INTERNATIONAL CONFERENCE

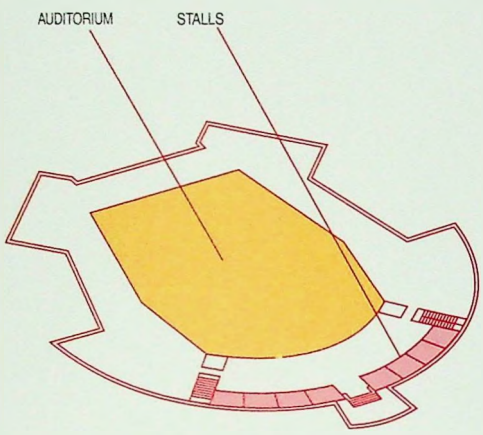
on "Antioxidants & Free Radicals in Health-Nutrition & Radio-protectors" and IV Annual Conference of the Society for Free Radical Research in India (SFRR)

10th-12th January-2005

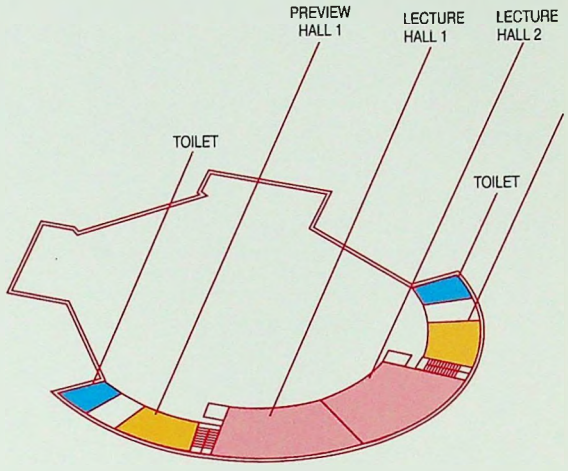
Under the Aegis of SFRR-India/Asia & in Collaboration with International Society for Free Radical Research

DEPARTMENT OF BIOCHEMISTRY & BIOPHYSICS
ST. JOHN'S MEDICAL COLLEGE

St. John's National Academy of Health Sciences, Bangalore 560034 INDIA. E-mail : conference@sjmc-sfrr.org Website : www.sjmc-sfrr.org



GROUND FLOOR PLAN



FIRST FLOOR PLAN

AUDITORIUM

Community Health Cell
Library and Information Centre
367, "Srinivasa Nilaya"
Jakkasandra 1st Main,
1st Block, Koramangala,
BANGALORE - 560 034.
Phone : 553 15 18 / 552 53 72
e-mail : chc@sochara.org

INTERNATIONAL CONFERENCE

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"Antioxidants & Free Radicals in Health-Nutrition & Radio-protectors"

and

IV Annual Conference of Society for
Free Radical Research in India (SFRR)

10-12th January 2005

St. John's National Academy of Health Sciences, Bangalore

The Organizing Commitee welcomes delegates to the
Conference and acknowledges the following
for their generous support

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Organized by :

St. John's Medical College
St. John's National Academy of Health Sciences
Bangalore 560034, India

A RADICAL VIEW OF ANTIOXIDANTS - DESTINATION INDIA

Dear Delegates,

"Wish you a very happy 2005"

A hearty welcome to this beautiful campus of St John's Medical College, which is hosting the International Conference on Antioxidants & Free Radicals in Health Nutrition & Radioprotectors and the IV Annual Conference of the Society for Free Radical Research in India (SFRR). The theme of the Meet is "A radical view of antioxidants- destination India".

The response to this conference has been overwhelming and we are very fortunate to get some outstanding scientists to be with us. A workshop on "Assuring Quality Research Data through accreditation" is being held on the 9th January conducted by Dr Kanagasabapathy, considered as Guru of quality control in India. This workshop, jointly sponsored by Randox and the Council for Scientific and Industrial Research, is expected to sensitize the young and middle level researchers on the importance of quality assurance in research.

Over the next three days we have a feast of scientific deliberations. We are extremely fortunate to have the key note address by Professor T. Yoshikawa. Diabetes mellitus is afflicting many people world-wide and India is no exception. Professor Yoshikawa's address should throw light on several aspects of this dreadful disorder. After diabetes mellitus it is the heart attack which hits the young adult. Professor B.M.Hegde, one of our leading clinicians, readily agreed to deliver the SFRR Oration.

We are indeed fortunate to have several scientists, from all over the world who are participating in the conference. The total number of invited speakers is 131 out of which 43 are from outside India. In all more than 600 participants are attending this conference.

We could make it possible mainly due to the total support and co-operation of St John's National Academy of Health Sciences, The Society for Free Radical Research (SFRR) India. The inputs of Dr T.P.A Devasagayam and his team were indispensable. Without the secretarial assistance of Dr Roopa, Dr Ravi Kishore, Mr N.Prabhakar and Mr M.B.Kadam it would have been impossible to bring out this book in time. We are also indebted to all the staff members of the department of Biochemistry and Biophysics for their help and support.

We hope that all of you will take back pleasant memories from Bangalore.

Prof. Thuppil Venkatesh
Organizing Secretary

Prof. C. V. Anand
Chairman of Scientific Committee

INTERNATIONAL CONFERENCE

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10-12th January 2005

St. John's National Academy of Health Sciences, Bangalore

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Society for Free Radical Research India (SFRR-India)
C/O Radiation Biology & Health Sciences Division
Bhabha Atomic Research Centre
Mumbai 400 085, India

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Website: Organized by: Punkaj Tanwar

INFORMATION IS POWER...

A participating laboratory in RIQAS (Clinical Chemistry) receives an average of 20,800 statistical data per year

RANDOX

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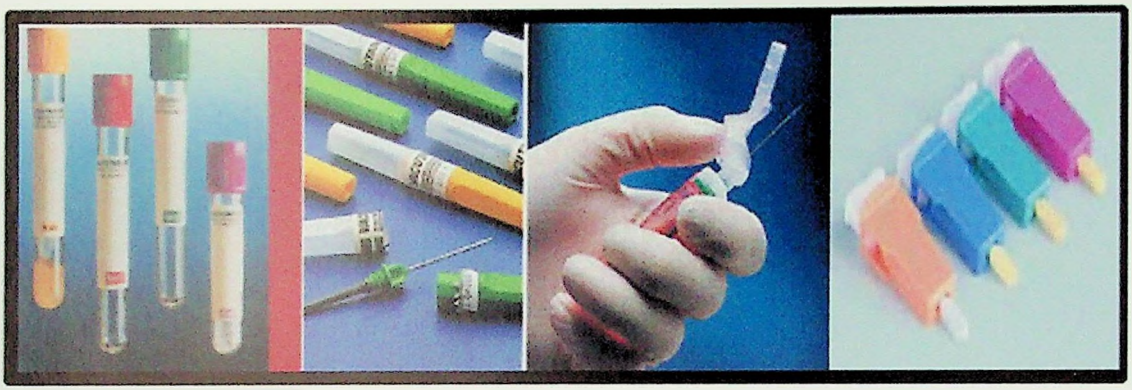

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Proceddings of

INTERNATIONAL CONFERENCE

on "Antioxidants & Free Radicals in Health-Nutrition & Radio-protectors"and

IV Annual Conference of Society for Free Radical Research in India (SFRR)

In

Memory of the

Tsunami Victims

CONFERENCE ORGANIZING COMMITTEE

Chief Patron:
Rev. Fr.Dr.Thomas Kalam
Director, SJNAHS

Patrons:
Rev.Fr.Sebastian
Rev.Fr.Linus Neli
Mary Ollapally
Anura Kurpad

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Raghunath T. N.

Treasurer:
Anitha Devanath

Support & Logistics:
G. Somashekarappa

Publications:
S. Muralidharan

Dear Delegates,

Cordially I would like to welcome you to St. John's National Academy of Health Sciences, Bangalore for the International Conference on Antioxidants and Free Radicals and the Annual Conference of the Society for Free Radical Research in India! These two conferences promote the very ideal enshrined in the motto of St. John's: "He shall live because of me."One of our Departments which is translating this motto into practice in letter and spirit is the Biochemistry Department under the leadership of Dr. Venkatesh. Ensuring the health of present and future generations is the greatest service that health care Institutions and professionals can render to humanity, instead of just taking care of the victims of an unhealthy environment and life style. Happy to note that participants of these Conferences are involved in both basic and applied medical research to improve the quality of life by bringing about clinical and nutritional interventions. The age-old association that India has with herbal medicinal practices should provide an ideal context for the deliberations of these Conferences. I am happy that St. John's has been chosen as the venue for this globally important meeting of leading scientists in the field. Wishing that the outcome of the Conferences will make the common man's life brighter in the future,

Chief Patron
conference
organzing Committee

Rev. Fr. Dr. Thomas Kalam
Director SJNAHS

'Sfrr india has made tremendous progress in recent years in both science and education by sponsoring conferences in india. At these conferences the indian scientific community and other scholars from international destinations have had the opportunity to exchange information,make friendships, establish scientific cooperation whichhas advanced the field of free radical research, oxygen biology, agricultural and biomedical applications. This field of research continues to be important for severalÊ reasons. These are that the science isinteresting and important for the human welfare and that research in this field of knowledge is rapidly moving forward my congratulations to sfrr india for their past and future efforts and look forward to the success of the january2005 conference

Lester packer, past president

Professor Lester Packer

Molecular Pharmacology & Toxicology

School of Pharmacy

University of Southern California

1985 Zonal Avenue

Los Angeles, CA 90089-9121

Tel.: +1 (323) 442 3355

Fax: +1 (323) 224 7473

E-mail: packer@usc.edu

E-mail: packer@socrates.berkeley.edu

Lester packer
University of Southern California

Message from President, SFRR-India

As President of the Society for Free Radical Research, India, I warmly welcome all the delegates of the "International Conference on 'Antioxidants and Free Radicals in Health, Nutrition and Radio-protectors" and the IV Annual Conference of SFRR-India, to be held at the St. John's National Academy of Health Sciences, Bangalore. Antioxidants that keep free radicals in check and are shown to protect from diseased conditions form an important strategy in preventive medicine and human nutrition as well as in radioprotection. Our country has a rich tradition of oriental medicine in the form of Ayurveda, which contains wealth of information on medicinal plants with potent antioxidant and other therapeutic properties. This will be of interest to all those who are attending this conference and working in the area of free radicals and antioxidants. I wish the delegates to have a highly fruitful and scientifically rewarding time at this international meeting, which has attracted participants from over 20 countries.

Padma Bhushan
Dr. R.D. Lele
president, SFRR - India

I am happy to write a message for the book of abstracts of the scientific papers to be presented at the International conference on Antioxidants and Free Radicals in Health, Nutrition and Radio-Protectors to beheld in St. John's National Academy of health Sciences from January 10-12, 2005. The conference which deals with basic science research in an area of great relevance to the better understanding of the pathogenesis of a large number of conditions both for good and harm. The conference has attracted a host of eminent scientists and researcher from around the world. I am sure that the talks, paper presentation and ensuing discussions will go a long way to further knowledge in this field and lead to improvement in health of all people.

As chairperson of the Organizing Committee I welcome all delegates to the conference and hope that your stay will be pleasant, enjoyable and fruitful.

DR. PREM PAIS, MD
DEAN
St. John's Medical College

Message from Secretary-General, SFRR-India

I warmly welcome all the delegates of the IV Annual Conference of SFRR-India and the accompanying "International Conference on 'Antioxidants and Free Radicals in Health, Nutrition and Radio-protectors". This new branch of SFRR-Asia had been formed just 4 years back with help and support from its parent societies, SFRR-Asia and SFRR-International. The main objective of this society is to promote interaction between basic scientists and clinicians from within India and abroad. With this in view, our society has organized 3 international conferences, and the 4th one is being organized in Bangalore. Like the earlier conferences, this one also has received a tremendous response from scientists from many different backgrounds coming from many states in India and several countries spread all over the globe. I request the delegates to give their best efforts for the success of this conference as well as our society. Another major activity of our society is the publication of the SFRR-India Bulletin. I also request the delegates to contribute their articles/tidbits/interesting information for the success of this journal. Finally I appeal to the delegates that they may utilize the friendships formed during the conference for the betterment of science and for the well-being of the human beings, especially the poor and the down-trodden.

Dr. T.P.A. Devasagayam
Secretary-General
SFRR INDIA


BANGALORE
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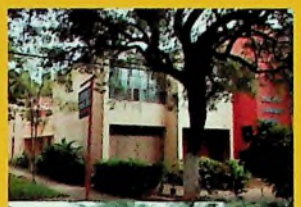








GENERAL INFORMATION

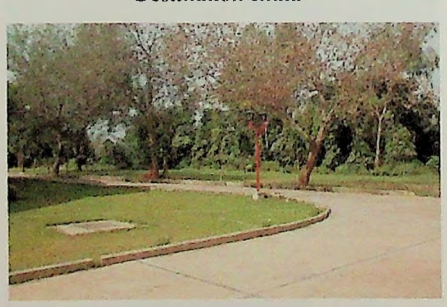
St. John's National Academy of Health Sciences main auditorium where the conference will be held

The International Conference on "Antioxidants & Free Radicals in Health Nutrition & radio-protectors" and the IV Annual Conference of the Society for Free Radical Research in India (SFRR) is being held at the Auditorium complex of St. John's National Academy of Health Sciences, John Nagara in Bangalore.

The venue is situated amidst thick greenery and natural surroundings. Ideally located just minutes away from St. John's Medical College and the Hospital are only 15-20 minutes drive from the Bangalore International Airport. Situated in an area of over 100 hectares of land has amenities such as post office, bank, telecommunication centers, canteen, guest house and Internet browsing centre.

Conference theme

"A Radical view of Antioxidants-Destination India"



Approach to the main auditorium is surrounded by lush green ambience

The Conference Secretariat is located in the department of Biochemistry & Biophysics on the 2nd floor of the Medical College building (Robert Koch Bhavan)

Delegates can contact the Secretariat on any of the following telephone numbers for help and assistance:

Office of the Organizing Secretary 080-2206 5058 / 2206 5050 / 25502341 / Residence of the Organizing Secretary 25532146.

Safe Drinking water

Safe drinking water is made available by the Aqua Guard of Eureka Forbes at several places in the conference venue. Every delegate is also provided with drinking water bottles in the delegate bags.

Conference sessions are held in the first floor of the auditorium

Main entrance to the SJMCH

Conference sessions are arranged in the SJNAHS auditorium complex located in the eastern side of the campus. The main auditorium has a seating capacity of 1200 with latest technology of acoustics and lighting facilities. Two auxiliary conference halls with a maximum capacity of 100 each is housed on the first floor of the auditorium. All sessions will be held at the above halls which is equipped with multimedia audiovisual facilities.

Message board

Conveniently located close to the registration desk is the place where you may check for messages. Please advise potential callers to

contact the registration desk.

Internet café

For your convenience the internet browsing centre is located behind the Zablocki learning centre (Library block). Registered delegates with their identity badges will have free access to the centre.

Coffee and Tea will be available throughout the conference hours outside the main hall.

Canteen is located close to the hospital annexe

Business Centre

All delegates can have access to the Fax, photocopying, telephone, computer and poster support materials which will be made available on payment of nominal charges at the business centre located in the 1st floor of the auditorium. Facilities for making long distance calls are also available at the STC /ISD booths located at many places as indicated in the enclosed layout of the campus.

Public call booths are located in the campus at many places.

People with special needs.

Every effort has been made to ensure people with special needs are catered to. Should you require any special assistance please contact the staff on duty at the registration desk on your arrival, to make your stay in Bangalore a pleasant and comfortable experience.

Simple and clean accommodation is arranged to delegates.

Institute of Population Research Guest house

Name badges

Please wear your conference delegate badge at all times as it is your entry to sessions and for meals. Name badges in utility pouch is provided

Registration Desk

Located in the foyer of the auditorium Registration will begin in the evening of Sunday the January 9th. Application forms for the SFRR (India) membership will be available at this venue.

"A Radical view of Antioxidants Destination India"

Another entrance to the auditorium

Conference Industry Exhibition

State of the art Laboratory Technology is the main theme of the exhibition. Stalls will be kept open during the days of the conference.

Accommodation is at hospital annex to student delegates

Parking

Facilities for four & two wheelers are available.

Security

There will be 24 hour watch and ward at the conference venue.

Photograph

Photographs of various events will be available at the photo desk. All delegates are required to assemble during the morning tea break on Tuesday the 11th January in front of the auditorium.

Tour information

Local tours can be undertaken. A desk will be functional providing the required information and registration and reservations for various tours mentioned in the conference second circular. Information can be had in our web site www.sjmc-sfrr.org

Amphitheater at the back of the auditorium

Associate meetings

Pre-conference work-shop on QC and Accreditation session will be held in the Cardinal Gracias Hall located in the east wing of the Robert Koch Bhavan, on Sunday the 9th January 2005.

Robert Koch Bhavan
Venue for the Pre Conference work-shop

Work-Shop will be conducted by Dr A S Kanagasabapathy, authority in India on the Clinical Chemistry Quality Control Program, is Consultant and Technical Committee member of the National Accreditation Board for Testing and Calibration of Laboratories, Government of India.

Registration. What is included?

- Attendance to all the scientific sessions
- Participation and visits to industry exhibition
- Breakfast round table sessions
- Tea
- Lunch
- Cultural events
- Banquet / Dinner

Not included for the pre-conference workshop.

Accompanying persons / associate delegate are welcome to attend social events, lunch, banquet and dinner.

Social events on Monday the 10th January 2005

1. Inaugural function commences at 0915 H in the main auditorium. Everybody should be seated by 0900 H. Dress code is formal.
2. Official Inauguration by Professor T Yoshikawa, President of SFRR (International).
3. Welcome reception. A taste of local Karnataka ethnic food from different parts of the state.

"A Radical view of Antioxidants Destination India"

Cultural Program on Tuesday the 11th January 2005

Classical Music and Dance performance by professional artistes will be arranged. This will be followed by fellowship and Banquet Dinner.

Poster Sessions

Between 1430 and 1630 H on all days of the conference poster sessions are arranged with panels provided for posters. Poster sessions are arranged in the cardinal Gracias hall of the Robert Koch Bhavan.

Organizing committee have instituted best poster award for every twenty posters. Panel of judges will be evaluating the posters.

Best Oral Presentation Award (ONLY FOR OL CATEGORY)

Under OL category of ten minutes duration one best oral presentation award will be announced during the concluding session on the final day of the conference.

Breakfast round table sessions

In order to facilitate academic interactions between young and experienced, round table breakfast sessions are planned on 11th and 12th January 2005.

Registration for the BF sessions is free of charges on a first come first served basis with a limited number of seats.

Accommodation

Delegates are accommodated based on their request in the accommodation registration from made by them well in time. Organizers have tried their best to provide accommodation at reasonably priced hotels or guest houses.

For students sponsored for local hospitality hostel type of accommodation is arranged separately for ladies and gents.

To senior scientists, guest house type accommodation is arranged at nearby places.

To invited speakers and members of the executive committee of SFRR, accommodation is arranged in the campus guest house.

List giving details of who is staying where will be available on request, at the registration counters.

Certification of attendance/ Participation in the conference

Certificate of participation is included in the delegate registration bags. Kindly check for any corrections needed in your certificate.

Late abstracts / on the spot submission of papers for presentation

Organizers have made adequate provision for the late submission of abstracts and late submission for oral presentation not exceeding ten minutes under the miscellaneous papers category.

Delegates can contact the registration counter for help and assistance. Copies of such abstracts will be photocopied and distributed to the attending delegates.

Special meeting with the quality managers and technical managers of accredited medical testing laboratories

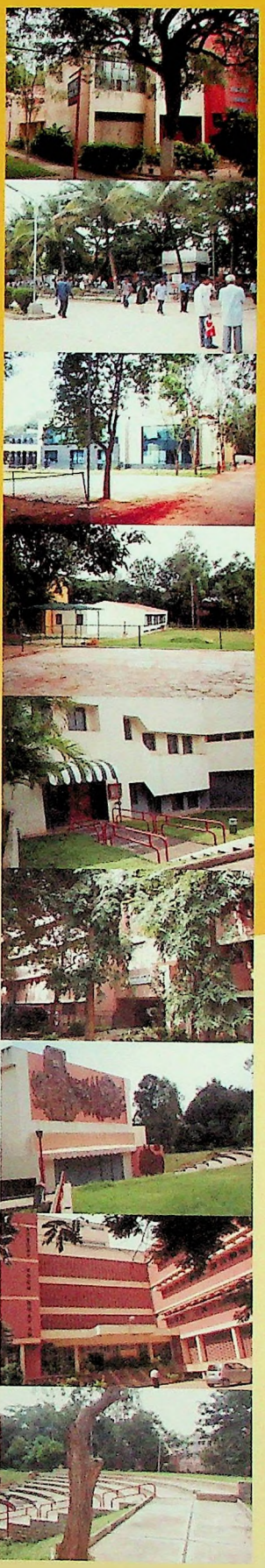
Delegates who are interested in undertaking clinical trials in accredited laboratories can attend a meeting with the quality and technical managers of the NABL accredited laboratories. Details in this regard will be available at the registration desk.

The organizers have invited over twenty such accredited laboratory representatives.

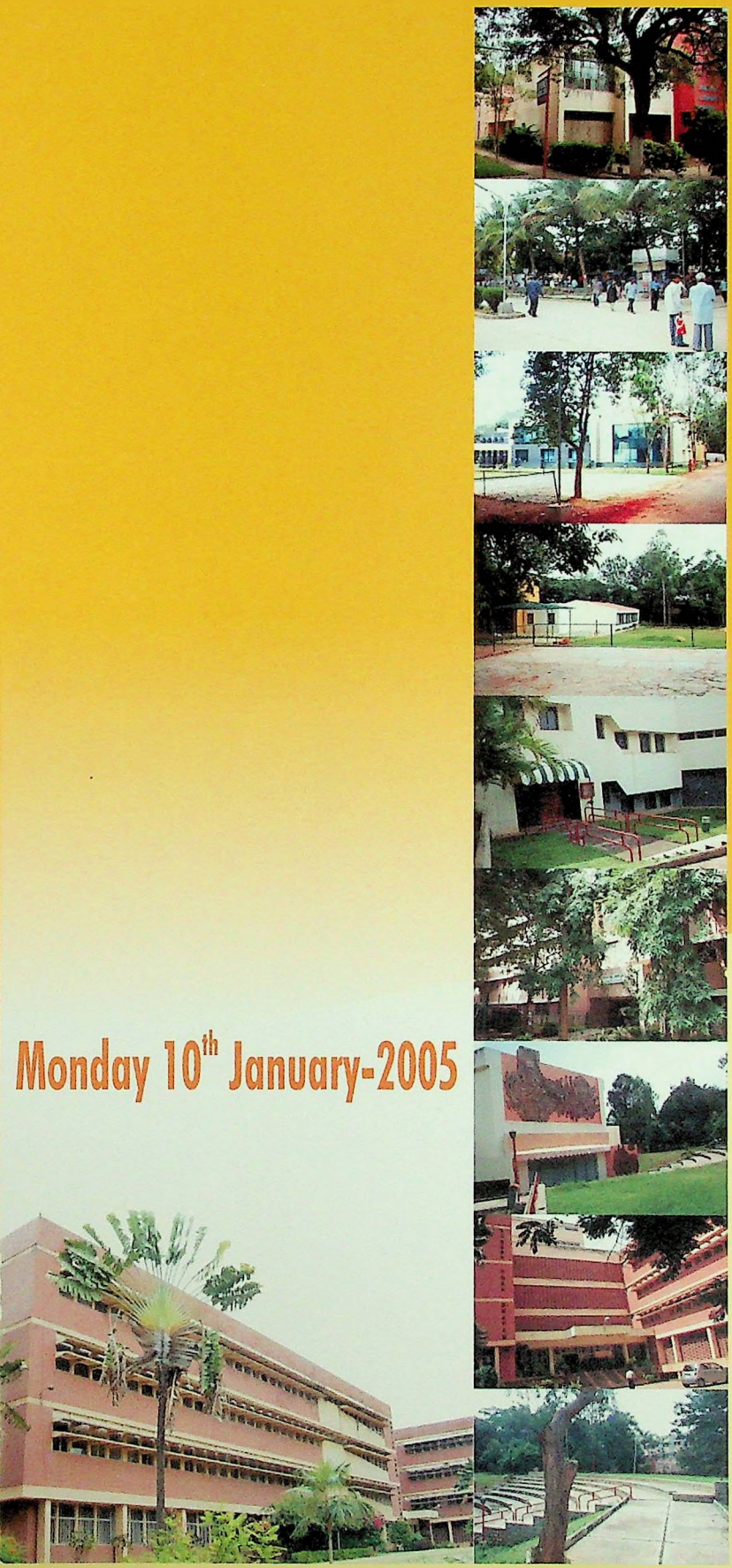
The meeting is scheduled in the VIP meeting room located in the ground floor of the conference auditorium on Tuesday the 11th January between 1430-1600 H

"A Radical view of Antioxidants Destination India"

Sunday 9th Jan-2005



SUNDAY		WORKSHOP		
Jan 9th 2005		PRE-CONFERENCE WORKSHOP ON "ASSURING QUALITY RESEARCH DATA THROUGH ACCREDITATION"		
		Topic : "ANTIOXIDANTS & FREE RADICALS IN HEALTH -NUTRITION & RADIO-PROTECTORS"		
	0830H		:	Registration
	0930 H		:	Inauguration
	1000 H		:	Tea Break
	1030 H	A. S. Kanagasabapathy	:	Quality Assurance and Quality Control
	1115 H	A. S. Kanagasabapathy	:	GLP with reference to Accrediation Standards
	1200 H	A. S. Kanagasabapathy	:	Uncertainty of Measurement, Calibration & traceability
	1230 H		:	Exercise, Group Discussion & Presentation
	0115 H		:	Lunch Break
	1400 H	T. Venkatesh	:	Assessor's view points on Laboratory Auditing
	1430 H		:	Equipment demonstration with respect to QC, calibration Uncertainty of Measurement, etc. - By "RANDOX"
	1430 H		:	Panel Discussion
	1600 H		:	Concluding Remarks
	1615 H		:	Tea



Monday 10th January-2005

MONDAY
Jan 10th 2005

0730 - 0900	REGISTRATION
0915 - 1000	INAUGURATION
1000 - 1045	KEY NOTE ADDRESS
1045 - 1100	TEA

1100 - 1330

SYMPOSIUM I
Sponsored by : RANDOX
Venue : MAIN AUDITORIUM

Topic : "FREE RADICALS & ANTIOXIDANTS IN MOLECULAR MEDICINE"

CHAIRPERSONS :
1. J P Mittal (India) 2. M P Barros (Brazil) 3. Harl Mohan (India)

PL-1	T. Ramasarma, (India)	: Whither oxidative stress?
IL- 1	B Epe (Germany)	: Generation and repair of endogenous oxidative DNA damage
IL-2	Hideyuki J Majima (Japan)	: Vitamin E protects against intracellular oxidative stress induced by X-irradiation
IL-3	Irfan Rahman (USA)	: Molecular antioxidant strategies in the potential management of lung diseases
IL-4	Panda B B (India)	: Some intriguing insights into metallo and oxi - adaptive responses to genotoxic stress in plant cells
IL-5	Ramlah D (India)	: Investigation of sensitizers based on squaraine moiety for photodynamic therapy
OL-1	Moinuddin (India)	: Peroxynitrite damaged DNA: implications in carcinogenesis

SYMPOSIUM II
Sponsored by : APL RESEARCH CENTRE
Venue : HALL A

Topic : "CARDIOVASCULAR DISEASES"

CHAIRPERSONS :
1.Sheila Uthappa (India) 2. Nick Hunt (Australia) 3. Palep HS (India)

PL-2	Dipak K Das (USA)	: Red wine and heart: a journey from grape to resveatrol
IL -6	S Basu (Sweden)	: Oxidative stress and inflammation in cardiovascular dysfunction:role of isoprostanes and prostaglandins
IL-7	Lindsay Brown (Australia)	: Controlling cardiovascular remodeling by controlling oxidative stress
IL-8	Nilanjana Maulik(USA)	: Effect of resveratrol on ischemic heart : the healthy heart miracle
IL-9	Prem Pais (India)	: Risk factors for IHD-Indian scenario
IL-10	APL sponsored speaker (India)	:
OL-2	S Shinde(India)	: Oxidative and antioxidant status of patients after off-pump and on-pump coronary artery by pass surgery
OL-3	Tilak JC (India)	: Antioxidant and DNA-protective properties of cardioprotective plant, terminalia arjuna, and its component, baicalein using various models

SYMPOSIUM III
Sponsored by : ASSOCIATION OF CLINICAL BIOCHEMISTS OF INDIA (ACBI)
Venue : HALL B

Topic : "FREE RADICALS AND ANTIOXIDANTS IN DIABETES MELLITUS"

CHAIRPERSONS :
1. K P Sinha (India) 2. Sambu Varma (USA) 3. H.A. Nadiger (Malaysia)

PL-3	Mukherjee T (India)	: Free radical pathways to the antioxidant action: physicochemical studies
IL-11	Praveen Sharma (India)	: Oxidative stress: an additive risk factor in metabolic syndrome
IL-12	Vijaya Haldankar (India)	:
IL-13	Balasubramanian M(India)	: Oxidative Stress: molecules and mechanisms with special reference to diabetes and its complications
IL-14	B. Ganapathi (India)	: Free radicals and antioxidants in diabetes mellitus
OL-4	S Srivastava (USA)	: Inhibition of the metabolism of lipid derived aldehydes exacerbates atherosclerosis in apo E-null mice
OL-5	Vinayaga Moorthy(India)	: Starvation- re-feeding cycles impairs antioxidant defense and increases risk for atherogenesis
OL-6	Usha Anand (India)	: Serum paraoxonase in diabetes mellitus

1330 - 1430	LUNCH
1430 - 1600	POSTER

1600 - 1830

SYMPOSIUM IV
Sponsored by VIJAYA DIAGNOSTICS, Hyderabad
Venue : HALL A

Topic : "FREE RADICALS AND ANTIOXIDANTS IN LIVER DISEASES"

CHAIRPERSONS :
1. R.K.Bhattacharya (India) 2. Vaidya AB (India) 3. Indu Paul Kaur (India)

IL-15	Adhikari S (India)	: Antioxidant prooxidant mechanism of bilirubin
IL-16	Balasubramanyam KA (India)	: Oxidative stress in the intestine in liver cirrhosis: role in spontaneous bacterial peritonitis
IL-17	Raj K Singh (India)	: Circadian periodicity of human circulating lipid peroxides and anti-oxidant enzymes as putative markers in cirrhosis of liver
IL-18	Venugopal Menon (India)	: Protective role of ferulic acid, a natural phenolic antioxidant on liver fibrosis
IL-19	Vishwanatha Jamboor (USA)	: Nicotine inhibits nitric oxide-induced apoptosis in oral epithelial cells
OL-7	Prabhu Daniel (India)	: Hepatoprotective and anti-oxidant potential of luffa acutangula (var) amara against CCL4 induced liver dysfunction
OL-8	Sayanti Bhattacharya	: Gastric ulcer healing by a potent herbal free radical scavenger Piper betle linn & its active compounds
OL-9	Subir Kumar Das (India)	: Effect of choline derivatives in the treatment of ethanol mediated free radical induced hepatotoxicity

SYMPOSIUM V
Sponsored by: ST. JOHN'S NATIONAL ACADEMY OF HEALTH SCIENCES
Venue : MAIN AUDITORIUM

Topic : "FREE RADICALS AND ANTIOXIDANTS IN NEUROLOGICAL DISEASES"

CHAIRPERSONS :
1. K. Taranath Shetty (India) 2. Bernd Epe (Germany) 3. Menon V P (India)

PL-4	Baolu Zhao (China)	: Natural antioxidants prevent neurodegeneration diseases
PL-5	Tilman Grune (Germany)	: Modulation of protein oxidation by antioxidants-implications for neuronal protection
IL-20	Mathangi DC (India)	: Does REM sleep deprivation result in oxidative stress?
IL-21	Nadiger HA (Malaysia)	: Regional distribution & age related changes in oxidative stress markers in different regions of SHR rat brain
IL-22	Neeraj Agarwal (USA)	: Neuroprotection of Rgc-5 cells against glutamate induced oxidative damage by a novel 2-adamantyl estrogen analogue, Zyc-3
OL-10	Nageshwari K (India)	: Therapeutic potential of antioxidants on cerebral ischemic reperfusion injury
OL-11	Sudha K (India)	: Erythrocyte antioxidant enzymes as the markers of oxidative stress in neurological disorders

SYMPOSIUM VI
Venue : HALL B

Topic : "MISCELLANEOUS TOPICS" - 1

CHAIRPERSONS :
1. Keshav Singh (USA) 2. Balasubramanyam K A (India) 3. Kalyanaraman B (USA)

IL-23	Bapat MM (India)	: Free radical damage, diabetes mellitus and dietary antioxidants
IL-24	Ilavazhagan (India)	:
IL-25	J. Bhattacharjee(India)	: Regulatory role of ros and rns in expression of transcription factor ap1 in breast cancer
IL-26	Srivastava KK (India)	: Herbs for enhancing mental performance
IL-27	Flora SJS (India)	: Metal induced oxidative stress and the role of antioxidant in chelation therapy
IL-28	Shambhu Varma (USA)	: Implications of oxygen free radicals in the formation of cataracts
IL-29	Janardhanan KK (India)	: Prevention of oxidative stress by mushroom derived antioxidants.
OL-12	Kusal K Das (India)	: Effect of antioxidant (L-ascorbic acid) on nickel induced alteration of nucleic acid concentration in rats

KEY NOTE ADDRESS

ON

OXIDATIVE STRESS IN DIABETES AND NUTRIGENOMICS

BY

Toshikazu Yoshikawa and Yuji Naito

Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Oxidative stress is implicated as an important mechanism by which diabetes causes nephropathy. Using a high-density oligonucleotide array, we recently investigated the transcriptome analysis for mesangial cells in mice with diabetic nephropathy. We confirmed the up-regulation of many genes associated with oxidative stress, pro-inflammatory cytokines, transforming growth factor, and collagen synthesis. Astaxanthin, which is found as a common pigment in algae, fish, and birds, is a carotenoid with significant potential for antioxidative activity. We examined whether chronic administration of astaxanthin could prevent the progression of diabetic nephropathy induced by oxidative stress in mice. We used female db/db mice, a rodent model of type 2 diabetes. After 12 weeks of treatment, the astaxanthin-treated group showed a lower level of blood glucose compared with the non-treated db/db group; however, both groups had a significantly high level compared with the db/m mice. The relative mesangial area calculated by the mesangial area/total glomerular area ratio was significantly ameliorated in the astaxanthin-treated group compared with the non-treated db/db group. The increases in urinary albumin and 8-OHdG at 12 weeks of treatment were significantly inhibited by chronic treatment with astaxanthin. The 8-OHdG immunoreactive cells in glomeruli of non-treated db/db mice were more numerous than in the astaxanthin-treated db/db mice. In this study, treatment with astaxanthin ameliorated the progression and acceleration of diabetic nephropathy in the rodent model of type 2 diabetes. Astaxanthin treatment reversed the expression of the up- and down-regulated genes, which were confirmed by GeneChip analysis. The results suggested that the antioxidative activity of astaxanthin reduced the oxidative stress on the kidneys and prevented renal cell damage. In conclusion, administration of astaxanthin might be a novel approach for the prevention of diabetes nephropathy.

SESSION - I

PL-1

WHITHER OXIDATIVE STRESS

T. Ramasarma

Centre for DNA Fingerprinting & Diagnostics, Hyderabad 500 076, and

Solid State & Structural Chemistry Unit and

Department of Biochemistry, Indian Institute of Science, Bangalore- 560 012.

Living cells are always exposed to atmospheric oxygen and deal with about 0.2 mM concentration of dissolved oxygen in the cytosol. The popular concept of oxidative stress therefore is not due to dioxygen molecule. The best-known cellular oxidant, NAD^+, is subject to redox turnover and occurs in small concentration. Then which is the oxidant responsible for stress? Is there oxidation in oxidative stress?

The most-talked about reactive oxygen species (ROS) is superoxide, derived by reduction of oxygen. This becomes a significant oxidant after further reduction to hydrogen peroxide or after complexing with nitric oxide to form nitroperoxide. Reduction and release of iron leads to peroxidation of lipids and generates hydroxyl radicals in presence of hydrogen peroxide.

Are the disease-nonspecific increase in lipid peroxidation products, F2-isoprostanes, a general stress response? Antioxidants that added a great value in this research are not mere reductants and act more by radical quenching. The antioxidant enzymes finally result in peroxicidal action. All these place at the center of action reduced forms of oxygen species, particularly hydrogen peroxide, and some explanation is needed how hydrogen peroxide is saved from the abundant powerful "antioxidant enzymes. It appears that process of reduction has inescapable role in "oxidative stress".

IL-1

GENERATION AND REPAIR OF ENDOGENOUS OXIDATIVE DNA DAMAGE

B. Epe

Institute of Pharmacy, University of Mainz, D-55099 Mainz, Germany.

Reactive oxygen species (ROS) are generated in all cells endogenously as by-products of the oxygen metabolism. There is no doubt that the generation of ROS constitutes a significant challenge for the integrity of the genome. Thus, basal levels of oxidative DNA modifications such as 8-hydroxyguanine (8-oxoG) can be observed in apparently all types of cells. The sources of the basal endogenous oxidative DNA damage have not yet been established. Surprisingly, ROS from the mitochondrial electron transport chain do not play a major role, as concluded from experiments with 0 cells, which lack mitochondrial DNA. More relevant appear enzymes such as the cytochrome P450 reductase, since its overproduction increases both the basal level of oxidative DNA base modifications and genomic instability. An interesting experimental approach to assess the consequences of the endogenous oxidative DNA damage *in vivo* without the interference of other ROS-mediated effects is offered by the generation of mice deficient in specific repair mechanisms dealing with oxidative DNA damage. In *ogg1*$^-$ null mice, which are deficient in the specific repair glycosylase for 8-oxoG, elevated endogenous levels of this lesion in the liver were associated with 2-3 fold increased spontaneous mutation rates. Our analysis of back-up repair mechanisms, which apparently prevent a severe phenotype of the mice, revealed an unexpected involvement of the *CSB* (Cockayne Syndrome B) gene product in the global repair of 8-oxoG. Accordingly, a several-fold increased age-related accumulation of 8-oxoG was observed in *ogg1/csb* double-knockout mice. The analysis of the spontaneous mutation rates in various organs and the effects of xenobiotic oxidants, promoters and antioxidants in these mice are expected to provide further information on the risk associated with a given level of oxidative DNA

IL-2

VITAMIN E PROTECTS AGAINST INTRACELLULAR OXIDATIVE STRESS INDUCED BY X-IRRADIATION

Hideyuki J. Majima1, Hiroko P. Indo1, Kazuo Tomita1 and Toshihiko Ozawa2

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We previously reported that the potential role of mitochondrial manganese superoxide dismutase (MnSOD) in protective activity to irradiation by analyzing the cell viability by a colony-formation assay, and by detecting apoptosis in stably human MnSOD gene-transfected stable clones of HLE (Cancer Res. 61:5382-5388, 2001). The results showed that overexpression of MnSOD reduced the levels of reactive oxygen species (ROS) in the mitochondria, intracellular phospholipid peroxidation product (4-Hydroxy-2-nonenal; HNE), and prevented apotosis. The results suggested that MnSOD might play an important role in protecting cells against radiation-induced apotosis by controlling the generation of mitochondrial ROS and intracellular lipid peroxidation. In this study, we further examined whether alpha-tocopherol could prevent against mitochondrial generation of ROS, lipid peroxidation and apoptosis. Our results showed X-irradiation increased in ROS, HNE, and apoptosis. Post-X-ray treatment with alpha-tocopherol protected against these processes and apoptosis. These results suggest that mitochondria are primary sites of X-ray-induced cellular oxidative injuries.

IL-3

MOLECULAR ANTIOXIDANT STRATEGIES IN THE POTENTIAL MANAGEMENT OF LUNG DISEASES

Dr. Irfan Rahman

Department of Environmental Medicine, Division of Lung Biology and Disease, University of Rochester Medical Center,

Rochester, NY 14642., USA.

Oxidative stress and inflammation are major hallmarks of various chronic lung diseases such as asthma, lung fibrosis, chronic obstructive pulmonary disease (COPD) and lung cancer. The sources of the increased oxidative stress in patients with chronic lung diseases derive from the increased burden of inhaled oxidants (cigarette smoke, environmental pollutants/gases), and from the increased amounts of reactive oxygen species (ROS) and reactive nitrogen species generated by inflammatory, immune and structural cells of the airways. Oxidative stress has important consequences on several events of lung physiology and for the pathogenesis of various chronic lung diseases. These include airway hyperresponsiveness/hyperreactivity, bronchial constriction, mast cell activation, epithelial detachment, oxidative inactivation of anti-proteases and surfactants, mucus hypersecretion, alveolar epithelial injury, mitochondrial dysfunction, proliferation, remodeling of extracellular matrix, and apoptosis. ROS and aldehydes play a key role in enhancing the inflammation through the activation and phosphorylation of MAP kinases and redox sensitive transcription factors such as NF-?B and AP-1 in lung diseases. Oxidative stress also alters nuclear histone acetylation and deacetylation leading to increased gene expression of pro-inflammatory mediators in the lung. Oxidative stress may have a role in the poor efficacy of corticosteroids in asthma and COPD. Since a variety of oxidants, free radicals and aldehydes are implicated in the pathogenesis of chronic lung diseases it is likely that a combination of antioxidants may be effective in the intervention of these diseases.

It is becoming increasingly clear that the antioxidant and/or anti-inflammatory effects of thiol molecules (glutathione and mucolytic drugs, such as N-acetyl-L-cysteine and N-acystelyn), dietary polyphenol (curcumin-diferuloylmethane, a principal component of turmeric),

resveratrol (a flavanoid found in red wine), ergothioneine (xanthine and peroxynitrite inhibitor), and the antioxidant beverage EM-X (derived from the ferment of unpolished rice, papaya and sea-weeds with effective microorganisms) control the NF-? B activation, regulation of glutathione biosynthesis gene, chromatin remodeling and subsequently inflammatory gene regulation in lung epithelial cells. Specific spin traps such as -phenyl-N-tert-butyl nitrone, a catalytic antioxidant (ECSOD mimetic), manganese (III)meso-tetrakis (N,N'-diethyl-1,3-imidazolium-2-yl) porphyrin (AEOL 10150 and AEOL 10113), and a SOD mimetic M40419 inhibited the cigarette smoke-induced inflammatory response (decreased number of neutrophils and macrophages) in animal models of lung diseases. Thus, the effective wide spectrum antioxidant therapy that has good bioavailability and potency is urgently needed to control the localized oxidative and inflammatory processes that occur during lung inflammation and in the management of chronic lung diseases.

Supported by Philip Morris External Research Program, USA., and an Environmental Health Sciences Center grant ES01247.

IL-4

SOME INTRIGUING INSIGHTS INTO METALLO - AND OXI - ADAPTIVE RESPONSES TO GENOTOXIC STRESS IN PLANT CELLS.

B. B. Panda and J. Patra

Genecology and Tissue Culture Laboratory, Department of Botany, Berhampur University, Berhampur 760 007

Genomic stability and adaptive evolution are of paramount importance for the species survival and fitness under stressful environment, and is the key for sustenance of the biodiversity. Because of their sedentary life style, plants are incapable of physically escaping potentially harmful environment, and therefore they have developed sophisticated cellular mechanisms to defend from adversity. The perception of stresses and signal transduction to switch on adaptive responses are critical steps in determining the survival and reproduction of plants under stressful environment. Of the different cellular targets, DNA is the target of genotoxic stress that could be evaluated by cellular responses manifested as chromosome aberration, micronucleus or comet. Evidences available over the recent past increasingly point to the involvement of reactive oxygen species (ROS) in metal-induced genotoxicity. Interestingly, metals and oxidative agents in low conditioning doses induce adaptive response that confer genomic protection when subsequently subjected to genotoxic challenge; referred as metallo- or oxi-adaptive response, respectively. The underlying mechanism of metallo- or oxi-adaptive response, however, remains elusive.

We present here an comparative account of adaptive responses induced in root meristem (Allium cepa) or embryonic shoot (Hordeum vulgare) cells of by two contrasting metals, cadmium (Cd2+) and aluminium (Al3+); two oxidative agents, hydrogen peroxide (H2O2) and paraquat (PQ); and a signalling phytohormone, salicylic acid (SA) against three different standard genotoxins namely maleic hydrazide (MH), a S-dependent clastogen that induces no DNA strand break; ethyl methane sulfonate (EMS), an alkylating mutagen; and methyl mercuric chloride (MMCl), an aneugen-cum-clastogen. The aforesaid conditioning agents induced oxidative stress, which was evident by accumulation of H2O2, increased lipid peroxidation, induction of one or more antioxidant enzymes (catalase, peroxidase, super oxide dismutase etc.) in plants. The pattern of genotoxic adaptation to MH, EMS and MMCl induced by the conditioning agents exhibited a remarkable difference between the metals (Cd and Al) as well as between the oxidative agents (H2O2 and PQ). Adaptive responses induced by Al and PQ on the other hand were similar. The fact that adaptive response induced by SA was quite comparable to that induced by Al or PQ, but differed from H2O2, underscored the possible involvement of a signal transduction pathway in the underlying adaptive response to genotoxic stress that perhaps does not involve H2O2.

IL-5

INVESTIGATION OF SENSITIZERS BASED ON SQUARAINE MOIETY FOR PHOTODYNAMIC THERAPY

D. Ramiah,*[1] K. T. Arun,[1] K. Jyothish,[1] I. Eckert,[2] L. Weidenfeller[2] and B. Epe[2]

[1]Photosciences and Photonics Division, Regional Research Laboratory (CSIR), Trivandrum 605 019, INDIA and [2] Institute of Pharmacy, University of Mainz, Germany

Photodynamic therapy (PDT) is a non-invasive technique for the treatment of both neoplastic and non-neoplastic diseases by the combined action of light and a photosensitizing drug.[1] The photosensitizer, when injected into the body, due to its inherent properties accumulates in the cancerous tissues and on irradiation with light of suitable wavelength generates cytotoxic agents, which can cause tumor necrosis. Contrary to the conventional treatments such as chemotherapy and radiotherapy, PDT is relatively a safer treatment since the induction of tumor necrosis ceases when the light is switched off. The recent advent of laser fiber optics, endoscopy and laproscopy has made it possible by PDT to alter only the irradiated area with minimal systemic toxicity, thereby extending the clinical application of PDT to a variety of cancers. Several photosensitizers including porphyrins, metallophthalocyanins, chlorins, porphycenes, purpurins and aminolevulenic acid-mediated porphyrins have been extensively studied for their use in PDT. With the I[st] generation photosensitizer, Photofrin® already in clinical use and several other photosensitizers under various phases of clinical trials, the search for more effective photosensitizers has become an important area of research in recent years. In this context, we have designed and synthesized a few heavy atom substituted squaraine dyes and have investigated their photophysical and photobiological properties under different conditions. These dyes possesses favorable properties and generate cytotoxic agents such as singlet oxygen in quantitative yields.[2,3] Cytotoxicity and mutagenicity studies in mammalian cells and bacterial strains revealed that these dyes are non-toxic in the dark but exhibit high cytotoxicity only when activated with visible light.[1] Cytotoxicity and DNA damage studies in cellular and cell-free conditions revealed that singlet oxygen is the major reactive species responsible for the photobiological activity of these dyes.[3] Our *in vitro* studies clearly indicate that sensitizers based on squaraine chromophore could form an effective alternate system to the well-studied porphyrin moiety for photodynamic therapeutical applications.

OL-1

PEROXYNITRITE DAMAGED DNA: IMPLICATIONS IN CARCINOGENESIS

Moinuddin, Kiran Dixit, Asif Ali

Department of Biochemistry, J.N. Medical College, A.M.U., Aligarh (INDIA)

Introduction: Reactive nitrogen species such as nitric oxide and its derivatives, produced by inflammatory cells, have been proposed to contribute to multistage carcinogenesis by inducing DNA or tissue damage. Increased levels of circulating autoantibodies directed against nucleus have been reported in the serum of patients with malignancies.

Methods: The effect of peroxynitrite ($ONOO^-$) generated by diethylamine NONOate (nitric oxide donor) and 1,4-hydroquinone (superoxide donor) on commercially available human placental DNA was monitored by UV and fluorescence spectroscopy, melting temperature studies, alkaline gel electrophoresis and nuclease S1 digestibility. The DNA antigenicity and repertoire of specificities of induced antibodies were evaluated by direct binding ELISA, Competition ELISA and gel retardation assay.

Results: DNA was found to be modified significantly when exposed to 0.1 mM DEA-NO and 0.1mM 1,4-hydroquinone in combination

However, DNA incubated with DEA-NO (0.1mM) alone and 1, 4-hydroquinone (0.1mM) alone did not cause any modification. UV spectra of the modified DNA showed 49% hyperchromicity while the fluorescence spectrum exhibited a decrease in fluorescence intensity. Alkaline agarose electrophoresis and nuclease S1 digestibility clearly demonstrated DNA strand breaks. Melting temperature of the modified DNA was found to be 71°C, whereas for native DNA it was 86°C. The modified DNA induced specific antibodies in experimental animals with a titre =1:12800 in ELISA. Modified DNA presented better epitopes to the cancer autoantibodies as compared to the native analogue.

Conclusions: Nitric oxide and superoxide alone did not cause perceptible damage to native DNA. However, the synergistic action of nitric oxide and superoxide, generating peroxynitrite, causes extensive damage to human DNA rendering it immunogenic. The modified DNA proved to be a better antigen for cancer autoantibodies thereby implicating its possible role in carcinogenesis.

SESSION - II

PL-2

RED WINE AND HEART: A JOURNEY FROM GRAPE TO RESVEATROL

Dipak K Das

Cardiovascular Research Center, University of Connecticut School of Medicine, Farmington, Connecticut, USA

The consumption of wine, particularly red wine, imparts beneficial effects in the prevention of coronary heart disease. Our study determined that mild to moderate wine consumption (equivalent to one to two glasses of wine/day) rendered the heart resistant to ischemia and heart failure. This gave rise to what is now popularly termed as the French paradox. A recent study determined that regular consumption of grapes also render the myocardium resistant to ischemic heart disease. In this study, the rats were given (orally) standardized grape extract (sge) (obtained from California table Grape commission) for a period of one month. After 30 days, the rats were sacrificed, hearts excised and made ischemic for 30 min followed by 2 hrs of reperfusion. At 100 mg/kg and at 200 mg/kg, grapes provided significant cardio protection as evidenced by improved post-ischemic ventricular recovery and reduced amount of myocardial infarction. sge reduced the malonaldehyde Content of the heart indicating reduction of oxidative stress during Ischemia and reperfusion.

The cardio protective effects of red wine have been attributed to several Polyphenolic antioxidants including resveratrol and proanthocyanidins that are present in the wine and the grapes. Our study determined that these Polyphenolic antioxidants provide cardioprotection by their ability to function as in vivo antioxidants.È These phenols as well as red wine triggered a signal transduction cascade initiated by the activation of Adenosine a1 and a3 receptors thereby activating map kinase signaling leading to a reduction of pro-apoptotic transcription factors and genes such as jnk-1 and c-jun and inducing redox-sensitive transcription factor nfkb thereby potentiating ischemia-mediated anti-death signal. This results in the reduction of cardiomyocyte apoptosis.È Resveratrol mediated anti-apoptotic signal appears to be potentiated by an upregulation of nitric oxide leading to the initiation of an angiogenic signal triggered by an Induction of vascular endothelial growth factor. The results, thus, indicate that not only do the red wine and grapes provide cardioprotection through their antioxidative properties, but also they have ability to trigger a survival signal through the polyphenolic antioxidants, especially Resveratrol.

IL-6

OXIDATIVE STRESS AND INFLAMMATION IN CARDIOVASCULAR DYSFUNCTION: ROLE OF ISOPROSTANES AND PROSTAGLANDINS

S. Basu

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Introduction: Non-enzymatic oxidation of arachidonic acid through free radical pathway and enzymatically through cyclooxygenases results in several short-half lived unique biologically active compounds in the mammalian body namely, isoprostanes and prostaglandins (PGs). These eicosanoids or their metabolites are shown to be reliable parameters of oxidative stress and inflammation in various clinical and experimental studies.8-Iso-PGF2?, a major F2 -isoprostane evokes vasocontriction in lung and kidney, and also serves as a reliable indicator of free radical mediated-oxidative stress. Prostaglandin F2? (PGF2?) is a potent vasocontrictory compound and is involved in various acute and chronic inflammatory situation. 15-Keto-dihydro-PGF2?, a major metabolite of cyclooxygenase-catalysed PGF2?, has shown to be an unique indicator of inflammatory response.

Methods: We have developed radioimmunoassays by raising highly specific antibodies for 8-iso-PGF2? and 15-keto-dihydro-PGF2? in the rabbits. The methods have been successfully applied for studies of these eicosanoids in various body fluids collected during endotoxin induced septic shock and acute inflammation, following cardiopulmonary resuscitation after cardiac arrest (CPR), during cardiopulmonary bypass (CPB), pecutaneous coronary intervention (PCI) and angiography, from type 2 diabetes patients and smokers.

Results: Rapid increase of these bioactive eicosanoids have seen in the body fluids in experimental septic shock, CPR, CPB, PCI/angiography and in patients with type 2 diabetes and smokers with a distinct kinetics of appearance and disappearance.

Conclusions: Both isoprostanes and prostaglandins are involved in various cardiovascular dysfunction (ARDS, dysfunction on systemic haemodynamics, ischemia-reperfusion etc.) and riskfactors. Thus, the simultaneous determination of isoprostanes and prostaglandin metabolite in body fluids opened exellent possibilities to study the role of both oxidative injury and inflammatory state in the pathogenesis of cardiovascular diseases and their riskfactors, and also in drug evaluation studies at these endpoints

IL-7

CONTROLLING CARDIOVASCULAR REMODELLING BY CONTROLLING OXIDATIVE STRESS

Lindsay Brown

Department of Physiology and Pharmacology, School of Biomedical Sciences, The University of Queensland, Australia.

Chronic cardiovascular disease is characterized by cardiovascular remodelling, especially excessive cellular growth (hypertrophy), excessive collagen deposition (fibrosis) and endothelial dysfunction. The trigger that initiates these changes may be an increased oxidative stress defined as increased reactive oxygen species (ROS) such as superoxide. This hypothesis has been investigated by studying the changes in cardiovascular structure and function following treatment with compounds that alter the production or availability of ROS. All experiments have been carried out in DOCA-salt hypertensive rats since this model is characterized by an excessive production of superoxide by vascular smooth muscle cells. DOCA-salt hypertension was produced in 8 week old male Wistar rats by uninephrectomy and administration of deoxycorticosterone acetate (DOCA)(25 mg sc every fourth day) and 1% NaCl in the drinking water for 28 days. DOCA-salt rats developed hypertension, ventricular hypertrophy, fibrosis and endothelial

dysfunction. NADPH oxidase is the major source of superoxide in this model; treatment with allopurinol (50 mg/kg/day), an inhibitor of xanthine oxidase, did not significantly change cardiovascular remodelling. NADPH oxidase is activated by endothelin through ETA receptors and angiotensin II through AT1 receptors. Administration of A-127722 (approx 10 mg/kg/day), a selective ETA receptor antagonist, reversed existing cardiac and vascular remodelling and also prevented further remodelling; cardiovascular function was also improved. Similar improvements were shown following treatment with candesartan (2 mg/kg/day), a selective AT1 receptor antagonist. L-arginine is the precursor of the paracrine vasodilator, NO, which reacts with superoxide eventually leading to the removal of free radicals. In DOCA-salt rats, administration of L-arginine (approx 3g/kg/day) significantly reduced the onset of hypertension and hypertrophy, prevented collagen deposition and the consequent increase in cardiac stiffness. Further, the loss of responsiveness of isolated thoracic aortic rings from DOCA-salt rats to acetylcholine was reversed by L-arginine. The antioxidant, resveratrol (1 mg/kg/day), prevented the cardiac and vascular remodelling in DOCA-salt hypertension and improved cardiovascular function. In summary, the DOCA-salt hypertensive rat rapidly develops significant cardiovascular remodeling. In this model, pharmacological interventions that decrease or remove ROS and therefore reduce oxidative stress induce a reversal of existing changes and prevent further cardiovascular remodelling.

IL-8 WITHDRAWN

EFFECT OF RESVERATROL ON ISCHEMIC HEART: THE HEALTHY HEART MIRACLE

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Ischemic coronary disease is the leading cause of morbidity and mortality. Therapeutic approaches to induce angiogenesis mostly aim to restore flow to a localized segment by angioplasty or bypass surgery. Among the various triggers of angiogenesis, tissue hypoxia/ischemia as well as pharmacological agents such as resveratrol (polyphenol) has been identified as being a very important stimulus/agent for the induction of new vessel growth. Occlusion of a main coronary depletes the blood supply to the myocardium and subsequently reduces cardiac function, which ultimately leads to heart failure. Progressive, chronic coronary artery occlusion has been shown to induce development of collateral arteries to reestablish and maintain blood flow to the myocardium at risk via the growth of new capillary vessels or angiogenesis. Studies from our laboratory as well as from others have already confirmed the protective role of collaterals against myocardial ischemia and cell death. We have successfully demonstrated in adult rat myocardium (LV) effect of resveratrol on significant upregulation of the protein expression profiles of vascular endothelial growth factor (VEGF) and its tyrosine kinase receptors (Flk-1 and Flt-1) as well as other angiogenic factors such as Ang-1, Ang-2 and their receptor Tie-2. Also, we were able to demonstrate increased capillary/arteriolar density, capillary to myocyte cross-sectional area (after 1-4 weeks and after 2 months) and decreased collagen volume fraction as well as improved LV function and blood flow by resveratrol preconditioning in a rat model of chronic myocardial infarction (MI) model.

IL-9

RISK FACTORS FOR IHD-INDIAN SCENARIO

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India is in a phase of epidemiological transition between a country with major morbidity and mortality from malnutrition and infectious disease to a stage of increasing burden of chronic disease especially cardiovascular disease. In addition, these diseases are striking at ages younger than in the developed economies. Over the last two decades a number of epidemiologic studies have demonstrated that standard risk factors explain much of the increased risk for CVD in Indians. These include smoking, dysglycemia, hypertension, disorders of lifestyle and possibly hyperlipidemia. Some novel risk factors have also been hypothesized including hymocysteine, LP(a), coagulation abnormalities and genetic and intrauterine factors. The epidemic of CVD promises to be so large that it is time to start prevention on a nationwide scale with the evidence already available. Such preventive strategies should consist of simultaneous programmes of population-wide strategies to lower population risk factor distribution as well as primary andk secondary prevention programme. Such programmes should be designed to reach as many people as possible at a cost that makes the programmes feasible yet effective.

IL-10

APL SPONSORED SPEAKER

OL-2

OXIDATIVE AND ANTIOXIDANT STATUS OF PATIENTS AFTER OFF-PUMP AND ON-PUMP CORONARY ARTERY BYPASS SURGERY

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***Introduction*:** The development of new surgical devices and techniques allow off pump coronary artery bypass surgery (OPCAB) without use of cardiopulmonary bypass (CPB). The aim of the study-oxidative stress marker and antioxidant status were studied in patients undergoing off-pump CABG when compared with patients undergoing on-pump CABG using CPB.

Methods: The study included 45 patients (30 males and 15 females) with mean age of 56.19.98 years undergoing CABG were divided in two groups: A cardiac stabilizer (Octopus Tissue Stabilizer, Medtronic Inc) was used on 25 patients to perform OPCAB surgery without CPB (Group 1) and 20 patients undergoing on pump CABG with CPB (Group 2). Arterial blood was drawn through the intra-catheter immediately after induction of anesthesia. Subsequent samples were collected at following specific times after surgery 1hrs., 6 hrs., 24hrs., 48hrs.,72hrs. The following biochemical parameters were estimated plasma levels of MDA, -Tocopherol as well as erythrocyte activities of superoxide dismutase (SOD) and Glutathione peroxidase (GPx).

Results: Concentration of antioxidant and oxidative stress levels is high in On-Pump CABG group than Off-Pump CABG. A significant difference was noted ($P<0.001$) between pre and postoperative levels of markers such as SOD, GPx, -Tocopherol and MDA in both the groups.

Conclusion: The data of the present study indicate that OPCAB without use of CPB reduces Lipid peroxidation and antioxidant levels were comparatively less in OPCAB than On-pump CABG. All of this may contribute to improve myocardial function and faster postoperative recovery from surgical revascularization procedures, particularly in critical ill patients

OL-3

ANTIOXIDANT AND DNA-PROTECTIVE PROPERTIES OF CARDIOPROTECTIVE PLANT, *TERMINALIA ARJUNA*, AND ITS COMPONENT, BAICALEIN USING VARIOUS MODELS

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Objective: Terminalia arjuna is an Indian medicinal plant known to possess cardiotonic, cardioprotective, antimutagenic and antigenotoxic properties. Baicalein (5,6,7-trihydroxy-2-phenyl-4H-1-benzopyran-4-one) is a constituent of T. arjuna credited with many beneficial effects. The antioxidant abilities, in relation to these observed beneficial properties have not been examined in detail earlier.

Methods: To examine the bioavailability in an animal model, we studied their stability and absorption in intestine, using an 'inverted loop model of rat intestine' and HPLC. Then DNA binding ability of baicalein was studied by spectofluorimetry. The ability of baicalein and T. arjuna extract to protect against DNA damage induced by potent generator of reactive oxygen species (ROS), -radiation, was assayed using plasmid pBR322 DNA as model system and single strand breaks (ssbs) as the end-point. Ability to inhibit intracellular ROS production was studied by using 2'-7'dichlorodihydrofluorescein diacetate (DCFDA) in NIH 3T3 cells. Antioxidant ability in relation to antiatherogenic effect was measured as plasma oxidation induced by biologically relevant peroxyl radicals and its inhibition by T. arjuna extracts and baicalein.

Results: Our studies showed that approximately 25% baicalein was absorbed in inverted rat intestine. Baicalein binds to calf thymus DNA in a concentration dependent manner. The compound, at the concentration of 50 M, and T. arjuna extracts, at a concentration of 0.05% can significantly prevent ssbs in pBR322 DNA. The DRF calculated for baicalein was 1.24. Baicalein protects against radiation-induced intracellular ROS generation. T. arjuna extracts as well as baicalein protect against plasma oxidation induced by peroxyl radicals.

Conclusion: Our results indicate that baicalein showed significant bio-availability and that T. arjuna extracts as well as baicalein are highly potent in protecting DNA strand breaks and intracellular ROS levels caused by -radiation-induced oxidative damage. Its mechanism of cardioprotection may involve inhibition of LDL oxidation.

SESSION III

PL-3

FREE RADICAL PATHWAYS TO THE ANTIOXIDANT ACTION: PHYSICOCHEMICALSTUDIES

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Radiation chemical and biochemical techniques work hand-in-hand in elucidating the mechanism of antioxidant action and drug action and toxic effects. In the cases where free radical mechanism is operative, the former method scores over the latter as free radicals can be studied by several novel techniques like pulse radiolysis and epr spectroscopy. A few salient features of these techniques will be summarized.

Results in some of our recent studies on rosmarinic acid, sesamol, folic acid, bakuchiol, resveratrol, capsaicin, melatonin, etc. will be highlighted. A comparison will be made about the efficacy of antioxidant action, radiation protection and repair mechanism, etc.

IL-11

OXIDATIVE STRESS: AN ADDITIVE RISK FACTOR IN METABOLIC SYNDROME

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Oxidative stress plays role in pathophysiology of many diseases including diabetes and cardiovascular disease. However, not much is known about the antioxidant status among individuals at high risk of developing these conditions i.e. metabolic syndrome. The metabolic syndrome is conceptualized as a constellation of anthropometric & metabolic abnormalities, which includes excess weight, hyperglycemia, elevated blood pressure, low concentration of HDL cholesterol and hypertriglyceridemia. In addition, various other abnormalities of uric acid, inflammation, hemostasis and fibrinolysis are often considered part of this syndrome. Not surprisingly, people with metabolic syndrome are at high risk for developing diabetes and cardiovascular diseases. If antioxidants play a protective role in the pathophysiology of diabetes and cardiovascular disease, understanding antioxidant status among people with metabolic syndrome is of interest. With this view present study was conducted on diabetic subjects, their first-degree relatives with and without diabetes and their spouses. Nutrients antioxidants- vitamin A, C & E levels and oxidative stress were measured. Diabetic subjects, first degree diabetic and non-diabetic relatives, as well as spouses with >3 risk factors (Metabolic Syndrome) had low status of vitamin A, C & E as compared to first degree non-diabetic relatives and spouses both with < 3 risk factors. Antioxidant status showed a significant ($P<0.001$) negative correlation with oxidative stress expressed by MDA level. More over subjects with presence of all the five risk factors (ATPIII criteria) had extremely low antioxidant status as compared to subjects with >3 risk factors. Further oxidative stress was found to be positively linked to LDL cholesterol and negatively with HDL cholesterol and decreased anti oxidant status. Sub optimal concentrations of antioxidants (vitamin A, C & E) in metabolic syndrome may explain increased risk of diabetes and cardiovascular disease.

IL-12

Vijaya Haldankar

IL-13

OXIDATIVE STRESS: MOLECULES AND MECHANISMS WITH SPECIAL REFERENCE TO DIABETES AND ITS COMPLICATIONS

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Oxidative stress has been proposed as a unifying hypothesis linking various molecular disorders of Type 2 diabetes. The theoretical importance of oxidative stress in diabetes is highlighted by its potential double impact, on metabolic dysfunction on one hand, on the vascular system on the other hand. Thus, pancreatic beta cells producing insulin as well as its target adipose or muscle cells can be negatively affected, as can blood elements and various cell types in the large and small blood vessels implicated in diabetic complications. From the epidemiological, pre-clinical and clinical studies, there is an indisputable evidence for a shift in the equilibrium between reactive oxygen species (ROS) and antioxidants in favour of oxidative stress in diabetes. Interestingly, most if not all of these reactions and abnormalities can already be evidenced in prediabtic states, long before diabetes is detected. Hyperglycemia and the cellular consequences of it later add to the list of potential causes of

oxidative stress. ROS is also a chemical inducer of gene expression acting through the activation of NFkB and activator protein-1 transcription factors and increases the transcription of IL-6 and TNFa, the proinflammatory factors that in turn induce ROS generation. Thus 'oxidation meets inflammation' and operates in a vicious cycle. Despite these, the proof of causal relationship of oxidative stress in the worsening of the metabolic control and/or the angiopathy characterizing diabetes has still to be investigated. A series of studies undertaken in our laboratory support a role for oxidative stress in the genesis and progression of diabetes and its complications. Increased oxidative damage was inferred from our various biomarker analyses: lipid peroxidation, glutathione levels, shortening of telomeres, glutathionylation of Hb, leukocyte DNA damage, increased NADPH oxidase mRNA levels etc. The reason that antioxidants are not received with great attention as a treatment option in diabetes is partly due to the failure of such approach in cardiovascular and atherosclerosis studies. However, none of the antioxidant trials to date has measured markers of oxidation to assess the degree of oxidative stress. Secondly, antioxidants such as Vitamin E work by concentrating in lipid bilayers whereas many of the oxidative reactions occur in cytosol and intracellular levels. It is also interesting to note that in clinical trials, administration of cardiovascular drugs and anti-diabetic agents, all of which show intracellular antioxidant activity, has resulted in beneficial diabetes treatment outcomes. These observations raise the possibility that controlling oxidative stress intracellularly may be an attractive therapeutic approach for diabetes and its angiopathies. The hope is that further deciphering of the free radical pathway will continue to lead to new therapies.

IL-14

FREE RADICALS AND ANTIOXIDANTS IN DIABETES MELLITUS

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Diabetes is the leading cause of new blindness in working-age adults, of new cases of end stage renal disease and of non-traumatic lower leg amputations and cardiovascular complications. Hyperglycemia leads to increased oxidative stress and endothelial dysfunction.Ê Oxidation of glucose can generate oxygen free radicals and excess reactive oxygen species such as superoxides. These molecules can promote lipid peroxidation, leading to excessive oxidative burden in patients with diabetes.Ê Oxidative stress can also influence the expression of multiple genes in vascular cells, including signaling molecules such as PKC, NFkB and ERK; overexpression of these genes may lead to endothelial dysfunction and, ultimately, to micro- and macrovascular disease. Molecules in the arterial wall can also be modified by glycation, which usually is associated with oxidation. The formation of advanced glycation end-products (AGEs) can occur on proteins, lipids and nucleic acids. Patients with diabetes appear to have decreased antioxidant defense capability, measured as lower levels of specific antioxidants, such as ascorbic acid (vitamin C) or vitamin E, or reduced activities of antioxidant enzymes, such as catalase, superoxide dismutase or glutathione peroxidase.

OL-4

INHIBITION OF THE METABOLISM OF LIPID DERIVED ALDEHYDES EXACERBATES ATHEROSCLEROSIS IN APO E-NULL MICE

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Oxidation of phospholipids generates products in which unsaturated fatty acids at the *sn*-2 position are oxidized to short chain aldehydes. These phospholipid aldehydes enhance the expression of adhesion molecules on endothelium, stimulate monocyte adhesion, promote smooth muscle cell proliferation and elicit immune responses. However little is known about the biochemical mechanisms by which these aldehydes are metabolized and detoxified. In the present study we examined the ability of various aldo-keto reductases in the reduction of phospholipid aldehydes. Our data suggest that aldose reductase (AR), fibroblast regulated protein-1, aldehyde reductase, and mouse vas deferens protein catalyze the reduction of aldehydes generated from the oxidation of 1-palmitoyl-2-arachidonyl-*sn*-glycero-3-phosphocholine and its 1-alkyl and 1-alkenyl analogs as well as the aldehydes generated from the oxidation of 1-palmitoyl-2-arachidonyl containing phosphatidic acid and phosphoglycerol. Of the enzymes tested, AR was the best catalyst for the reduction of phospholipid aldehyde- 1-palmitoyl-2-(5-oxovaleroyl)-*sn*-glycero-3-phosphatidylcholine (POVPC) with a K_m of 10 ?M. Incubation of COS-7 and THP-1 cells with 10 ?M POVPC resulted in the accumulation and reduction (30-40 %) of the parent aldehyde. AR inhibitors sorbinil and tolrestat prevented the reduction of POVPC by 35-50 % in these cells. Transfection of COS-7 cells with AR cDNA enhanced the reduction of POVPC by > three fold in AR^{+} cells. Feeding of sorbinil or tolrestat increased the atherosclerotic lesion formation by 1.8 fold in apo E-null mice. These observations suggest that AR catalyzed reduction of phospholipid aldehydes could play a pivotal role in regulating the pro-atherogenic effects of oxidized phospholipids.

OL-5

STARVATION- REFEEDING CYCLES IMPAIRS ANTIOXIDANT DEFENSE AND INCREASES RISK FOR ATHEROGENESIS.

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Introduction: Stress is a universal feature in human life. Formation of excessive free radicals due to stressful conditions is a major internal threat to cellular organisms. Recently, attention has been focused on the significance of psychosocial factors and life style in the aetiology of a number of diseases, especially in coronary artery disease. Hence, a feeding experiment was conducted to examine the effect of multiple cycles of starvation- refeeding on free radical scavenging defense mechanisms and plasma parameters on male Wister rats.

Methods: Male Wister rats weighing 150-180 g at the beginning of the study were maintained in standard laboratory conditions. Animals (n = 5/ group) were fed either rodent chow ad libitum or subjected to 48 hours starvation and 24 hours refeeding with chow diet for five cycles. After five cycles body weight, epididymal fat weight were measured. Blood samples collected were used for various analyses.

Results: We found that body weight and epididymal fat weight of starved-refed animals reduced significantly compared to control animals ($p<0.02$). The level of plasma triglycerides, fasting glucose and erythrocyte reduced glutathione decreased significantly ($p<0.05$). On the other hand, the plasma cholesterol and malondialdehyde levels increased significantly ($p<0.05$). The erythrocyte catalase and glutathione peroxidase activity was significantly elevated.

Conclusions: Although there is a reduction in adipose tissue weight and plasma triglycerides concentrations, our results suggest that multiple cycles of starvation re-feeding increases oxidative stress along with total cholesterol, the most powerful predictors of risk for developing coronary artery disease.

OL-6

SERUM PARAOXONASE IN DIABETES MELLITUS

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Introduction: Paraoxonase (PON), an arylesterase (EC 3.1.8.1), circulates in association with HDL. Its physiological role is still uncertain, although evidence exists for a protective effect of PON against oxidative stress. Because dyslipidemias are a common occurrence in diabetes mellitus, PON activities and lipid profile were assayed in patients with type 2 diabetes mellitus.

Methods: PON activities were assayed in 100 male non-smoking diabetic patients (duration of diabetes > 2 years) and in 30 age-matched controls. Patients who were on lipid lowering drugs were excluded from the study. Fasting blood glucose, total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C) were estimated using the Dade Behring Dimension AR Clinical Chemistry analyzer. Low density lipoprotein cholesterol (LDL-C) was calculated using the Friedwalde formula. PON was assayed by the spectrophotometric method using p-nitrophenyl acetate as the substrate.

Results: Serum PON activities were significantly lower in diabetics when compared with age-matched controls ($p<0.001$). A positive correlation was observed between PON and HDL-C. There was no such correlaton between PON and TC, TG and LDL-C.

Conclusion: PON is known to function as an antioxidant and lower levels of PON could lead to an increase in the steady state levels of lipid peroxides. The higher levels of oxidized LDL known to be present in diabetics could be partly due to low PON activity.

PROTECTIVE EFFICACY OF *MENTHA PIPERITA* AGAINST ARSENIC INDUCED RENAL DAMAGES IN SWISS ALBINO MICE

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SESSION IV

IL-15

ANTIOXIDANT PROOXIDANT MECHANISM OF BILIRUBIN

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Introduction: Bilirubin (BR), a toxic metabolite of heme was regarded as a waste to be excreted. An impaired excretion results in jaundice, a well recognizable symptom of liver disease. Only in 1987, Stocker et al. have shown for the first time that BR can act as an antioxidant *in vivo* at a micromolar concentration and can inhibit lipid peroxidation initiated by peroxyl radicals. BR has been reported to protect cells from neurotoxicity and myocardial ischemia. Recently a multiplied effect in the antioxidant effect of BR via a redox cycling involving BR-ROS-BV and biliverdin reductase has been proposed. Of late the potential function of BR and BV against the damaging effects of uncontrolled NO production has also been suggested. All these studies provide a motivation to study the reactions of BR with bio-relevant free radicals in order to understand the mechanistic pathway.

Methods: The experiment was carried out with a cyclic voltammeter (Acochemie Autolab, model PGSTAT 20) using a three-electrode system *viz.* Ag/AgCl as the reference electrode, a glassy carbon electrode as the working electrode and a platinum wire as a counter electrode. The pulse radiolysis system using 7 MeV electrons has been used to follow the reactions.

Results: The mechanism for the reaction of BR with oxidizing radicals as reported so far is the following. The hydroxyl radical on reacting with BR forms a tetrapyrole pigment via a radical adduct. One electron oxidizing radicals like $N_3^{\cdot}$, $Br_2^{\cdot-}$, $CCl_3OO^{\cdot}$ form the radical cation. A detailed mechanistic study for the reaction of BR with hydroxyl, glutathiyl, linoleic acid peroxyl and nitrogen dioxide radicals is reported here. Direct evidence of hydrogen abstraction mechanism for oxidation of BR has been observed and will be discussed. This study demonstrates that hydroxyl, glutathiyl and methyl radicals abstract hydrogen from BR and forms a carbon-centered radical. In presence of oxygen the carbon-centered radical of bilirubin forms a peroxyl radical. In contrast to $CCl_3OO^{\cdot}$ radical reactions reported earlier, linoleic acid peroxyl radical reacts via hydrogen abstraction. In the case of $NO_2^{\cdot}$ radical reaction, BR radical cation is produced.

Conclusions: The antioxidant action of bilirubin is generally via radical scavenging. For physionlogically relevant radicals abstraction of a hydrogen atom from central methylene group of bilirubin is the predominant reaction pathway.

IL-16

OXIDATIVE STRESS IN THE INTESTINE IN LIVER CIRRHOSIS: ROLE IN SPONTANEOUS BACTERIAL PERITONITIS

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Liver cirrhosis is a pathological condition that reflects irreversible injury of the hepatic parenchyma in association with extensive fibrosis. Spontaneous bacterial peritonitis (SBP) is a common illness in patients with cirrhosis and bacterial translocation from the gut plays an important role. This study looked at oxidative stress in the intestine, alterations in the luminal bacterial flora and changes in the surface sugars in the intestinal epithelium during development of liver cirrhosis. Liver cirrhosis was induced by intraperitoneal injection of thioacetamide (200mg / kg body weight). Development of the disease was confirmed by histology, serum markers and hepatic hydroxy proline content. Surfactant like particles and brush border membranes and mitochondria were isolated from the intestine and looked for oxidative stress and glycosylation changes during development of cirrhosis. Ceca and cecal luminal contents were harvested from control and cirrhotic rats and the luminal bacteria flora were quantitated and their adherence property tested *in vitro*. Mild oxidative stress was seen in the intestine at 1 and 2 months of treatment which was increased significantly after the development of cirrhosis. The surface sugars such as sialic acid, fucose, hexose and hexosamine were increased in both surfactant like particles and brush border membranes in experimental liver cirrhosis and was associated with increased bacterial adherence. There was significant increase in total number of both aerobic and anaerobic bacteria, predominantly E.coli and bacterioids in cirrhosis as compared to control. These studies suggest that liver cirrhosis is associated with oxidative stress and surface sugar alterations in the intestinal epithelium along with qualitative and quantitative alterations in the luminal bacteria resulting in increased bacterial adherence. This might facilitate bacterial translocation leading to spontaneous bacterial peritonitis

IL-17

CIRCADIAN PERIODICITY OF HUMAN CIRCULATING LIPID PEROXIDES AND ANTI-OXIDANT ENZYMES AS PUTATIVE MARKERS IN CIRRHOSIS OF LIVER.

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Introduction: The chronome (from chronos, time, and nomos, rule), or time structure of lipid peroxidation and anti-oxidant defense mechanism may relate to prevention and curative chronotherapeutic efficacy and management.

Patients and Methods: 50 patients with cirrhosis of liver, 25 to 45 years of age and 60 age-matched clinically healthy volunteers were synchronized for one week with diurnal activity from about 06:00 to about 22:00 and nocturnal rest. Breakfast was around 08:30, lunch around 13:00 and dinner around 20:30. Drugs known to affect the free radical system (its nature, rhythm and concentration) were not taken. Blood samples were collected at every 6-hourly intervals for complete 24 hours under standardized, presumably 24-hour synchronized conditions. Determinations included plasma lipid peroxides, in the form of malondialdehyde (MDA), blood superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx)

, glutathione reductase (GR) activities and serum total protein, albumin, ascorbic acid, and uric acid concentrations.

Results: A marked circadian variation was demonstrated for each variable in each group by population -mean cosinor ($P<0.01$). In addition to overall anticipated differences in overall mean value (MESOR), patients differed from healthy volunteers also in terms of their circadian pattern.

Conclusion: Mapping the broader time structure (chronome), with age and multifrequency rhythm characteristics of anti-oxidants and pro-oxidants is needed for exploring their putative therapeutic role as markers in cirrhosis of liver chronoprevention, if any, and their management.

IL-18

PROTECTIVE ROLE OF FERULIC ACID, A NATURAL PHENOLIC ANTIOXIDANT ON LIVER FIBROSIS

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Alcohol related disabilities are one of the world's major public health concerns. Ethanol is a powerful inducer of liver fibrosis and other associated pathological abnormalities. The alcohol-induced fibrosis is further aggravated when diets rich in polyunsaturated fatty acid are consumed. At present there is a resurgence of interest in natural principles for the treatment of various ailments. Ferulic acid (FA), a natural phenolic compound with largest bioavailability receives lot of attention in the research world because of its potent antioxidant activity. This prompted us to investigate on the biological activity of ferulic acid against alcohol and thermally oxidized sunflower oil (Ä PUFA) induced fibrosis. We tested the antifibrotic potential of ferulic acid by analyzing its influence over lipid peroxidative indices, antioxidant status, Matrix Metalloproteinases (MMPs), Tissue Inhibitors of Matrix Metalloproteinases (TIMPs) and the levels of collagen the markers of fibrotic changes. Our result showed administration of FA significantly reduced the extent of lipid peroxidation, and improved the antioxidant status, reduced the levels of collagen and TIMPs and positively modulated the activities of MMPs in alcohol and/or Ä PUFA treated rats. These results suggest that FA is an effective anti-fibrotic agent and can provide substantial protection against alcohol and ÄPUFA induced toxicity.

IL-19

NICOTINE INHIBITS NITRIC OXIDE-INDUCED APOPTOSIS IN ORAL EPITHELIAL CELLS

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Development of oral cancer is clearly linked to the usage of smokeless tobacco. However, the molecular mechanisms involved in this process are not well understood. Towards this goal, we have investigated the effect of smokeless tobacco exposure on apoptosis of oral epithelial cells. Exposure of oral epithelial cells to smokeless tobacco extract (STE) induces apoptosis in a dose-dependent manner, until a threshold level of nicotine is achieved upon which apoptosis is inhibited. Nicotine inhibits apoptosis induced by STE in these cells. Exposure of cells to nicotine alone has no effect on apoptosis, but nicotine inhibits apoptosis induced by other agents present in STE. The anti-apoptotic action of nicotine is specifically associated with the down-regulation of nitric oxide (NO) production. By using specific inducers of NO, we have demonstrated that inhibition of apoptosis by nicotine is through down-regulation of NO production. We further demonstrate that cyclooxygenase-2 (COX-2) activity is significantly down-regulated during inhibition of apoptosis by nicotine. Inhibition of apoptosis is a hallmark of many tumor suppressors and may lead to development of cancer. Thus, our data indicate that inhibition of STE-induced apoptosis

OL-7

HEPATOPROTECTIVE AND ANTI-OXIDANT POTENTIAL OF Luffa acutangula (var) amara AGAINST CCL4 INDUCED LIVER DYSFUNCTION

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INTRODUCTION: Carbon tetrachloride (CCl4) is a potent hepatotoxicant producing liver fibrosis. In liver fibrosis cell death occurs due to destruction of plasma membrane by various mechanisms including free radicals. CCl4 is biotransformed to trichloromethyl radical. This free radical reacts with oxygen to form trichloromethyl peroxy radical, which attacks lipids on the membrane. In the present study CCl4 used to induce liver damage and the hepatoprotective nature of the extracts of Luffa acutangula (var) amara is evaluated.

METHODS: Leaves of Luffa acutangula (var) amara were extracted with Ethyl acetate (EAELA) and Ethanol (EELA) and used for the study. Albino rats of either sex (150-200g) were divided into 5 groups with 6 animals each. All the groups (II, III, IV, V) recived CCl4 in olive oil (1:1) at a single dose of (3ml/kg/i.p). Animals in group III, IV, V received silymarin (25mg/kg/p.o), EAELA (200mg/kg/p.o), EELA (200mg/kg/p.o) respectively for five days prior to challenge. Group I & II served as control and received only vehicle and CCl4 on the 5th day. On the 6th day animals were sacrificed by decapitation. Blood and liver is collected and processed for the estimation of biochemical parameters.

RESULTS: Animals in CCl4 treated groups showed significant increase in liver enzyme marker levels. Pretreatment with silymarin, EAELA, EELA showed significant ($p<0.001$) reversal of the elevated levels of the marker enzymes in liver. Both enzymatic and non-enzymatic anti-oxidants levels decreased in CCl4 treated animals and reversed to normal in silymarin ($p<0.001$), EAELA ($p<0.01$), EELA ($p<0.001$)

treated rats.

CONCLUSION: The present study revealed that both extracts of Luffa acutangula (var) amara (EAELA, EELA) showed marked antioxidants, vitamins and hepatoprotective drugs are some of the therapeutic options.

OL-8

GASTRIC ULCER HEALING BY A POTENT HERBAL FREE RADICAL SCAVENGER: PIPER BETLE LINN & ITS ACTIVE COMPOUNDS

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INTRODUCTION: Role of free radicals in the pathogenesis of peptic ulceration is now well known. Oxygen derived free radicals has also been shown to be involved in the pathogenesis of acute gastric ulceration induced by an NSAID, Indomethacin. Thus after acid, pepsin and Helicobacter pylori, the generation of free radicals could well become another major factor to contend with in the management of peptic ulcers. In our present study, we have aimed for a plant drug , having potent free radical scavenging property with safety and efficacy to be used as an anti-ulcerogenic drug.

METHODS: Ethanolic extract of Piper betle Linn .(PBE) is tested against NSAID induced gastric ulcer in Male Wister rats(200g avg wt.).The oxidized metabolites and cellular antioxidants levels were measured.

Besides, in vitro free radical scavenging activity of PBE for various ROS (LOO``, OH``, O2` `, etc) was seen. The in vivo experiments to determine the Lymphoproliferative effect of PBE was also done.The Epidermal Growth Factor level in the gastric tissue was also measured. The active components from PBE were isolated and tested against the similar parameters.

RESULT: PBE and its active components have shown reduction in ulcer index (P*0.001), increased protein content, excellent free radical scavenging action (both in vivo and in vitro) (P*0.001), and significant increase in Epidermal growth Factor content (P*0.001).. They have lymphoproliferative property as well.Active component P1 has shown somewhat better effect than P2 in all the tests. CONCLUSION:All these data suggested that PBE and its active compounds can exert a strong anti-ulcer action via its antioxidant and immunomodulatory mechanism.

OL-9

EFFECT OF CHOLINE DERIVATIVES IN THE TREATMENT OF ETHANOL MEDIATED FREE RADICAL INDUCED HEPATOTOXICITY

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Liver damage due to consumption of alcohol may be caused by oxygen radicals such as superoxide and hydroxyl radicals, generated during the metabolism of ethanol by the microsomal oxidizing system. Lecithin, an important class of phospholipids contains choline, which is considered as lipotropic factor. The effects of this lecithin as a hepatoprotective drug on body weight and other biochemical parameters (especially liver function tests and antioxidant status) of ethanol exposed rats were studied. The results were compared with the effects of á-tocopherol (vitamin E). From the present study, it can be concluded that ethanol-induced stress can be partly prevented by á -tocopherol (vitamin E). Abstination from alcohol also involved for little hepatic regeneration. Supplementation of lecithin showed a minimal effect on reversing the effect of ethanol induced liver damage in the present study. Moreover, preventive measures were found to be better than curative treatment. This study further suggested that the oxidative stress is one of the proposed mechanisms for Alcoholic liver diseases. However, abstinence from alcohol, proper nutrition, supplementation of

SESSION V

PL-4

NATURAL ANTIOXIDANTS PREVENT NEURODE GENERATION DISEASES

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Tea catechins (TC) are usually expected as scavengers of free radicals. However not all the actions of TC are necessarily beneficial. Here we demonstrated TC could protect PC12 cells against apoptosis caused by 6-OHDP but promote SH-SY5Y cells against apoptosis caused by NO free radicals. We investigated the effects of exposure of PC12 cells to 6-OHDA alone or associated with pre-treatment of TC. Exposure of PC12 cells to 6-OHDA induced a concentration dependent decrease in cell viability determined by MTT assay and apoptosis of PC12 cells observed by flow cytometry, fluorescence microscopy and DNA fragmentation technique. TC displayed significantly inhibitory effects against PC12 cell death. EGCG and ECG were more effective that TC but EGC, EC and (+)-C were less effective.

The neuroprotective effect of genistein against A?25-35- induced apoptosis in cultured hippocampal neurons was studied. It was found that A?25-35-induced apoptosis, indicated by decreased cell viability, neuronal DNA condensation and fragmentation, is associated with the increase of intracellular free CA2+ level, the accumulation of reactive oxygen species (ROS), and the activation of caspase-3. All these phenotypes induced by A?25-35- are reverted by genistein. Our results further show that at nanomolar level, genistein protects neurons from A? 25-35- induced damages largely via the estrogen receptor (ER)-mediated pathway and at micromolar level, the neuroprotective effect of genistein is mainly mediated by its antioxidative properties.

Flavonoids extracted from Crataegus (CF) on brain ischemic insults were investigated in Mongolian gerbil stroke model. Results showed that pretreatment of the animals with CF decreased ROS, TBARS, and nitrite/nitrate in brain homogenate, increased the brain homogenate antioxidant level in a dose dependent manner. And pretreatment with CF increased the amount of biological available NO. At same time, the content of nitrite/nitrate increased NO, while oral pretreatment with CF decreased the nitrite/nitrate content in the brain homogenate and increased the biological available NO concentration. iNOS was implied in delayed neuron death after brain ischemic damage and it was found that pretreatment with CF could decrease the protein level of TNF-? and NFkB, and increase the mRNA level of NOS estimated by western blotting and RT-PCR. There were more neurons survived and less cells suffered apoptosis in the hippocampal CA1 region of CF treated animal brain tested.

PL-5

MODULATION OF PROTEIN OXIDATION BY ANTIOXIDANTS-IMPLICATIONS OR NEURONAL PROTECTION

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Oxidative stress plays an important role in cell death associated with many diseases. Such a condition is always connected with the formation of oxidatively modified proteins. Oxidatively modified proteins are selectively recognized and degraded by the proteasomal system. The isolated proteasome is able to degrade moderately oxidized proteins, whereas severe oxidized

model proteins are poor substrates of the protease. Therefore, these severely oxidized proteins accumulate and might facilitate the disease. Such a role of oxidized protein aggregates is postulated in aging and neurodegenerativediseases. Several lines of evidence demonstrate that the recognition of oxidized proteins by the proteasome is due to unfolding and to the exposure of hydrophobic moieties on the protein surface. In living mammalian cells we were able to demonstrate that the proteasome is the proteolytic system responsible for the degradation of oxidized proteins and that the exposure of cells to oxidants is followed by an enhanced protein turnover. Since protein oxidation is one of the potential pathophysiological factors in a number of oxidative stress related diseases it is important to prevent this process. Therefore, we undertook the attempt to test whether antioxidants are able to protect the proteins from oxidation in in vitro systems. Furthermore, several synthetic compounds and plant extracts were tested by us for the ability to protect the intracellular protein pool from oxidation.

IL-20

DOES REM SLEEP DEPRIVATION RESULT IN OXIDATIVE STRESS?

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India

Introduction: Free radicals and the resulting oxidative stress have been implicated as one of the causes for the effects of sleep deprivation like increased food intake and weight loss. Hence effect of REM sleep deprivation (REMSD) on brain oxidative stress was investigated in the current study.

Method: Wistar strain male rats weighing between 150-180g were deprived of REM sleep using the inverted flower pot technique. The animals were divided into four subgroups of six animals each based on the duration of REMSD 24, 48, 72 and 96 hours. Following the specified duration of REMSD animals were sacrificed and discrete regions of the brain, hypothalamus, midbrain, hindbrain and cerebral cortex, were dissected out for the study of lipid peroxidation, superoxide dismutase (SOD), catalase (CAT), total reduced glutathione (GSH) and glutathione peroxidase (GPX). All these results were compared with REM control animals as well as cage control animals. The effectiveness of restorative sleep in returning back these changes to baseline values were also investigated by allowing the animals to sleep in their home cages for 12, 18 and 24 hrs after depriving them of REM sleep for 96hrs. All the results obtained were analyzed using two way analysis of variance with time and group as main effects.

Results: REM sleep deprivation resulted in increase in lipid peroxidation and significant decrease in the levels of the antioxidant enzymes SOD, CAT and also GSH and GPX in all the regions studied. These changes were also time dependent. All these changes reverts back to baseline value gradually by 24 hours of restorative sleep

Conclusion: This study shows REM sleep deprivation (24h 96h) results in oxidative stress, which is reversible.

IL-21

REGIONAL DISTRIBUTION & AGE RELATED CHANGES IN OXIDATIVE STRESS MARKERS IN DIFFERENT REGIONS OFSHR RAT BRAIN

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Introduction: Oxidative stress has been implicated in the pathogenesis of organ damage associated both with normal ageing and hypertension. Age related changes in oxidative damage & antioxidant enzyme activities in brain reported in normotensive and a few hypertensive animal models but rarely in SHR, have been controversial and inconclusive. Regional distributions and age related changes in oxidative stress markers & activities of NaKATPase and Ach.esterase in the Cerebral Cortex, Cerebellum and Brain stem of WKY and SHR rats were studied to understand their role in hypertensive brain damage.

Methods: Six animals from WKY and SHR strains obtained from the same colony were sacrificed serially at 6, 12, 18, 24, 32, 40, 48 & 56 weeks of age. Contents of TBARS, Protein carbonyls, GSH, GSSG and activities of SOD, Catalase, GSH, GR, GST, NaKATPase, Ach. Esterase were determined in cerebral cortex (CC), cerebellum (CB) and brain stem (BS).

Results: SHR rats showed high SBP and low body wts at all time points. TBARS from wk. 24 and prot. Carbonyls from wk. 32 onwards increased in all the brain regions. GSH content and GSH/GSSG ratio were low in SHR at all time points and were lowest in BS.GPx, GR, GST, SOD, NaKATPase, Ach. esterase were low in all the brain regions but showed differences in the time course of their change. Catalase activity was low in CB from wk.32 but in CC and BS showed varying levels at different time points.

Conclusions: Oxidative damage to lipids and proteins is increased in all brain regions with increasing SBP in SHR. Activities of NaKATPase and Ach.esterase decrease with increasing SBP. There are regional differences in the contents and the time course of changes in the antioxidant enzyme activities. Oxidative stress increases with increasing SBP in SHR brain despite the fact that SHR are not prone to develop stroke Critical levels of oxidant/antioxidant imbalance and coping mechanisms to combat the oxidative stress may play important roles in hypertensive end organ damage.

IL-22

NEUROPROTECTION OF RGC-5 CELLS AGAINST GLUTAMATE INDUCED OXIDATIVE DAMAGE BY A NOVEL 2-ADAMANTYL ESTROGEN ANALOGUE, ZYC-3

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Introduction: Synthetic estrogen analogues, with minimal affinity for estrogen receptors, may provide a highly effective and safe alternative to native estrogens as neuroprotectants.

Methods: Estrogen and analogue receptor binding assays were performed with an enzyme fragment complementation assay kit. The antioxidant capacity of 17-estradiol and ZYC-3 was assessed via lipid peroxidation, using TBARs assay. Neuroprotective effects of 17-estradiol and ZYC-3 was assessed by neutral red dye uptake assay in RGC-5 cells, pretreated with 17-estradiol or ZYC-3, in the presence or absence of ICI compound, followed by an insult with l-glutamic acid. To assess if glutamate-cystine antiporter is involved in neuroprotection by ZYC-3, cystine uptake was examined in RGC-5 cells pretreated with ZYC-3, followed by glutamate challenge, by a ^{35}S-cystine uptake assay. -glutamylcysteine synthetase levels were examined by western blot analysis. Glutathione levels were measured by HPLC.

Results: ZYC-3 had a minimal or no binding to estrogen receptors. Glutamate treatment resulted in 50-60% RGC-5 death. EC_{50} values for inhibition of TBAR levels were 20 fold lower for ZYC-3 than 17-estradiol. 17-estradiol and ZYC-3 (0.5 to 1.0M) protected RGC-5s against glutamate cytotoxicity. These compounds worked independent of estrogen receptors, as inclusion of 100 nM ICI compound did not

reverse their neuroprotective properties against glutamate insult. Cystine uptake and glutathione levels were 3 fold higher in ZYC-3 pretreated cells as compared to glutamate treated cells. -glutamylcysteine synthetase levels were enhanced over both control and glutamate treated samples.

Conclusions: ZYC-3 may function as a potent antioxidant by scavenging oxidative free radicals. ZYC-3 may upregulate components of the glutathione synthesis pathyway. Taken together this compound has demonstrated powerful anti-oxidant capabilities both as a direct scavenger of free radicals and by enhancing glutathione synthesis. Thus, it may be used in treatment of neurodegenerative diseases. Supported by AHAF-National Glaucoma Program (NA) and AG10485 and AG22550 (JWS).

OL-10

THERAPEUTIC POTENTIAL OF ANTIOXIDANTS ON CEREBRALISCHEMIC REPERFUSION INJURY

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Oxidative stress is important in the pathophysiological mechanisms underlying acute central nervous system (CNS) injury. The discovery and development of potent antioxidant agents has been one of the most interesting and promising approaches in the search for treatment of CNS injury. Antioxidants of varying chemical structures have been investigated as therapeutic agents in the treatment of acute CNS injury. Although some of the antioxidants showed efficiency in animal models, most of them did not show beneficial effect in clinical trials performed to date. To achieve efficacy, the antioxidant must be given during the "time window" available between the vascular event and irreversible neuronal loss and also these agents might be particularly important not only in those patients who cannot receive thrombolysis but also in those who, undergoing this type of treatment, are at risk for so-called reperfusion injury. Reoxygenation during reperfusion provides oxygen to sustain neuronal viability and also provides oxygen as a substrate for numerous enzymatic oxidation reactions that produce reactive oxidants. In addition, reflow after occlusion often causes an increase in oxygen to levels that cannot be utilized by mitochondria under normal physiological flow conditions. During reperfusion, perturbation of the antioxidative defense mechanisms is a result of the overproduction of oxygen radicals, inactivation of detoxification systems, and consumption of antioxidants in the ischemic brain tissue. Reactive oxygen species may cause peroxidation of lipids, DNA damage, and oxidative injury of several key molecules essential for cell survival. Better understanding of the underlying pathological mechanisms of acute CNS injury and improvement of the molecular design of antioxidants will open a full spectrum of possibilities for treatment of various types of injuries.

OL-11

ERYTHROCYTE ANTIOXIDANT ENZYMES AS THE MARKERS OF OXIDATIVE STRESS IN NEUROLOGICAL DISORDERS

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Oxidative stress is one of the causes of the complications in neurological disorders.Several antioxidants are involved in the defence mechanisms against oxidants. Superoxide dismutase (SOD), Catalase (CT), Glutathione peroxidase (GP), Glutathione reductase (GR) are some of the most important antioxidant enzymes. Hence present study was designed to estimate these enzymes in erythrocytes of patients with neurological disorders and compare the values with those of normal subjects, and use these parameters as markers of oxidative stress.

Random venous blood samples were collected from 109 patients with various neurological disorders and 50 age and sex matched normal subjects. Patients with neurological disorders included 46 hemorrhagic strokes, 29 epilepsy, 19 meningitis, 15 Parkinson's disease cases. RBCs were separated from plasma and used for the estimation of SOD, CT, GP and GR in both the groups. These findings were statistically compared

RBC GR activity was significantly decreased in all types neurological disorders compared to controls. Stroke patients showed significantly low SOD activity. GP and CT levels remained normal in the patients irrespective of the type of the disease.

It can be concluded that functional insufficiency of RBC GR activity plays an essential role in the development of oxidative stress in the RBCs of the patients with brain disorders.

SESSION-VI

IL-23

FREE RADICAL DAMAGE, DIABETES MELLITUS AND DIETARY ANTIOXIDANTS

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Introduction: Free radical damage such as those induced by ionizing radiation and photosensitization has been implicated in various diseased states including diabetes. Oxidation of low density lipoprotein has been thought to be one of the possible factors in atherogenesis. Such damage may also be induced by increased level of oxidative stress during exposure to radiation. The free radical damage in the form of lipid peroxidation induced by photosensitization in diabetic patients and rats was examined. Antioxidants derived from dietary sources would have the potential application in preventing the cellular damage induced by free radicals and thus the disease. *Garcinia indica*, (kokam) a commonly used Indian spice has been considered to have many medicinal properties. The antioxidant property of kokam in various forms was investigated in this connection.

Methods: Experimental diabetes in rats was induced by streptozotocin injection. Oxidation of LDL and tissue fractions was carried out in the presence of copper sulphate or methylene blue plus visible light on photoexcitation. The generated singlet oxygen, thiobarbituric acid reactive substances, conjugated dienes and lipid hydroperoxides formed were estimated.

Results: The potential for peroxidation, induced by photosensitization and copper sulphate was high in blood of diabetic patients and rats. Photochemically induced peroxidation in rat brain and liver on other hand was low during diabetes. It is likely that tissues in diabetic rat contain a higher level of singlet oxygen quenchers than the respective controls. Blood from diabetics may be poorer in antioxidants due to the enormous amount of glucose and other secondary metabolites present in blood which may affect the delicately maintained balance between peroxidants and antioxidants. It was found that various fractions of kokam show antioxidant action at different level. The standardization of proper doses of dietary sources which show antioxidant property would be useful in control of diabetes as well as CVD and may be other diseases.

IL-24

Ilavazhagan,

IL-25

REGULATORY ROLE OF ROS AND RNS IN EXPRESSION OF TRANSCRIPTION FACTOR AP1 IN BREAST CANCER

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Background: Reactive oxygen species such as superoxide (O^{2-}), hydrogen peroxide (H_2O_2), hydroxyl radical (OH) and reactive nitrogen species (RNS) like nitric oxide (NO), peroxynitrite (ONOO) have been shown to play a significant role in mutagenesis and tumorogenesis. AP1 is a composite transcription factor (activator protein). It is a homo or heterodimer DNA binding protein composed of either 2-jun family members (c-jun, jun-B, jun D) or one jun and one fos family protein (c-fos, fos B, fra 1, fra2). ROS and RNS have been shown to induce c-fos and c-jun oncoproteins, which can lead to carcinogenesis.

Aim: To study nitric oxide and scavenger enzymes in one hand and c-fos& c-jun expression on other hand in breast cancer patients.

Materials and Methods: 25 women with breast cancer were taken to evaluate the blood levels for oxidative damage markers and antioxidants (like MDA, NO, GSH, GPx and SOD) and cancerous breast tissue to evaluate the level of expression of transcription factors c-fos and c-jun.25 age and sex matched healthy women without any breast disease served as control for the study of blood parameters. Tumor free adjacent healthy breast tissue from mastectomised breast of 25 breast cancer patients of study group and healthy breast tissue from 5 benign breast disease patients served as control for the study of transcription factors c-fos and c-jun.

Results: The mean serum levels of NO were higher in study group than controls ($p=0.013$). A comparison between the study and control group showed higher levels of MDA in the study group ($p=0.064$). The difference between the mean values of GSH in the study group and the control group was also statistically significant ($p=0.042$). The SOD and GPx levels showed no statistically significant difference between the two groups. The expression of c-fos and c-jun in the cancer patients ranged from high to very high, whereas the expression of c-fos and c-jun in the control group ranged from nil to moderate ($p<0.001$).

Conclusion: The increased levels of nitric oxide and glutathione in the blood of patients and the high levels of expression of c-fos and c-jun may further lend credence to the fact that transcription factors are redox regulated. The mechanisms involved in the regulation of AP-1 needs to be defined before we can think of using redox status to study the expression of this transcription factor.

IL-26

HERBS FOR ENHANCING MENTAL PERFORMANCE

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Several herbs have been prescribed in oriental systems of medicine for enhancing mental performance, Dhi, Dhriti and Smriti, dependant on age of the individual. Several of these have been experimentally tested and commercialized as well.Ayurveda prescribes some single herbs for enhancing mental performance. Some of the important ones are: Vaca (Acorus calamus), Shankhapushpi (Convolvulus pluricaulis), Mandukpami (Centella asiatica), Guduci (Tinospora cordifolia), Yasthimadhu (Glycirrhiza glabra) and Brahmi (Bacopa monnieri). A basket of such herbal extracts, Composite Indian Herbal Preparation (CIHP), was investigated for avoidance learning during endurance performance in albino rats using Runimax, a circular runway. The oral dose of CIHP was 47.86 mg/100 gm body wt. once a day for 5 days /week in a cross over experiment involving 5 weeks of drug intake and 4 weeks of withdrawl. Learning ability and memory retention was evaluated by counting the number of electrical stimuli recieved/avoided during the endurance run. The number of stimuli decreased in the group given drug. Removal of drug increased the number of stimuli but gradually over the period of four weeks.Brahmi extract, one of the important constituent of CIHP, had similar effect. The endurance run was increased in rats receiving drugs as compared with the controls. In high mountains, the mental performance of man gets highly compromised due to hypoxia. A different CIHP containing another basket of herbal extracts and minerals was able to relatively restore higher cognitive functions in man.

The mechanism by which CIHPs and Brahmi extracts enhanced mental performance is little understood though the active constituents have been characterised.However,the enhanced mental performnace could be due to increase in the availability of tissue oxygenation, availability of nutritional factors leading to improved neurotransmitter regeneration and/or improvement in free radical scavenging system.

IL-27

METAL INDUCED OXIDATIVE STRESS AND THE ROLE OF ANTIOXIDANT IN THE CHELATION THERAPY

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It is well known that number of transition metals acts as catalysts in the oxidative deterioration of biological macromolecules and therefore, the toxicities associated with these metals may be due at least in part to oxidative tissue damage. Metals like lead and metalloids like arsenic are known to deplete glutathione and protein bound sulfhydryl groups resulting in the production of reactive oxygen species as superoxide ions, hydrogen peroxide and hydroxyl radicals. As a consequence, enhanced lipid peroxidation. DNA damage and altered calcium and sulfhydryl homeostasis occur. Consequently, it is suggested that metal induced oxidative stress in cells can be partially responsible for the toxic effects of metals. It is now clearly defined that oxidative stress is one of the important mechanisms of lead and arsenic induced pathogenesis. There have number of studies being done to determine the effect of antioxidant supplementation following heavy metal exposure. Data suggest that antioxidant may play an important role in abating some hazards of heavy metals. It is thus, expected that co-administration of an antioxidant should be an important component of an effective chelation therapy. We recently reported more pronounced beneficial effects of co-administration of n-acetylcysteine (NAC) with meso 2, 3-dimercaptosuccinic acid (DMSA) in the depletion of arsenic and lead accompanied by significant recoveries in altered biochemical variables compared to the treatment with DMSA alone. We also recently reported an encouraging role of -lipoic acid in reducing oxidative stress in lead poisoned rats when administered with DMSA or monoisoamyl DMSA (MiADMSA). Beneficial role of taurine when administered along with a thiol chelator for the treatment of chronic lead poisoning too was reported recently by us. Two mechanisms were proposed for the antioxidant effects of taurine might be protecting cells via intercalating into the membrane and stabilizing it. A pronounced beneficial role of vitamin E (-tocopherol acetate) and vitamin C (ascorbic acid) when administered along with DMSA/MiADMSA in the recovery of lead and arsenic induced oxidative stress and body metal burden was also reported.

Thus, use of antioxidants thus brings another level option to the therapy i.e. the possibility of therapeutic intervention without removing the patient from the source of toxic metal exposure. Antioxidants are recognized as safe molecules and may be given to subjects with low level metal concentrations in their blood even when it is not possible to remove them from exposure to metals.

IL-28

IMPLICATIONS OF OXYGEN FREE RADICALS IN THE FOMATION OF CATARACT

Shambhu Verma,

IL-29

PREVENTION OF OXIDATIVE STRESS BY MUSHROOM DERIVED ANTIOXIDANTS

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Introduction: Our recent investigations showed that extracts of medicinal mushrooms namely, Ganoderma Lucidum, and Phellimus rimosus possessed significant in vitro antioxidant activity. Hence we examined the effect of these mushrooms derived antioxidants to prevent oxidative stress. Two experimental models, carbontetrachloride-induced hepatotoxicity in rats and cisplatin-induced nephrotoxicity in mice, were used to evaluate this ability of the mushroom preparations.

Methods: Chronic hepatotoxicity in rats was induced by the intoxication with CCl4 (i.p) 3 times a week for 5 weeks. Methanolic extract of G.lucidum (500 / 1000 mg/kg) and ethyl acetate extract of P.rimosus (25/50 mg/kg) were given orally to animals 1 hr before each CCl4 administration. Nephrotoxicity in mice was induced by a high dose of cisplatin (16 mg/kg). Methanolic extract of G.lucidum (250/500 mg/kg) or ethyl acetate extract of P.rimosus (25/50 mg/kg) was administered 1 hr. prior to cisplatin treatment.

Results: Chronic exposure to CCl4 caused depletion of antioxidant defense in the liver resulting in oxidative stress. The activities of SOD, CAT and GPx in the liver were significantly elevated ($p<0.01$) GSH level enhanced and lipid peroxidation (MDA) reduced significantly by the treatment with mushroom extracts. The high dose treatment of cisplatin significantly reduced real SOD, CAT, GPx ($p<0.001$) and GSH level and increased lipid peroxidation ($p<0.001$) indicating oxidative stress. The administration of mushroom extracts significantly restored the renal antioxidant defense.

Conclusions: Experimental results reveal that P.rimosus and G.lucidum extracts protect the antioxidant defense in the lever and kidney. The findings suggest the usefulness of medicinal mushroom extracts to prevent oxidative stress in the vital organs.

OL-12

EFFECT OF ANTIOXIDANT (L-ASCORBIC ACID) ON NICKEL INDUCED ALTERATION OF NUCLEIC ACID CONCENTRATION IN RATS.

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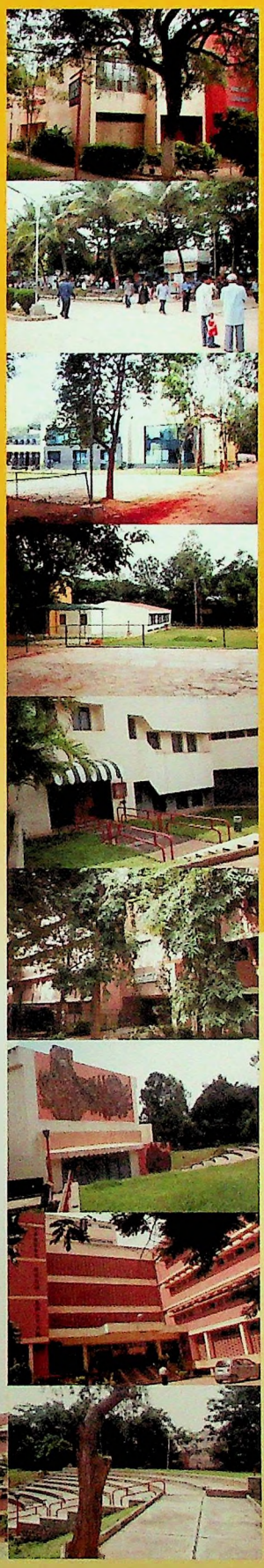
Introduction: Nickel exhibit the ability to produce reactive oxygen species (ROS) or free radicals resulting in lipid peroxidation, DNA damage, depletion of sulfhydryl and altered calcium homeostasis. The present study was designed to elucidate the effect of L-ascorbic acid on nickel sulfate induced hepatic nucleic acids concentration in rats.

Methods: Adult male Wister strain rats (160 ± 5g) were divided into four groups (n=6). Group I served as an untreated control. Group II rats were administered nickel sulfate (2.0 mg / 100 g body weight, i.p.) on alternate days until the tenth dose. Group III rats were treated orally with L-ascorbic acid (50mg / 100 g. b.wt.) and Group IV rats were given nickel sulfate and ascorbic acid simultaneously. Hepatic total protein, RNA and DNA concentration were determined by the standard methods.

Results: Nickel induced a significant decrease in hepatic DNA, RNA and protein content in the Group II rats in comparison to untreated control (Group I). Whereas simultaneous administration of L- ascorbic acid with nickel sulfate (Group IV) resulted in a remarkable improvement of hepatic nucleic acids and total protein concentration in comparison with rats treated with nickel sulfate alone (Group II).

Conclusions: Nickel sulfate appears to be a potential hepatotoxic heavy metal that affects adversely to the expression of genetic information by reducing DNA, RNA and protein concentrations in the liver of albino rats. But simultaneous treatment with L-ascorbic acid relatively prevents

Tuesday 11th Jan-2005



TUESDAY Jan 11th 2005

0730 - 0830 — BREAK FAST ROUND TABLE

0830 - 0900 — SFRR ORATION BY B. M. HEGDE ON Topic : "ANTIOXIDANTS AFTER HEART ATTACK" Venue : MAIN AUDITORIAUM CHAIRPERSONS : PREM PAIS & P. R. KRISHNA SWAMY

0915 - 1130

SYMPOSIUM VII
Sponsored by : M.S. RAMAIAH MEDICAL COLLEGE & HOSPITALS
Venue : MAIN AUDITORIUM

Topic : "FREE RADICALS AND ANTIOXIDANTS IN CANCER"

CHAIRPERSONS :
1. RD Lele (India) 2. Chancerelle Y (France) 3. Chandan K Sen (USA)

- IL-30 A Jaya Deep (India) : Role of long chain omega-3 fatty acids on plasma antioxidant status in human subjects
- IL-31 Kanthimathi (Malaysia) : The effect of phytosterols on breast cancer cell proliferation
- IL-32 Keshav Singh (USA) : Mitochondrial oxicative stress and nuclear genome instability
- IL-33 Nagini S (India) : Combination chemoprevention by tomato and garlic in the hamster buccal pouch carcinogenesis model
- IL-34 Shahab Uddin(S. Arabia) : Curcumin induces growth inhibition of leukemic cells
- IL-LS Roisin Molloy (UK) : Antioxidants the future in disease management
- OL-13 Tranum Kaur(India) : Relationship of molecular biomarkers and anti-oxidant defense system in esophageal carcinoma
- OL-14 Asha S Raste (India) : Antioxidant status in disseminated cancer

SYMPOSIUM VIII
Venue : HALL A

Topic : "FREE RADICALS AND ANTIOXIDANTS IN INFECTIOUS DISEASES AND IMMUNITY"

CHAIRPERSONS :
1. Ragini Macaden (India) 2. Umah R. Kuppuswamy (Malaysia) 3. Panda B B (India)

- PL-6 Nicholas Hunt(Australia) : Radicals, antioxidants and malaria
- IL-35 Tuli Biswas India) : Oxidative modification of band 3 in the reduced survival of erythrocytes in visceral leishmaniasis
- IL-36 Neeta Singh (India) : Gene expression profiling in practitioners of sudarshan kriya
- OL-15 Benedicta D'Souza(India) : Comparative study on lipid peroxidation and antioxidants in falciparum and vivax malaria
- OL-16 Brijesh Rathore (India) : Comparative studies of different organs of N.arbor tristis in modulation of cytokines in rheumatoid arthritis
- OL-17 Meena Shelgaonkar(India) : Oxidative stress and the role of antioxidants in the treatment of pulmonary tuberculosis

SYMPOSIUM IX
Sponsored by : EUREKA FORBES
Venue : HALL B

Topic : "FREE RADICALS AND ANTIOXIDANTS IN ENVIRONMENTAL BIOLOGY"

CHAIRPERSONS :
1. TPA Devasagayam (India) 2. Kalanithi Nesarethnam (Malaysia) 3. Khanduja K L (India)

- IL-37 Abhay Kumar(India) : Alkaline water as an antioxidant for healthier life
- IL-38 Anand CV (India) : Anti-Oxidant defences in aortae of cigarette smoke-exposed rats, and the effect of supplementation with Vitamin E
- IL-39 Asha Devi (India) : The possible effects of Vitamin E and exercise on rat erythrocytes to intermittent hypobaric hypoxia and oxidative stress
- IL-40 Barros MP (Brazil) : Antioxidant efficiency of astaxanthin in phosphatidyl choline liposomes as a pH-dependent event
- IL-41 Bhattacharya RK (India) : Suppression of arsenic toxicity by antioxidant tea polyphenols
- IL-42 Goswami K (India) : Ascorbic acid therapy in lead exposed jewellery workers of Kolkata

1130 - 1145 — TEA

1145 - 1400

SYMPOSIUM X
Venue : MAIN AUDITORIUM

Topic : "FREE RADICALS AND ANTIOXIDANTS IN FOOD SCIENCES"

CHAIRPERSONS :
1. Samar Basu (Sweden) 2. Lindsay Brown (Australia) 3. Singh R K (India)

- PL-7 Kalyanaraman (USA) : Mitochondria targeted antioxidants and SOD mimetics a new class of therapeutic antioxidants
- IL-43 Hettiarachchy Navam (USA) : Total phenolics, phenolic acid constituents, anitioxidant activities and antimutagenic activities of selected plant extracts including bitter melon (bitter gourd).
- IL-44 Kalanithi Nesarathnam (Malaysia): Potential health benefits of palm tocotrienols
- IL-45 Kiran Ahuja (Australia) : Serum concentration of carotenoids in healthy adults on various carotenoid controlled diets
- IL-46 U.R. Kuppuswamy (Malaysia): Antioxidant enzyme activities in trace element exposed mononuclear and ovarian cancer cells
- OL-18 Kruthika Desai (India) : Spirulina platensis as a novel source of antiaging enzyme superoxide dismutase
- OL-19 Pugalendi (India) : Effect of excessive intake of fresh and thermally oxidized edible oils on redox status in the plasma and tissues of rats

SYMPOSIUM XI
Venue : HALL A

Topic : FREE RADICALS AND ANTIOXIDANTS IN HUMAN REPRODUCTION AND INFERTILITY"

CHAIRPERSONS :
1. Dipak K Das (USA) 2. Debasis Bagchi (USA) 3. Poonam Kakkar (India)

- PL-8 Chandan K Sen (USA) : New horizons in Vitamin E neuroprotection
- IL-47 Abbas Ali Mahdi (India) : Seminal plasma antioxidant status in cigarette smokers
- IL-48 Haegeman (Belgium) : Soy phytoestrogens counteract age related cytokine gene expression
- IL-49 Palep HS (India) : Role of cap. torchnil, a herbal immunomodulator and antioxidant,in recurrent pregnancy loss
- OL-20 Sukanya Shetty (India) : Plasma ceruloplasmin levels in pregnancy with pre-eclampsia
- OL-21 Vijayalakshmi B (India) : Alterations in lipid metabolism and free radical levels in pregnancy induced hypertension

SYMPOSIUM XII
Sponsored by : NATIONAL REFERRAL CENTRE FOR LEAD POISONING IN INDIA.
Venue : HALL B

Topic : "FREE RADICALS AND ANTIOXIDANTS IN TOXICOLOGY"

CHAIRPERSONS :
1. Mukherjee T (India) 2. Kanthimathi (Malaysia) 3. Rao B S M (India)

- IL-50 Chaubey RC (India) : Modulation of hydrogen peroxide induced oxidative damage to DNA by taxifolin in mouse
- IL-51 Jawali N (India) : Genetic evidence for the involvement of reactive oxygen species in bactericidal action of ciprofloxacin
- IL-52 Kyung-Sun Kang(Korea) : Chinese cabbage extracts and sulforaphane can protect H_2O_2 induced inhibition of gap junctional inercellular communiation through the inactivation of Erk1/2 and P38 map kinases
- IL-53 Mishra KP (India) : Radiation induced reactive oxygen species mediated cell death and its implication in tumor radiotherapy
- IL-54 Mugesh G (India) : Antioxidant activity of selenoenzymes and selenium compounds

TUESDAY	1400 - 1430	LUNCH		
Jan 11th 2005	1430 - 1600	POSTER		
	1600 - 1830	SYMPOSIUM XIII Venue : MAIN AUDITORIUM	SYMPOSIUM XIV Sponsored by : Venue : HALL A	SYMPOSIUM XV Venue : HALL B
		Topic : "FREE RADICALS AND ANTIOXIDANTS IN AGEING & APOPTOSIS"	Topic : "FREE RADICALS AND ANTIOXIDANTS IN RADIATION BIOLOGY"	Topic : "NITRIC OXIDE"
		CHAIRPERSONS : 1. Hideyuki Majima (Japan) 2. Ramsarma T (India) 3. Chainy G B N (India)	CHAIRPERSONS : 1. Kanagasabapathy (India) 2. Chandan K Sen (USA) 3. Virupaksha H. S. (India)	CHAIRPERSONS : 1. Kang K S (Korea) 2. Parameshwaran (Australia) 3. T. Malati (India)
		PL -9 Lele RD(India) : Ageing and free radicals: A review	IL-59 Chancerelle Y (France) : Treatment of local exposition to radiation injury: the french experience	PL-11 Gerald Wolf (Germany) : Mitochondria, Nitrosative/Oxidative stress, and the crossroads for damaging and protective pathways
		PL-10 Sainis KB (India) : Differential responses of cells to natural compounds In Vitro and in Vivo	IL-60 Huilgol N.(India) : A Phase i trial of tocoferol monoglucoside (Tmg) in patients undergoing hemi-body radiation	IL-65 Malini Krishna(India) : Inhibition of radiation induced tyrosine nitration of proteins by curcumin and nicotinamide.
		IL-55 Aroor (India) : Role of oxidetive stress in alcohol suppression of immune response	IL-61 Nair C K K (India): : Possible use of antioxidants as radioprotectors	IL-66 Poduval TB (India) : L-Arginine treatment rescues mice from heat stroke induced death. role of nitrosative and oxidative stress
		IL-56 Devasagayam TPA (India) : Free radical damage to mitochondria and its possible prevention by natural compounds: A review of our studies	IL-62 Prasad MNV (India) : Radiophytoremediation IL-63 Sandip K Bandyopadhyay : Natural antioxidants and radioprotection	IL-67 Suvro Chatterjee(India) : Time, space and nitric oxide: The three dimensions of NOS
		IL-57 Suhel Pervez (Germany) : Blockade of mitochondrial permeability transition by Dopamine -D2- Receptor agonists and possible role in neuroprotection	IL-64 Dandekar SP (India) : Radiation inactivation of an Alanine Aminopeptidase - A Probe into the active site composition	IL-68 Udayan Ray (Australia) : The inhibition of insulin induced nitric oxide synthesis by blood platelets in chronic cigarette smokers
		IL-58 Indu P Kaur (India) : Cutaneous photoageing: Prevention and repair using antioxidant approach	OL-23 Kaushik P (India) : Influence of the leaf extract of mentha piperita (Linn) on radiation induced damage in swiss albino mice	OL-25 Ilangovan Govindaswamy (USA) : Hyperthermia induced attenuation of mitochondrial hydroxyl radicals in cardiac H9C2 cells
		OL-22 Srinivasulu N Pattipati (India): U74500a, a 21-Aminosteroid ameliorates haloperidol-induced perioral movements and associated memory dysfunction	OL-24 Samarth RM (India) : Modulatory influence of mentha piperita (Linn) leaf extract on hepatic antioxidant status and lipid peroxidation against gamma radiation in swiss albino mice	

SFRR ORATION BY
BM HEGDE

ON

"ANTIOXIDANTS AFTER HEART ATTACK"

Oxygen, an essential element for life, can create damaging by-products during normal cellular metabolism-called oxidants. Antioxidants counteract these cellular by-products, called free radicals, and bind with them before they can cause damage. If left unchecked, free radicals may cause heart damage, cancer, cataracts, and a weak immune system.

Antioxidants work by: binding to the free radicals; transforming them into non-damaging compounds; or repairing cellular damage. Antioxidants come in a variety of forms and include Vitamin C, Vitamin E, the Carotenoids, and Selenium.

Good sources of antioxidants include fruits and vegetables. The highest concentrations are found in the most deeply or brightly colored fruits and vegetables (spinach, carrots, red bell peppers, tomatoes).

There is widespread scientific agreement that eating adequate amounts of fruits and vegetables can help lower the incidence of cardiovascular disease and certain cancers. With respect to antioxidants and other phytochemicals, the key question is whether supplementation has been proven to do more good than harm. So far, the answer is no, which is why the FDA will not permit any of these substances to be labeled or marketed with claims that they can prevent disease.

Our own studies, both in animal models and patients suffering from acute myocardial infarctions, have shown very elegantly that cell damage by ischaemia does release large amounts of free radicals as measured by bio-chemical parameters. We have also shown that pretreatment with a combination of anti-oxidants does prevent cell damage post-infarction. Treatment with the same anti-oxidants after the cell injury has settled down does not seem to help to the same extent possible.

This is an important finding, as reperfusion injury in patients with heart attacks given thrombolytic therapy (routine now) is of grave concern to the medical profession. This often sends quite a few patients to meet their maker in heaven prematurely. With further large scale human studies we would be able to make it therapeutically available. Another important finding brought out in our many studies (published extensively already) is that individual anti-oxidants in isolation do not seem to work.
The last finding is an indicator how the reductionist science in medicine does not seem to fit into the dynamic human physiology that follows the non-linear laws for time evolution. The talk would give an overview of all these concepts.

IL-30

ROLE OF LONG CHAIN OMEGA-3 FATTY ACIDS ON PLASMA ANTIOXIDANT STATUS IN HUMAN SUBJECTS

A. Jayadeep [1*], P. R. Sudhakaran [1], V. P. Menon [2] and P. P. Nair [3, 4]
[1] Department of Biochemistry, University of Kerala, Trivandrum- 695 581, India; [1*] Central Food Technological Research Institute, Mysore, India; [2] Department of Biochemistry, Annamalai University, Tamil Nadu, India; [3] Department of International Health, Johns Hopkins University, Maryland, USA.

Long chain n-3 fatty acids like eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) present in fish and fish oil are reported to have a number of beneficial effects in the prevention of cardiovascular diseases and cancer. Beneficial effects are attributed to the effects of lipoxygenase and cyclo-oxygenase mediated products, and lipid lowering action. In addition to that n-3 fatty acids enhance the bioavailability of fat soluble antioxidants and resultant health beneficial effects through the prevention of oxidative stress in the body. In order to assess the effect of long chain n-3 fatty acids on plasma antioxidants, levels of retinol, beta-carotene, lycopene and alpha-tocopherol were analyzed in fish consuming and vegetarian subjects. In addition to that, effect of supplementation of n-3 fatty acids in hyper-cholesterolemic non-vegetarian and vegetarian subjects on plasma antioxidant status, and bioavailability studies with carotene rich *spirullina* on plasma antioxidants in vegetarian and fish eating subjects were also carried out. Results of the studies clearly show that long chain omega-3 fatty acids have definite role in plasma antioxidant status in human subjects.

IL-31

THE EFFECT OF PHYTOSTEROLS ON BREAST CANCER CELL PROLIFERATION

M.S. Kanthimathi[1], JW Chai[1], UR Kuppusamy[1], C Wiart[2]
[1]Department of Molecular Medicine, [2]Department of Pharmacy, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia.

This study was conducted to provide scientific evidence to corroborate the ethnopharmacologic use of *Cyrtandra cupulata* plant parts by the aboriginal people of Malaysia *('orang asli')*. A mixture of phytosterols, namely, campesterol, stigmasterol and beta-sitosterol, was purified from crude methanolic extracts of *Cyrtandra cupulata* leaves. This mixture inhibited the proliferation of the estrogen-sensitive breast cancer cell line, MCF-7 by 30%, as measured by the microculture tetrazolium formazan (MTT) assay. The total antioxidant capacity and total phenolic content were estimated to be about 200 mmol ferrous sulphate equivalents/100 grams of lyophilized extract, and 1583 mg gallic acid equivalents/ gram of lyophilized extract, respectively. The total phenolic content and the antioxidant capacity each correlated well with the inhibitory effect on MCF-7 proliferation. The leaf extract also induced alkaline phosphatase activity in MCF-7 cells, in a dose-dependent manner. The induction of alkaline phosphatase activity has been used to indicate estrogenic activity, using estradiol as a reference. The postulation that the cytotoxic components in the extract had an estrogenic nature was further strengthened by the observation that the proliferation of another breast cancer cell line, MDA-MB-231, was not inhibited. The MDA-MB-231 cell line is estrogen-insensitive, while MCF-7 is estrogen-sensitive. Data on differential protein expression studies and estrogen receptor-binding assays will be presented.

IL-32

MITOCHONDRIAL OXIDATIVE STRESS AND NUCLEAR GENOME INSTABILITY

Keshav Singh

Associate Professor of Cancer Genetics

Roswell Park Cancer Institute

Using two cellular model systems we have analyzed the consequences of disrupting mitochondrial function on nuclear genome stability and cell death. Our studies suggest that mitochondrial dysfunction leads to genomic instability in the nucleus and resistance to apoptosis. We measured the frequency of canavanine resistant colonies as a measure of nuclear mutator phenotype in Saccharomyces cerevisiae model. Our data suggest that mitochondrial dysfunction leads to increased nuclear genomic instability when oxidative phosphorylation is blocked in wild type yeast by antimycin A and in mitochondrial mutant strains lacking the entire mitochondrial genome (rho0) or those with deleted mitochondrial DNA (rho-). Blockage of oxidative phosphorylation by antimycin A treatment led to increased intracellular levels of ROS. In contrast, inactivation of mitochondrial activity (rho- and rho0) led to decreased intracellular levels of ROS. Our study revealed that in rho0 cells the REV1, REV3 and REV7 gene products all implicated in error-prone translesion DNA synthesis control mutagenesis in the nuclear genome. However, TLS was not involved in nuclear DNA mutagenesis caused by inhibition of mitochondrial function by antimycin A. Studies conducted in a mammalian cell line model also suggest that like the yeast model system mammalian rho0 cells contained lower ROS than parental cells. Our analysis revealed that depletion of the mitochondrial genome did not affect either the expression of superoxide dismutase or its activity. However, catalase expression and its activity were decreased. Decrease in catalase activity resulted in increased lipid peroxidation, increased oxidative damage to nuclear genome, impaired DNA repair and resistance to apoptosis. Studies are now under way to determine the nature of nuclear genome instability and its role in resistance to apoptosis.

IL-33

COMBINATION CHEMOPREVENTION BY TOMATO AND GARLIC IN THE HAMSTER BUCCAL POUCH CARCINOGENESIS MODEL

S.Nagini

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Combination chemoprevention by functional foods with antioxidant properties is an attractive strategy to control reactive oxygen species (ROS)-induced diseases such as oral cancer. We used the hamster buccal pouch (HBP) carcinogenesis model to evaluate the chemopreventive potential of tomato, a functional food rich in the antioxidant carotenoid lycopene, both alone and in combination with garlic, a commonly used spice containing antioxidants and bioactive substances. Chemoprevention was biomonitored using a range of markers, including the cellular redox status, carcinogen detoxification enzymes, incidence of bone marrow micronuclei and apoptosis. HBP carcinomas induced by 7,12-dimethyl-benz[a]anthracene displayed decreased susceptibility to lipid peroxidation coupled with antioxidant adequacy, genotoxicity as reflected by increased frequency of bone marrow micronuclei, altered balance in the activities of phase I and phase II carcinogen-metabolizing enzymes and evasion of apoptosis, which may confer a selective growth advantage on tumour cells. Although tomato paste significantly suppressed the incidence of HBP carcinomas, tomato in combination with garlic was more effective in chemoprevention. Combined administration of tomato and garlic exerted antigenotoxic effects modulated the oxidant-antioxidant status and carcinogen-metabolising enzymes and induced apoptosis. The results indicate that broad spectrum of anticancer properties with less adverse effects can be achieved through effective combination of functional foods.

IL-34

CURCUMIN INDUCES GROWTH INHIBITION OF LEUKEMIC CELLS

Shahab Uddin

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Curcumin has been shown to possess variety of biological functions including anti-inflammatory, anti-tumor and antioxidative. The mechanism by which curcumin inhibit cell proliferation remains poorly understood. In the present report we investigated the effect of curcumin on the activation of apoptotic pathway in T malignant cells. Our data demonstrate that curcumin causes the dose dependent suppression of several T cell line proliferation. Curcumin treatment causes the suppression of constitutively active AKT, FOXO transcription factor and GSK3. Cumin also induces release of cytochrome c accompanied by activation of caspase-3 and PARP cleavage. In addition, zVAD-fmk, a universal inhibitor of caspases, prevents caspase-3 activation as well as PARP cleavage induced by curcumin treatment. Taken together, our finding suggest that curcumin suppresses constitutively activated targets of PI3'-kinase (AKT, FOXO and GSK3) in T cells leading to the inhibition of proliferation and induction of caspase-dependent

OL-13

RELATIONSHIP OF MOLECULAR BIOMARKERS AND ANTI-OXIDANT DEFENSE SYSTEM IN ESOPHAGEAL CARCINOMA

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Esophageal carcinoma has high incidence in India, but its etiology is unknown. The disease is multifactorial and the etiological factors and genetic disposition may depend upon geographical variations. The oxidant-antioxidant balance is thought to be important in the initiation, promotion, and therapy resistance of cancer. Therefore, the present study was carried out with a aim to evaluate expression profiles of p53, bcl-2, c-myc, nos-2 and cox-2, and to identify prognosticators of esophageal carcinoma in northern part of India. The antioxidant defense status in tumor and normal mucosa of esophageal patients were also evaluated. Patients were divided into two groups. The first group did not receive any chemotherapy, whereas, the second group received pre-operative chemotherapy comprising of cisplatin (30 mg/mt2/day) and 5-FU (750 mg/mt2/day) for 3

days followed by surgery after 4 weeks. Results obtained by Western blotting showed a significant difference in the tumor bcl-2 protein expression pattern between patients who had undergone neoadjuvant therapy (NAT) and those who had no therapeutic intervention (Mann-Whitney Test, P=0.0244). Correlation studies revealed that there was a significant negative correlation between bcl-2 and c-myc expression in tumor tissue of patients with and without NAT. Whereas, a positive correlation between bcl-2 and cox-2 in tumor tissue in response to NAT indicates the tumor promoting tendency even after chemotherapy. Immunohistochemistry studies showed both the nuclear and cytoplasmic localization of p53 and c-myc, whereas mainly cytoplasmic localization was seen in case of bcl-2. Clinicopathological parameters (age, sex, dysphagia, grade, smoking, alcohol, location and length of lesion, lymph node involvement, differentiation and histological types) and their relationship with the various cancer proteins were found to be non-significant. Analysis of antioxidant defense system showed significant decrease in superoxide dismutase, catalase and reduced glutathione levels and increased glutathione peroxidase activity in tumor tissue as compared to normal mucosa of patients with NAT. This study broadens the insight into the relationships of various oncoproteins, which might be helpful in adjusting the apoptotic threshold in clinical setting for esophageal cancer.

OL-14

ANTIOXIDANT STATUS IN DISSEMINATED CANCER

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Department Of Biochemistry &* Radiation Oncology

Humans have evolved with antioxidant systems, that protect them against free radicals. These systems include antioxidants produced in the body, both endogenous and supplied from the diet and exogenouses.Oxidative stress has been proposed to play a major role in cardiovascular infectious diseases, cancer, diabetes and neuro degenerative pathologies.

Various anti-oxidant enzymes Superoxide Dismutase ,Glutathione Peroxidase, Glutatione reductase are involved in stress response and cancer progression.There is no published data on the normal values for these anti-oxidants in healthy Indian population nor in cancer patients.

As part of an ongoing study we measured the serum Superoxide Dismutase Glutathione Peroxidase, Glutatione reductase along with the total antioxidant status in 29 healthy adult volunteers(medical & paramedical staff) and 72 patients with widely disseminated cancer.

Result : In the healthy adult Indians, the mean levels of Glutathione Reductase was 54.99 $\pm$ 6.35 U/L with a range of 41.28 66.92 U/L, Glutathione Peroxidase had a mean of 6846.2 $\pm$ 2738.0 U/L and a range of 3452 18552 U/L. In comparison, for cancer, the levels of Glutathione Reductase was 132.7 $\pm$ 91.7 U/L with a range of 46.12 618.62 U/L was significantly higher($p < 0.001$), Glutathione Peroxidase had a mean of 4171.0 $\pm$ 2186.0 U/Land a range of 129 8828 U/L and the levels were significantly lower.

IL - LS

ANTIOXIDANTS - THE FUTURE IN DISCEASE MANAGEMENT*

Rolsin Molloy, UK.

SESSION VIII

PL-6

RADICALS, ANTIOXIDANTS AND MALARIA

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About 1% of people infected with *Plasmodium falciparum* develop cerebral malaria (CM) and around 25% of them die. Previous studies in humans and in mouse models of malaria have suggested, on the basis of indirect evidence, that phagocyte-derived reactive oxygen species (ROS) may be important in the host immune response against the malaria parasite and in the pathogenesis of CM. Other studies have suggested that glutathione peroxidase-1 (Gpx1) protects the malaria parasite against oxidative damage. Haptoglobin, a molecule that binds to haemoglobin and may have antioxidant activity *in vivo*, has some known associations with the progression of human malaria infections. To further investigate these phenomena, we have used the following experimental systems: (i) $gp91^{phox}$ -/- mice, whose phagocytes cannot generate ROS; (ii) Gpx1 -/- mice; (iii) Hp -/- mice..

Our studies with $gp91^{phox}$ -/- mice suggested that phagocyte-derived ROS

are not important in malaria immunity or in the pathogenesis of CM. Work with the Gpx1 -/- mice showed that the parasitaemia associated with *P. berghei* ANKA infection, but not *P. chabaudi* infection, increased more rapidly in the absence of this enzyme. There also was a modest enhancement of susceptibility to CM in these mice. The rate of recrudescence of *P. chabaudi* infection was significantly higher in Gpx1 -/- mice than in Gpx1 +/+ animals. The peak parasite burden in *P. chabaudi*-infected Hp -/- mice was greater than in Hp +/+ mice. Hp -/- mice survived *P. berghei* ANKA infection (a CM model) significantly longer than did Hp +/+ mice.

Thus, oxidation and antioxidation play some roles in malaria parasite growth / survival, and haptoglobin may have some involvement in the pathogenesis of CM.

IL-35

OXIDATIVE MODIFICATION OF BAND 3 IN THE REDUCED SURVIVAL OF ERYTHOCYTES IN VISCERAL LEISHMANIASIS.

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Structural deformability of erythrocytes plays an important role in the premature hemolysis and development of anemia during visceral leishmaniasis.The disease is associated with marked degradation of integral membrane protein band 3 leading to ionic imbalance and membrane destabilization in red cells which eventually promotes their untimely removal from circulation in the infected condition .The structure of band 3 consists of a transmembrane domain mediating anion exchange across the plasma membrane and a cytoplasmic domain which is anchored to the cytoskeleton of the membrane by binding with ankyrin.Present study depicts the effect of structural modification of band 3 on phosphate transport during leishmaial infection using ^{31}P NMR .Downregulation of phosphate transport by the oxidation of this anion channel protein and subsequent reversal by reduction using dithiothreitol suggest the contribution of sulfhydryl groups in the cytoplasmic domain of band 3 resulting in the impaired functioning of this protein under the diseased condition..Band 3 protein provides the binding site for the oxidized denatured hemoglobins to the erythrocyte membrane..Binding between the two propagated into a macroscopic copolymer formation which increased gradually with the progress of infection. This phenomenon is likely to be responsible for the redistribution of band 3 in the plane of the membrane leading to membrane destabilization and altered permeability of erythrocytes which favours their reduced survival in leishmanial infection.

IL-36

GENE EXPRESSION PROFILING IN PRACTITIONERS OF SUDARSHAN KRIYA

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Introduction: Oxidative stress or free radicals may contribute to the pathophysiology of atherosclerosis and other chronic diseases associated with aging.

Methods: Because psychosocial stress has been shown to increase oxidative stress, we have looked at the effect of stress reduction with the help of Sudarshan Kriya, a breathing technique on long term practitioners (n=26) of Sudarshan Kriya in both males and females. The control group(n=25) comprised of age and sex matched subjects practicing unstylized rest. We have estimated Superoxide dismutase (SOD), Catalase and Glutathione in practitioners of Sudarshan Kriya and their age and sex matched controls. Alterations were seen in genes involved in DNA damage such as p53, antioxidant genes Catalase, Mn-SOD, Cu-Zn SOD, Glutathione peroxidase and Glutathione S-transferase (GST), Heat Shock Protein-70 (HSP-70), cell cycle regulators such as c-jun, c-fos and c-myc, aging related TERT, and apoptosis related genes such as Cox-2, Bcl-2, Bcl-X_L using RT-PCR and Western blotting.

Results: We found that there was a three fold higher level of Glutathione in practitioners as compared to their controls. The practitioners of SK showed higher antioxidant defence as seen by higher levels of Glutathione, SOD and Catalase activities. There was an increased level of Catalase, GST and Glutathione peroxidase mRNA in practitioners as observed by RT-PCR. A small increase seen in hTERT in SK practitioners indicates a delayed senescence and perhaps a longer life span. An increased expression of Heat shock protein (HSP70) was also seen which indicates a better cyto-protection in SK practitioners.

Conclusions: The findings of this study suggest that a better antioxidant/antistress status is seen in subjects doing regular practice of Sudarshan Kriya. This technique may therefore provide a mechanism for reducing incidence of coronary heart disease and improvements in other age-related and ROS associated disorders.

OL-15

COMPARATIVE STUDY ON LIPID PEROXIDATION AND ANTIOXIDANTS IN FALCI PARUM AND VIVAX MALARIA

Prasannachandra, V.D'Souza, **B.D'Souza**

Introduction: Malarial parasite activates the immune system of body causing release of reactive oxygen species. This study was undertaken to assess the role of lipid peroxidation and antioxidant Vitamins E and C in malaria patients.

Methods: The study group consisted of 28 untreated malaria patients between the age group 16 to 52 years of both sexes. Of the 28 patients, 19 had vivax malaria and 9 had falciparum malaria. The control group included 26 healthy individuals of both sexes between 20 to 55 years. Malondialdehyde (MDA), Vitamin E and Vitamin C were estimated by standard methods.

Results: The increase in MDA in malaria patients is highly significant ($p< 0.001$) when compared to control subjects. Increase in MDA is more in falciparum malaria compared to vivax malaria. The plasma vitamin E concentration decreased significantly ($p<0.001$) in malaria patients and the decline was more in falciparum malaria. The plasma Vitamin C concentration in malaria patients decreased significantly ($p<0.001$) compared to control subjects. Maximum decline was observed in vivax malaria. A weakly positive correlation was obtained between MDA and Vitamin E concentration in study group. A negative correlation was obtained between MDA and Vitamin C in the study group, whereas a strong negative correlation was obtained between MDA and Vitamin C in the control group.

Conclusion: Invasion of human erythrocytes by malaria parasite results in generation of lipid peroxides which causes the lysis of erythrocytes and alteration of major antioxidants. The decrease in antioxidant Vitamins E and C in the patient group might be due to their transfer to red cell membrane to counteract increased oxidative stress. The administration of Vitamins E and C after adequate treatment for parasite clearance may be fruitful to avoid malarial anaemia.

OL-16

COMPARATIVE STUDIES OF DIFFERENT ORGANS OF N.ARBOR TRISTIS IN MODULATION OF CYTOKINES IN RHEUMATOID ARTHRITIS

Brijesh Rathore, Bholanath Paul, Abbas Ali Mahdi*, Bhushan P Chaudhury**, Ashok Kumar Saxena, Anand Prakash Sahu*** and Yogendra Kumar Gupta

Immunobiology Laboratory, **Central Pathology Laboratory, ***Preventive Toxicology Laboratory, Industrial Toxicology Research Centre, MG Marg, Lucknow.

*Dept. of Biochemistry, King George Medical University, Lucknow.

Introduction: Rheumatoid arthritis is a disease characterized by joint pain followed by bone and joint destruction. Cytokines play a major role in arthritis. Overabundance of pro-inflammatory cytokines (TNF-â, IL-1 â and IL-6) and inadequate anti-inflammatory cytokines (IL-4 & IL-10) has been reported in rheumatoid arthritis. Earlier reports suggest a possible role of pro-inflammatory cytokines in arthritis and that they are a potential target for therapy. The effect of water soluble fraction of ethanol extract of leaf of Nyctanthes arbor tristis (NAT) on TNF-â level in arthritic and soluble protein A treated mice plasma has been studied and it was found depleted. Although leaves of NAT have been extensively studied for their anti-inflammatory property, however, little is known about the other parts of the plant. In the present study, we studied different parts of NAT for their anti-inflammatory properties.

Methods: Arthritis was induced in female mice (25-30g) by injecting Freund's complete adjuvant in the subplantar region of the right hind paw. A booster dose was injected at the same site on the 12th day. Water soluble ethanol extract of fruits, seeds and leaves was prepared under sterile conditions and administered at a dose of 24mg/kg body weight to each mouse till day-47. Footpad swelling was measured with the help of eclipse circumference formula 2ð x ?(a^2+ b^2)/2 using Vernier caliper. Joint homogenate was prepared in ice cold PBS containing 0.5% tween-20 and it was used for cytokine assay. TNF-á, IL-1â, IL-6 and IL-10 were evaluated using solid phase sandwich ELISA.

Results: Oral administration of NAT extract from day of induction of arthritis with Freund's complete adjuvant showed significant reduction in the pro-inflammatory cytokine levels, improved mobility and reduced joint inflammation. Daily oral administration of leaf and fruit extracts of NAT in arthritic mice reduced the proinflammatory cytokine TNF-á, IL-1â, IL-6 levels in inflamed joint on 2nd, 14th and 47th day in comparison to untreated mice, while extract of seed was found ineffective. Anti-inflammatory cytokine IL-10 was found elevated on both the time points i.e. 14th and 47th day.

Conclusion: The results of the present study demonstrate that NAT leaf and fruit extract preparation can be used to treat rheumatoid arthritis as also other inflammatory disorders, thus providing a newer and safer therapeutic measure.

OL-17

OXIDATIVE STRESS AND THE ROLE OF ANTIOXIDANTS IN THE TREATMENT OF PULMONARY TUBERCULOSIS

M.Shelgaonkar, 1 Dr. R. Munje, 2 Dr. S.Shelgaonkar3, Dr. S. Umathe4

1. Institute of Diploma in Pharmacy, Nagpur, 2. Govt.Medical College, Yavatmal, 3. Govt.Medical College, Nagpur, 4. Pharmaceutical Sciences, Nagpur

Introduction: Plit ML(1998) reported that even after six months of apparently successful antimicrobial chemotherapy, pulmonary tuberculosis is associated with increased oxidative stress. The present study was undertaken to evaluate whether reduction in oxidative stress by addition of a chain breaking antioxidant to first line antituberculosis agents will improve the clinical outcome

Methods: Randomized control clinical trial approved by institutional ethical committee was undertaken in newly diagnosed cases of pulmonary tuberculosis (PTB), of either sexes exhibiting sputum AFB. Control group A (n=50) was treated with routine 2EHRZ regime daily for initial phase of two months while study group B received Vit E and Vit C concurrently daily along with 2EHRZregime. Lipid peroxidation levels were used as markers of cellular damages.

Results: Statistical significant reduction in LPO, augmentation of Sputum AFB negativity, and Radiological improvement was noted in study group receiving antioxidants.

Conclusion: Better clinical improved in cases of pulmonary tuberculosis, receiving concurrent antioxidants, as evidenced by early sputum AFB.

SESSION IX

IL-37

ALKALINE WATER AS AN ANTIOXIDANT FOR HEALTHIER LIFE

Abhay Kumar

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Water is our most important nourishment and fundamental for good health. A human being consists of 65 - 70 % water. All body fluids contain water. Water adjusts the body's temperature and through urination and perspiration, is the main way to rid the body of toxins. Most of us do not drink enough water and are, therefore, dehydrated to some extent. For the body to function properly, it is imperative to be properly hydrated. Drinking the alkaline water on a daily basis will assist the body in flushing out toxic or acidic wastes. Alkaline Water acts as an antioxidant, scavenging for and neutralizing free radicals. Because Alkaline Water has the ability to give up electrons, it can effectively neutralize and block free radical damage to the body. Ionized Alkaline Water seeks out free radicals and converts them into oxygen, which your body can use for energy production and tissue oxygenation.

Antioxidants are nutrients found naturally in the body and in plants such as fruits and vegetables. Common antioxidants include vitamin A, vitamin C, vitamin E, and certain compounds called carotenoids (like lutein and beta-carotene). Ionized water has two antioxidant qualities, its negative charge and the presence of Hydroxyl ions. It can retard the onset of disease, as well as the aging process itself. All liquids have an Oxidation Reduction Potential (ORP). Normal water has an ORP of +300 to +400 mV. It does not have any potential for reducing oxidation because its ORP is positive.

Only a negative ORP can reduce or negate oxidation. Water produced by a quality Water Ionizer typically has an ORP of about -200 mv, meaning it can act as an antioxidant that can reduce oxidation, neutralize harmful free radicals, and retard the aging process. Our body systems work to keep our blood and the fluids surrounding our cells slightly alkaline. The process of metabolism - the digestion and burning of our foods to produce energy - results in waste products. These waste products are acidic. If conditions were ideal, we'd get rid of our acidic wastes as fast as they formed through breathing and through the kidneys, bowels and skin. Many health experts agree that an overly acidic system also burdens the immune system and leads to disease. HOW CAN WE FLUSH OUT THESE ACIDIC WASTES? Drinking alkaline water daily assists the body to flush out the build-up of toxic acidic wastes. It is rich in oxygen. Electrolysis separates water molecules into acidic water-positively charged hydrogen ions (H+) and alkaline water-negatively charged hydroxyl ions, which have both oxygen and a hydrogen atom (OH-). The alkaline water is, therefore, rich in oxygen. Alkaline Minerals such as Calcium, Magnesium, Potassium, Manganese, and Sodium have a positive charge and are called Alkaline-forming Minerals. Many health researchers also point to free radicals as the cause of disease and aging. Antioxidants are, therefore, recommended to scavenge free radicals. Our bodies as part of the chemical reactions in cell respiration produce

abundance of free radicals. A free radical is an unstable, or active, form of oxygen with an urgent need to find an electron. They usually rip these electrons from cell membranes. When too many free radicals are produced, they attack the membranes of healthy cells. Over time, the damage shows up as a disease or the signs of aging. More research studies and scientific evidence are required to establish the theory of alkaline water as an antioxidant..

IL-38

ANTI-OXIDANT DEFENCES IN AORTAE OF CIGARETTE SMOKE-EXPOSED RATS, AND THE EFFECT OF SUPPLEMENTATION WITH VITAMIN E

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Introduction: Cigarette smoke is is a known source of oxidants which are injurious to the artery.

Methods: The study was carried out on three groups (8 in each group) of rats- smokers (group I), non-smokers (group II), and smokers supplemented with vitamin E (group III). The antioxidant enzymes glutathione reductase(GR), glutathione peroxidase (GSH Px), glucose 6-phosphate dehydrogenase (G-6PD), superoxide dismutase (SOD) and catalase (CAT) were assayed in the rat aorta after exposure to cigarette smoke (cs). Group I and III animals were exposed to cs, in a specially designed polypropylene chamber, with two holes- one to introduce a burning commercial cigarette and the other to let in air of 0.4kg/cm^2. They were exposed to cs three times a day, six days a week, for 26 weeks. During this period group III also received vitamin E (50 mg tocopherol acetate/kg body wt/day) orally. Group II received only air.

Results have shown that the activities of GR and G-6PD were higher ($p<0.001$) in group II when compared with group I. The activities of GSH Px and SOD were lower ($p<0.001$) in group II when compared with group I. The CAT activity did not differ between these groups, although its activity was higher in groupIII when compared with I and II.

Conclusion: Cs exposure perturbs the antioxidant defences in the aorta of the rat. The weak antioxidant shield may be responsible for endothelial dysfunction. These perturbances were, to a significant extent, reversed by vit E (in group III). The study was funded by the Indian Council for Medical Research.

IL-39

THE POSSIBLE EFFECTS OF VITAMIN E AND EXERCISE ON RAT ERYTHROCYTES TO INTERMITTENT HYPOBARIC-HYPOXIA AND OXIDATIVE STRESS

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Introduction: Lipid peroxidation (LPO) and proteolysis activation are seen when erythrocytes are challenged with free-radicals. This study evaluated the effects of 1) swim training and, 2) vitamin E at sea level, followed by intermittent hypobaric-hypoxia on LPO and antioxidant (AO) defense in these cells.

Methods: One set of adult male rats were swim trained in normoxic condition and then exposed to altitudes of 5,700 m for 90 min/day for 9 days (AL_1). A second trained set was exposed to 6,300 m for 30 min/day and for 15 days (AL_2). Whole erythrocytes and membranes were studied for their fragility and hemoglobin (Hb) along with superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px) activities. Malondialdehyde (MDA), lipofuscin (LF) and protein carbonyl content were also determined.

Results: Hb increased in the trained and untrained when exposed to 5,700m with an increased fragility in the trained. Increases were seen in SOD and CAT at 6,300 and 5,700m respectively. Membrane MDA increased at 6,300m while protein carbonyl increased at both the altitudes. Vitamin E supplemented showed insignificant effect at both the altitudes. Increased hemolysis was seen in the supplemented when exposed to AL_2. Concomitant increases were seen in SOD and CAT activities in the supplemented, with the latter elevating in the supplemented sedentary too. Significant increase in MDA was seen in the supplemented and altitude-exposed animals.

Conclusion: Animals subjected to intermittent hyobaric-hypoxia were benefited by a pre-supplementation schedule of vitamin E with a noticeable up-regulation the AO enzymes and insignificant changes in their LPO. However, the increase in Hb could be due to exercise *per se* and not as a response to vitamin E.

IL-40

ANTIOXIDANT EFFICIENCY OF ASTAXANTHIN IN PHOSPHATIDYLCHOLINE LIPOSOMES AS A pH-DEPENDENT EVENT

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Introduction: The ketocarotenoid astaxanthin (AST) is a red pigment common to several aquatic organisms including microalgae, salmonids and lobsters. The scavenging efficiency of AST against reactive oxygen/nitrogen species (ROS/RNS) is believed to have a key role in the amelioration/prevention of several human pathological processes such as skin UV-mediated photooxidation, inflammation, prostate and mammary carcinogenesis, ulcer's *Helicobacter pylorii* infection, and age-related diseases. However, based on several contradictory trials, mostly all carotenoids perform fluctuating antioxidant activities due to unchecked specific conditions at the microenvironment of free radical reactions.

Objectives and Methods: The aim of this work is to evaluate the pH-effect in the levels of lipoperoxidation products (thiobarbituric-acid reactive substances and HPLC-malondialdehyde determinations) triggered by different ROS/RNS in AST-loaded egg-yolk phosphatidylcholine unilamellar liposomes.

Results: The preliminary data suggest that under harsh oxidative/nitrosative conditions (imposed by concomitant 0.15 mM peroxynitrite and 0.15 mM cytochrome c treatments), AST performed efficient antioxidant activity in all tested pH values, but remarkably proximal to physiological conditions (pH 7.4). In contrast, under more moderate oxidative conditions (0.15 mM KO_2), AST could not significantly inhibit lipoperoxidation, especially at pH 6.2 when a hypothetical pro-oxidant activity is even suggested.

Conclusions: Consensually, the mechanism of ROS/RNS scavenging process is perceived to be more dependent on the nature of the radical species than on the carotenoid structure. This fact might explain the pH-dependent antioxidant efficiency of AST in liposomes taking, at least, three major factors into account: (i) protonated superoxide radical (HO_2) diffusion throughout membranes; (ii) kinetics of HO_2 spontaneous dismutation; and (iii) pH-dependent peroxynitrite chemistry.

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IL-41

SUPPRESSION OF ARSENIC TOXICITY BY ANTIOXIDANT TEA POLYPHENOLS

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Arsenic is one of the most important global environmental contaminants. Millions of people all over the world are being exposed to inorganic arsenic through geologically contaminated drinking water. West Bengal in India and adjoining districts in Bangaladesh are facing severe arsenic contamination of ground water, the level being 200-600 g/l in some areas whereas the WHO recommended limit is 10 g/l. Arsenic-induced skin lesions have been noticed in some endemic regions due to long term exposure to high levels of arsenic in drinking water. Chronic exposure to inorganic arsenic, particularly in drinking water, causes a wide range of adverse health effects including cancer. At the cellular level, arsenic induces single strand breaks, DNA-protein crosslinks and apurinic sites in DNA. Genetic instability and DNA damage are the pre-requisites for induction of carcinogenesis. Prevention of DNA damage therefore is considered an important strategy to control arsenic calamity. Natural compounds particularly polyphenols are known to prevent DNA damage. Tea, the most popular beverage containing several polyphenols, has been extensively studied as a chemopreventive agent against cancer. The role of tea extract as well as its polyphenols in the modulation of arsenic-induced damage is an important area to look into. The present study conducted along this line clearly shows that the cytotoxic, genotoxic and clastogenic effects of arsenic in Chinese hamster male lung fibroblast cells (V-79) are greatly influenced by different tea compounds. Investigation on the mechanistic approach lying behind the antioxidant effects of tea suggests that arsenic is believed to cause deleterious effects by increasing the levels of reactive oxidants and decreasing the level of antioxidant capacity. Experiments have been designed to investigate whether tea can modulate the level of phase II detoxification enzymes catalase, superoxide dismutase and glutathione peroxidase. Induction of these antioxidant enzymes may be the causative factor for the reversal of arsenic-induced damage in mammalian cells as observed in the present study. Tea, the most preferred global beverage, thus can be considered an important source of antioxidant polyphenols to confront the disastrous effect of arsenic.

IL-42

ASCORBIC ACID THERAPY IN LEAD EXPOSED JEWELLERY WORKERS OF KOLKATA

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Introduction: The exposure among the lead smelting factory workers is still an acute problem; free radicals damage tissue both at cellular and sub cellular levels by causing lipid peroxidation in the cell membrane and inactivation of membrane bound enzymes. Ascorbic acid plays an important role in microsomal hydroxylative enzyme mediated detoxication. The present investigation analyzed the interaction between free radicals and lead and the effect of ascorbic acid in blood of normal person and jewellery workers.

Methods: A total of 54 male jewellery workers who had been exposed to the fumes and dust of lead for the previous 10 to 25 years and 22 controls matched for age and economic status were compared with respect to lipid peroxidation, antioxidant levels and copper, zinc status in relation to lead toxicity.

Results: Blood hemoglobin, serum copper, zinc and vitamin E, and red cell superoxide dismutase were found to diminished, with no changes observed in red cell glutathione peroxidase and gluthione reductase activity in the jewellery workers. The concentrations of lipid peroxidation products were high. Ascorbic acid supplement, an antioxidant, could partially restore the serum copper and zinc levels and red cell superoxide dismutase, leading to a significant decrease in the mean blood lead concentration of jewellery workers.

Conclusions: Dietary supplementation with ascorbic acid can complement other efforts to prevent lead exposure and reduce lead toxicity.

SESSION X

PL-7

MITOCHONDRIA-TARGETED ANTIOXIDANTS AND SOD MIMETICS-A NEW CLASS OF THERAPEUTIC ANTIOXIDANTS.

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The mitochondria-targeted drugs mitoquinone(Mito-Q), mitovitamin-E (MitoVit-E), and mitoproxyl nitroxide (Mito-Proxyl)are a new class of antioxidants containing the triphenylphosphoniumcation moiety that facilitates drug accumulation in mitochondria. In this talk, I will discuss the potential beneficial effects of these targeted antioxidants and SOD mimetics in mitigating oxidant-induced mitochondrial damage and apoptosis in endothelial cells. The mitochondria-targeted antioxidants are more effective inhibitors of mitochondrial oxidative damage than the corresponding "untargeted" counterparts. The use of targeted antioxidants potentially enables one to "pinpoint" exactly whether mitochondria is the site of ROS generation.

IL-43

TOTAL PHENOLICS, PHENOLIC ACID CONSTITUENTS, ANITIOXIDANT ACTIVITIES AND ANTIMUTAGENIC ACTIVITIES OF SELECTED PLANT EXTRACTS INCLUDING BITTER MELON (BITTER GOURD).

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Bitter melon is traditionally known for its medicinal properties such as antidiabetic, anticancer, and cholesterol lowering effects. It contains many phenolic compounds that may have the potential as antioxidant and antimutagen. Although the value of bitter melon is realized, scientific information on phenolic composition of bitter melon and antioxidant and antimutagenic activities of its extracts from food grade solvents are limited. Phenolics were extracted using methanol/ethanol/water system, and total phenolics and phenolic acid composition were determined using Folin-Ciocalteu's reagent and HPLC, respectively. Antioxidant and antimutagenic activities were determined by methyl linoleate model system and Ames test, respectively. Total phenolics of flesh and seed extracts ranged from 11.41-20.78 and 12.55-22.44 mg as CAE / g extract, respectively. Catechin, chlorogenic acid, epicatechin, and *t*-cinnamic acid were the main phenolics in flesh extracts, while gallic acid, gentisic acid, catechin, and chlorogenic acid were predominant in seed extracts. Antioxidant activities of the extracts from flesh and seed ranged from 71.31-82.29% inhibition and 71.22-81.48% inhibition, respectively. Antimutagenicity against benzo(a)pyrene (mutagen) with Salmonella TA98 and TA100 ranged from 91.6-100% and 78.7-86.2%, respectively.

The total phenolics and antioxidant activities of fenugreek, green tea, black tea, grape seed, ginger, rosemary, gotu kola, and ginkgo extracts, vitamin E, and tert-butylhydroquinone, were also determined. The total phenolics of these plant extracts ranged from 24.8 to 92.5 mg of CAE/g dry material. The antioxidant activities of methanolic extracts determined by conjugated diene measurement of methyl linoleate were 3.4 86.3%. The antioxidant activity of the extracts using chicken fat by

an oxidative stability instrument (4.6-10.2 h of induction time) followed a similar trend in antioxidant activity as determined by the Folin-Ciocalteu method. Seven phenolics in grape seed and green tea extracts were identified that ranged from 15.38 to 1158.49 and 18.3 to 1087.02 mg/100 g of extract, respectively.

Bitter melon, tea and grape seed extracts can be potential sources of antioxidant and antimutagen. We have also demonstrated that green tea and grape seed extracts containing polyphenols minimized lipid oxidation caused by irradiation in meat system. The phenolics present in bitter melon, green tea, and grape seed extracts can be potential sources of antioxidants in minimizing/preventing tumors and can have health benefits. These extracts can find application in food products, and dietary supplements.

IL-44

POTENTIAL HEALTH BENEFITS OF PALM TOCOTRIENOLS

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Studies of the role of nutrition in cancer prevention and treatment have paid a great deal of attention to certain vitamins and vitamin analogues. One such vitamin is the fat soluble vitamin E. It comprises the two major homologous series of compounds known as tocopherols and tocotrienols. Although the chemical structure of these compounds is very similar, direct comparisons show that tocotrienols display significantly more potent anticancer and cardiovascular protective effects than tocopherols. The etiology of cardiovascular disease is a multi-step process that involves many contributing factors. Tocotrienols have been shown to effectively inhibit many of these events associated with the development of atherosclerosis, including inhibiting hydroxymethylglutaryl coenzyme A reductase activity, the rate limiting enzyme in cholesterol synthesis, as well as inhibiting the oxidation of LDL, monocyte-endothelial cell adhesion, platelet aggregation and vascular smooth muscle proliferation. Tocotrienols have also been shown to significantly inhibit mitogen-induced proliferation and initiates apoptosis in preneoplastic and neoplastic mammary epithelial cells at treatment doses that have no effect on normal epithelial cell growth or viability. Although additional studiers are required to clarify the exact intracellular mechanisms mediating the chemoprotective effects of tocotrienols, experimental evidence strongly suggests that dietary supplementation of tocotrienols may provide significant health benefits in lowering the risk of cardiovascular disease and breast cancer;.

IL-45

SERUM CONCENTRATION OF CAROTENOIDS IN HEALTHY ADULTS ON VARIOUS CAROTENOID CONTROLLED DIETS

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Introduction: It is thought that the absorption and serum levels of fat-soluble antioxidants and carotenoids like lycopene, â-carotene, â-carotene, â-cryptoxanthin and lutein may depend on the amount and type of fat present in the diet as well carotenoid content. However little data is available to support this suggestion. We investigated the effects of a high and a low fat diet on serum carotenoid concentrations, especially lycopene.

Methods: Two separate randomized crossover dietary intervention studies were undertaken. The participants included healthy volunteers aged 22 to 70 years (n = 18 study one, n = 21 study two). The dietary periods comprised a high monounsaturated fat diet (MUFA) and a high carbohydrate low fat (HCLF) diet for 16 and 10 days, on study 1 and study 2, respectively. The diets were controlled for other macronutrients, and were high in lycopene but low in other carotenoids. Dietary lycopene was lower in study 1 (~15mg/day) than study 2 (20mg/day). Fasting blood samples obtained at commencement and end of each dietary period were analysed for serum carotenoids using HPLC.

Results: For each study, serum carotenoids changed similarly on the two (MUFA and HCLF) diets. Serum â-cryptoxanthine and á -carotene concentrations fell ($p<0.05$). In study 1, serum lycopene increased on the MUFA diet ($p < 0.05$); however there was no difference at the end of the two dietary periods. In study 2, serum lycopene increased ($p < 0.01$) on both the diets to similar and higher levels.

Conclusion: These results suggest that, at least for short terms (10-16 days), serum carotenoid concentration is dependent on dietary carotenoid intake, and is not influenced by a change of dietary fat from 15% - 38% of energy.

IL-46

ANTIOXIDANT ENZYME ACTIVITIES IN TRACE ELEMENT EXPOSED MONONUCLEAR AND OVARIAN CANCER CELLS

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Introduction: The trace elements, copper, zinc and selenium are essential micronutrients which play an important role as immune-modulators and essential co-factors of the antioxidant enzymes. Lately, trace elements have gained recognition as adjuvant therapy in the treatment of cancer especially to boost the immune system. In the present study, the effects of zinc, copper and selenium on human peripheral mononuclear cell (PBMC) and ovarian cancer (CaOV-3) cell proliferation as well as antioxidant enzyme activities were determined.

Method: The PBMC and CaOV-3 cells were cultured in the presence of trace elements for 48 hours in an appropriate condition. The cell number was estimated, washed, ruptured (sonicated) and centrifuged at 13,000xg. The supernatant was used to determine the antioxidant enzyme activities.

Results: Zinc and copper stimulated the PBMC proliferation in a dose-dependent manner within the dose range of 0-200µmol/L. SOD and GPx activities in PBMC exposed to zinc was inhibited whilst catalase activity was unaffected. All the three antioxidant enzymes in the cells exposed to copper were inhibited. Selenium exerted more potent inhibition of the cell proliferation while causing stimulation of the PBMC antioxidant enzymes at the lowest dose (25µmol/L) than at the highest dose (200µ mol/L) tested. A significant negative correlation was observed between proliferation and antioxidant enzyme activities in trace element exposed PBMC. In contrast selenium which exerted a dose dependent inhibition of CaOV-3 cells, showed a positive correlation with the antioxidant enzymes (SOD and Catalase).

Conclusion: This study provides evidence that the immune and cancer cell proliferation and modulation involves the enzymatic antioxidant system but the responses to trace elements are different.

OL-18

SPIRULINA PLATENSIS AS A NOVEL SOURCE OF ANTIAGING ENZYME SUPEROXIDE DISMUTASE.

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Introduction: *Spirulina platensis* is used as a food supplement and is becoming popular for its medicinal properties. It is a photosynthetic cyanobacterium and shows the presence of pigments like chlorophyll, phycocyanin, and carotenoids. It is subjected to oxidative stress and is endowed with enzymatic and non-enzymatic antioxidant systems.

Methods: To study its antioxidant properties, the cells were sonicated and chlorophyll and phycocyanin containing fractions were separated by ammonium sulphate fractionation. Three fractions, green, blue and colourless, were used for the determination of the antioxidant ability by DPPH and ABTS assay. Compared to the pigment containing fractions, the colourless fraction showed higher free radical scavenging ability. Antioxidant enzymes studied include superoxide dismutase, catalase, ascorbate peroxidase, glutathione reductase which peaked around 12-15th days of growth. Superoxide dismutase showed the highest specific activity and was purified using conventional methods like ammonium sulphate fractionation and anion exchange chromatography using DEAE-52.

Results: The final purified enzyme was electrophoretically homogenous. This enzyme was identified as iron containing superoxide dismutase based on inhibition by H_2O_2. The active site amino acids have been identified by the use of group specific chemical modifiers. The amino acid composition as well as active site amino acids showed similarity to other iron and manganese containing superoxide dismutases.

Conclusion: *Spirulina platensis* grows on simple inorganic nutrient medium. The purification of this enzyme is easy and simple The enzyme is stable over a broad range of pH and temperature. *Spirulina platensis* can be exploited for the large-scale production of superoxide dismutase. The pigment containing fractions can also be used as antioxidant agents. Superoxide dismutase is used as an antiaging agent and is incorporated in various skin lotions as well as in liposomes for the treatment of various oxidative stress related diseases.

OL-19

EFFECT OF EXCESSIVE INTAKE OF FRESH AND THERMALLY OXIDIZED EDIBLE OILS ON REDOX STATUS IN THE PLASMA AND TISSUES OF RATS.

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Introduction: Sesame, groundnut and coconut oils are widely used, either fresh or fried, in various food preparations in South India. Effect of these edible oils, fresh or thermally oxidized, as high fat diet, on lipid peroxidation and antioxidants status were studied.

Methods: Male Wistar rats were divided into seven groups, including control-group, of six animals each. The experimental animals received totally 20% (as high fat diet) of either fresh or thermally oxidized sesame or groundnut or coconut oils mixed with the diet. After 2 months, the animals were sacrificed and plasma and tissues (liver, heart & brain) collected for various estimations.

Results: Lipid peroxidation markers such as thiobarbituric acid reactive substances, lipid hydroperoxide and conjugated dienes increased in the plasma and tissues of all the experimental animals and more so in the plasma and tissues of corresponding thermally oxidized oil-fed group. Lipid peroxidation was less pronounced in sesame oil-fed groups when compared with the corresponding other oils-fed groups. Nonenzymatic antioxidants such as vitamin C and reduced glutathione decreased and vitamin E increased in all the experimental animals, and more decrease in vitamin C and GSH and less decrease in vitamin E were observed in thermally oxidized oils-fed animals. Superoxide dismutase, catalase and glutathione peroxidase decreased in the tissues of all the experimental animals and more decrease in the thermally oxidized oils-fed animals. The decrease of enzymic and nonenzymic antioxidants is less in sesame oil-fed groups when compared with the other oils-fed groups.

Conclusions: Our results show that lipid peroxidation is high in oils having more saturated fatty acid than unsaturated fatty acid.

SESSION XI

PL-8

NEW HORIZONS IN VITAMIN E NEUROPROTECTION

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Our knowledge of the neuroprotective properties of vitamin E is almost wholly derived from the study of ?-tocopherol. In nature, the vitamin E family consists of tocopherols and tocotrienols (T3). The current work is based on our striking evidence that in neuronal cells nM concentrations of ?-T3, but not ?-tocopherol, blocked glutamate-induced death by suppressing early activation of c-Src kinase (*J Biol Chem* 275:13049,2000). A later independent study reporting that Src blockade provides cerebral protection following stroke (*Nature Med* 7:222,2001) enhanced the significance of our finding that ?-T3 possesses c-Src regulatory effects. While previous reports have suggested that dietary ? -T3 is not available to the brain, we have recently observed that gavaging of pregnant rats with Tocomin??50% (Carotech Sdn Bhd, Perak, Malaysia) clearly increased the levels of ? -T3 in the brains of both adult mother as well as fetal rats (*FEBS Lett.* 530:17,2002). Interestingly, the enrichment was more in fetal brain tissue. Long-term time-lapse imaging studies revealed neurons and their axo-dendritic network is fairly motile under standard culture conditions. Such motility is arrested in response to glutamate challenge. T3-treated primary neurons maintained healthy growth and motility even in the presence of excess glutamate (see video in JBC online; 278:43508). Studies on HT4 as well as immature primary cortical neurons indicate a central role of 12-lipoxygenase (LOX) in executing glutamate-induced neurodegeneration (*JBC* 278:43508, 2003). Neurons isolated from 12-LOX-deficient mice were resistant to glutamate-induced death. Importantly, glutamate-induced 12-LOX activation is subject to T3 control. *In silico* docking studies identified that ?-T3 may hinder the access of arachidonic acid to the catalytic site of 12-LOX by binding to the opening of a solvent cavity close to the active site. Following glutamate challenge 12-LOX is Tyr-phosphorylated and migrates from the cytosol to the membrane. The phosphorylation seems to be c-Src dependent and T3-sensitive. The single neuron microinjection approach has revealed that sub-attomolar amounts of T3, but not tocopherol, protect cultured neurons from glutamate when injected to the cytosol or overlayed on the cell membrane. Nuclear injections failed to protect. These findings are consistent with the key targets of T3, c-Src and LOX, in the cytosol. *In vivo* stroke studies lend substantial credence to our in vitro findings supporting that tocotrienol is a potent neuroprotective form of natural vitamin E.

IL-47

SEMINAL PLASMA ANTIOXIDANT STATUS IN CIGARETTE SMOKERS

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Introduction: The possible effect of men's smoking on fertility and pregnancy has been extensively studied. It is well established that cigarette smoke contain substances which are not only carcinogens and mutagens but they also affect pulmonary vasculature and also generates oxygen centered free radicals. In view of above considerations, present study was planned to assess the seminal plasma for vitamin c, uric acid and lipid peroxide levels and activities of enzymes superoxide dismutase and catalase in smokers and non-smokers.

Materials and Methods: Study was set up with two groups viz. Study group and Control group. Study group comprised of 49 smoker male partners of couples attending the infertility clinic of department of Obstetrics and Gynaecology, Queen Mary's Hospital, King George's Medical University, Lucknow, and a control group comprised of 50 non-smoking males who had previously initiated at least one pregnancy and exhibited normal semen profile. The study group was further divided into 2 sub groups; (1) people who smoke 1-19 cigarette per day (n=22), (2) people who smoke more than 20 cigarette per day (n=27). Seminal plasma was used for the estimation of lipid peroxide, Superoxide Dismutase, Catalase, urate and Ascorbic acid levels.

Results: The results of the present study showed that the sperm count was significantly low in smoker sub group 1 and 2 as compared to non-smoker group. Sperm motility was also observed reduce in smoker groups. Abnormal sperm morphology and more dead sperms were found in smoker sub group 1 and 2. Seminal plasma Lipid peroxide levels in non-smoker males were found to be 1.56 0.12 nmol MDA/ml (Mean S.D.), while in smoker group, they were found significantly elevated. Superoxide dismutase and catalase activities in cigarette smokers were found significantly low as compared to non-smokers. Similarly, seminal plasma ascorbic acid and urate levels were also observed reduced in smokers as compared to non-smoker group.

Conclusion: The results of the present study reveal that smoking even in low quantity affects sperm count and motility as well as disturbs the balance of oxidants and anti-oxidant defence system.

IL-48

SOY PHYTOESTROGENS COUNTERACT AGE-RELATED CYTOKINE GENE EXPRESSION

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After menopause or andropause, loss of the normally inhibiting sex steroids (estrogen, testosterone) results in elevated IL6 levels, which are further progressively increasing with age. This aberrant gene expression accounts for several disease-associated pathologies and phenotypical changes of advanced age, such as osteoporosis, rheumatoid arthritis, multiple myeloma, neurodegenerative diseases, frailty. Excessive IL6 expression also promotes tumorigenesis (breast, prostate, lung, colon, ovarian) and serum IL6 levels are currently regarded as a diagnostic marker for tumor progression and prognosis in various cancers. In order to prevent these types of complaints and to maintain the important physiological balance, estrogens and SERMs (such as raloxifene, tamoxifen) have long been recommended in hormone replacement therapy (HRT). Unfortunately, both pharmacological compound groups have been associated with severe negative side effects. In this view, plant-derived estrogens (phytoestrogens), particularly those found in soy products (such as genistein), are considered as putative beneficial alternatives in HRT. We have analysed in more detail how soy isoflavones (genistein, daidzein, biochanin) inhibit expression of the 'geriatric' cytokine IL6. TNF-induced IL6 production in fibroblasts mainly depends on nuclear translocation of the transcription factor NF-B, as well as on the activation of p38 and p42/p44 MAPKs, and consequent cofactor recruitment to the IL6 promoter. Recently, our research unit identified the dual MAPK (p38, ERK)-responsive MSK1, as an important player for nuclear NF-B phosphorylation (transactivation), besides chromatin components (i.e. H3), for optimal IL6 gene transcription. With respect to molecular targets of soy isoflavones, our results demonstrate that soy phytoestrogens, but not synthetic17b-estradiol, can counteract MSK-dependent NF-kB transactivation on selective target genes in fibroblasts and aggressive tumor cells, most probably via its tyrosine kinase inhibitor and antioxidant properties. As soy isoflavones integrate both hormonal ligand activities and interference with signaling cascades, therapeutic use may not be restricted to hormonal ailments only, but may have applications in cancer chemoprevention and/or NF-B-related inflammatory disorders as well.

IL-49

ROLE OF CAP. TORCHNIL, A HERBAL IMMUNOMODULATOR AND ANTIOXIDANT IN RECURRENT PREGNANCY LOSS

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INTRODUCTION: Recurrent pregnancy loss (RPL) is defined as three or more consecutive spontaneous losses of pregnancy. RPL is a diagnostic challenge and frustrating therapeutic experience despite the tremendous scientific and technological advances in modern medicine. Nearly 43% of pregnancy losses are categorized as unexplained etiology. The immune responses and oxidative stress play a great role in the successful outcome of the pregnancy. Ayurvedic texts such as Charak and Sushrut Samhita has advised certain herbs which are immunomodulatory and antioxidant in nature. Cap Torchnil is a combination of 11 such herbs

MATERIALS AND METHODS: 69 patients of BOH were studied in relation to TORCH infection as etiological factor as well as in non-TORCH infections. The study group in either category was given Cap. Torchnil and in controls, the standard model line of treatment included low dose aspirin, prednisolone and heparin.

RESULTS: The results showed significant improvement in outcome, in the study group, in both the categories, TORCH as well as non-TORCH groups was observed.

CONCLUSION: Cap Torchnil plays an important role in RPL because of its immunomodulatory, antioxidant and antimicrobial actions, which are characteristics of all herbal rasayanas.

OL-20

PLASMA CERULOPLASMIN LEVELS IN PREGNANCY WITH PRE-ECLAMPSIA

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Introduction : Pre-eclampsia is a pregnancy specific disorder complicating 5 to 7% of pregnancies and characterized by elevated blood pressure, proteinuria, edema and activation of haemostatic system. The cause of pre-eclampsia is unknown although several factors have been shown to contribute. Pre-eclampsia is more common in women during their first pregnancy, who have diabetes, gestational hypertension. In the present study plasma ceruloplasmin levels have been evaluated in pregnancy with pre-eclampsia and compared with normal pregnancy.

Methods : 15 normal subjects, 15 pregnant women and 15 pre-eclamptic patients were selected for the study. The blood samples were analyzed for plasma ceruloplasmin by ortho - Dianisidine method.

Results : Plasma ceruloplasmin level in pregnant women was significantly higher ($P < 0.001$) than the normal subjects. A highly significant increase ($P < 0.05$) is also found in pregnancy with pre-eclampsia when compared to normal pregnancy.

Conclusion : Ceruloplasmin is an acute phase protein in normal pregnancy.It is said to have oxidase activity towards polyamine and polyphenol substrates and also acts as a copper donor for monoamine oxidase and diamine oxidase enzymes. Because of antioxidant property of ceruloplasmin, which prevents peroxidation and free radical formation, increased ceruloplasmin level is found in pregnancy with pre-eclampsia

OL-21

ALTERATIONS IN LIPID METABOLISM AND FREE RADICAL LEVELS IN PREGNANCY INDUCED HYPERTENSION (PIH)

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Introduction: In pregnancy Induced Hypertension (PIH) alterations in lipid metabolism has been reported. Normal metabolisms of lipids follow extra mitochondria system. But turn over of lipids exceed the normal value as in PIH, the metabolism takes up the altered pathway, ie., the microsomal system. This in turn evolves oxygen free radicals causing increased peroxidation of membrane lipids. Therefore we planned the present study to quantitate free radical level in the serum of PIH subjects and correlate it with altered lipid metabolism.

Methods: Ninety random samples were studied in three groups. 1. Normotensive non-pregnant women (n = 30). 2. Normotensive pregnant women (n = 30). 3. Women with PIH (n = 30). Fasting Blood samples were analysed for Melon Dialdehyde (MDA) according to the method of Nadiger et al. and High Density Lipoproteins (HDL) Triglyceride (TGL) and Cholesterol by standard methods.

Results: Our result showed that, MDA level was higher in pregnant women than non-pregnant women. However it further increased significantly in PIH subjects ($P < 0.001$). There was also significant increase in the level of cholesterol ($P < 0.001$) TGL ($P < 0.001$), and significant decrease in HDL level ($P < 0.01$) in PIH.

Conclusion: There is change in lipid metabolism in PIH, which has resulted in, increased in lipid peroxide levels. Melon Dialdehyde (MDA), an end product of lipid peroxidation is therefore increased in PIH resulting in an imbalance between oxidant and anti oxidant levels. This increased oxidant level could be due to derangement in lipid metabolism, which starts off a vicious cycle of autoxidation. Therefore we suggest that, increased lipid peroxidation could be the contributing factor for PIH.

SESSION XII

IL-50

MODULATION OF HYDROGEN PEROXIDE INDUCED OXIDATIVE DAMAGE TO DNA BY TAXIFOLIN IN MOUSE

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Introduction: The exposure of human beings to toxic agents generates oxygen derived reactive oxygen species (ROS), which can be the possible initiators of various chronic diseases. When levels of free radicals exceed that of antioxidants during oxidative stress, sensitive bio-molecules such as lipids, proteins and DNA in particular can be damaged. Effect of Taxifolin, a flavonoid on Hydrogen Peroxide induced DNA damage was studied in mouse peripheral blood leukocytes one hour prior to administration of hydrogen peroxide (10mg/kg b.w.).

Methods: DNA strand breaks were estimated by alkaline comet assay in blood withdrawn, one hour after administration of hydrogen peroxide. Modulation of hydrogen peroxide induced antioxidant enzymes by taxifolin was studied in 10% liver homogenate and blood lysate. Taxifolin (100mg/kg b.w.) was administered one hour prior to intra-peritoneal administration of hydrogen peroxide and after one hour the activities of the anti oxidant enzymes, such as catalase, glutathione peroxidase and super oxide dismutase were estimated.

Results: On analyzing the results with respective controls a major amount of DNA damage induced by Hydrogen Peroxide was protected by Taxifolin, in terms of Comet Tail length, 75%, protection in terms of tail moment, 83% and in percent DNA in tail, 77% protection was observed respectively. Levels of all the three enzymes were observed to be elevated on administration of hydrogen peroxide in liver homogenate and blood lysate. Administration of Taxifolin decreased the levels of all the three enzymes to different extent both in liver and blood.

Conclusion: The mode of antioxidant action of this flavonoid appears to be by scavenging free radicals and reactive oxygen species.

IL-51

GENETIC EVIDENCE FOR THE INVOLVEMENT OF REACTIVE OXYGEN SPECIES IN BACTERICIDAL ACTION OF CIPROFLOXACIN

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Quinolones are a group of low molecular weight extremely potent antimicrobial agents and ciprofloxacin is an important and commonly used member of the quinolone family. Ciprofloxacin inhibits DNA topoisomerase II and DNA topoisomerase IV, thereby interrupting DNA breakage and resealing steps during the process of DNA supercoiling. In addition increase of reactive oxygen species in the bacterial cells in response to ciprofloxacin has been shown. Whether ROS have a role in the bactericidal action of ciprofloxacin was investigated by studying the effect of some antioxidant compounds on the sensitivity of *E.coli* strain MG1655 to ciprofloxacin. Ascorbic acid or glutathione provided substantial protection against ciprofloxacin. Role of O_2^- and H_2O_2 in the action of ciprofloxacin analyzed using superoxide dismutase and catalase knockout strains of *E.coli*. The results indicate that bactericidal action of ciprofloxacin is partly mediated through superoxide anion. This observation is of significance as quinolones are the only oral anti pseudomonal antibiotics currently available and the effectiveness of these antibiotics may be widely affected the dietary intake and cellular levels of antioxidants.

IL-52

CHINESE CABBAGE EXTRACTS AND SULFORAPHANE CAN PROTECT H_2O_2 INDUCED INHIBITION OF GAP JUNCTIONAL INERCELLULAR COMMUNIATION THROUGH THE INACTIVATION OF ERK1/2 AND p38 MAP KINASES

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Consumption of cruciferous vegetables has been proposed to protect against various cancers. The cruciferous vegetable such as Chinese cabbage and broccoli contain Sulforathane (SFN) that is an anticancer photochemical. Gap junction channels are structures in the plasma membranes of most of cell type and a direct cell to cell pathway for the movement of molecular information through exchange of small molecules and ions. This is known as gap junctional intracellular communication (GJIC) and functions l homeostasis, cell growth and differentiation, and many of he physiological processes. Inhibition of GJIG by either chemical-tumor promoter or oncogenes is suspected to be involved in the mechanism of tumor promotion and progression. In the present study, we examined the anti-crcinogenic properties of some Chinese cabbage esxtract and SFN on the inhibition of gap junctional intercellular communications (GJIC) induced by hydrogen peroxide i WB-F344 rat liver epithelial cell. Our results showed that Chinese cabbage extracts and SFN were able to prevent the inhibition of GJIC through the blocking of connectin 43 phosphorylation and inactivation of ERK ½ and p38 MAP Kinase. Therefore, our results suggest that cruciferous vegetable and its component, SFN, may exert the anticancer effect by targeting the GLIC as functional dietary chemopreventive agent. This study was supported by a grant from BioGreen 21 program, Rural development Administration, Republic of Korea.

IL-53

RADIATION INDUCED REACTIVE OXYGEN SPECIES MEDIATED CELL DEATH AND ITS IMPLICATION IN TUMOR RADIOTHERAPY

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Introduction: Investigations on radiation/drug-induced free radicals in the mechanism of apoptotic mode of cell death have been gaining increasing importance in cancer biology and radiotherapy Evidences are accumulating to suggest that a correlation existed between radiation induced reactive oxygen species (ROS) and apoptotic cell death of cancer cell. It is generally accepted that free radicals play a role in cancer induction and treatment. This talk gives a review of the current developments concerning the role of radiation generated intracellular ROS in the mechanism of cancer induction in normal cell and radiation and/or drug induced ROS mediated killing of tumor cells.

Methods: Fluorescence and Electron Spin Resonance techniques have been used to detect and quantify radiation generated ROS in the normal and tumor cells. Moreover, annexin V fluorescence and electrophoresis techniques have provided methods for measurement of apoptosis in cells. Microsciopic examinations were carried out to examine normal and apoptotic cells in vitro.

Results: Research in our laboratory has been focused to investigate molecular mechanism of radiation/drug induced cell death in a variety of tumor cell e.g. EAC, MCF-7, HL-60, HeLa. We have studied the mechanism of radiation induced oxidative damage in model system as well as in cultured cells. Results have shown the involvement of oxidative damage in lipid bilayer and in cellular membrane. Measurements of lipid peroxidation have shown that radiation triggered the induction of cell death through the production of ROS.

Conclusions: Modifications of radiation-induced cytotoxicity have also been shown by antioxidants suggesting significant role of ROS in radiation induced cell death. Present findings suggest a possible new approach, which involves the modulation of intracellularly generated ROS. These findings would provide a scientific basis to develop effective guideline for treatment of cancer in patients in clinical settings.

IL-54

ANTIOXIDANT ACTIVITY OF SELENOENZYMES AND SELENIUM COMPOUNDS

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Selenoenzymes such as glutathione peroxidase (GPx), thioredoxin reductase (TrxR) and selenoprotein P are known to act against reactive oxygen and nitrogen species. GPx, in particular, plays an important role in the reduction of various hydroperoxides by using cellular thiol reducing equivalents such as glutathione (GSH). The enzyme catalytic site includes a selenocysteine residue in which the selenium undergoes a redox cycle involving the selenol (ESeH) as the active form that reduces hydrogen peroxides and organic peroxides. The selenol is oxidized to selenenic acid (ESeOH), which reacts with reduced glutathione (GSH) to form selenenyl sulfide adduct (ESeSG). A second glutathione then regenerates the active form of the enzyme by attacking the ESeSG to form the oxidized glutathione (GSSG). Recently, some simple organoselenium compounds have been shown to mimic the GPx activity. Among them the most promising drug was Ebselen (PZ 51, 2-phenyl-1,2-benzoisoselenazol-3-(2*H*)-one, 1), a heterocyclic compound that functions as an antioxidant. (Figure 1). In addition to the GPx activity, ebselen also reduces peroxynitrite.

SESSION XIII

PL-9

AGEING AND FREE RADICALS: A REVIEW

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Introduction: One of the main causes of ageing has been considered to be accumulation of cellular damage due to free radicals and decreased antioxidant defense. Recent studies indicate caloric restriction, resulting in decreased generation of reactive oxygen species (ROS), may be able to increase longevity in certain organisms. This presentation reviews recent advances in the above areas.

Methodology: Literature survey has been carried out using indexing services such as 'PubMed' and some papers and reviews have been selected along with other general articles on ageing from popular/scientific literature.

Results and Conclusions: Several recent studies implicate the role of ROS in various aspects of ageing and altered gene regulation that accompany ageing. Among the cellular organelles, mitochondria seem to play a key role in the generation of ROS and its possible role in various cellular activities associated with ageing, gene expression and apoptosis. Altered gene regulation during ageing also has been ascribed to damage/ signaling induced by ROS. These areas will be discussed in detail.

PL-10

DIFFERENTIAL RESPONSES OF CELLS TO NATURAL COMPOUNDS *IN VITRO* AND *IN VIVO*

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Introduction: Most of the natural compounds examined for antioxidant activity are tested in pure chemical or cell free systems. However, their activities at cellular level *in vitro* as well as after administration to animal/ human consumption may be different depending on their uptake, metabolism, intracellular concentration etc. There are several cellular responses such as proliferation, phagocytosis, immune responses, nitric oxide generation etc which involve free radicals and such responses can be influenced by exogenous antioxidants. The present studies were aimed at assessing the effect of some natural compounds at cellular level under conditions of induced oxidative stress or during their specific physiological functions. Chlorophyllin (CHL), a water-soluble analogue of the green plant pigment chlorophyll and a purified immunomodulator (PPI / G1-4A) from a medicinal plant *Tinospora cordifolia* were used in these studies.

Material and methods: Spleen cells from both BALB/c and C3H mice were used. Different doses of CHL and PPI / G1-4A were administered to mice intraperitoneally or lymphocytes and macrophages were incubated *in vitro* with various concentrations of these agents. Gamma radiation and a peroxyl radical initiator (AAPH) were used to induce oxidative stress. Intracellular ROS, phagocytosis and cell proliferation were measured by flow cytometry. Antibody and cell mediated responses were generated using sheep red blood cells (SRBC) as an antigen.

Results: CHL entered spleen cells, scavenged radiation-derived intracellular free radicals in these cells *in vitro* and inhibited peroxyl radical induced lipid peroxidation. However, *ex vivo* studies showed that both basal and induced ROS levels varied depending on the concentration and time after administration to mice. CHL exhibited 50 % protection against whole body irradiation induced apoptosis and lipid peroxidation in mice. CHL enhanced phagocytic activity and B and T cell immune responses in mice. It also enhanced cell survival. In contrast, it inhibited mitogen induced T cell proliferation *in vitro*. The immunomodulator from *Tinospora cordifolia* scavenged radiation and AAPH-induced free radicals in cell free systems but its administration to mice had prooxidant effect resulting in increased basal and induced levels of ROS and a marginal increase in apoptosis.

Conclusions: While the benefits of natural antioxidants could be evinced in the context of specific end points, their pleiotropic effects on other targets and functions cannot be ignored.

IL-55

ROLE OF OXIDATIVE STRESS IN ALCOHOL SUPPRESSION OF IMMUNE RESPONSE

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Background: A plethora of atypical immune responses including suppression of lymphocyte mitogenesis and apoptosis of lymphocytes have been linked to chronic ethanol consumption. This study addressed the possibility that the effect ethanol has on ethanol induced apoptosis of lymphocytes may be due oxidative stress induced by altering phospholipid metabolism, and supporting phosphatidylethanol (PEth) synthesis.

Methods: Jurkat T lymphocytes were treated with ethanol, and concanavalin A.. Apoptosis of Jurkat T lymphocyte was determined by flow cytometry by analyzing hypodiploid cells and phosphatidylserine expression. Oxidative stress was assessed by measuring DCF florescence.

Results: Ethanol caused apoptosis of Jurkat T lymphocytes, and enhanced the entry of cells into S phase and decreased the number of cells in G_2/M phase. Ethanol enhanced concanavalin A induced apoptosis and cell cycle dysregulation. Ethanol caused increase in reactive oxygen intermediates and potentiated concanavalin A induced accumulation of reactive oxygen species. The effects of ethanol were mimicked by hydrogen peroxide and phosphatidylethanol.

Conclusions: The apoptosis of lymphocytes is dependent on oxidative stress dependent dysregulation of cell cycle. Phosphatidylethanol is a potential mediator of ethanol induced apoptosis of Jurkat T lymphocytes

IL-56

FREE RADICAL DAMAGE TO MITOCHONDRIA AND ITS POSSIBLE PREVENTION BY NATURAL COMPOUNDS: A REVIEW OF OUR STUDIES

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Introduction: Mitochondria are crucial subcellular organelles whose damage can lead to serious consequences for the cell including loss of many cellular functions. Adverse alteration to mitochondria also has been implicated in many diseased states such as neurodegenerative diseases, cardiomyopathy, multi-organ system failure in sepsis and in the process of ageing. Hence we have examined the susceptibility of mitochondria to free radicals and related reactive species generated by different physiologically relevant model systems and its possible prevention by some natural compounds.

Methods: Mitochondria were isolated from rat liver/brain and exposed to free radical generating systems such as -radiation, photosensitization, peroxyl radicals, ascorbate-Fe^{2+}, NADPH-ADP-Fe^{3+} and peroxynitrite. Damage to mitochondria was assessed by measuring products of lipid peroxidation in terms of conjugated dienes, lipid hydroperoxides and thiobarbituric acid reactive substances (TBARS); protein oxidation in terms of protein carbonyls and protein hydroperoxides; loss of protein sulphydryls, and mitochondrial enzymes besides depletion of antioxidants such as reduced glutathione (GSH). The natural compounds examined for their ability to protect against such damage, included baicalein, caffeine, chlorophyllin, plumbagin, tocotrienols and vanillin.

Results: Mitochondria from both rat liver and brain are susceptible for free radical induced damage, the latter being more sensitive. Lipid peroxidation seems to be the initial event followed by protein damage. Among the compounds examined, baicalein was the most effective protector followed by tocotrienol, chlorophyllin, vanillin, plumbagin and caffeine, in a concentration-dependent manner.

Conclusions: These natural compounds derived from medicinal plants and dietary substances can help to protect mitochondria against free radicals generated by different means. Their higher intake in the form of dietary constituents of supplements may help in reducing the incidence of diseased conditions/radiation damage/process of ageing in which free radicals have been implicated.

IL-57

BLOCKADE OF MITOCHONDRIAL PERMEABILITY TRANSITION BY DOPAMINE-D2-RECEPTOR AGONISTS AND POSSIBLE ROLE IN NEUROPROTECTION

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Introduction: The mitochondrion has been shown as the link between different signaling pathways involved in neurodegenerative diseases. The formation of the mitochondrial permeability transition pore (PTP) involves phenomena such as the dissipation of the mitochondrial electrochemical potential and the release of substances like apoptosis inducing factor (AIF) and cytochrome c from the membrane cleft. We investigated the role of dopamine-D2-receptor agonists in blocking the PTP and thus elucidating neuroprotection by these substances.

Methods: Mitochondria were prepared by homogenizing freshly dissected rat livers by several steps of centrifugation. Single channel currents were recorded from mitoplasts by the patch-clamp technique. Analysis was done using the PClamp software (Axon-Instruments). Permeability transition was monitored by measuring mitochondrial swelling as change in light scattering measured by a photometer and membrane potential changes were determined by the safranine fluorescence measurement.

Results: Analysis of patch clamp experiments showed that the dopamine-agonists pramipexole and ropinirole block the PTP dose-dependently with an IC50 of 500nm and 3.2 µM respectively. Protection of Ca^{2+}-induced permeability transition (PT) by pramipexole as measured by swelling assay in both energized and non-energized mitochondria. A dose-dependent block of the PT by ropinirole could also be seen in energized mitochondria. Additionally, we showed in safranine fluorescence assays a protection of the membrane potential by ropinirole after a Ca^{2+} stimulation of the PTP.

Conclusion: The frequently described neuroprotective effect of dopamine-D2-receptor agonists like ropinirole and pramipexole in patients suffering from neurodegenerative diseases could be due to a delayed cell death by PTP mediated apoptosis. Designing pharmaceuticals capable of interfering with the functions of mitochondrial PTP could delay the decline of motor scores in Parkinson

IL-58

CUTANEOUS PHOTOAGEING: PREVENTION AND REPAIR USINGANTIOXIDANTAPPROACH

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In general aging is a progressive accumulation of changes with time, and is characteristically described as a time dependent functional decline leading to the cell's disability to withstand external and internal changes which accompany advancing age. It represents a biological attrition at cellular level resulting in cellular senescence and/ or cell death. Human skin like all other organs undergoes chronological aging. In addition, unlike all other organs skin is in direct contact with the environment and therefore undergoes aging as a consequence of environmental damage. Oxidative stress is regarded as one of the most important spontaneous phenomena responsible for aging. Reactive oxygen species which are formed as a result of oxidative stress are dramatically enhanced by exposure to the UV- radiation. UV- induced signal transduction pathways mediate damage to skin connective tissue, degrade skin collagen and reduce the ongoing procollagen synthesis in severely photodamaged and chronologically aged skin. Skin is equipped with a network of enzymatic and non-enzymatic inherent antioxidant systems. However, at times these protective molecules may be inadequate to counter the induced oxidative attack. In the present situation, extrinsically applied free radical scavengers and antioxidants can provide both an immediate and long term protection. Nutritional supplements in the form of antioxidants are long being proposed for their antiaging effects, but their cutaneous availability is a point of concern and debate. In this presentation, the usefulness of topical antioxidants, an as yet under explored group of agents as suitable moieties for combating photoaging, in addition to the diet, shall be highlighted along with suitable examples from literature and the authors own research work. The proposed pathways which can counteract oxidative injury and the oxidative stress markers which can be used for evaluating the extent of photodamage will also be discussed. Various oxidative stress markers whch can be used for assessing the extent of damage and the efficacy of topical antiaging formulations is also included.

OL-22

U74500A, A 21-AMINOSTEROID AMELIORATES HALOPERIDOL-INDUCED PERIORAL MOVEMENT, AND ASSOCIATED MEMORY DYSFUNCTION

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Introduction: Tardive dyskinesia is one of the major side effects of long-term neuroleptic treatment. The pathophysiology of this disabling and commonly irreversible movement disorder is still obscure. Oxidative stress and products of lipid peroxidation are implicated in the etiopathology of TD. Chronic treatment with neuroleptics is reported to increase free radical production and oxidative stress. The objective of the study was to study the effect of U74500A a lazaroid with potent antioxidant activity on haloperidol-induced orofacial dyskinesia and cognitive dysfunction.

Methods: Orofacial dyskinesia (perioral movements) in rats was induced by chronic treatment with haloperidol (1 mg/kg, i.p.) for a period of 21 days. Memory impairment was assessed by using elevated plus maze and passive avoidance paradigms. Behavioral measurement was carried out 24 h after the last dose of haloperidol or U74500A. Biochemical estimations were carried out immediately after behavioral measurements.

Results: Chronic haloperidol (1.0 mg/kg for 21 days) treatment significantly induced vacuous chewing movements and tongue protrusions in rats. Co-treatment with U74500A (10-50mg/kg) significantly attenuated the development of haloperidol-induced orofacial dyskinesia (VCMs and TPs). Haloperidol treated rats showed poor performance on elevated plus maze and passive avoidance paradigms indicating memory impairment and U74500A significantly reversed the haloperidol-induced memory impairment. Biochemical analysis revealed that chronic haloperidol treatment significantly induced lipid peroxidation, elevated the nitrite levels and decreased the glutathione levels. U74500A significantly reduced the haloperidol-induced lipid peroxidation and nitrite levels and restored the decreased glutathione levels in rats.

Conclusions: The major findings of the present study suggest that oxidative stress-induced neuronal death might play a significant role in neuroleptic-induced orofacial dyskinesia and cognitive dysfunction. In conclusion, U74500A could be a useful neuroprotective agent for the treatment of haloperidol-induced orofacial dyskinesia and memory dysfunction.

SESSION XIV

IL-59

TREATMENT OF LOCAL EXPOSITION TO RADIATION INJURY: THE FRENCH EXPERIENCE.

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The use of radioactive materials offer a wide range of benefits. Precautions are however, necessary in order to protect people from the detrimental effects of radiation and exposition to radiation injury may have severe consequences for the individuals affected. Nevertheless, in spite of precautions, accidents with radiation sources continue to occur. When the amount of radioactive material is substantial, as in the case of radiotherapy sources or industrial or military sources, extreme care is needed to prevent accidents which may have severe consequences. As a result of exposure to sources, most of the patients suffer from localized radiation injury requiring plastic surgery.

After presentation of some effects of radiation injury, the objective of the presentation is to focus on two radiological accidents for witch the French army burn center provided support and assistance, and to the treatment of lesions and skin injuries. We will look at the development of extended radiation induced skin injuries and the management of medical and chirurgical treatment from initial to skin grafting with two examples . The first is related to an accident occurring at Lilo (Georgia) in an old camp of the Russian army. Several frontier guards from Georgia were exposed during several months to missing sources of ^{137}Cs of medium activity, devoted to formation. The victims were irradiated for approximately one year and four of them were then treated in France. Each of them suffered from one or more acute localized irradiation lesions of various seriousness. The second concern a Peruvian worker who found a metal disk and conserved it in her pocket for several hours. This was an iridium source with activity of 36,75Ci. After hospitalization in Peru, the patient was transferred to the French army burn center for treatment.

IL-60

A PHASE I TRIAL OF TOCOFEROL MONOGLUCOSIDE (TMG) IN PATIENTS UNDERGOING HEMI-BODY RADIATION

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Purpose: To evaluate Tocoferol monoglucoside (TMG), a water soluble vit. E. in a phase I trial, as a radiation protector in those undergoing hemi-body radiation for disseminated disease.

Methods & Materials: Patients scheduled to receive modified hemi-body radiation were accrued for the study. Patients not only had disseminated skeletal disease but, were heavily pretreated Seven patients were accrued for the study. Patients received 1 and 2gms of TMG 30-40 minutes before hemibody radiation. A dose of 600cGy was delivered on telecobalt equipment at mid plane. Immediate Toxicities were evaluated as well as response to pain.

Results: All the seven patients underwent radiation uneventfully. There was no drug related toxicity. Pain relief was adequate.

Conclusion: Tocoferol monoglucoside an effective antioxidant with no significant acute toxicity, when administered in a dose of 1 or 2g per oral route. TMG being water-soluble can have global antioxidant & radio protective effects. This needs further clinical evaluation.

IL-61

POSSIBLE USE OF ANTIOXIDANTS AS RADIOPROTECTORS

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Introduction: Ionizing radiations produce free radicals and reactive oxygen species which cause damage to biomolecules. Antioxidants are known to protect cells from the damage caused by the free radicals. Radioprotective compounds are also of importance in clinical radiotherapy for better tumour control with higher doses. The paper will present an overview of some of the recent work on protection of biological systems against ionizing radiation induced damages by the antioxidant compounds- troxerutin and tocopherol minoglucoside (TMG).

Methods: In *in vitro* studies conversion of the ccc form of the plasmid DNA to oc and linear forms and peroxidation lipids in microsomal and mitochondrial membranes on exposure to gamma-radiation were monitored. For *in vivo* studies single cell gel electrophoresis (comet assay) was carried out to examine radioprotection of cellular DNA in tumour and various tissues such as blood luecocytes, liver, bone marrow and spleen, in murine system.

Results: Presence of troxerutin and TMG during irradiation protected the plasmid DNA from radiation induced strand breaks as evidenced from the decrease in the conversion of super coiled DNA to the oc and linear forms. These compounds protected membrane-lipids from radiation induced peroxidative damage. Protection, due to administration of troxerutin and TMG, of cellular DNA against radiation induced strand breaks, was discernible in the cells of normal tissues such as liver, blood leukocyes, bone marrow and spleen, but not in the cells of fibrosarcoma tumour, as evidenced from decrease in comet parameters.

Conclusions: The administration of troxerutin and TMG immediately after exposure to gamma-radiation could preferentially protect normal tissues against radiation damages in tumour bearing animals. These radioprotective compounds are of importance for their potential use in clinical radiotherapy

IL-62

RADIOPHYTOREMEDIATION

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Radiophytoremediation is an emerging biogeotechnological application based on the "green liver concept". It is an environmental cleanup strategy in which plants are employed to remove or contain, or radionulides. This technology operates on the principles of biogeo-chemical cycling. Radiophytoremediation projects have been successfully implemented in developed nations for the cleanupmetal radioactively contaminated soils. Extensive diversity of native and non-native plants have been applied in this strategy. This paper reviews the recent advances to cleanup of radionuclides in soils for sustainable development.

Specie of *Alternanthera* are known for weedy and garden ornamentals. Species like *A. sessiles* (L.) DC and *A. philoxeroides* (Mart.) Griseb are used as green vegetables and/or as fodder. It is the most dominant aquatic weed in contaminated/polluted waters (natural water and industrial polluted). This is a native to south America and naturalized in

India. Iron content is very high (2%) and used as pot-herb and leaf vegetable. It is an accumulator of radionuclides and other potentially toxic elements. Accumulation of radionuclides by tree, grass, and forb species and their application in phytoremediation for the helath "Human and biosphere" are presented.

IL-63

NATURAL ANTIOXIDANTS AND RADIOPROTECTION

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The importance of usage of ethnomedicine are nowadays increased as they have less or no side effects, less cost and often accessibility to the common people. There are evidences that even prehistoric man had the idea of pharmacological effects of plants. Today, almost one half of the pharmaceuticals uses plant products in the preparation as safe and effective medicine. *Piper betle* Linn., commonly known as Tambula (Sanskrit); Pan (Hindi and Bengali) of Piperaceae family is a widely growing plant in the topical humid climate of South-East Asia. In the traditional medicinal system it has been reported to possess the wound healing activity and enhancement of digestion. The ancient literature, AtharbaVeda, as early as 3000-2500 BC mentioned this plant (Vedic name: Saptasira) against various diseases. The extract of *Piper betle* leaves possesses antimicrobial, antifungal, anti-inflammatory activity. The extract also exhibited gastro-cytoprotective properties on experimentally induced gastric lesions by antioxidative mechanism.

Our present study approaches towards the search for the antioxidative property of the plant itself in relation to the radio-protective activity. The radioprotective activity of ethanolic extract of the leaves of *Piper betle* Linn.has been studied using Rat Liver Mitochondria and p BR 322 plasmid DNA as two model *in vitro* system . the extract could effectively prevent the ?ray induced lipid-peroxidation as assayed by measuring TBARS, LOOH, 4-HNE, and Conjugated Diene. Likewise, it prevented radiation induced DNA strand break in a concentration dependant manner. The radioprotective activity of the extract of *Piper betle* could be attributed by its hydroxyl and superoxide scavenging property. In vitro study also demonstrate that the extractive has a potential to scavenge a nitrogen centred stable free radical DPPH. The radical scavenging activity of the extract was primarily due to its constituent Phenolic component which were isolated and identified as chevitol and chevibetol Ê

IL-64

RADIATION INACTIVATION OF AN ALANINE AMINOPEPTIDASE - A PROBE INTO THE ACTIVE SITE COMPOSITION

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Introduction: Interaction of free radicals play an important role in the biochemical processes often leading to pathological conditions such as carcinogenic and mutagenic events ultimately causing cellular lethality. Radiation chemistry of proteins and enzymes is assuming importance since such studies provide information on the properties of the enzyme active site and migration of free radicals through the macromolecule.

Methods: The present study reports on the radiation response of an important protease: aminopeptidase. This was purified to homogeneity from chicken intestine which is a rich source of proteins and proteolytic enzymes.

Results: The aminopeptidase purified from chicken intestine had a molecular weight of 158 kDa and migrated as a heterodimer of 97 kDa and 66 kDa on SDS PAGE. It showed a differential response to radiation in different atmospheric conditions. The inactivation was in the order N2O > N2 > Air, indicating a predominant OH radical mediated inactivation.

Conclusions: It can be concluded that the mechanism underlying radiation inactivation of aminopeptidase involves an OH mediated destruction of crucial tryptophan residues. The chicken intestinal aminopeptidase is sensitive to gamma and UV radiation. The radiation inactivation studies have thus proved a good tool to probe into the active site composition of a protein.

OL-23

INFLUENCE OF THE LEAF EXTRACT OF *MENTHA PIPERITA* (LINN) ON RADIATION INDUCED DAMAGE IN SWISS ALBINO MICE

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Introduction: To investigate the radioprotective activity of 50% ethanolic extract of Mentha piperita leaves (ALM) in Swiss albino mice exposed to different doses of gamma radiation.

Methods: To study the radioprotective effect of ALM, mice were administered different doses, 50, 100, 200, 400 mg/kg body weight of ALM orally for 3 consecutive days before exposure to 8 Gy gamma radiation. The optimum dose (100 mg/kg body weight/day) of ALM was administered before exposure to 6,8,10Gy gamma radiation along with their respective controls (radiation alone). Reduced glutathione and lipid peroxidation were estimated in total surviving animals of all groups on day 30 post irradiation. The radioprotective effect of Mentha piperita was further analyzed on bone marrow chromosomes at 1, 3,7,14,30day post-irradiation.

Results: The optimum radioprotective dose was 100 mg/kg body weight/day of ALM where the highest survival (75%) to 8 Gy radiation was observed .The irradiation caused a dose dependent decrease in survival, while treatment of mice with ALM enhanced survival. The dose reduction factor (DRF) was 1.44. Irradiation caused a dose dependent decline in the levels of glutathione accompanied by an elevation in lipid peroxidation, ALM pretreatment arrested glutathione decline and lipid peroxidation elevation significantly. A significant reduction in chromosomal aberrations was observed in ALM treated groups.

Conclusion: The significant reduction in radiation induced chromosomal aberrations suggests the anti-mutagenic effect of Mentha piperita. The possible mechanism of radioprotection might be free radical scavenging and arrest of lipid peroxidation accompanied by an elevation of glutathione.

OL-24

MODULATORY INFLUENCE OF MENTHA PIPERITA (LINN) LEAF EXTRACT ON HEPATIC ANTIOXIDANT STATUS AND LIPID PEROXIDATION AGAINST GAMMA RADIATION IN SWISS ALBINO MICE

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The radiomodulatory influence of aqueous extract of leaves of Mentha piperita Linn. (1gm/kg body weight/day) was studied on hepatic antioxidant status; glutathione content (GSH), glutathione peroxidase (GPX), glutathione reductase (GR), glutathione S-transferase (GST), superoxide dismutase (SOD), catalase (CAT) and lipid peroxidation (LPO) were assessed in Swiss albino mice. A significant decrease in the activities of glutathione content (GSH, P<0.001), glutathione peroxidase (GPX, P<0.50), glutathione reductase (GR, P<0.05), glutathione-S-transferase (GST, P<0.05), superoxide dismutase (SOD, P<0.50) and catalase (CAT, P<0.50) were observed in the liver of mice exposed to 8.0 Gy gamma radiation. Also, a significant increase in malondialdehyde formation (MDA) in liver was observed in these animals. However, animals pretreated with Mentha extract and exposed to 8.0 Gy gamma radiation showed a significant increase in the activities of reduced glutathione content (GSH, P<0.001), glutathione peroxidase (GPX, P<0.50), glutathione reductase (GR, P<0.50), glutathione S-transferase (GST, P<0.50), superoxide dismutase (SOD, P<0.50), and catalase (CAT, P<0.50). Mentha extract pretreated irradiated group showed significant decrease in malondialdehyde (MDA) formation in liver, suggesting its role in protection against radiation induced membrane damage. Mentha extract has significantly induced the activities of glutathione peroxidase (GPX, P<0.50) and superoxide dismutase (SOD, P<0.50) in the present study. The present study also reveals that Mentha extract can significantly attenuate radiation induced oxidative stress by modulating cellular enzymatic and non-enzymatic antioxidant defense system. Antioxidant influence mediated by Mentha piperita Linn. was assessed by its efficacy to modulate the basal level of the specific activities of glutathione peroxidase and superoxide dismutase in liver of Swiss albino mice.

SESSION XV

PL-11

MITOCHONDRIA, NITROSATIVE/OXYDATIVE STRESS AND THE CROSSROADS FOR DAMAGING AND PROTECTIVE PATHWAYS

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Traditionally, mitochondria have been viewed as the "powerhouse" of the cell, i.e., the site of the oxidative phosphorylation machinery involved in ATP production. But in recent years a large body of knowledge have come to recognize that mitochondria also participate in other important processes such as the intracellular calcium levels, the initiation and performance of cell death programs and aging. Moreover, mitochondria constitute a primary locus for the intracellular formation and conversion of reactive oxygen and nitrogen species (ROS, RNS). These processes are pivotal for the modulation of critical cellular functions, where nitric oxide (NO) forms the crossroads for oxydative and nitrosative pathways and for damaging and protective actions as well. The NO-related formation and opening behavior of the mitochondrial permeabilty transition pore (mtPTP) is suggested to play a particular role in this context. As to brain tissue, preconditioning induced by NO pre-adaption can increase the tolerance to nitrosative/oxidative stress, although the underlying neuroprotective mechanisms are not fully understood. Accordingly we show that not only the concentration but also the time point of the NO exposure determines the outcome of NO actions as demonstrated by the intracellular calcium dynamics and mtPTP opening in response to the activation of glutamate receptors (NMDA-subtype). The ways by which antioxidants may be involved is extremely complicated.

IL-65

INHIBITION OF RADIATION INDUCED TYROSINE NITRATION OF PROTEINS BY CURCUMIN AND NICOTINAMIDE.

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Nitric oxide has been implicated as an important signaling molecule that is activated by various kinds of stress. Ionizing radiation has been shown to induce NO production via activation of iNOS (inducible nitric oxide synthase) in various cell lines. SAPK/JNK pathway has been shown to be involved in iNOS activation. One of the components of NO production is the nitration of proteins. Proteins nitrated on tyrosine have been isolated from pathophysiological tissues; nitration was therefore attributed to pathological conditions. However, the role of nitration in cell signaling has just begun to be unraveled, where many crucial signaling proteins were found to be the targets. In this study the pattern of nitration has been studied following gamma irradiation and the modulatory effect of curcumin, nicotinamide and JNK inhibitor has been studied.

The noteworthy observation of this study was that the increase in NO production did not parallel the iNOS expression but was similar to the nitration of proteins. After LPS activation and irradiation, the increase in iNOS was not as much as the increase in iNOS activity. This implies that iNOS, apart from being regulated at the transcriptional/translational level by LPS and ionizing radiation, may also be under post-translational control by these inducers. The subsequent nitration of proteins was found to parallel nitric oxide production and not iNOS expression.

This study therefore indicates that there are two phases at which NO production is monitored, one that lies prior to iNOS activation and the second that lies distal to NO production. The first phase where NO is produced by iNOS activation is under the control of JNK and NF-ê B and the second phase, where nitration of proteins takes place, is also under the control of JNK. The activation or inhibition of iNOS does not reflect the posttranslational modification (nitration) of the proteins and should not be taken as a measure for NO production. The ultimate nitration of proteins is the critical parameter that should be used for interpreting the effects of NO production.

IL-66

L-ARGININE TREATMENT RESCUES MICE FORM HEAT STROKE INDUCED DEATH. ROLE OF NITROSATIVE AND OXIDATIVE STRESS

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Heat stroke and burn injury are major killers world wide. The consequence of heat waves have been appalling, both in the West as well as the East, both in tropical and temperate regions of the world. The recent heat waves in 2003 killed more than 35,000 people in Europe and more than 1600 people in India.. Research findings have shown that heat stroke results from thermoregulatory failure coupled with an exaggerated acute phase response. The ensuing multi-organ injury results from a complex interplay among the cytotoxic effect of the heat and the inflammatory and coagulation responses of the host. There are no therapeutic approaches to handle these major catastrophes. Thermal hazard associated with burns kills more than 1 lakh people in India. Hypothermia is poor prognostic indicator not only in burn victims but also in other critically ill patients. Since nitric oxide(NO) is an early molecule, which plays a role in the host stress response, including the thermoregulation of the host, we used an amino acid L-arginine, a substrate for NO in modulating the mortality. We used a mouse model of heat stroke to test the therapeutic efficacy of L-arginine a semi-

essential amino acid, which is needed in large quantity during stress, in rescuing the mice from death. Heat stroke mice injected with L-arginine had significantly elevated rectal temperature, compared to the only heat stressed or heat stressed mice injected with either D-arginine or saline. L-arginine treatment resulted in significantly improved survival. Studies which looked at the molecular markers suggested decreased levels of heat stress proteins in the liver and decreased nitrite and inflammatory cytokines in the plasma compared to the heat stressed mice which are not treated, or treated with D-arginine. This L-arginine induced homeostasis both at the physiological and molecular level, which is favourable to the survival of the heat stressed mice. L-arginine, which is the least toxic amino acid, which ahs been clinically widely used can be used to treat heat stroke due to either environmental or exertional heat. This can also be considered in handling stroke, and critically ill patients, who are hypothermic and hypothermia is a poor prognostic indicator for such

IL-67

TIME, SPACE AND NITRIC OXIDE: THE THREE DIMENSIONS OF NOS

Suvro Chatterjee

AU-KBC Research Centre, Anna University, Chennai

Nitre Oxide Syntahse (NOS) is a heme containing dimer protein which produces Nitric Oxide (NO). Robust co-translational and post-translational control machineries involving palmitoylation, myristoylation, protein-protein interactions and sub-cellular trafficking evolved for the control of NO production from NOS. Sub-cellular trafficking of NOS has been implicated in the eNOS activity and control. NOS in endothelial cells, known as eNOS, is mainly distributed in two sub-cellular domians, plasma membrane and perinuclear region close to Golgi area. Membrane localization of eNOS attributes to acylation of c-terminal cysteine residues. Point mutation experiments with critical acylated cysteines suggest that plasma membrane distribution of eNOS is imporatnt for the activity of eNOS. Results of our experiments prove that agonist such as bradykinin promotes physical movement of eNOS proteins from plasma membrane to peri-nuclear Golgi area. Sub-cellular trafficking of eNOS proteins also asured a surge in the production of NO. Further, we showed that both the localization and activity of eNOS are associated with a large GTPase protein, dynamin-2. These observations suggest that spatial distribution of NOS proteins in the endothelial cells tune the temporal production of NO along with other eNOS associating proteins.

IL-68

THE INHIBITION OF INSULIN INDUCED NITRIC OXIDE SYNTHESIS BY BLOOD PLATELETS IN CHRONIC CIGARETTE SMOKERS.

U Ray, 3, K Chakraborty1, G Reddy1, N Sinha1, S Karmohapatra1, & A K Sinha1, 2.

Sinha Institute of Medical Science & Technology, Calcutta, India1, Mount Sinai Medical Center, NY, USA2, Royal Hobart Hospital Hobart, Tasmania, Australia3.

Background: Chronic cigarette smoking has been established to be a major risk factor for the coronary artery disease (CAD) in men. However, pathophysiological mechanism that leads to CAD due to cigarette smoking remains largely obscure. From this laboratory it has been reported earlier that insulin is an essential humoral factor for the prevention of CAD through the systemic generation of nitric oxide (NO), a potent inhibitor of platelet aggregation catalysed through insulin activated nitric oxide synthase (IANOS) on platelet membrane (BioEssays 2003 26(1): 91-98). The aim of the present study was to determine the role of cigarette smoking on the synthesis of NO through IANOS and consequent effect on platelet aggregation leading to CAD.

Methods: Blood was collected either from chronic cigarette smokers for > 3 years (M= 20, age: 23-75 years) or sex and age matched normal volunteers with no systemic hypertension or diabetes mellitus. The inhibitor protein against IANOS was isolated by chromatography on DEAE-Cellulose and Sephadex G50 gel filtration. Nitric oxide was determined as described before (IUBMB Life. 2000 May; 49(5): 441-50). Aggregation of platelets was determined using aggregometer as described before (Platelets 2003 (14) 4:203-210).

Results: While the incubation of normal washed platelets in Tyrode's buffer with 200 µunit insulin/ml produced 3.3 nmol NO /107 platelets/h, incubation of the suspension with 7.5 µg inhibitor/ml for 60 min at 370C reduced the insulin induced NO synthesis to 1.3 nmol/107 platelets/h under similar condition. Incubation of normal platelet-rich plasma with the same amount of the inhibitor under identical conditions resulted in the blockade of insulin-induced inhibition of platelet aggregation by 70% induced by different aggregating agents. Isolated inhibitor from the plasma of chronic smoker was found to be a homogeneous protein with molecular weight of 29 KD as determined by polyacrylamide gel electrophoresis.

Conclusion: We conclude that chronic cigarette smoking results in the systemic appearance of an inhibitory protein for the synthesis of NO through IANOS, and in the reduction of insulin stimulated synthesis of NO in the circulation. The consequent enhanced platelet aggregation predisposes chronic cigarette smokers to increased CAD due to the impairment of insulin induced thromboprotection.

This work was supported by the Philip Morris Inc, USA (External Research Program).

OL-25

HYPERTHERMIA INDUCED ATTENUATION OF MITOCHONDRIAL HYDROXYL RADICALS IN CARDIAC H9C2 CELLS

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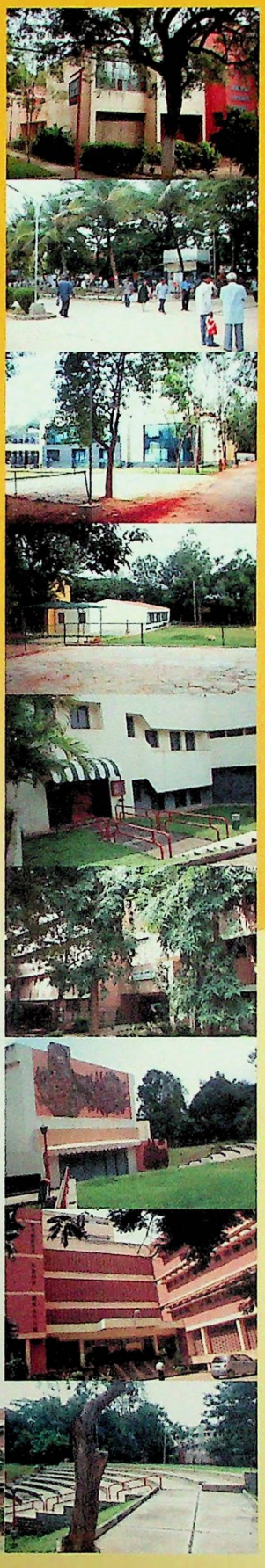
Hyperthermia, in terms of mild and non-lethal heat shock, protects cellular death from various diseases by expressing heat shock proteins which can accumulate with time after the hyperthermia treatment. Particular interest of these proteins in the field of cardiology is their effective role in protecting the myocardium in combination with the nitric oxide synthase (NOS) enzyme. It has been previously reported that the ischemic injury is very much reduced for the animals which are treated by hyperthermia (42-45?C for 1-3 hrs) prior to subjecting them to ischemia reperfusion protocol, indicating a possible therapeutic intervention with the heat shock proteins. Though such an observation of improved myocardial recovery was observed, the actual mechanism of cardioprotection still remains unsolved. Using cardiac H9c2 cells as model system, recently we reported that the heat shock induced HSP90 activates the eNOS to increase the production of NO and the produced NO can block the respiration. Thus reduced respiration of myocytes in the intact heat stressed myocardium might be one of reasons for the reduced injury. The present presentation will focus on some of the recent results obtained in our laboratory on the generation of reactive oxygen species in hyperthermia treated cells, using EPR and DCF-2A fluorescent staining. The results have shown that hyperthermia attenuates the generation of OH radicals through reducing the mitochondrial aconitase activity. Results and evidences for possible binding of heat shock proteins with m-aconitase will be presented and discussed.



Wednesday 12th Jan-2005

WEDNESDAY | **Jan 12th 2005**

0730 - 0830 — **BREAK FAST ROUND TABLE**

0900 - 1130

SYMPOSIUM XVI Venue : HALL-A	SYMPOSIUM XVII Sponsored by : LAILA IMPEX Venue : MAIN AUDITORIUM	SPECIAL SYMPOSIUM Venue : HALL B
Topic : "RECENT ADVANCES IN MARKERS IN OXIDATIVE STRESS"	**Topic : "HERBAL ANTIOXIDANTS""**	**Topic : "GENES TO GENOMICS AND PROTEOMICS IN HEALTH AND DISEASE"**
CHAIRPERSONS : **1. CKK Nair (India) 2. Baulo Zhao (China) 3. Jawail N K (India)**	CHAIRPERSONS : **1. Abbas A Mahdi (India) 2. Udayan Ray (Australia) 3. Mishra K P (India)**	CHAIRPERSONS : **1. Hari S. Sharma, (Netherlands) 2. Ramesh Chandra (India) 3. Haegeman (Belgium)**
IL-69 Harimohan (India) : Generation and reactions of singlet oxygen with organic molecules	IL-74 Debasis Bagchi (USA) : Molecular mechanisms of weight management by a Novel (-)-Hydroxycitric Acid (Hca-Sx) Extract	Nilanjana Maulik (USA) : Antibody array as a tool to asses altered proteins: implications to cardiovascular diseases.
IL-70 Kuppuswamy P (USA) : Cardioprotective effects of nitroxyl-conjugated derivatives of trimetazidine against ischemia-reperfusion injury	IL-75 GC Jagetia (India) : Chemopreventive effect of naringin on the benzo (A)Pyrene -induced forestomach carcinoma in mice	Ramesh Chandra (India) : Role of metalloporphyrins in therapeutics of cardiovascular complications during hypoxic stress.
IL-71 Madhu Dikshit (India) : Neutrophil functions and ascorbic acid: an exploration	IL-76 Manish K Pandit (USA) : Antioxidant effects of withania somnifera on glutamic acid induced neurodegeneration in hippocampus and cerebral cortex of swiss albino mice	Peter van der Spek (Netherlands) : Recent developments in data analysis after DNA microarray experiments.
IL-72 MNA Rao (India) : In praise of oxidant stress	IL-77 Padma PR (India) : Differential response of different sources of DNA to protection by antioxidant rich plant extracts	Luke Janssen (Canada) : Isoprostanes: New mediators in airway and vascular functions.
IL-73 Sudhakaran PR (India) : Oxidant stress and production of superoxide dismutase (SOD) By monocyte-macrophage in culture	IL-78 S Pandey (Canada) : Role of oxidative stress in neuronal cell death: Neuroprotection by Coenzyme Q10.	Hari S. Sharma (Netherlands) : Myocardial gene profiling during human cardiac hypertrophy and failure
	IL-79 Subbaraju (USA) : Novel Anti-Inflammatory Properties of 5-Loxin, Akba Enriched *Boswellia* Extract	
	IL-80 GJ Sharma (India) : Plant-Based Anti-oxidants against sulfur free radical-induced damages	

1130 - 1145 — **TEA**

1145 - 1400

SYMPOSIUM XVIII Venue : MAIN AUDITORIUM	SYMPOSIUM XIX Venue : HALL A	
Topic : "MISCELLANEOUS TOPICS - II"	**Topic : "MISCELLANEOUS TOPICS-III"**	
CHAIRPERSONS : **1. Irfan Rahman (USA) 2. Adhikari S (India) 3. Sainis K B (India)**	CHAIRPERSONS : **1. MNA Rao (India) 2. Hideyuki Majima (Japan) 3. Dandekar S. P. (India)**	
IL-81 Chainy GBN (India) : Thyroid hormone-induced oxidative stress in the submitochondrial particles of rat liver	OL-28 Reddanna P (India) : Antioxidant, anti-inflammatory and anti-cancer properties of clerodendron serratum extracts	OL-34 Molly Jacob (India) : Alterations in the intestinal glycocalyx and bacterial flora in response to oral indomethacin
IL-82 Poonam Kakkar (India) : Exploration of antioxidant capacity of herbs: A target specific approach	OL-29 Patel VH(India) : Antioxidant capacity of commonly consumed vegetables of gujarat.	OL-LS Senthil Murugan(India) : Compensatory role of a 182 kda protein, a cardiac isoform of 2m in the free radical mediated cellular damage in pathological conditions.
IL-83 Ram Vatnani (India) : Antioxidants and free radicals in health	OL-30 Singh HV (India) : Serum apolipoproteins A-I, A-II, B, C-II, C-III, E and total antioxidant status in angiographically proved CAD cases.	
IL-84 Farhath Khanum (India) : Rhodiola: A versatile adaptogen	OL-31 Rani P (India) : Influence of selenium status on the cellular defence against oxidative damage during aging in the Insect C. cephalonica	
OL-26 Biswas SK (India) : Effect of rubia cordifolia, fagonia cretica linn and tinospora cordifolia on free radical generation and lipid peroxidation during oxygen glucose deprivation in rat hippocampal slices	OL-32 Vijay K Kutala (USA) : Spirulina prevents doxorubicin-induced free radical release and apoptosis in cardiomyocytes in vitro	
OL-27 Pari L (India) : Antioxidant role of tetrahydro curcumin (Thc): effect on lipid peroxidation and antioxidant status in chloroquine induced toxicity	OL-33 Govindarajan R (India) : Effect of desmodium gangeticum on antioxidant enzymes in streptozotocin induced diabetic rats.	

1400 - 1430 — **LUNCH**

1430 - 1600 — **POSTER SESSION**

1600 - 1700 — **CONCLUDING SESSION FOLLOWED BY VALEDICTORY FUNCTION & HIGH TEA**

SESSION XVI

IL-69

GENERATION AND REACTIONS OF SINGLET OXYGEN WITH ORGANIC MOLECULES

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Bhabha Atomic Research Centre, Trombay, Mumbai-400 085

Singlet molecular oxygen ($^1O_2$) is a reactive oxygen free radical which plays an important role in the photodynamic therapy of cancer. It is oxidizing in nature and various biochemical reactions generates singlet oxygen *invivo*. Some peroxidase are also known to proceed through singlet oxygen intermediate. There are several dyes which are used as the generators of $^1O_2$, while some cellular organelles and other biomolcules like antioxidants have high reactivity. In order to exploit photodynamic action in therapy, it is necessary to quantitatively evaluate the yield and reactivity of singlet oxygen. For this, a new transient luminescence spectrometer (TL900, Edinburgh Instruments, UK) was used. The instrument is designed to produce singlet oxygen by photosensitization and measure luminescence decays at 1270 nm. The signal using germanium detector is measured by an oscilloscope through an emission monochromator.

The life time of $^1O_2$ in acetonitrile and benzene was found to be 67 and 30 s, respectively. In presence of the quencher, the lifetime decreased. The decrease in lifetime in presence of varying concentrations of the quencher was used to determine the quenching rate constant for a number of organic compounds. Antioxidants like curcumin, resveratrol, caffeic acid and ferulic acid showed quenching rate constants of $1.3x10^8$, $1.1x10^6$, $8.1x10^5$ and $4.0x10^5$ M^{-1} s^{-1} respectively. The reaction of singlet oxygen with organoselenium compounds such as ebselen and its analogues have also been studied. Good correlation was observed between the observed rate constants and electron density at selenium.

IL-70

CARDIOPROTECTIVE EFFECTS OF NITROXYL-CONJUGATED DERIVATIVES OF TRIMETAZIDINE AGAINST ISCHEMIA-REPERFUSION INJURY

P. Kuppusamy, M. Khan, V. K. Kutala, K. Hideg*

Davis Heart and Lung Research Institute, Ohio State University, Columbus, OH, USA and *Institute of Organic and Medicinal Chemistry, University of Pecs, Pecs, Hungary

Myocardial ischemia followed by reperfusion induces the formation of deleterious oxidants, such as, $O_2^{\cdot}$ H_2O_2, OH, ROO, and Fe (IV). These oxidants inflict significant functional injury to the heart leading to inefficient cardiac contractility and/or arrhythmias and cell death. Prior studies have shown that exogenous SOD, catalase and other antioxidant enzymes can prevent the postischemic reperfusion injury. However, the protective effect of SOD and catalase is limited because of their large molecular size and their inability to get into cells. We have synthesized cyclic amino/nitroxide derivatives of some commonly used anti-arrhythmic and anti-ischemic drugs. The amino/nitroxyl derivatizations enable these drugs to function as anti-oxidants. Previously, we have reported that the antioxidant compound 2,2,5,5-tetramethyl-3-carboxamide prevented the postischemic myocardial injury. Trimetazitidine (TMZ, 1[-(2,3,4-trimethoxypheynyl) methyl] piperazine) has been used as an anti-anginal and anti-ischemic agent over the last two decades. In the present study, we have investigated the efficacy of various derivatives of TMZ with an antioxidant moiety, on isolated rat hearts subjected to ischemia (30 min) and reperfusion (45 min). Hearts were either untreated or treated with 50 μ M of TMZ and TMZ-derivatives for 1 min before ischemia. The hemodynamic, biochemical and histological parameters have been used to assess the cardiac function and damage. The results demonstrated that some of the TMZ derivatives showed significant cardioprotection. Both TMZ-NH and TMZ-NHO(N-phenyl-substituted) showed cardioprotection with a more than 3-fold increased recovery of contractile function compared to control hearts. Thus, the new class of compounds with dual functions exhibit potent antioxidant action and protection against myocardial injury in the postischemic heart.

IL-71

NEUTROPHIL FUNCTIONS AND ASCORBIC ACID: AN EXPLORATION

Madhu Dikshit

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Neutrophils or polymorphonuclear leukocytes (PMNs), the first line of defense, against the invading microbes generate both reactive oxygen species (ROS) and nitric oxide (NO). Ascorbic acid, though present in large concentrations in the PMNs does not have a defined physiological relevance. Role of ascorbic acid and its cell permeable analogue, dehydroascorbic acid (DHA) on the PMNs functions such as phagocytosis, apoptosis, free radical generation and modulation of platelet aggregation was the subject of present study. Ascorbate and DHA did not affect the phagocytosis but enhanced ROS generation and apoptosis following treatment with *Escherichia coli*, FMLP, phorbol ester (PMA) or arachidonic acid (AA). DHA also increased hydrogen peroxide (H_2O_2), peroxynitrite (ONOO-) generation from PMNs, and inhibited platelet aggregation in the presence of PMNs. Early apoptosis marker, Annexin V was significantly increased after bacterial phagocytosis in the ascorbate/dehydroascorbate treated cells.

Nitric oxide synthase (NOS) activity, as measured by nitrite content, diaminofluorescein fluorescence or conversion of L-[^{3}H]-arginine to L-[^{3}H]-citrulline was enhanced in rat, monkey or human PMNs after ascorbate or DHA treatment. The increase in NO generation following ascorbate treatment was due to the intracellular ascorbate as iodoacetamide mediated inhibition of DHA to ascorbate conversion attenuated the DHA mediated increase in NO synthesis. The augmentation of NOS activity in the PMNs homogenate by tetrahydrobiopterin was significantly enhanced by ascorbate, while ascorbate alone did not influence the NOS activity. NOS activity was also reduced significantly in the scorbutic guinea pig PMNs. Ascorbate mediated enhancement of NOS activity in the cultured PMNs was significantly reduced in the presence of biopterin synthesis inhibitors. Ascorbate thus seems to regulate the NOS activity in the PMNs through tetrahydrobiopterin. Detailed investigation on the DHA mediated increase in the ROS generation indicated that, inhibitors of DHA uptake, NADPH oxidase, NO synthase, or ROS scavengers attenuated ROS generation. The response was also attenuated in presence of NO scavengers, hemoglobin and PTIO, and by ROS scavenger, SOD and catalase, while MPO inhibitor had no effect. Iodoacetamide, an inhibitor of intracellular conversion of dehydroascorbate to ascorbate; high glucose (10 mM), an inhibitor of dehydroascorbate uptake reduced ascorbate/dehydroascorbate induced NO and peroxynitrite generation from PMNs. Thus ascorbate mediated ROS and RNS generation might mediate cytotoxicity towards the ingested microbes and subsequently augmented PMNs apoptosis. The talk will focus on the role of ascorbate in the regulation of neutrophil functions.

IL-72

IN PRAISE OF OXIDANT STRESS

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Oxygen is the essence of life. Without oxygen, life probably would not have progressed beyond the ocean and earth would have ended up like Mars, full of red iron oxide and without any sign of life. It is oxygen that has given diversity to life, in the form of a variety of microorganisms, plants and animals. Contrary to the common belief that the antioxidant system developed in order to fight against oxygen, life had learnt to take care of excess oxidant stress well before oxygen accumulated in the atmosphere. In fact, certain amount of oxidant stress is essential for the proper functioning of cells. Many transcription factors require oxidant stress for activation. NFê B, Nrf-2, AP-1, P53, etc. require oxidation before migrating to the nucleus where they activate transcription by binding to DNA. Although a large number of diseases are attributed to oxidant stress, antioxidant therapy has not yet thrown up any miracle cure . Many antioxidants are known to act as prooxidants in a different situation. It is likely that we are designed to be refractory to excess dietary antioxidants so that the beneficial effects of oxidant stress is not affected.

IL-73

OXIDANT STRESS AND PRODUCTION OF SUPEROXIDE DISMUTASE (SOD) BY MONOCYTE-MACROPHAGE IN CULTURE

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Introduction: Peripheral blood mononuclear cells (PBMC) undergo transendothelial migration and differentiate to macrophages, which take up oxidatively modified LDL and become foam cells. The macrophages are known to produce H2O2 whose content increases when they are subjected to oxidant stress, which inturn is attributed to increased dismutation activity of SOD. The present study was designed to evaluate the production and secretion of SOD by mo-m? system under conditions of oxidant stress using PBMC in culture.

Methods: PBMC was isolated from human peripheral blood and maintained in culture for different time intervals in RPMI-1640 medium and supplemented with oxidized LDL. The culture medium and cell layer were collected at different time intervals and the activity of SOD was assayed.

Results: Analysis of down regulation of monocyte specific markers like MPO and CD14 and upregulation of m? specific functions like ? -glucuronidase, MMPs and CD71 showed that monocytes in culture undergo differentiation to macrophages when subjected to oxidant stress. Mo-m?in culture produces SOD, which was distributed into extracellular (EC) and intracellular parts. Treatment of these cells with oxidatively modified protein caused an increase in the level of EC-SOD indicating that cells respond to oxidative stress by secreting more of EC-SOD. It appears that the production of superoxide is dependent on a membrane bound NADPH oxidase, which is otherwise dormant and may be activated in response to certain stimuli including oxidant stress.

Conclusions: The results indicate that mo-m? system when subjected to oxidant stress produce and secrete SOD to the extracellular space, which may be important in protecting the cell surface, and ECM from superoxide mediated damage.

SESSION XVII

IL-74

MOLECULAR MECHANISMS OF WEIGHT MANAGEMENT BY A NOVEL ()-HYDROXYCITRIC ACID (HCA-SX) EXTRACT

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Garcinia cambogia-derived HCA has shown promise in weight management. We have recently demonstrated the broad spectrum safety and bioavailability of Super CitriMax (HCA-SX, a 60% calcium-potassium salt of HCA). HCA-SX promotes weight loss in both humans and animals, fat oxidation and inhibits ATP-citrate lyase. A recent clinical study in 90 subjects exhibited that HCA-SX reduces body weight, BMI, serum leptin, LDL, triglycerides and total cholesterol, and enhances the excretion of urinary fat metabolites. HCA-SX acts as a mild serotonin receptor reuptake inhibitor (SRRI) and enhances the availability of serotonin in the brain tissues. HCA-SX feeding marginally increased five neurotransmitters including serotonin, dopamine, DOPA-C, 5-HIAA and HVA in the brain, which might explain its appetite suppressive effect. Recently, the effects of low-dose oral HCA-SX was investigated on the body weight and abdominal fat transcriptome in rats. Sprague-Dawley rats were fed either control or HCA-SX for 8 weeks. Total RNA was extracted from abdominal fat and microarray Genechip analysis was conducted. Data analyses were conducted using Affymetrix Microarray Suite 5.0. Results were validated on selected genes by conducting Real Time PCR. HCA-SX restricted body weight gain in rats and lowered abdominal fat leptin expression. High-density microarray analysis of 9960 genes and ESTs present in the fat tissue identified a small set of specific genes sensitive to dietary HCA-SX and weight loss. Mitochondrial/nuclear proteins necessary for fundamental support of the tissue were not affected by HCA-SX, which demonstrated the safety of HCA-SX. Functional characterization of HCA-SX sensitive genes revealed that up-regulation of genes encoding serotonin receptors represents a distinct effect of HCA-SX on appetite suppression. Taken together, these results reconfirm the ability of HCA-SX in appetite suppression and obesity regulation by modulating a set of key functional genes.

IL-75

CHEMOPREVENTIVE EFFECT OF NARINGIN ON THE THE BENZO(A)PYRENE -INDUCED FORESTOMACH CARCINOMA IN MICE

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The chemopreventive activity of 1, 2.5, 5, 10, 25, 50, 100 or 250 mg/kg b. wt. naringin, a citrus flavanone was studied on the benzo(a)pyrene (BaP)-induced forestomach carcinoma in female Swiss albino mice. Naringin was given before, after or both (before & after) orally or intraperitoneally to mice receiving BaP for the induction of chemical carcinogenesis. The optimum chemopreventive dose was found to be 10 mg/kg p.o. and oral administration was more effective than the intraperitoneal treatment. A maximum chemopreventive activity of naringin was observed when it was given during and after the termination of BaP treatment. The tumor incidence and tumor multiplicity were reduced in a dose dependent manner, highest reduction of 78% in tumor multiplicity was observed at 10 mg/kg, where a 20% reduction in tumor incidence was also observed. However, a reduced chemopreventive effect was observed when naringin was given either before or after chemically induced carcinogenesis. These observations were further confirmed by PCNA labeling where naringin pretreatment

reduced the PCNA labeling index by four folds. The micronuclei analysis in splenocytes also confirms to the chemopreventive activity of naringin. BaP treatment increased the frequency of micronuclei bearing splenocytes (MNBNC) by six folds. Naringin treatment during and after BaP administration reduced the frequency of MNBNC in a dose dependent manner up to 10 mg/kg where a highest reduction in MNBNC was observed, thereafter the frequency of MNBNC showed a marginal increase up to a dose of 250 mg/kg naringin however it was two folds lower than BaP treatment alone. A similar effect on MNBNC decline was observed for pre or post-naringin treated group however, the degree of decline in MNBNC was lesser when compared to pre-post naringin treatment. Our study demonstrates that the naringin possess chemopreventive activity and this may be due to reduction in DNA damage as evidenced by lower frequency of MNBNC in the group treated with naringin during and after chemical carcinogenesis.

IL-76

ANTIOXIDANT EFFECTS OF WITHANIA SOMNIFERA ON GLUTAMIC ACID INDUCED NEURODEGENERATION IN HIPPOCAMPUS AND CEREBRAL CORTEX OF SWISS ALBINO MICE

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Introduction: Oxidative stress participates in the etiology of neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. The brain with its high lipid content, low levels of free radical eliminating enzymes may be prime target of free radical damage. Plant flavonoids have significant effect on protection of brain against free radicals. Withania somnifera (Ashwagandha) has a profile of activity that is consonant with putative antistress and antioxidant activity. In the present work, we examined the neuroprotective effects of Withania somnifera against lipid peroxidation (LPO) in parallel with the level of reduced glutathione (GSH) in Hippocampus and Cerebral cortex regions mouse brain.

Methods: Glutamic acid was injected intraperitoneally in three concentrations (1.0, 5.0,10.0 mg/kg body weight) for 10 days. Methanolic extract of Withania somnifera was administered orally in concentration of 250 mg/kg body weight. Free radical induced oxidative damages was assayed by lipid peroxidation assay as described by Okahwa et al. (1979). Endogenous antioxidative defense system was assayed by the analysis of reduced glutathione as described by Jollow et al. (1974.).

Results: Extract of Withania somnifera (250 mg/kg body weight) protected both hippocampus and cerebral cortex neurons against oxidative damage as evidenced by significant ($p<0.05$) decline in lipid peroxidation. The GSH content was significantly ($p<0.05$) increased after the treatment with extract of Withania somnifera.

Conlusion: From results we conclude that the extract of Withania Somnifera has significant antioxidant property which may prevent the progression of neuronal cell injury.

IL-77

DIFFERENTIAL RESPONSE OF DIFFERENT SOURCES OF DNA TO PROTECTION BY ANTIOXIDANT RICH PLANT EXTRACTS

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The role of herbal constituents in preventing and combating oxidative damage is unquestionably proven by many studies conducted the world over. The exact mechanism of action of many such preparations, however, eludes the researcher. In-depth studies into the molecular mechanisms of action of herbal extracts should be conducted to understand the biochemical mechanism of action of the components. One promising herbal candidate that has been well recognized for its memory-enhancing properties is Bacopa Monnieri, commonly known as Brahmi. The exact mechanism of action of this herb in preventing oxidant-induced damage is as yet unclear. Earlier studies conducted in our laboratory showed that Bacopa monnieri could significantly decrease the extent of DNA damage induced by the oxidant H2O2. As a first step towards understanding the mechanism of the damage prevention different sources of DNA (viral, bacterial, haploid animal and diploid animal) were treated with H2O2, in vitro or in intact cells, in the presence and absence of the extracts of Bacopa monnier. Another herb, Alternanthera sessilis, which bears a remarkable morphological similarity to Bacopa Monnieri, was also tested in a similar manner. The results showed that all the types of DNA were damaged significantly by the in vitro exposure to H2O2. The extent of damage was significantly reduced by the co-exposure of leaf extracts of both Alternanthera sessilis and Bacopa monnieri. However, the extent of damage was not completely reversed by the extracts at the dose level tested in the in vitro systems. However, in the intact cells, the reversal of DNA damage was complete, where the extent of damage was found to reach the basal levels after exposure to the leaf extracts. This indicated that the phytochemicals present in Alternanthera sessilis and Bacopa monnieri leaves exert a better DNA-protective action in the presence of some endogenous component in the intact cell. This observation has a lot of bearing under in vivo conditions, the understanding of which will potentiate the use of these herbs in the preparations used against a variety of oxidant-induced disorders and diseases.

IL-78

ROLE OF OXIDATIVE STRESS IN NEURONAL CELL DEATH: NEUROPROTECTION BY COENZYME Q10

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Recent research has indicated that neuronal cells are highly sensitive to reactive oxygen species such as free radicals. It has been hypothesized that mitochondrial dysfunction and consequent production of ROS may induce neuronal cell death occurring in neurodegenerative disorders such as hypoxic-ischemia, Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis.

In the present study, we have demonstrated that external oxidative stress induces mitochondrial dysfunction leading to increased ROS generation and ultimately apoptotic cell death in neuronal cells. Furthermore, we have investigated the role of Coenzyme Q10 as a neuroprotective agent.. Our results indicate that total cellular ROS generation was inhibited by Coenzyme Q10. Further, pre-treatment with Coenzyme Q10 maintained mitochondrial membrane potential during oxidative stress and reduced the amount of mitochondrial ROS generation. Preliminary in vivo studies have shown that Coenzyme Q10 helped in improving cognition in rats when oxidative stress was induced using paraquat. The levels of

lipid peroxidation were higher and low GSH levels in the brain tissues in rats that were not fed with Coenzyme Q10 prior to paraquat treatment. While those fed with Coenzyme Q10 prior to paraquat treatment showed lower lipid peroxidation and higher GSH levels. Our study suggests that water-soluble Coenzyme Q10 acts by stabilizing the mitochondrial membrane when neuronal cells are subjected to oxidative stress. Therefore, Coenzyme Q10 has the potential to be used as a therapeutic intervention for neurodegenerative diseases.

IL-79

NOVEL ANTI-INFLAMMATORY PROPERTIES OF 5-LOXIN, AKBA ENRICHED *BOSWELLIA* EXTRACT

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Osteoarthritis (OA) is a common, chronic, progressive, skeletal, degenerative disorder. NSAIDs represent the current therapeutic option for the treatment of inflammation and pain associated with OA. In Ayurvedic medicine, the gum of *Boswellia serrata* is purported to have good anti-inflammatory and anti-arthritic activities. The acute oral LD_{50} of 5-LOXIN, an enriched fraction of Boswellic acid with ~30% 3-acetyl-11-keto-?-boswellic acid (AKBA), is >5.0 gm/kg in rats, acute dermal LD_{50} is >2.0 gm/kg, primary dermal irritation index is 0.0, and scored mildly irritating in ocular irritation tests. TNF-? is known to play a major causative role in the pathophysiology of numerous inflammatory disorders including OA. We investigated the molecular mechanisms underlying the purported anti-inflammatory properties of 5-LOXIN. Inflammatory response was induced in human microvascular endothelial cells (HMEC) by treating cells with TNF-ng/ml). 5-LOXIN was first tested for its potential cytotoxic properties by LDH assay in HMEC. No toxic effect was observed up to a dose of 50 ?g/ml. To identify the genome-wide effects of 5-LOXIN in an inflammatory situation, GeneChip (Affymetrix) analysis was conducted using human genome U133 Plus 2.0 GeneChip. This array analyzes the expression level of over 47,000 transcripts and variants, including 38,500 well-characterized human genes. HMEC were either pre-treated or not with 5-LOXIN for 48h. After this duration, cells were treated with TNF-? and harvest after another 6h. Global transcriptome analysis identified a specific set of 5-LOXIN-sensitive inflammatory genes including vascular cell adhesion molecule-1 (VCAM-1). The expression of VCAM-1 microvascular endothelial cells is recognized as an early feature in the pathogenesis of inflammatory diseases such as OA. Additional experiments employing quantitative real-time PCR technique to assess gene expression confirmed that TNF-inducible VCAM-1 expression in HMEC is down-regulated by 5-LOXIN treatment. These results warrant further evaluation of 5-LOXIN in an *in vivo* model of inflammation.

IL-80

PLANT-BASED ANTI-OXIDANTS AGAINST SULFUR FREE RADICAL-INDUCED DAMAGES

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Natural anti-oxidants' role in countering free radical-mediated macromolecular damages leading to a variety of human diseases has been very well understood and documented in the literature. The emerging trend in anti-oxidant research aims at bioprospecting bio-active molecules from various conventional and non-conventional medicinal plants possessing anti-oxidant properties. The rich mega-biodiversity hotspot of the north-east India offers invaluable gene pools for several endemic medicinal plants requiring immediate attention. Rapid screening protocols have already been developed to evaluate the anti-oxidant potentials of members belonging to family Zingiberaceae. Rhizome extracts of these members are widely utilized in dietary intakes and traditional system of medicine. Crude methanol rhizome extracts of elite species have been evaluated for the presence of anti-oxidant potentials using sulfur free radical reactivity with curcumin as reference indicator. Sulfur free radicals (GS) can be generated by irradiating 15 mM glutathione (GSH) solution using a 5100 Ci cobalt-60 gamma irradiator (BARC, India). In vitro depletion of pure curcumin (Sigma, USA) determined by simple spectrophotometric measurement is used as reference indicator for reactivity with sulfur free radicals. Addition of the supernatant from crude extracts (after homogenization and centrifugation at 5000 rpm) to the reaction mixtures can significantly decrease the depletion of curcumin, thereby indicating that these extracts do possess anti-oxidant properties. Varying magnitudes of curcumin protection can be achieved in treatments at different doses of irradiation. Relative curcumin depletions by crude extracts against sulfur free radicals in the elite species have shown that significant anti-oxidant properties could be detected in all the members with Zingiber cassumunar Rose providing the maximum activity thereby indicating that this species possesses significant potentials[1]. Some of these results are briefly discussed in this paper.

SESSION XVIII

IL-81

THYROID HORMONE-INDUCED OXIDATIVE STRESS IN THE SUBMITOCHONDRIAL PARTICLES OF RAT LIVER

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Introduction: Thyroid hormones are known to influence several mitochondrial functions including oxygen consumption, oxidative phosphorylation, proton leak and biogenesis. The present study aims to investigate the effect of thyroid hormone on the integrity of mitochondrial inner membrane.

Methods: Submitochondrial particles (SMPs) were prepared from the liver of hypothyroid and hyperthyroid adult male Wistar rats by the administration of 0.05% 6-n-propylthiouracil (PTU) for 45 days and by daily injection of 20 g T_3/100g body weight for 3 days to the PTU-treated rats, respectively. Control rats received vehicle for the same period. The primary index of membrane damage viz., lipid peroxidation and protein carbonylation were compared among the SMPs of the three sets of rat.

Results: Endogenous lipid peroxidation and protein carbonylation change significantly in both hypo- and hyperthyroid rat SMPs in comparison to euthyroid ($P < 0.05$). *In vitro* lipid peroxidation induced by the redox couple $FeSO_4$ / ascorbate as well as ADP/ Fe^{3+} did not register significant change in any of the altered thyroid states ($P < 0.05$). Among the oxidants, tert-butylhydroperoxide induced significant peroxidation in both hypo- and hyperthyroid rat SMPs, while hydrogen peroxide could induce peroxidation only in the hypothyroid rat SMPs ($P < 0.05$).

Conclusions: The results suggest that thyroid dysfunction makes the submitochondrial particles of liver of rats highly susceptible to oxidative damage, thus ultimately affecting the mitochondrial membrane function

IL-82

EXPLORATION OF ANTIOXIDANT CAPACITY OF HERBS: A TARGET SPECIFIC APPROACH

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Traditionally used herbs are gaining unforeseen popularity due to revelation of their scientifically validated efficacy using modern methods. A large number of herbal products with antioxidant capacity are available as neutraceuticals, cosmetics and over the counter functional foods. We explored some therapeutically important medicinal herbs for their antioxidant potential. Since herbal extracts are a mixture of many chemical constituents, efforts were made to address some pertinent issues. Is one free radical quenching assay sufficient to know the antioxidant capacity of herbs? Will a battery of assay systems with different free radicals as targets generate differential response? What would be the response of herbal extracts in different cell types as targets? Selected medicinal plants i.e. *Acorus calamus, Azadirachta indica, Nelumbo nucifera,, Phylanthus emblica* and *Terminalia chebula* were subjected to exploration of antioxidant capacity using ABTS radical assay, SOD mimetic activity, LPO inhibitory potential, total thiol content and plasma oxidisability inhibition. Studies were also conducted to see the effect of these standardized extracts on the viability of K-562 cells and primary rat hepatocytes subjected to oxidative stress using MTT assay. The same extracts were also explored for their quenching capacity of NO released by stimulated alveolar macrophages. The results show differential response of extracts to different target free radical species and cell types. The approach is beneficial in selecting herbal antioxidants for use in specific disease/stress condition.

IL-83

ANTIOXIDANTS AND FREE RADICALS IN HEALTH

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The new millennium has ushered in E-business, E-commerce and gamut of E-activities in all walks of life. This era, in turn, has introduced a stressful mindset in the society at large. The high level in any aspect of life coupled with intense competition is leading to a general erosion of value systems all around. By and large, people in Asia who have adopted both to the life style and eating habits of west have lower fiber and accompanied by an increase in obesity, cardiovascular and digestive problems coupled with higher stress levels. The Asians are thus faced with a rapid increase in the diseases of the Western hemisphere.

Conversely, in the US and other western countries, where cardiovascular diseases and obesity have already reached epidemic levels, there is a noticeable move in the reverse direction. Fiber for long, a staple food of Asian / Japanese diets, is one of the hottest ingredients in the US, with soya, oats and whole grains gaining official approval highlighting various health claims.

We also pollute our external environment with toxic wastes of the mind-boggling diversity, not to mention, noise and smoke. Small wonder then that we live with an under current of anxiety which only reinforces the vicious cycle. At the same time, we don't stop inflicting further damage on ourselves with a life style brimming with fast food, cola, tobacco, sleep deprivation and many more items. Any way, from whatever angle we look at it, our life, toady, is not natural, and our life style is taking us further and further away from what the mother nature would have liked. Such a transition gets translated into excessive demands on our metabolic process, which eventually, leads to higher oxidative stress on all body tissues and organs. For instance, blood vessels all over the body, irrespective of their size, undergo changes over the period of years as a result of oxidative damage to their inner lining. The resulting decrease in blood flow leads to impaired functioning of various organs including vital ones like **heart, kidneys, brain, eyes**. Similarly, our body's defense mechanism too gets affected by the oxidative damage, reducing our immunity to infections and external challenges. Oxidative damage of another kind exposes us to the development of cancer and many other illnesses. The need of the hour is to prevent as well as manage such high levels of oxidative stress. It is here that the naturally occurring vitamins and antioxidants have values beyond compare. While the role of vitamins has been known for a long time, antioxidants are steadily emerging as dietary forces of the new millennium.

Well, we now understand that free radicals are produced in the body and may have potential for tissue damage, free radicals damage accumulates with age.

Antioxidants are nutrients (vitamins and minerals) as well as enzymes (proteins in our body) that assist in chemical reactions). They are thought to protect the body against the destructive effects of free radicals.

Antioxidants neutralize free radicals by donating one of their electrons, ending the electron- stealing reaction. Antioxidants act as scavengers, helping to prevent cell and tissue damage that could lead to cellular damage and disease.

Antioxidnats such as VitaminE, Mixed-Carotenoids, Vitamin-C, Lutein, Enzymes, and trace elements and minerals block the process of oxidation by neutralizing free radicals. In doing so, the antioxidants themselves become oxidized. That is why there is a constant need to replenish our antioxidant resources. In a healthy or normal person, the body is adequately provided with, to handle free radicals.

IL-84

RHODIOLA: A VERSATILE ADAPTOGEN

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Rhodiola rosea belonging to the family *Crassulaceae* is a popular medicinal plant in Russia and Scandinavia. Extracts of this plant have been found to favourably affect a number of physiological functions including neurotransmitter levels, central nervous system activity, cardiovascular function etc. It is being used to stimulate nervous sytem, decrease depression, enhance work performance, eliminate fatigue and prevent high altitude sickness. Most of these effects have been attributed to the constituents such as salidrosides, rosavins and p-tyrosol. It has been found to strong antioxidant and anticarcinogen due to the presence of several phenolic compounds. In India the plant has been growing wild in high altitudes of Himalayas. Defence Research and Development Organisation has taken up the responsibility of its conservation, development of multiplication management practices and development of health foods, supplements and nutraceuticals in India. During the presentation, the physiological effects on the humans, mechanisms of actions, and its exploitation for development of nutraceuticals will be discuused

OL-26

EFFECT OF RUBIA CORDIFOLIA, FAGONIA CRETICA LINN AND TINOSPORA CORDIFOLIA ON FREE RADICAL GENERATION AND LIPID PEROXIDATION DURING OXYGEN GLUCOSE DEPRIVATION IN RAT HIPPOCAMPAL SLICES

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Introduction: The major damaging factor during and after

ischemic/hypoxic insult, is the generation of free radicals, which leads to apoptosis, necrosis and ultimately neuronal cell death. *Rubia cordifolia* (RC), *Fagonia cretica linn* (FC) and *Tinospora cordifolia* (TC) have been reported to contain a wide variety of antioxidants and have been in use in the eastern system of medicine for various disorders.

Methods: Rat hippocampal slices were subjected to OGD (oxygen glucose deprivation) and divided into 3 groups, control, OGD and OGD + drug treated. Cytosolic reduced glutathione (GSH), nitric oxide [NO, measured as nitrite (NO2)]. RT-PCR was performed for the three herbs to assess their effect on the expression of gamma-glutamylcysteine ligase (GCLC), iNOS, and GAPDH gene expression.

Results: All the three herbs were effective in elevating the GSH levels and expression of the GCLC. The herbs also exhibited strong free radical scavenging properties against reactive oxygen and nitrogen species as revealed by diminished expression of iNOS gene, NOS enzyme activity, ONOO generation and lipid peroxidation. RC, FC and TC also increased Cu-Zn SOD gene expression and activity.

Conclusions: Therefore RC, FC and TC attenuate oxidative stress mediated cell injury during OGD and exert the above effects at both the cytosolic as well as at gene expression level and may be effective alternative therapeutic tool against ischemic brain damage.

Acknowledgements: NIV, Pune, India, British Heart Foundation, UK.

OL-27

ANTIOXIDANT ROLE OF TETRAHYDRO CURCUMIN (THC): EFFECT ON LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN CHLOROQUINE INDUCED TOXICITY

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Introduction

Tetrahydrocurcumin (THC) is one of the major colourless metabolite of Curcumin, the biologically active principle from the rhizomes of Curcuma longa (Turmeric). In the present investigation THC was evaluated for its antioxidant role against the conventional antimalarial drug chloroquine (CQ) induced toxicity in rats.

Methods

Chloroquine (970mg/kg) toxicity was developed with single oral administration. THC (80mg/kg) administered orally for 8 days before single administration of CQ (970mg/kg) and treatment with THC followed for 7 more days. At the end of experimental period, the activities of serum enzymes (aspartate transaminase, alanine transaminase and alkaline phosphatase), bilirubin, serum lipids, liver lipid peroxidation indices (TBARS and hydroperoxides) and antioxidants (enzymic and nonenzymic) were estimated. Histopathological changes in liver were also observed. The effect of THC was compared with curcumin.

Results

The increased activities ($p<0.05$) of serum hepatospecific enzymes and the levels of bilirubin, serum lipids (cholesterol, triglycerides, phospholipids and free fatty acids) and hepatic lipid peroxidation were observed in rats treated with CQ. In addition, the decreased levels of antioxidants (superoxide dismutase, catalase, glutathione peroxidase and reduced glutathione) in liver were also observed in CQ treated rats. Administration of THC and curcumin significantly decreased ($p<0.05$) the serum hepatospecific markers and the level of lipid peroxidation in liver with enhancement of cellular antioxidant defense against CQ challenge. All these observations were supplemented by histopathological examination of liver.

Conclusion

The results of this study revealed that the antioxidative action of THC is responsible for its protective activity against CQ induced hepatic damage. THC has more prominent effect than curcumin

OL-28

ANTIOXIDANT, ANTI-INFLAMMATORY AND ANTI-CANCER PROPERTIES OF CLERODENDRON SERRATUM" EXTRACTS

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Introduction: Growing popularity and worldwide acceptance of alternative medicine has drawn attention of many researchers towards exploration and identification of drug candidates from natural sources that can cure chronic diseases effectively. The present study scientifically validates the antioxidant, anti-inflammatory and anticancer properties of *Clerodendron serratum* root extracts.

Methods: The roots were first extracted with alcohol, and then fractionated with petroleum ether, diethyl ether, ethyl acetate, ethyl methyl ketone and n-butanol, according to increasing polarity. These fractions were checked for cytotoxicity. Among these fractions ethyl acetate fraction showed relatively more cytotoxicity followed by ethyl methyl ketone fraction. Based on this, ethyl acetate (EA) fraction was selected for testing its anti-inflammatory and anticancer properties *in vitro* and *in vivo*. Antioxidant effects of the extracts was studied by its ability to scavenge DPPH free radical by ESR method. The anti-inflammatory properties of ethyl acetate fraction were tested in carrgeenan induced rat air-pouch model of inflammation. Anti-cancer activity of EA fraction was proved by testing their anti-proliferative effect in chronic myeloid leukemia (CML) cell line K562. The active ingredients of EA fraction were isolated and further characterized on LC/MS, Proton and C^{13} NMr, HRMS

Results: ESR studies show promising DPPH radical scavenging activities of EA extracts of *C. serratum*. In the carrageenan induced rat air-pouch model of inflammation, decrease in exudate volume and total cell population in the EA fraction treated animals was observed compared to carrageenan treatment alone. In carrageenan treated animals oxidative stress was found to be increased in the pouch tissue as evidenced by an increase in lipid peroxidation and oxidized glutathione levels. The decreased levels of antioxidant enzymes such as catalase, glutathione peroxidase and glutathione reductase, indicate the induced oxidative stress in animals during inflammation. These levels were restored in EA fraction treated animals, and thus showing its anti-inflammatory properties.

EA fraction showed potent anti-proliferative effects on chronic myeloid leukemia cell line, K562. "Classical laddering" of DNA, which is regard as a marker of apoptosis, was clearly detected in cells treated with EA fraction. Flow cytometric analysis of the K562 cells treated with EA fraction (10 g/ml) showed of 41% cell in sub G0/G1 phase i.e undergoing apoptosis. Flow cytometric analysis of treated cells showed the increase of hypodiploid apoptotic cells in a concentration-dependent manner and decrease of the cells at S and G2 phase of cell cycle. These results thus suggest the induction of apoptosis in chronic myeloid leukemia cells by ethyl acetate fraction of the plant. Further purification of EA fraction on HPLC revealed one major and one minor peak. These peaks were identified as saponin glycosides with molecular weights of 774 and 755.

OL-29

ANTIOXIDANT CAPACITY OF COMMONLY CONSUMED VEGETABLES OF GUJARAT STATE.

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Introduction: Epidemiological studies have demonstrated an inverse association between consumption of fruits and vegetables and degenerative diseases. As plant foods contain many different classes and types of antioxidants, knowledge of their total antioxidant capacity (TAC), which is the cumulative capacity of food components to scavenge free radicals, would be useful for epidemiological purpose.

Methods: Total eighteen vegetables were analyzed for their TAC along with vitamin-C, ß-carotene and total phenols .The TAC of pure vitamin-C and gallic acid was also studied.

Results: The content of vitamin-C, ß-carotene and total phenols in studied vegetables ranged from 1.1 to 132.5 mg%, 4.56 to 5436.52 µ g% and 46.52 to 1056.22 mg%, respectively. Six vegetables showed TAC values more than 60.0%, five vegetables showed TAC values in between 40-60% and seven vegetables showed TAC values less than 40%. Coriander leaves showed highest amount of all three studied antioxidants as well as TAC value. The TAC of pure vitamin-C and gallic acid (at 40 µg/ ml concentration) was found to be 20.57 and 37.27 %, respectively. Comparing the TAC of all vegetables with pure compounds it was found that 17 vegetable showed higher TAC values than vitamin-C while 11 vegetables showed higher TAC than gallic acid. The correlation and regression analysis of the antioxidant compounds and TAC of vegetables showed positive but insignificant relationship.

Conclusion: Most of the vegetables showed better TAC values than the pure compounds. Hence, it is recommended that the supplementation of natural antioxidants through balance diet containing enough vegetables could be the most effective measure in protecting the body against various oxidative stresses.

OL-30

SERUM APOLIPOPROTEINS A-I, A-II, B, C-II, C-III, E AND TOTAL ANTIOXIDANT STATUS IN ANGIOGRAPHICALLY PROVED CAD CASES

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Introduction: Lipoproteins & apolipoproteins in ethnic Indians vis a vis other ethnic grouApolipoproteins are being studied in coronary artery disease for their possible role in the formation and reduction of atherosclerotic plaques. Many unsubstantiated reports have generated intense interest in the role of antioxidants in preventing heart disease. In the present study however, it is an attempt to study the same in Indian population.

Methods: 124 healthy individuals were selected after screening them for normal lipid profile, x-ray chest, TMT, ECG and for diabetes; where as 121 angiographically proved cases were selected for the present work, in which 76 CAD cases were found to be diabetic.

Results: The mean values for apolipoprotein A-I, A-II, B, C-II, C-III, E and total antioxidant status were 94.75 ± 27.48 mg/dl, 23.04 ± 7.67 mg/dl, 90.65 ± 28.57 mg/dl, 4.63 ± 3.38 mg/dl, 7.52 ± 3.26 mg/dl, 2.73 ± 1.48 mg/dl , 52.13 ± 48.32 mg/dl and TAS 0.92 ± 0.18 m mol/L respectively for diabetic CAD cases ; where as in healthy controls mean serum value for apoA-I was 118.81 ± 21.88 mg/dl, apoA-II was 28.43 ± 6.01 mg/dl, apoB was 87.14 ± 21.68 mg/dl, apoC-II was 3.33 ± 2.38 mg/dl, apoC-III was 7.20 ± 2.76 mg/dl, apoE was 2.69 ± 1.50 mg/dl and lp(a) was 20.98 ± 18.66 mg/dl and TAS 1.10 ± 0.14 m mol/L respectively.

Conclusion: Mean levels of apolipoprotein A-I ($P<0.001$), A-II ($P<0.001$) and TAS ($P<0.001$) were significantly decreased in CAD cases than the control group; where as ApoC-II ($P<0.001$) and Lp(a) levels ($P<0.001$) were significantly increased in angiographically proved CAD cases.

OL-31

INFLUENCE OF SELENIUM STATUS ON THE CELLULAR DEFENCE AGAINST OXIDATIVE DAMAGE DURING AGING IN THE INSECT *C.cephalonica*

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Introduction: Aging results from the deleterious effect of free radicals produced in the course of cellular metabolism. Age associated changes reported in antioxidant enzymes seems to lack uniformity. In the present study the extent of oxidative stress mediated by oxygen free radicals during aging of the insect *C.cephalonica* was assessed with respect to Selenium status.

Methods: Se deficiency was created in the insect model *C.cephalonica* by formulating Se deficient diet. Age associated changes in broad spectrum of antioxidants and indicators of oxidative stress were assessed in both Se deficient experimental and Se supplemented (1.0 ppm) control group.

Results and conclusions: Se deficiency in experimental model *Corcyra cephalonica* resulted in impaired mitochondrial substrate oxidations and lowered thiol levels. Decline in antioxidant defense mechanism with aging process was also evident as shown by continuous drop in GSH/GSSG ratio accompanied with linear increase in lipid peroxidation. While SOD and GST activity increased with aging process, catalase and GSH-Px activity enhanced upto third instar followed by drop in late instar stages. In Se deficient group, the extent of increase in antioxidant enzymes with aging were low compared to Se supplemented group which is directly correlated with high level of lipid peroxidation, pointing to the prevalence of oxidative stress in Se deficiency. Electron microscopic observations revealed structural changes such as loss cristae with proliferative and degenerative changes of mitochondria in Se deficiency. Involvement of Se in maintaining the redox balance and thereby delaying the aging process is evident from the present study.

OL-LS

COMPENSATORY ROLE OF A 182 KDA PROTEIN, A CARDIAC ISOFORM OF 2M IN THE FREE RADICAL MEDIATED CELLULAR DAMAGE IN PATHOLOGICAL CONDITIONS

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Extensive studies on the characterization of a 182-kDa protein that appears in the blood sera of animals subjected to aortic constriction have shown it to play a crucial signaling role in the development of cardiac hypertrophy. Further molecular characterization has shown it to be the cardiac isoform of 2M, a liver specific stress protein. Based on the sequence homology of 2M, the growth factor binding domain and protease inhibitor domain of the 182-kDa protein have been characterized. A similar protein has been found in induced levels in the sera of patients with hypertrophy suffering from various cardiac ailments such as ventricular septal defect, atrial septal defect, aortic regurgication

and aortic stenosis. Recently we have reported the possible compensatory contribution of this protein in cardiac cellular damage and its expression in other secondary cardiac ailments including Hansen's disease and Diabetes. The prominent high-level induction of this protein in leprosy and in diabetes has further triggered our thrust to unravel its global role in several pathological conditions. The protease inhibitor effect of this protein has received much attention and a new dimension of its compensatory mechanism in free radical damage has been highlighted. It is proposed that the 182-kDa protein may interfere with the rate limiting step in the conversion of xanthine dehydrogenase to xanthine oxidase. It is suggested that the calcium overload during the hypertrophic condition may trigger the Protease mediated conversion of xanthine dehydrogenase to Xanthine oxidase during the reoxygenation phase, which ends up in the production of free radicals and ultimately the tissue damage. The 182-kDa protein may interfere to bring down the level of free radicals by inhibiting the conversation and thereby may prevent the cellular damage in several pathological conditions

RANDOX LECTURE

ANTIOXIDANTS THE FUTURE IN DISEASE MANAGEMENT

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Antioxidant and free radical involvement in disease processes have been documented in the literature for many years. Antioxidant measurement methods however have not progressed and are seen as a research tool in development laboratories with restricted sample throughput due to laborious preparation and processing of patient samples. Some laboratories utilise in-house methods of measurement for many markers, which lack standardisation and present conflicting results in collaborative studies involving different laboratories.

Antioxidant markers are now available for use on high throughput, automated, clinical chemistry analysers, complete with standardised controls and calibrator samples. Excellent assay precision, standardisation, minimal sample volumes and preparation and ease of use, are just some advantages of automated antioxidant testing.

Therapeutic potential of the numerous antioxidant markers in disease processes will only be recognised with large scale clinical studies in different sample groups. These comprehensive clinical studies require analysis of large sample numbers for a broad range of markers to elucidate the relationship and effectiveness of antioxidant markers both separately and in combination.

This paper presents results that demonstrate the clinical utility of antioxidant marker and introduces the practical implications of utilising automated analysis over the more conventional manual and in-house methods.

OL-33

EFFECT OF *DESMODIUM GANGETICUM* ON ANTIOXIDANT ENZYMES IN STREPTOZOTOCIN -INDUCED DIABETIC RATS

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Introduction: The elevated levels of blood glucose in diabetes produces oxygen free radicals, which cause membrane damage due to peroxidation of membrane damage due to peroxidation of membrane lipids and protein glycation. Desmodium gangeticum (L.) DC. (Family Leguminaceae) has been used in Indian system of medicine as a bitter tonic, febrifuge, digestive and in treatment of various other inflammatory conditions. Present study was undertaken to study the effect of Desmodium gangeticum on antioxidant enzymes in diabetic rats.

Methods: Streptozocin -induced diabetic rats were treated with D. gangeticum extract and its fractions and the levels of antioxidant enzymes were estimated. The effect was assessed on lipid peroxidation (LPO) and the antioxidant defense enzymes like GSH and SOD in rat tissues.

Results: Flavanoid fraction demonstrated hypoglycemic effect in the diabetic rats significantly at 25 mg/kg within three hours after administration whereas the alkaloid fraction did not have any significant reduction. Oral administration of the flavanoid fraction reduced the hepatic TBARS (1.83 nmoles/ mg protein as compared to 3.78 nmoles/ mg protein of control), GSH level (5.47 nmoles/ mg protein as compared to control of 3.86 nmoles/ mg protein) and SOD activity (7.56 units/ mg protein as compared to 13.97 of control).

Conclusions: The results indicate that the flavanoids fraction of D. gangeticum possess anti-oxidant properties in diabetic conditions.

OL-32

SPIRULINA PREVENTS DOXORUBICIN-INDUCED FREE RADICAL RELEASE AND APOPTOSIS IN CARDIOMYOCYTES IN VITRO

M Khan [1,2], **V.K. Kutala** [1,2], S.Varadharaj[1], J.C.Shobha[2], M.U.R.Naidu[2], P.Kuppusamy[1]

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Doxorubicin (DOX) is a highly potent antineoplastic agent, but its use is limited by the risk of developing cardiomyopathy. Redox activation of DOX to form reactive oxygen species (ROS) and apoptosis has been implicated in DOX-induced cardiotoxicity. In our recent study, we have demonstrated that Spirulina, blue - green algae containing antioxidants protected the mice against DOX-induced cardiotoxicity. In this study, we investigated the effect of Spirulina and C-phycocyanin, one of the main constituent of Spirulina, against DOX -induced ROS generation and apoptosis in isolated rat cardiomyocytes in vitro. Cardiomyocytes were pretreated with Spirulina (50 µg/ml) and C-phycocyanin (25 µM) for 1 h followed by DOX (10 µM) and incubated for 24 h. The ROS generation in cardiomyocytes was evaluated by dicholorofluorescein (DCF), hydroethidine (HE) and cell death by measuring LDH in the cell culture supernatant. Apoptosis was assessed by measuring annexin V-FITC/propidium iodide double staining using flow cytometry, DNA laddering by gel electrophoresis and caspase-3 activity by spectrophotometric assay. Treatment with the DOX produced significant loss in cell viability, and apoptosis, indicated by the presence of increase in the fraction of annexin-V-FITC positive fluorescent cells. The DOX-induced increase in ROS was reduced to control levels in cells treated with Spirulina and C-phycocyanin. Pretreatment with Spirulina and C-phycocyanin reduced the number of positive fluorescent cells. Doxorubicin-induced DNA fragmentation to a clear ladder pattern, while Spirulina and C-phycocyanin prevented DNA fragmentation. Caspase-3 activity was significantly increased with DOX whereas Spirulina and C-phycocyanin inhibited the caspase-3 activation. Our results suggest that C-phycocyanin, a potent free radical scavenger protected against DOX-induced cardiotoxicity by decreasing ROS and apoptosis in cardiomyocytes.

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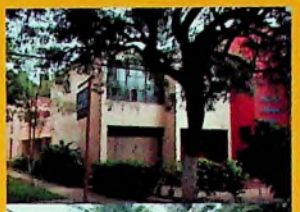
See P-154

Posters Programme










POSTER: SESSION I Symposia 1 to 6
Date: 10TH JANUARY 2005
Time: 1430-1600 H
Venue: Cardinal Gracias Hall, Ground Floor St. John's Medical, College Robert Koch Bhavan

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN MOLECULAR MEDICINE

P1 **OFR-MODIFIED NUCLEOSOME: A NEO-ANTIGEN FOR SYSTEMIC LUPUS ERYTHEMATOSUS**
Farah Mansoor and Rashid Ali
Department of Biochemistry, Jawaharlal Nehru Medical College, A.M.U., Aligarh 202 002

P2 ***IN VITRO* AND *IN VIVO* PROTECTION BY T. CHEBULA FROM GAMMA-RADIATION INDUCED DNA AND MEMBRANE DAMAGES**
N. M. Gandhi, **S. Vetrivel** and C. K. K. Nair
Radiation Biology and health sciences Division, Bhabha Atomic Research Centre
Trombay, Mumbai 400 085 India

P3 **SCID-A SMOKE CONDENSATE INDUCED NOVEL DNA DAMAGING FACTOR FROM HUMAN LYMPHOCYTES**
L. Srinivas, R.P.Rao
Adichunchanagiri Biotechnology and Cancer Research Institute, B.G.Nagara-571 448, India.

P4 **STUDIES ON ALACHLOR MODIFIED PLASMID DNA**
Suraiya Jabeen and Khursheed Alam
Department of Biochemistry, Jawaharlal Nehru Medical College,
A.M.U., Aligarh 202 002

TOPIC: CADIOVASCULAR DISEASES

P5 **EFFECT OF ASCORBIC ACID ADMINISTRATION IN POST-REPERFUSED PATIENTS OF MYOCARDIAL INFARCTION.**
P. Bhakuni, M. Chandra*, M.K. Misra
Department of Biochemistry, Lucknow University, Lucknow
*Department of Medicine, KG Medical University, Lucknow, India.\

P6 **EFFECT OF SPERMACOCE HISPIDA LINN. (SEED EXTRACT) ON REDOX STATUS IN HYPERLIPIDEMIC PATIENTS WITH AND WITHOUT DIABETES MELLITUS**
K.Kaviarasan, M.M.Arjunan, K.V. Pugalendi*
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Department of Biochemistry, Faculty of Science,
Annamalai University, Annamalainagar - 608 002, Tamilnadu, India.

P7 **ENHANCED OXIDATION OF LDL IN HYPERCHOLESTEROLEMIA AND ITS REVERSAL BY ASCORBIC ACID AS A HYPOTHESIS OF PREVENTING ATHEROSCLEROSIS**
S. Das, A.Manocha, Snehlata, N.Das and L.M.Srivastava
Department of Biochemistry, Sir Ganga Ram Hospital and All India Institute of Medical Sciences, New Delhi., India

P8 **STATUS OF SOME FREE RADICAL SCAVENGING ENZYMES IN BLOOD OF THE PATIENTS REPERFUSED AFTER MYOCARDIAL INFARCTION.**
V. K. Dwivedi, M. Chandra, P.C. Misra and M.K. Misra
Department of Biochemistry, Lucknow University, Lucknow Department of Medicine, K.G's Medical University, Lucknow, India.

P9 **SPIRULINA PREVENTS DOXORUBICIN-INDUCED FREE RADICAL RELEASE AND APOPTOSIS IN CARDIOMYOCYTES IN VITRO**

M Khan [1,2], **V.K. Kutala** [1,2], S.Varadharaj[1], J.C.Shobha[2], M.U.R.Naidu[2], P.Kuppusamy[1]
[1]Ohio State University, Columbus, OH, USA, [2]Nizam's Institute of Medical Sciences, Hyderabad, India

P10 **CARDIOPROTECTIVE EFFECT OF S-ALLYL CYSTEINE ON ISOPROTERENOL-INDUCED MYOCARDIAL INFARCTION IN RATS**

M. Padmanabhan and P. Stanely Mainzen Prince
Department of Biochemistry, Annamalai University, Annamalainagar, Tamil Nadu, India.

P11 **EFFECT OF BALSAMODENDRON MUKUL ON THE OXIDANT-ANTIOXIDANT STATUS IN HYPERTENSIVE PATIENTS**

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P12 **REDOX STATUS AND GLYCOPROTEIN COMPONENTS IN HYPERTENSIVE PATIENTS TREATED WITH MELOTHRIA MADERASPATANA LEAF EXTRACT**

B.Raja, M.M.Arjunan, K.V. Pugalendi
Siddha Division, Govt. Kamaraj Hospital, Chidambaram. Department of Biochemistry, Annamalai University

P13 **EFFECT OF AEGLE MARMELOS ON LIPID PEROXIDES AND LIPIDS ON ISOPROTERENOL-INDUCED MYOCARDIAL INFARCTION IN RATS**

M. Rajadurai and P. Stanely Mainzen Prince
Department of Biochemistry, Annamalai University, Annamalainagar, Tamil Nadu, India.

P14 **LIPID PEROXIDATION & GLUTATHIONE SYSTEM IN CARDIAC DISEASES**

Rajni R. Shivnani and Vijaya A. Haldankar
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Professor & Head Dept. of Biochemistry, T.N. Medical College & B.Y.L. Nair Ch. Hospital, Mumbai 400 008

P15 **EFFECT OF VITAMIN E ON HUMAN BLOOD XANTHINE OXIDASE IN ISCHEMIC MYOCARDIAL DISORDERS.**

Rashmi Raghuvanshi, M. Chandra, P.C. Misra and M.K. Misra
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P16 **EFFECT OF ATORVASTATIN ON OXIDATIVE STRESS.**

V. Save*, G Rajadhykshya**, N Patil*
* Department of Biochemistry, ** Department of Medicine,
L.T.M.Medical College, Sion, Mumbai

P17 **HOMOCYSTEINE AND OXIDATIVE STATUS IN ISCHEMIC HEART DISEASE**

A S Yadav, V R Bhagwat, I. M. Rathod Department of Biochemistry, M. I. .M. S. R. Medical College, Latur- 413531 Maharashtra-INDIA

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN DIABETES MELLITUS

P18 **ANTIDIABETIC AND ANTIOXIDANT EFFECT OF PTEROSTILBENE ON STREPTOZOTOCIN INDUCED DIABETIC RATS**

M. Amarnath Satheesh and L.Pari
Department of Biochemistry, Annamalai University, Annamalainagar, Tamil Nadu, India.

P19 **ANTIOXIDATIVE AND HYPOLIPIDEMIC EFFECTS OF INDIAN HERBAL PREPARATIONS STREPTOZOTOCIN INDUCED DIABETIC RATS**

Anu Chandra, Abbas Ali Mahdi and R.K.Singh
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P20 **EFFECT OF *DESMODIUM GANGETICUM* ON ANTIOXIDANT ENZYMES IN STREPTOZOTOCIN - INDUCED DIABETIC RATS**

R. Govindarajan, M. Vijayakumar, Ch. V. Rao, A.K.S. Rawat and P. Pushpangadan
Pharmacognosy and Ethnopharmacology Division, National Botanical Research Institute, Lucknow 226 001

P21 **OXIDATIVE PROTEIN & LIPID DAMAGE IN TYPE 2 DIABETES MELLITUS**

K.N. Kalaivanam*, M. Dharmalingam#, S.R. Marcus*
Depts of Biochemistry* and Endocrinology#, M.S.Ramaiah Medical College, Bangalore, 560 054, India

P22 **ANTIDIABETIC ACTIVITY OF HYDRO-ALCOHOLIC EXTRACT OF *CRATEVA NURVALA BUCH.* IN ALLOXAN-INDUCED DIABTES IN RATS**

A. Kasliwal, N. Raut, N. Gaikwad
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P23 **ANTIOXIDANTS ROLE IN THE CONTROL OF IN TYPE II DIABETES MELLITU**

E.P. Kumar*,Senthil. R, Girish S. Parhate, B.Suresh.
JSS College of Pharmacy, Ooty.

P24 **LEVEL OF INCREASED METHYL GLYOXAL AND REDUCED ANTI OXIDANT STATUS ARE THE INDICATIONS OF SEVERITY OF COMPLICATIONS IN DIABETES MELLITUS.**

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P25 **IMPACT OF UMBELLIFERONE ON OXIDATIVE STRESS IN PLASMA AND LIVER OF STREPTOZOTOCIN DIABETIC RATS**

B. Ramesh and K.V. Pugalendi
Department of Biochemistry, Annamalai University, Annamalainagar 608 002, Tamilnadu, India.

P26 **POSTPRANDIAL LIPEMIA, OXIDATIVE STRESS AND NITRIC OXIDE END PRODUCTS IN TYPE 2 DIABETIC PATIENTS WITH MACROANGIOPATHY**

Ritu Saxena, JK Gambhir, *SV Madhu, Rimi Shukla, KM Prabhu
Departments of Biochemistry and *Medicine; Univ College of Medical Sciences & GTB Hospital, Shahdara, Delhi-110095

P27 **EVELOPMENT OF A NOVEL MODEL FOR SCREENING ANTIDIABETIC ACTIVITY BY INDUCING HYPERGLYCEMIA WITH PYROGALLOL, A PROOXIDANT**

A. There, Y. Mundhada, M. Wanjari, P. Dixit, S. Umathe.
Dept. of Pharmaceutical Sciences, Nagpur University, Nagpur.

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN LIVER DISEASES

P28 **ANTIOXIDANT ACTIVITY OF VEDIC GUARD IN ANTI-TUBERCULAR DRUGS INDUCED HEPATOTOXICITY IN RATS**

Rema Razdan, **Amar dev**
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P29 **ALTERATION OF LIVER LIPID PEROXIDATION AND ANTIOXIDANT ENZYMES IN EXPERIMENTAL DIABETES: ROLE OF N-BENZOYL-D-PHENYLALANINE AND METFORMIN**

N.Ashok Kumar and L.Pari
Department of Biochemistry, Annamalai University, Annamalainagar - 608002, Tamil Nadu, India.

P30 **OXIDATIVE STRESS DURING LIVER CIRRHOSIS RESULTS IN MODIFICATION OF METAL BINDING CAPACITY OF SERUM ALBUMIN**

Anup Ramachandran, Jayasree Basivi Reddy, C.E. Eapen & K.A. Balasubramanian
Wellcome Trust Research Laboratory, Department of Gastrointestinal sciences

P31 **EFFECT OF ANTIOXIDANT (L-ASCORBIC ACID) ON NICKEL INDUCED ALTERATION OF NUCLEIC ACID CONCENTRATION IN RATS.**

Nazmun L, Raisa NK, Swastika Das*, AM Patil**, SA Dhundasi , KK Das
Department of Physiology, Department of Pathology**, Al Ameen Medical College ,Bijapur-586108 ,Department of Chemistry*, BLDEA's College of Engineering, Bijapur - 586103, India.

P32 **HEPATOPROTECTIVE ACTIVITY OF ARIEL ROOTS OF FICUS BENGALENSIS**

V.R Mallurwar, A.K. Pathak
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P33 **INFLUENCE OF DIALLYL DISULFIDE ON OXIDATIVE STRESS IN N- NITROSODIETHYLAMINE INDUCED HEPATOCARCINOGENESIS**

T. Manivasagam and P. Subramanian
Department of Biochemistry, Annamalai University, Annamalainagar - 608002, Tamil Nadu, India.

P34 **DIALLYL TETRASULPHIDE ATTENUATES CADMIUM INDUCED OXIDATIVE DAMAGE IN RAT LIVER**

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P35 **ANTIOXIDANT AND HEPATOPROTECTIVE ACTIVITY OF ARJUNOLIC ACID**

Prabu Daniel 1, Anbalagan.N1., Moni Mallika2, Balakrishna K 3.
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2 Department of Microbiology, Sri Ramachandra Medical College and Research Institute (Deemed University), Chennai.
3 Department of Phytochemistry, Captain Srinivasamurty Research Institute for Siddha, Arumbakkam, Chennai.

P36 **FREE RADICAL SCAVENGING AND HEPATOPROTECTIVE ACTIVITY OF BORRERIA HISPIDA**

Prabu Daniel 1, Anbalagan.N1., Moni Mallika2, Balakrishna K 3.
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2 Department of Microbiology, Sri Ramachandra Medical College and Research Institute (Deemed University), Chennai.
3 Department of Phytochemistry, Captain Srinivasamurty Research Institute for Siddha, Arumbakkam, Chennai.

P37 **INFLUENCE OF A NOVEL SYNTHETIC CURCUMINOID ON FIBROTIC MARKERS IN ALCOHOL AND PUFA INDUCED TOXICITY.**

R. Rukkumani and Venugopal P. Menon
Department of Biochemistry, Annamalai University,
Annamalai Nagar - 608 002, Tamilnadu, India

P38 **OXIDATIVE STRESS IN EXPERIMENTAL LIVER MICROVESICULAR STEATOSIS: ROLE OF MITOCHONDRIA AND PEROXISOMES**

N. Sathish kumar, C.E. Eapen, Anna B. Pullimood
and Kunissery..A.Balasubramanian
Wellcome Trust Research Laboratory, Department
of Gastrointestinal sciences

P39 **ANTI-OXIDANT ACTIVITY OF GLYCYNHIZA GLABRA LINN, ON CARBON TETRACHLORIDE INDUCED HEPATO-TOXICITY IN RAT**
K. Shaheena, Ziyaunahman AR, MH Dehghan
M.E.S. Society's Allana College of Pharmacy, Pune 411001

P40 **HEPATOPROTECTIVE AND ANTI-OXIDANT POTENTIAL OF VENTILAGO MADRASPATANA ROOT BARK EXTRACTS IN RATS**
Shanmuganathan.K, Raju Ilavarasan S.Venkataraman, Prabu Daniel.E, K.Sujith, Chandra Mohan.P
C.L.Baid Metha College OF Pharmacy, Chennai-965

P41 **FERULIC ACID, A NATURAL PROTECTOR AGAINST CARBON TETRACHLORIDE INDUCED LIVER TOXICITY**
M. Srinivasan and Venugopal P. Menon
Department of Biochemistry, Annamalai University, Annamalai Nagar - 608 002, Tamilnadu, India

P42 **HEPATOPROTECTIVE EFFECT OF LUPEOL AND ITS ESTER DERIVATIVE ON EXPERIMENTAL HYPERCHOLESTEROLEMIA**
V. Sudhahar, S. Ashok kumar, P. Varalakshmi
Department of Medical Biochemistry,
Dr. ALM. Post Graduate Institute of Basic Medical Sciences,
University of Madras, Taramani Campus, Chennai 600 113.

P43 **ANTIINFLAMMATORY, ANALGESIC AND ANTIOXIDANT EFFICACY OF BARLERIA LUPULINA LINDL**
V.Suba, V.Ramarao, R.Kumaravelrajan
Department of Pharmacology, Vels College of Pharmacy, Chennai

P44 **HEPATOPROTECTIVE AND ANTITUMOR ACTIVITY OF SOY ISOFLAVONES**
Tajdar Husain Khan, Lakshmi Prasad, Tamanna Jahangir & Sarwat Sultana*
Section of Chemoprevention and Nutrition Toxicology Department of Medical Elementology and Toxicology Jamia Hamdard (Hamdard University), Hamdard Nagar New Delhi 110062, India.

P45 **ANTIOXIDANT TOLERANCE OF LIVER AFTER CADMIUM INDUCED HEPATIC INJURIES**
R. Shukla A. Sharma & M. Kumar
Cell & Molecular Bio. Lab. Department of Zoology,

P46 **INFLUENCE OF OXIDATIVE STRESS-INDUCED GASTROINTESTINAL ALTERATIONS ON PHARMACOKINETICS OF METFORMIN IN RATS**
M. Wanjari, A. There, A. Joharapurkar, C. Chopde, S. Umathe.
Dept. of Pharmaceutical Sciences, Nagpur University, Nagpur.

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN RENAL DISEASES

P47 **LIPID AND RENAL OXIDATIVE INJURY: ROLE OF EICOSAPENTAENOATE-LIPOATE (EPA-LA) DERIVATIVE**
S. Ashok Kumar, V Sudhahar and P Varalakshmi.
Department of Medical Biochemistry, Dr ALM PGIBMS, University of Madras, Taramani Campus, Chennai 600 113

P48 **NITRIC OXIDE LEVELS IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS**
S. R. Meenakshi, Rajni Agarwal,
Department of Biochemistry, M.S.Ramaiah Medical College, Bangalore, India.

P49 PROTECTIVE EFFICACY OF *MENTHA PIPERITA* AGAINST ARSENIC INDUCED RENAL DAMAGES IN SWISS ALBINO MICE

***Mukesh Kumar Sharma,** Ambika Sharma and Madhu Kumar
*Department of Zoology, S.N.K.P. Govt. (P.G.) College, Neem Ka Thana-332713, Distt-Sikar, (Rajasthan), Department of Zoology, University of Rajasthan, Jaipur-302004 (India)

P50 SSESSMENT OF ANTIOXIDATIVE POTENTIAL OF *TERMINALIA CHEBULA* AGAINST Fe-NTA INDUCED RENAL PROLIFERATIVE RESPONSE AND TOXICITY

Lakshmi Prasad, Tajdar Husain Khan, Tamanna Jahangir & Sarwat Sultana*
Section of Chemoprevention and Nutrition Toxicology Department of Medical Elementology and Toxicology Jamia Hamdard (Hamdard University), Hamdard Nagar New Delhi 110062, India.

P51 IMPACT OF URSOLIC ACID ON ETHANOL-MEDIATED OXIDATIVE DAMAGE IN RAT KIDNEY

R. Saravanan, K.V.Pugalendi
Department of Biochemistry, Faculty of Science, Annamalai University, Annamalai Nagar 608 002, Tamilnadu, India

P52 ROLE OF METHYL GLYOXAL IN ASSOCIATION WITH FREE RADICAL DAMAGE AND ANTIOXIDANT STATUS IN UREMIA.

S. Mukhopadhyay [1], **S. Sen**, M kar [1], A K Ghosh
Department of Biochemistry, Nilratan Sircar Medical College and Hospital, Kolkata 700014, W B, India

P53 RENAL OXIDATIVE STRESS BY PULCHA LANCEOLATA (RASNA)

Tamanna Jahangir, Tadjar Hussan Khan, Lakshmi Prasad & Sarwat Sultana
Section of Chemoprevention and Nutrition Toxicology, Department of Medical Elementology and Toxicology Jamia Hamdard (Hamdard University) Hamdard Nagar, New Delhi 110062 , India

P54 PROTEIN THIOLS AND FREE IRON IN UREMIA

S. Upadhya, M. Prakash
Department of Biochemistry, Kasturba Medical College, Manipal

TOPIC: FREE RADICALS AND ANTI OXIDANTS IN NEUROLOGICAL DISORDERS

P55 EFFECT OF CYCLOOXYGENASE-2 (COX-2) ON RESTRAINT STRESS INDUCED ALTERATIONS IN DIFFERENT BEHAVIORAL AND BIOCHEMICAL PARAMETERS

Ashish Dhir, Pattipati S Naidu and S.K Kulkarni
Pharmacology Division
University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh-160014, India

P56 BRAIN OXIDATIVE STRESS AND COGNITIVE IMPAIRMENT IN ACUTE TREATMENT OF 3-NITROPROPIONIC ACID-INDUCED NEUROTOXICITY AS AN ANIMAL MODEL OF HUNTINGTON'S DISEASE

PK. Bansal, N. Sehgal, SSV. Padi, SN. Pattipati, A. Kumar
Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India

P57 OXIDATIVE STRESS, VITAMIN E, ASCORBIC ACID AND REDUCED GLUTATHIONE STATUS IN SCHIZOPHRENICS

Gora Dadheech, Sandhya Mishra, Praveen Sharma & Shiv Gautam*
Department of Biochemistry and Department of Psychiatry*
S.M.S. Medical College and Hospital, Jaipur, Rajasthan

P58 ROLE OF HOMOCYSTEINE IN AETIOPATHOGENESIS AND CONTROL OF EPILEPSY

S.K. Handa, S. Prabhakar, S. Majumdar

Department of Neurology and Experimental Medicine, PGIMER, Chandigarh, India.

P59 **PROANTHOCYANIDIN SUPPLEMENTATION MODULATES CHOLINERGIC SYSTEM IN ADULT RAT BRAIN**

Jolitha, A.B and Asha Devi, S
Lab.Gerontology, Department of Zoology, Bangalore University, Bangalore 560056, India

P60 **DOES REM SLEEP DEPRIVATION RESULT IN OXIDATIVE STRESS?**

D.C. Mathangi,
Department of Physiology, Sri Ramachandra Medical College and Research Institute, Porur, Chennai 600 116 India

P61 **POSSIBLE ROLE OF FREE RADICALS IN A MODEL OF NEUROPATHIC PAIN IN RATS WITH CHRONIC CONSTRICTION NERVE INJURY**

S. S .V. Padi, SK. Kulkarni
Pharmacology Division, University Institute of Pha

P62 **NICOTINE OXIDATIVE AND ANTIOXIDANT PROPERTIES IN CNS**

Prabu Daniel.E* , Suba.V, Kumaravelrajen.R
*C.L.Baid Metha College Of Pharmacy, Chennai-96
Vels College Of Pharmacy, Chennai

P63 **ROLE OF NITRIC OXIDE IN THE EXPERIMENTAL MODELS OF PARKINSON'S DISEASE**

Sarika Singh and M. Dikshit
Central Drug Research Institute

P64 **EFFECT OF CARVEDILOL ON OXIDATIVE STRESS-RELATED NEUROTOXICITY AND COGNITIVE IMPAIRMENT IN A RAT MODEL OF HUNTINGTON'S DISEASE**

N. Sehgal, PK. Bansal, SSV. Padi, A. Kumar, SN. Pattipati
Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India.

POSTER: SESSION II Symposia 7 to 15
Date: 11TH JANUARY 2005
Time: 1430-1600 H
Venue: Cardinal Gracias Hall, Ground Floor St. John's Medical, College Robert Koch Bhavan

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN CANCER

P65 **THERAPEUTIC EFFECT OF Semecarpus anacardium LINN NUT EXTRACT ON MITOCHONDRIAL TCA CYCLE AND RESPIRATORY CHAIN ENZYMES IN MAMMARY CARCINOMA RATS**
G. Arathi AND P. Sachdanandam
Dr. A.L.Mudaliar post Graduate Institute Of Basic MedicaL ScienceS, Department Of Medical Biochemistry, University OF MadraS, Taramani campus, ChennaI- 600113. India

P66 **REGULATORY ROLE OF ROS AND RNS IN EXPRESSION OF TRANSCRIPTION FACTOR AP1 IN BREAST CANCER**
J. Bhattacharjee and M.L. Sherpa
Department of Biochemistry, Lady Hardinge Medical College, New Delhi.

P67 **LIPID PEROXIDATION IN CANCER**
Javapraksh Babu N, Ratnakumar C H and V Sriramulu
Department of Biochemistry, Rangaraya Medical College Kakinada 533008

P68 **CHEMOPREVENTIVE EFFECT OF GINGER ON CIRCULATORY LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN 1,2-DIMETHYL HYDRAZINE INDUCED COLON CANCER.**
Manju, V and Nalini N
Department of Biochemistry, Annamalai University, Annamali nagar Tamil Nadu India.

P69 **SERUM GLUTATHIONE-S-TRANSFERASE IN ORAL CANCER**
K. Prabhu, G Bhat and D.M. Vasudevan
Dept of Biochemistry Kasturba Medical College Manipal 576104, Amritha Institute of Medical Sciences, Cochin 682026

P70 **ACTIVITIES OF ENZYMES OF RESPIRATORY BURST IN THE NEUTROPHILS FROM ORAL CANCER PATIENTS SUBJECTED TO RADIOTHERAPY**
Reshma K, A. V.Rao, Vasudevan D.M.,
Department of Biochemistry
Centre for Basic Sciences
Kasturba Medical College
Mangalore

P71 **MODULATORY EFFECT OF TERMINALIA ARJUNA ON GLYCOPROTEIN LEVELS ON DIETHYLNIROSAMINE INDUCED LIVER CANCER IN RATS**
S.Sivalokanathan, M. Ilayaraja and M.P. Balasubramanian
Department of Pharmacology and Environmental Toxicology,
Dr. ALM Post Graduate Institute of Basic Medical Sciences,
University of Madras, Taramani, Chennai-600 113, India.

P72 **MODULATORY EFFECT OF RESVERATROL ON COLONIC MUCOSAL LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN 1,2-DIMETHYLHYDRAZINE INDUCED COLON CARCINOGENESIS**
M. Sengottuvelan and N. Nalini
Department of Biochemistry, Faculty of Science, Annamalai University,
Annamalai Nagar- 608 002, India.

P73 **LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN PATIENTS WITH PAPILLARY THYROID CARCINOMA**

N. Senthil, S. Manoharan
Department of Biochemistry, Faculty of Science,
Annamalai University, Annamalai Nagar 608 002.

P74 **CHEMOPREVENTIVE EFFICACY OF MENTHOL**

Shalini Shukla, Priti Saraswat and Ashok Kumar
Cancer and Radiation Biology Laboratory,
Department of Zoology, University of Rajasthan, Jaipur-302004. . India

P75 **ETIOLOGY, PREVENTION AND CLINICAL TREATMENT OF CERVICAL CANCER IN RAJASTHAN**

N.Sharma, A. Kumar, and A. Bhargav,
Department of Zoology, University of Rajasthan, Jaipur

P76 **BERBERINE CHLORIDE ENHANCES RADIATION RESPONSE IN MICE BEARING EHRLICH ASCITES CARCINOMA**

Shaival Kamalaksha Rao and Ganesh Chandra Jagetia

P77 **EFFECT OF GALLIUM NITRATE ON TAMOXIFEN TREATED BREAST CANCER RELATED HYPERCALCEMIA WITH REFERENCE TO CALCIUM AND MAGNESIUM IN RATS**

D. Sugapriya, P. Sachdanandam and P. Shanthi
Dr. A.L.Mudaliar Post- Graduate
Institute Of Basic Medical Sciences,
University Of Madras, Taramani Campus,
Chennai- 600113. India

P78 **EFFECT OF KALPAAMRUTHAA ON LIPID PEROXIDATION AND ENZYMIC ANTIOXIDANTS IN DMBA INDUCED MAMMARY CARCINOMA**

K.Veena and P. Sachdanandam
Department of Medical Biochemistry,
Dr.A.L.Mudaliar Post-Graduate institute of Basic Medical Sciences,
University of Madras, Taramani Campus, Chennai-600113, India.

TOPIC: FREE RADICAL AND ANTIOXIDANTS IN INFECTIOUS DISEASES AND IMMUNITY

P79 **MEASUREMENT AND SIGNIFICANCE OF 3-NITROTYROSINE IN SLE PATIENTS**

Fozia Khan and Rashid Ali
Department of Biochemistry, Jawaharlal Nehru Medical College, A.M.U., Aligarh 202 002

P80 **EFFECT OF VITAMIN C ON ANTIOXIDANTS IN PULMONARY TUBERCULOSIS**

S.Garg, H. C. Mehta, K. B. Gupta
Department Of Biochemistry, PGIMS, Rohtak, India

P81 **ROLE OF FLAVONOIDS IN THE ALLEVIATION OF ANEMIA ASSOCIATED WITH VISCERAL LEISHMANIASIS**

Gargi Sen, Tuli Biswas
Department Of Physiology, Indian Institute Of Chemical Biology, Kolkata-700032

P82 **ANTIOXIDANT VITAMINS AND IMMUNE FUNCTION IN LEPROSY.**

S.Girish P.Bulakh R.Melinkeri
Ph.D.Student ,Ex-Professor & Head ,Professor & Head
Department of Biochemistry, B. J. Medical College, Pune.

P83 **OXIDATIVE STRESS AND THE ROLE OF ANTIOXIDANTS IN THE TREATMENT OF PULMONARY TUBERCULOSIS**

M.Shelgaonkar,1 Dr. R. Munje,2 Dr. S.Shelgaonkar3, Dr. S. Umathe4
1. Institute of Diploma in Pharmacy, Nagpur, 2. Govt.Medical College, Yavatmal, 3. Govt.Medical College, Nagpur, 4. Pharmaceutical Sciences, Nagpur

P84 **ELEVATION OF METHYL GLYOXAL IN ASSOCIATION WITH FREE RADICAL MEDIATED DAMAGE IN RHEUMATOID ARTHRITIS.**

S. Mukhopadhyay[1], B. Majhi, S. Sen, M. Kar[1], A. K. Ghosh..

P85 **TUBERCULOSIS PATIENTS EXPRESSING HIGH LEVELS OF ANTI-INDUCIBLE NITRIC OXIDE SYNTHASE (INOS) ACTIVITY EXHIBITED CIRCULATING MYCOBACTERIUM ANTIGEN 85B COUPLED TO IGG IN SERUM**

Najmul Islam, Manish Kumar Varshney and Jawed Iqbal
Department of Biochemistry, J.N. Medical College, A.M.U., Aligarh 202 002
Department of Biochemistry, Nilratan Sircar Medical College and Hospital, Kolkata 700014, W B, India

P86 **COMPARITIVE STUDY OF VITAMIN E, A AND C LEVELS IN LEPROSY SUBTYPES**

C.V. B. Prasad, M.V.Kodliwadmath
Department of Biochemistry, J.N.Medical College, Nehru Nagar, Belgaum-590010, Karnataka, INDIA.

P87 **ENDOTHELIAL FUNCTION AND CARDIOVASCULAR DISEASE**

P.R.Usha, M U R Naidu,
Nizam's Institute of Medical Sciences, Hyderabad.

P88 **PEROXYNITRITE INDUCED MODIFICATION OF HUMAN DNA: IMPLICATIONS IN ETIOPATHOGENESIS OF SLE**

Safia Habib, Moinuddin, Rashid Ali
Department of Biochemistry, J.N. Medical College, A.M.U., Aligarh (INDIA)

P89 **OXIDATIVE STRESS IN RHEUMATOID ARTHRITIS**

S.Singh, Z. Ali, S.K. Tiwari
Department of Biochemistry, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN ENVIRONMENTAL BIOLOGY

P90 **OXIDATIVE STREE IN COPD- IS CHULLA SMOKE MORE DANGEROUS THAN TOBACCO SMOKE?**

J. Bardapurkar, D. Bokankar, S. Javed, S. Bardapurkar, V. Patil.
Biochemistry department, Government Medical College, Aurangabad, Maharastra, India.

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN FOOD SCIENCES

P91 **NUTRITIONAL INTERVENTION IN REDUCING THE ALTERATIONS IN ANTIOXIDANT ENZYMES CAUSED BY LEAD**

Herman Sunil D'souza, Geraldine Menezes, VenkateshT.
National Referral Center for Lead Poisoning in India
Department of Biochemistry, St. John's Medical College, Bangalore, Karnataka, India

P92 **ANTI-RADICAL ACTIVITY OF TEA POLYPHENOLS**

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Radiation Chemistry & Chemical Dynamics Division, Bhabha Atomic Research Centre, Mumbai- 400 085. and
[†]Tobacco Carcinogenesis Group, Advanced Centre for Treatment Research and Education

P93 **FREE RADICAL REACTIONS AND ANTIOXIDANT ACTIVITIES OF SESAMOL: PULSE RADIOLYTIC AND BIOCHEMICAL STUDIES**

Ravi Joshi[1], M. Sudheer Kumar[2], M. K. Unnikrisnan[2] and T. Mukherjee[1]
[1]Radiation Chemistry & Chemical Dynamics Division, Bhabha Atomic Research Centre, Mumbai 400085, INDIA.
[2]College of Pharmaceutical Sciences, Manipal 576119, INDIA.

P94 **FREE RADICAL SCAVENGING AND RADIATION PROTECTION BY TOCOPHEROL MONOGLUCOSIDE**

V Salvi and CKK Nair
Radiation Biology & Health Sciences Division, Bhabha Atomic Research Centre, Trombay, Mumbai-400085, India

P95 **ROLE OF ANTIOXIDANTS IN THE TREATMENT OF IRON DEFICIENCY ANAEMIA**

Rukhsana Ab. Rub, Ziyaurrehman, Rashmi Tambe.
M.C.E. Society's Allana College of Pharmacy, Pune 1.

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN HUMAN REPRODUCTION AND INFERTILITY

P96 **SIGNIFICANCE OF CHANGES IN LIPID PEROXIDATION AND ANTIOXIDANT STATUS AFTER SUPPLEMENTATION OF VITAMIN-E AND C IN WOMEN AT RISK OF PRE-ECLAMPSIA.**

S.B.Patil, M.V.Kodliwadmath* , Sheela M.Kodliwadmath**.
Research fellow, Dept. of Biochemistry*, Dept. of OBG**
J.N.Medical College, Belgaum. 590010. Karnataka.

P97 **FREE RADICALS MEDIATED TESTICULAR LESIONS BY CADMIUM CHLORIDE AND MODULATION BY PANAX GINSENG**

S. Sharma, M. Sharma & M. Kumar
Cell & Molecular Bio. Lab. Department of Zoology,
University of Rajasthan, Jaipur.

P98 **MALONDIALDEHYDE FOR PREDICTION OF PRE-ECLAMPSIA**

P.C. Sindu, K. Parvathi, Saboora Beegum
Department of Biochemistry, Govt.Medical College, Calicut.

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN DENTISTRY

P99 **LIPID PEROXIDATION AND ANTIOXIDANTS STATUS IN PATIENTS WITH PERIODONTITIS**

K.Panjamurthy1, S. Manoharan1, C.R. Ramachandran2
1Department of Biochemistry, Faculty of Science, Annamalai University, Annamalai Nagar - 608 002. India.
2Dean . Rajah Muthiah Dental College and Hospital Annamalai University, Annamalai Nagar 608002. India.

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN TOXICOLOGY

P100 **PROTECTIVE EFFECTS OF CURCUMIN AGAINST NICOTINE-INDUCED PULMONARY FIBROSIS IN WISTAR RATS.**

C. Kalpana and Venugopal P. Menon
Annamalai University, Annamalai Nagar-608 002, Tamilnadu, India.

P101 **COMPARATIVE EFFECTS OF CURCUMIN AND ITS ANALOG IN CARBON TETRACHLORIDE INDUCED HEPATOTOXICITY IN RATS**

N. Kamalakkannan and Venugopal P. Menon
Department of Biochemistry, Annamalai University, Annamalainagar, Tamil Nadu, India.

P102 **IRON AND ZINC INTERACTIONS AT THE SITE OF ABSORPTION IN RATS: RELEVANCE TO INTESTINAL PEROXIDATIVE DAMAGE**

K. Madhavan Nair and B. Sreedhar
Biophysics Division, National Institute of Nutrition (ICMR),
Jamai -Osmania, Hyderabad, India 500007

P103 **PROTECTIVE EFFECT OF FERULIC ACID AGAINST NICOTINE INDUCED OXIDATIVE STRESS IN BRONCHOALVEOLAR LAVAGE (BAL)**

A. Ram Sudheer and Dr. Venugopal P. Menon
Department of Biochemistry, Annamalai University,
Annamalai Nagar - 608 002, Tamilnadu, India.

P104 **EFFECT OF LUPEOL AND ITS ESTER ON CYCLOPHOSPHAMIDE INDUCED LIPEMIC-OXIDATIVE STRESS**

P. T. Sudharsan, Y. Mythili, P. Varalakshmi.
Department of Medical Biochemistry, Dr. ALM PGIBMS, University of Madras, Chennai 113, India.

P105 **ALCOHOL AND THERMALLY OXIDIZED PUFA INDUCED OXIDATIVE STRESS: ROLE OF N-ACETYLCYSTEINE**

P. Suresh Varma and Venugopal P. Menon
Department of Biochemistry, Annamalai University,
Annamalai Nagar - 608 002, Tamilnadu, India.

P106 **OXIDANTS AND ANTIOXIDANTS IN MYOCARDIAL INFARACTION AND REPERFUSION**

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Department of Biochemistry and Cardiology, Christian Medical College and Hospital, Ludhiana.

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN AGEING

P107 **AGE RELATED CAHNGES IN LIPID PEROXIDATION AND ANTIOXIDANTS IN ELDERLY PEOPLE.**

Akila, V Prashanth, H Harish Chandra, V D'Souza, and B D'Souza Department of Biochemistry K M C Mangalore India

P108 **FREE RADICALS AND ANTIOXIDANTS IN AGEING**

Satish Balasaheb Nimse*, Dilipkumar Pal**
Division of Pharmaceutical Chemistry, Seemanta Institute of
Pharmaceutical Sciences, Jharpokharia, Mayurbhanj - 757086, Orissa, India.

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN RADIATION BIOLOGY

P109 **RADIATION-AND FREE RADICAL-EXPOSURE AND REGULATION OF PROTEIN SYNTHESIS BY HEME REGULATED EUKARYOTIC INITIATION FACTOR 2 KINASE**

Abhijeet P. Kulkarni[1], T. P. A. Devasagayam[2] and Jayanta K. Pal[1]*
[1]Department of Biotechnology, University of Pune, Pune 411 007 and [2]Radiation Biology and Health Sciences Division, Bhabha Atomic Research Centre, Mumbai 400 085

P110 **RADIATION-AND FREE RADICAL-EXPOSURE AND REGULATION OF PROTEIN SYNTHESIS BY HEME REGULATED EUKARYOTIC INITIATION FACTOR 2 KINASE**
RADIOPROTECTION OF SWISS ALBINO MOUSE BY TINOSPORA CORDIFOLIA

Jaimala and S. Pahadiya
Dept. of Zoology, University of Rajasthan, Jaipur-302004.

P111 **TREATMENT OF ASCORBIC ACID IMPROVES HEALING OF EXCISION WOUNDS IN MICE EXPOSED TO DIFFERENT DOSES OF ?-RADIATION**
K. V. N. Mallikarjun Rao, Ganesh Chandra Jagetia and Rajanikant G. K.
Department of Radiobiology, Kasturba Medical College, Manipal 576 104.

P112 **RADIO-PROTECTION OF DNA BY FERULIC ACID**
DK Maurya, V Salvi and CKK Nair
Radiation Biology & Health Sciences Division, Bhabha Atomic Research Centre, Trombay, Mumbai-400085, India.

P113 **A NOVEL METHOD OF TESTING RADIOPROTECTIVE EFFECT OF OCIMUM SANCTUM IN PATIENTS UNDERGOING HEMI BODY IRRADIATION (HBI).**
Prasad D, Ghadge M, Sarin R, Raste A, et al, Tata Memorial Hospital.

P114 **RADIOPROTECTIVE EFFECT OF SESAMOL ON ?-RADIATION INDUCED CELLULAR CHANGES IN CULTURED HUMAN BLOOD LYMPHOCYTES**
N. Rajendra Prasad, Venugopal P. Menon and K.V. Pugalendi
Department of Biochemistry, Faculty of Science, Annamalai University, Annamalainagar - 608 002, India.

P115 **RADIOPROTECTIVE EFFECTS OF *SPINACIA OLERACEA* ON BIOCHEMICAL ACTIVITY IN BRAIN OF SWISS ALBINO MICE AFTER GAMMA EXPOSURE**
Rajesh Kumar Verma*, Dhankesh Meena, R. Sisodia and A. L. Bhatia
Department of Zoology, Univ. of Rajasthan, Jaipur (India) 302004

P116 **RADIOMODULATORY INFLUENCE OF NUTMEG (*MYRISTICA FRAGRANS*) EXTRACT IN SWISS ALBINO MICE AFTER WHOLE BODY EXPOSURE TO GAMMA RADIATION**
M. Sharma, S. Sharma & M. Kumar
Cell & Molecular Bio. Lab. Department of Zoology,
University of Rajasthan, Jaipur.

P117 **RADIO PROTECTIVE ROLE OF ACETONE EXTRACT OF *CENTELLA ASIATICA* AGAINST GAMMA RADIATION INDUCED LESION IN PERIPHERAL BLOOD OF MICE'**
R. Sharma, Jaimala
Department of Zoology, University of Rajastan, Jaipur 302004 India

P118 **MODULATION OF RADIATION INDUCED ALTERATION IN THE ANTIOXIDANT STATUS OF MICE BY NARINGIN.**
D. Subba Reddy, Tiyyagura Koti Reddy and Ganesh Chandra Jagetia
Department of Radiobiology, Kasturba Medical College, Manipal 576 104.

P119 **ELISA TO MONITOR AMPLIFIED HAEMOLYSIS BY THE COMBINED ACTION OF OSMOTIC STRESS AND RADIATION : APPLICATION IN MONITORING RADIO PROTECTOR AND MEMBRANE STABILIZERS.**
Saurabh Chatterjee, Sudha Premachandran, R S Bhagewadikar and T B Poduval.
Immunology and Hyperhermia section, Radiation Biology and Health Sciences Division, Baba Atomic Research Centre Trombay, Mumbai 400085 India.

POSTER: SESSION III Symposia 16-20 and Free poster presentation
Date: 12TH JANUARY 2005
Time: 1430-1600 H
Venue: Cardinal Gracias Hall, Ground Floor St. John's Medical, College Robert Koch Bhavan

TOPIC: FREE RADICALS AND ANTIOXIDANTS IN APOPTOSIS

P120 **INHIBITION OF CELL PROLIFERATION AND INDUCTION OF APOPTOSIS BY GENISTEIN IN EXPERIMENTAL HEPATOCELLULAR CARCINOMA**
Dechen Chodon and D Sakthisekaran
Department of Medical Biochemistry
Dr ALM Post Graduate Institute of Basic Medical Sciences
University of Madras, Taramani, Chennai-600113, India

P121 **ANTIOXIDANT AND IMMUNOMODULATORY PROPERTIES OF CHLOROPHYLLIN IN *VITRO* AND *IN VIVO***
D. Sharma, S. Santosh Kumar, B. Shankar and K. B. Sainis
Bioscience Group, Bhabha Atomic Research Centre, Mumbai-400 085, India

TOPIC: NITRIC OXIDE

P122 **ALTERATIONS OF ARGINASE ACTIVITY IN SWISS MICE AS A RESPONSE TO WHOLE BODY HYPERTHERMIA (WBH)**
R. S. Bagewadikar, Saurabh Chatterjee, Sudha Premachandran, and T.B.Poduval
Immunology and Hyperthermia Section, Radiation Biology and Health Sciences Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400 085, India.

P123 **IRRADIATION INDUCED NITRIC OXIDE PRODUCTION, iNOS ACTIVATION AND INHIBITION BY CURCUMIN AND NICOTINAMIDE.**
H. Narang and M. Krishna
Radiation Biology and Health Sciences Division, B.A.R.C, Mumbai, India

P124 **SYNTHESIS AND EVALUATION OF ANTI-OXIDANT ACTIVITY OF DERIVATIVES OF GALLIC ACID**
Natrajan Ramalakshmi, Thiyagarajan Saraswathy1, Subramani Arun kumar2
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2.Department of pharmaceutical chemistry S.R.M college of pharmacy.

TOPIC: RECENT ADVANCES IN MARKERS IN OXIDATIVE STRESS

P125 **GLUTATHIONE REDOX PARADIGM IN BLOOD, A BIOMARKER OF OXIDATIVE STRESS IN EPIDEMIC DROPSY PATIENTS**
Kishore Babu, Subhash K.Khanna, Mukul Das
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TOPIC: USE OF NATURAL PRODUCTS IN HUMAN HEALTH

P126 **PROTECTIVE EFFECT OF *EMBLICA OFFICINALIS* WITH SPECIAL REFERENCE TO ARSENIC INDUCED MICRONUCLEI FORMATION IN MOUSE BONE MARROW**
Ambika Sharma, Mukesh Kumar Sharma and Madhu Kumar
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P127 **KINETICS OF OXIDATION OF CURCUMIN BY T-BUTOXYL RADICALS IN WATERACETONITRILE MEDIUM.**
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P128 **QUERCETIN A BIOFLAVONOID, ATTENUATES LIPOSACCHARIDES INDUCED HEPATOTOXICITY AND OXIDATIVE STRESS IN RAT LIVER**
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P129 **INFLUENCE OF *Terminalia bellarica* ON THE RESPONSE OF *Saccharomyces cerevisiae***
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P130 **ANTI-OXIDANT ACTIVITY OF EXRACTS OF BALIOSPERMUM MONTATUM**
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P131 **IN VITRO INHIBITION OF LIPID PEROXIDATION IN FISH BY TURMERIC (CURCUMA LONGA)**
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P132 **ANTI-OXIDANT ACTIVITY OF POLYPHENOLICS ENRICHED ETHANOLIC EXTRACT OF *POLYGALA CHINENSIS* LINN.**
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P133 **FREE RADICAL- INDUCED MEMBRANE DAMAGE AN ANTIOXIDATIVE/RADIOPROTECTIVE ROLE OF HERBAL PRODUCTS**
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P134 **ANTIOXIDANT ACTIVITY OF SOME COMMON PLANTS OF MEDICINAL VALUE : A COMPARATIVE STUDY**
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P135 **ANTARTH, A POLYHERBAL PREPARATION PROTECTS AGAINST THE DOXORUBICIN-INDUCED TOXICITY WITHOUT COMPROMISING ITS ANTINEOPLASTIC ACTIVITY**
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P136 **CHEMOPREVENTIVE & ANTIMUTAGENIC PROPERTIES OF *ACACIA NILOTICA* (LINN.) ON 7,12-DIMETHYLBENZ(A) ANTHRACENE INDUCED SKIN PAPILLOMAGENESIS IN SWISS ALBINO MICE**
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P137 **FREE RADICAL SCAVENGING POTENTIAL OF HELICTERES ISORA.L**
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P138 BIOACTIVITY GUIDED FRACTINATION OF CORONOPUS DIDYMUS: A FREE RADICAL SCAVENGING PERSPECTIVE

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P139 IN VITRO ANTIOXIDANT ACTIVITY OF METHANOL EXTRACT OF CITRUS AURANTIFOLIA FRUITS

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P140 ANTIOXIDANT PROPERTIES OF GERMINATED FENUGREEK SEEDS

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P141 ANTIOXIDANT EFFECT OF GREEN LEAFY VEGETABLES

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P142 ANTI-INFLAMMATORY AND ANTIOXIDANT ACTIVITIES OF CASSIA FISTULA LINN BARK EXTRACTS

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P143 ANTIARTHRITIC AND FREE RADICAL SCAVENGING ACTIVITY OF RICINUS CUMMUNIS ROOT EXTRACT

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P144 ANTIINFLAMMATORY, ANALGESIC AND ANTIOXIDANT EFFICACY OF BARLERIA LUPULINA LINDL

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P145 FREE RADICAL QUENCHING EFFECT OF SEMECARPUS ANACARDIUM LINN. NUT EXTRACT AGAINST ADJUVANT ARTHRITIS.

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P146 **ORAL ADMINISTRATION OF GINGER (ZINGIBER OFFICINALE ROSC.), PROTECTS AGAINST THE RADIATION-INDUCED MORTALITY**

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P147 **HERBAL RELEIF FROM FREE RADICAL STRESS.**

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P148 **STUDY ON FREE RADICAL SCAVENGING &PROTECTIVE EFFECT OF Hybanthus enneaspermus UPON ISOLATED HEPATOCYTES**

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P149. **A NOVEL BIOACTIVE ANTIOXIDANT MOLECULE THAT PROTECTS CELLS AGAINST XENOBIOTIC-INDUCED CELL INJURY**

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P150 **ANTIOXIDANT PROPERTIES OF WHEATGRASS (*TRITICUM AESTIVUM* L.) EXTRACTS AS A FUNCTION OF THEIR GROWTH**

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P151 **EFFECT OF NARINGIN ON FERRIC IRON INDUCED OXIDATIVE DAMAGE IN VITRO**

Tiyyagura Koti Reddy and Ganesh Chandra Jagetia

P152 **STUDIES ON ANTIDIABETIC AND ANTIOXIDANT ACTIVITIES OF CAESALPINIA CRISTA**

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P153 **FREE RADICAL SCAVENGING ACTIVITY OF EXRACTS OF LUFFA ACUTANGULA VARAMARA**

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P154 **ALTERATIONS IN THE INTESTINAL GLYCOCALYX AND BACTERIAL FLORA IN RESPONSE TO ORAL INDOMETHACIN**

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P155 **LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN SICKLE CELLANAEMIA.**

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P156 **OXIDATIVE STRESS AND ENZYMATIC ANTIOXIDANT RESPONSE IN NEONATES SUFFERING FROM RESPIRATORY DISORDERS.**

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P157 **ANTIOXIDANTS IN NEONATAL HYPERBILIRUBINEMIA**
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P158 **OXIDATIVE STRESS AND ANTIOXIDANT STATUS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)**
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P159 **EFFECT OF ROS AND PROTEINASE INHIBITOR IN RHEUMATOID ARTHRITIS**
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P160 **GLUTATHIONE PEROXIDASE (GPx)-LIKE ANTIOXIDANT ACTIVITY OF ANTITHYROID DRUGS.**
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P-161 **A STUDY ON THE ROLE OF RNI AND ROI IN SLE**
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P-162 **ANTIOXIDANT MECHANISM OF HYDROXY CINNAMIC ACIDS**
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P163 **BINDING OF BILIRUBIN TO ERYTHROCYTES FROM CANCER PATIENTS**
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P164 **OXIDATIVE STRESS IN THYROTOXICOSIS**
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P165 **INFLUENCE OF BEEDI SMOKING ON LIPID PEROXIDATION STATUS**
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P166 **ANTIOXIDANT ACTIVITY OF COLEUS AROMATICUS**
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P167 **OXIDATIVE STRESS AND ANTIOXIDANT SYSTEM IN CEREBROVASCULAR ACCIDENTS.**
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P168 **MELATONIN IMPROVES CIRCULATORY ANTIOXIDANT LEVELS DURING N-NITROSODIETHYLAMINE - INDUCED HEPATOCARCINOGENESIS IN RATS**

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P169 **RADIO PROTECTION OF SWISS ALBINO MICE BY SEED EXTRACT OF BRASSICA COMPESTRIS (VAR SARASON)**

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P170 **RADIO PROTECTIVE EFFECT OF ALCOHOLIC EXTRACT OF MENTHA PIPERITA LINN IN SWISS ALBINO MICE**

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P171 **EVALUATION OF CHEMOPREVENTIVE ACTION AND ANTIMUTAGENIC EFFECT OF THE STANDARDIZED PANAX GINSENG EXTRACT, EFLA400, IN SWISS ALBINO MICE**

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P172 **ANTI-OXIDANT ACTIVITY OF *HYGROPHILA AURICULATA* IN STREPTOZOTOCIN-INDUCED DIABETIC RATS**

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P-173 **TOXICITY OF PENTACHLOROPHENOL METABOLITES TO HEPG2 CELLS IN CULTURE**

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P-174 **DYSLIPIDEMIA, OXIDATIVE STRESS AND ANTIOXIDANT STATUS IN PREGNANCY INDUCED HYPERTENSION**

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P-175 **GINSENG EXTRACT EXHIBITS ANTIMUTAGENIC ACTIVITY AGAINST MUTAGENESIS IN VARIOUS STRAINS OF SALMONELLA TYPHIMURIUM**

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P-176 **PROTECTIVE EFFECT OF GINGER EXTRACT AND ITS FORMULATION IN OXIDATIVE STRESS (ETHANOL)-INDUCED GASTRIC MUCOSAL LESIONS IN EXPERIMENTAL RATS**

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P-177 **EVALUATION OF ROLE OF OXIDANTS STRESS IN REHEUMATOID ARTHRITIS**

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P-178 OVEREXPRESSION OF CONNEXIN 43 ATTENUATES NITRIC OXIDE PRODUCTION IN ENDOTHELIAL CELLS: AN EPIPHENOMENON OF CELL DENSITY DEPENDENT ENOS DISTRIBUTION IN ENDOTHELIAL CELLS

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P-179 FLY ASH LEACHATE INDUCES CYTOTOXIC EFFECT IN CLUTURED HEPATOCYTES OF FRESH WATER FISH *CHANNA PUNCTATA* (BLOCH) AN IN-VITRO ASSESSMENT

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P-180 PROTECTIVE ROLE OF *Piper betle* (L) ON CCl_4 INDUCED OXIDATIVE STRESS *IN VITRO*

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P-181 ANTIOXIDANT STATUS OF TWO VARIETIES OF *Solanum nigrum* (L)

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P-182 PROTECTIVE EFFECT OF *Moringa oleifera* ON ETHANOL AND CCl_4 INDUCED OXIDATIVE STRESS IN RATS

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P-183 MOLECULAR STUDIES ON THE EFFECT OF *Withania somnifera* USING Hep 2 CELL LINE.

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P-184 COMPARATIVE STUDY OF SELECTED ANTIOXIDANTS IN FLOWERS AND LEAVES OF WHITE AND VIOLET VARIETY OF *Clitoria ternateae* (SANGU PUSHPAM)

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P-185 PREVENTIVE EFFECTS OF *Artemisia vulgaris* LEAVES AGAINST DNA DAMAGE INDUCED *IN VITRO* BY OXIDANTS

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P-186 EVALUATION OF THE PROTECTIVE EFFECTS OF *Triticum aestivum* AGAINST OXIDATIVE STRESS IN SELECTED *IN VITRO* MODELS

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P-187 EFFECT OF THYROID STATE ON HYDROPEROXIDE METABOLISING ENZYMES OF RAT TESTES

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P-188 ***INVITRO*** **ANTIOXIDANT ACTIVITY OF FICUS GLOMERATA**
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P-189 **MODULATION OF RADIOSENSITIVITY OF BREAST CANCER CELL LINE MCF-7 BY TOCHOPHEROL SUCCINATE**
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P-190 **AMELIORATIVE EFFECT OF IRRADIATED CURCUMIN AND FERULIC ACID IN EXPERIMENTAL DIABETES**
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P-191 **ANTI-OXIDANT ACTIVITY OF MURRAYA KOENIGII IN ALLOXAN-INDUCED DIABETIC RATS**
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P-192 **INFLAMMATORY MARKERS IN CORONARY ARTERY DISEASE**
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P-193 **TOTAL ANTIOXIDANTS AND OXIDATIVE STRESS IN LIVER CIRRHOTICS**
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P-194 **EFFECT OF VITAMIN E ADMINISTRATION ON ALCOHOL LEAD INTERACTIVE NEUROTOXICITY**
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P-195 **EFFECTS OF VITAMIN E ADMINISTRATION ON ALCOHOL LEAD INTERACTIVE HEPATOTOXICITY**
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P-196 **OXIDATIVE STRESS AND PRE-ECLAMPSIA**
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P-197 **PARAOXONASE ACTIVITY AND OXIDATIVE STRESS IN NON INSULIN DEPENDENT DIABETES MELLITUS WITH AND WITHOUT MICROALBUMINURIA**
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P-198 **TOTAL ANTIOXIDANT STATUS IN CHRONIC RENAL FAILURE (CRF) PATIENTS ON HEMODIALYSIS (HD) AND CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD).**
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P-199 **ANTIOXIDANT ENZYMES AS BIOMARKERS FOR LEAD TOXICITY**
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P-200 AN EVALUATIN OF ANTIOXIDANT AND NUTRITIONAL STATUS OF NON-INSULIN DEPENDENT DIABETES MELLITUS SUBJECTS

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P-201 EVALUATION OF TOTAL ANTIOXIDANT STATUS IN THYROID DYSFUCTION

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P-202 THE TOTAL ANTIOXIDANT CAPACITY IN TYPE II DIABETIC PATIENTS

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P-203 OXIDATIVE STRESS, PROTEIN GLYCATION AND DYSLIPIDEMIA IN ESSENTIAL HYPERTENSION

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P-204 EVALUATION OF SERUM MARKERS IN ALCOHOLICS

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P-205 REFERENCE INTERVALS FOR SERUM APOLIPOPROTEINS A-I, A-II, B, C-II, C-III, E IN HEALTHY INDIAN

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P-206 GLUCOSE CATALYSED OXIDATION OF AMINO ACIDS IMPLICATIONS IN ATHEROSCLEROSIS

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P-207 COMPARATIVE *IN VITRO* STUDY OF WATER- AND LIPID-SOLUBLE FREE RADICAL INITIATORS IN RAT ERYTHROCYTES

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P-208 PLASMA CERULOPLASMIN LEVELS IN PREGNANCY WITH PRE-ECLAMPSIA

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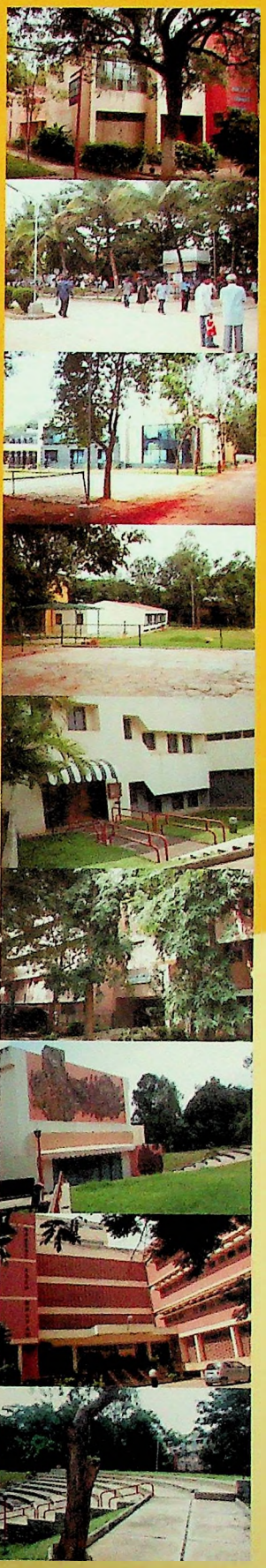
Posters Abstracts



Date : 10th January 2005

Time : 1430-1600 H

Chairpersons : Mahadevappa. K L India
Irfan Rahman USA

FREE RADICALS AND ANTIOXIDANTS IN MOLECULAR MEDICINE

P-1

OFR-MODIFIED NUCLEOSOME: A NEO-ANTIGEN FOR SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Free radicals and other reactive oxygen species (ROS) have been implicated in the etiology of a number of human diseases including systemic lupus erythematosus (SLE). It is a prototype autoimmune disease characterized by the production of antibodies to components of the cell nucleus in association with a diverse array of clinical manifestations. Nucleosome, the fundamental and structural unit of chromatin, is emerging as the most reactive substrate among nuclear antigens. The aim of the present study is to evaluate the binding of circulating autoantibodies in SLE to OFR (oxygen free radicals)-modified nucleosome.

Methods: Nucleosome isolated from goat liver was modified by hydroxyl radical generated by illumination of hydrogen peroxide at 254 nm UV light. Modifications incurred in nucleosome were analyzed by various physico-chemical techniques. Sera from thirty SLE patients were studied for their binding to native and modified nucleosome by direct binding and inhibition ELISA.

Results: UV absorption spectrum of nucleosome modified by hydroxyl radical showed decrease in absorbance with hypochromicity of 52% at 260 nm. Nuclease S1 digestion and thermal denaturation studies confirmed the generation of single stranded regions upon modification of nucleosome by hydroxyl radical. The possible role of OFR-modified nucleosome in SLE was probed by evaluating the binding of thirty SLE sera to native and hydroxyl-modified nucleosome. Nearly all sera showed higher binding with hydroxyl-nucleosome as compared to native nucleosome, and a p value of < 0.001 indicated significant difference in binding of these antigens.

P-2

IN VITRO AND *IN VIVO* PROTECTION BY T. CHEBULA FROM GAMMA-RADIATION INDUCED DNA AND MEMBRANE DAMAGES

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Introduction: Search of the radioprotecting chemical is one of the problems addressed by the radiobiologists. Although a large number of chemicals were screened which can protect cells from radiation damage, very few has shown promise due to the toxicity problems. *T. Chebula*, popularly known as *Harde* in Ayurvedic system of medicine, is used as laxative, diuretic and as a cardiotonic.

Methods: Plasmid pBR322 (250-300 ng) was exposed to ā-radiation at various doses, in presence and absence of plant extract. The DNA was electrophoresed in 1% agarose gel using 0.8 mM Tris-Borate/2mM EDTA buffer at pH 8.3 and the bands were visualised after staining with Ethidium bromide under uv light and photographed using AAB GelDoc system. The supercoiled (ccc) and opencircular (oc) forms of DNA were estimated. Exposure to radiation results in conversion of the ccc form of plasmid DNA to oc form. For ex *vivo* protection studies the peripheral blood leucocytes were irradiated in presence and absence of plant extract, and were analyzed for the DNA damage using the alkaline single cell gel electrophoresis (comet assay).

Results: Aqueous abstract of this plant fruit, protected the DNA both *in vitro* and ex *vivo*. In *in vitro* test, plasmid pBR322 was protected by the presence of the extract from the ā-radiation. Above 50 Gy gamma-irradiation, The 100% of plasmid gets converted to open circular form; presence of plant extract prevented the conversion by 83.93% at 50 Gy and 77.87% at 100 Gy. Cellular DNA of the human peripheral blood leucocytes were protected form undergoing damage *ex-vivo* from the gamma-radiation, as there was the decrease in the radiation-induced damage measured as tail moment.

Conclusion: The results suggest the ability of the plant extract -which is safe and non-toxic- is protecting the cellular DNA and membranes from the radiation-induced damages, and hence a promising agent for the radioprotection.

P-3

SCID-A SMOKE CONDENSATE INDUCED NOVEL DNA DAMAGING FACTOR FROM HUMAN LYMPHOCYTES

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Introduction: Oxygen is needed by all aerobic organisms to carryout vital functions, but can turn into truant radical causing extensive damage to biomolecules. Smoke condensate from cow dung cake, containing polycyclic aromatic hydrocarbons (PAH), is a potent prooxidant, acting on the membrane lipids inducing peroxidation, and generating HPETE and HETE. The present work is on the intracellular events following oxidative DNA damage by smoke condensate (SC).

Methods: Smoke condensate was prepared by smouldering cow dung cake for 15 minutes and condensed into PBS (10mM, pH 7.4). The condensate was used at 1: 100 dilution corresponding to OD of 1 at 271nm-the signature of PAH. Conditioned media was obtained by incubating human lymphocytes with 100l condensate, dialyzed, the active DNA damaging peak fractioned by G25, purified by RP HPLC. ESI was done for mass determination. All other important parameters to evaluate DNA damage were carried out.

Results: The active DNA damaging factor was released at 20th minute on SC treatment into the medium from human lymphocytes, showing a single peak in RP-HPLC and the mass was 3495 daltons with at 210nm indicating a peptide nature. The active factor was named as SCID, showed the presence of amino acids and absence of S-S groups, and sugar residues. SCID generated superoxide radical, hydroxyl radicals and induced DNA damage (60% at 6nM) induced by SCID was vented by SOD. A threshold 60% DNA damage appeared to be a prerequisite for the release of SCID and SCID induced DNA damage was prevented by SOD to 85%.

Conclusions: SCID is possibly a very novel membrane housed DNA damaging agent and the phenomenon could be referred to as " **membrane mediated DNA damage**".

P-4

STUDIES ON ALACHLOR MODIFIED PLASMID DNA

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Introduction: Alachlor-[2-Chloro-N-methoxymethyl-N-(2,6-diethylphenyl) acetamide] is a chloracetanilide herbicide used to control weeds. The extensive use of Alachlor and exposure to it either directly or through contamination of crops and water evaluates genotomic risk to humans. It is also a potential carcinogen.

Methods: The plasmid DNA (p-DNA) pUC 18 was isolated from E.coli (strain TB 1) and purified. The purified p-DNA was then allowed to interact with Alachlor for 72 hr at 370C in dark and dialyzed extensively. The reaction mixture was then subjected to various physicochemical studies such as UV spectroscopy, thermal denaturation, S1 nuclease and ECoRI digestion. Antibodies against control plasmid and its modified form was then raised in experimental animals. The titre and specificity of induced antibodies was monitored by Immunological techniques.

Results: The UV absorption spectroscopy of Alachlor modified p-DNA showed hyperchromicity as compared to native p-DNA. Treatment of p-DNA with higher concentrations of herbicides induced structural perturbations and was the cause of melting of modified p-DNA comparedto control plasmid, which did not show melting under identical conditions. Nuclease S1 treatment of modified and control plasmid showed generation of single strand breaks in Alachlor modified p-DNA. Restriction mapping of p-DNA and its analog with ECoRI showed the modification of ECoRI specific restriction site. Alachlor modified p-DNA was found to be more Immunogenic in comparison to native p-DNAas assessed by direct binding and inhibition ELISA.

Conclusions: All these physicochemical studies show that herbicide Alachlor causes structural changes in p-DNA rendering it immunogenic as compared to native p-DNA

CARDIOVASCULAR DISEASES

P-5

EFFECT OF ASCORBIC ACID ADMINISTRATION IN POST-REPERFUSED PATIENTS OF MYOCARDIAL INFARCTION.

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Introduction: Myocardial infarction (MI) results in severe oxidative stress causing alterations in the anti-oxidant system of blood. Reperfusion of the infarcted myocardium leads to the generation of toxic reactive oxygen species (ROS) due to burst of oxygen consumption. These ROS have deleterious effects and increase cardiovascular morbidity and mortality. Ascorbic acid is a powerful anti-oxidant capable of detoxifying free radicals and sparing other endogenous anti-oxidants.

In the present study, we have assessed the effect of administration of 500 mg. ascorbic acid for three days on the status of some representative anti-oxidant systems of the blood in the post reperfused patients of MI.

Methods: Anti-oxidants assayed were superoxide dismutase (SOD), ascorbic acid, total thiols along with the levels of cholesterol and malondialdehyde (MDA; as an index of free radical mediated damage) in 15 patients before and after administration of ascorbic acid.

Results: Significant increase in the levels of SOD ($p<0.05$), total thiols ($p<0.025$) and significant decrease in the levels of MDA ($p< 0.1$) and cholesterol ($p< 0.1$) has been observed in the patients after administration of ascorbic acid.

Conclusions: Our findings suggest that administration of ascorbic acid is beneficial for the patients under investigation as it causes augmentation of systems anti-oxidant mechanisms and lowers the levels

P-6

EFFECT OF SPERMACOCE HISPIDA LINN. (SEED EXTRACT) ON REDOX STATUS IN HYPERLIPIDEMIC PATIENTS WITH AND WITHOUT DIABETES MELLITUS

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Introduction: An imbalance in the antioxidant defense system seems to result from the accumulation of LDL or VLDL in the course of hyperlipidemia. Oxidative modification of LDL plays central role in atherosclerosis. Several medicinal plants including Spermacoce species were screened for antioxidant and ROS inhibitory activities. In this study we have analyzed the antioxidant properties of S. hispida on hyperlipidemic and diabetic hyperlipidemic patients

Materials and methods: Twenty patients with hyperlipidemia and fifteen patients with diabetic hyperlipidemia were chosen from Govt. Kamarajar hospital, Chidambaram and given the seed extract of S. hispida. Eighteen subjects served as control. Fasting blood samples were collected at the beginning (baseline) and after 45 days of treatment. The collected blood samples were analysed for lipid peroxidation markers, enzymatic and non enzymatic antioxidants.

Results: The lipid peroxidation markers such as thiobarbituric acid reactive substances (TBARS) and conjugated dienes increased significantly while enzymatic (superoxide dismutase, catalase and glutathione peroxidase) and non enzymatic antioxidants (vitamin C, vitamin E and reduced glutathione) decreased in hyperlipidemic and diabetic hyperlipidemic patients as compared with control. After 45 days of seed extract consumption, a significant reduction in lipid peroxidation markers and elevation in enzymatic and non enzymatic antioxidants were observed in seed extract consumed patients.

Conclusion: Our results show that the plant S. hispida Linn seed extract possess antioxidant properties.

P-7

ENHANCED OXIDATION OF LDL IN HYPERCHOLESTEROLEMIA AND ITS REVERSALBY ASCORBIC ACID AS A HYPOTHESIS OF PREVENTING ATHEROSCLEROSIS

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Hypercholesterolemia is a major risk factor for atherosclerosis (Ath)and related occlusive vascular disease. Oxidative modification of low density lipoprotein (LDL) has been implicated in the pathogenesis of Ath. This evidence led to study the effects of antioxidants on LDL oxidation which by preventing or suppressing prooxidant state can act as antiatherogens. In light of antioxidant properties of ascorbate and our earlier studies on prevention of Ath by AA, we have studied its role on *invitro* oxidative modification of LDL. LDL isolated from fasting normal controls and hypercholesterolemic patients were oxidised in presence and absence of AA and its oxidation level was studied. *Invitro* treatment of LDL with AA prevented oxidative modification, however the dose needed to prevent the oxidation of LDL isolated from controls was lower (40lM) as compared to LDL isolated from patients (80iM). LDL so treated also exhibited decreased electrophoretic mobility. In addition, we have studied the total antioxidant status (TAS) of controls and hypercholesterolemic patients. The (TAS) of patients was significantly less as compared to controls. These observations highlight the benevolent effects of AA in the prevention of LDL oxidation, which is one of the major causative factors of atherosclerosis.

P-8

STATUS OF SOME FREE RADICAL SCAVENGING ENZYMES IN BLOOD OF THE PATIENTS REPERFUSED AFTER MYOCARDIAL INFARCTION.

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Introduction: Oxygen derived free radicals are the cause/consequence of many cardiovascular disorders. Reperfusion of the infracted myocardium results in the burst of oxygen consumption with resultant generation of free radicals and their derivatives. If not scavenged off efficiently by the anti-oxidant system of the body, these may have deleterious effects because these are capable of causing structural and functional alterations in the essential macromolecules. Free radicals also cause lipid peroxidation and modifications in the low density lipoproteins which ultimately results in the formation of atherosclerotic lesions.

In the present communication, we have assessed the levels of some of the anti-oxidant enzymes and extent of free radical mediated damage caused by reperfusion of the patients of myocardial infarction.

Methods: Seventeen patients of myocardial infarction after reperfusion were included in the study. Fifteen age and sex matched healthy persons served as control. Levels of catalase, superoxide dismutase and glutathione reductase were assayed in the blood. As a marker of free radical mediated damage, level of malondialdehyde was also measured.

Results: Our findings show that all the anti-oxidant enzymes studied, show statistically significant decreased levels in the patients compared to control (superoxide dismutase p 0.005; catalase p 0.0005 and glutathione reductase p 0.01). The level of malondialdehyde is significantly (p 0.005) enhanced in the patients.

Conclusions: The results show that reperfusion therapy for myocardial infarction is not completely safe as it impairs the anti-oxidant machinery and thus promotes free radical mediated damage of the tissues, which at times, may result in fatal consequences. Administration of anti-oxidant vitamins may be of help.

P-9

SPIRULINA PREVENTS DOXORUBICIN-INDUCED FREE RADICAL SPIRULINA PREVENTS DOXORUBICIN-INDUCED FREE RADICAL RELEASE AND APOPTOSIS IN CARDIOMYOCYTES IN VITRO

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Doxorubicin (DOX) is a highly potent antineoplastic agent, but its use is limited by the risk of developing cardiomyopathy. Redox activation of DOX to form reactive oxygen species (ROS) and apoptosis has been implicated in DOX-induced cardiotoxicity. In our recent study, we have demonstrated that Spirulina, blue - green algae containing antioxidants protected the mice against DOX-induced cardiotoxicity. In this study, we investigated the effect of Spirulina and C-phycocyanin, one of the main constituent of Spirulina, against DOX -induced ROS generation and apoptosis in isolated rat cardiomyocytes in vitro. Cardiomyocytes were pretreated with Spirulina (50 µg/ml) and C-phycocyanin (25 µM) for 1 h followed by DOX (10 µM) and incubated for 24 h. The ROS generation in cardiomyocytes was evaluated by dicholorofluorescein (DCF), hydroethidine (HE) and cell death by measuring LDH in the cell culture supernatant. Apoptosis was assessed by measuring annexin V-FITC/propidium iodide double staining using flow cytometry, DNA laddering by gel electrophoresis and caspase-3 activity by spectrophotometric assay. Treatment with the DOX produced significant loss in cell viability, and apoptosis, indicated by the presence of increase in the fraction of annexin-V-FITC positive fluorescent cells. The DOX-induced increase in ROS was reduced to control levels in cells treated with Spirulina and C-phycocyanin. Pretreatment with Spirulina and C-phycocyanin reduced the number of positive fluorescent cells. Doxorubicin-induced DNA fragmentation to a clear ladder pattern, while Spirulina and C-phycocyanin prevented DNA fragmentation. Caspase-3 activity was significantly increased with DOX whereas Spirulina and C-phycocyanin inhibited the caspase-3 activation. Our results suggest that C-phycocyanin, a potent free radical scavenger protected against DOX-induced cardiotoxicity by decreasing ROS and apoptosis in cardiomyocytes.

P-10

CARDIOPROTECTIVE EFFECT OF S-ALLYL CYSTEINE ON ISOPROTERENOL-INDUCED MYOCARDIAL INFARCTION IN RATS

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Introduction: In the present study, we have evaluated the pretreatment effect of S-allyl cysteine (SAC) in isoproterenol (ISO) induced myocardial infarction (MI) in albino Wistar rats.

Methods: Rats were orally pretreated with SAC for a period of 45 days and then subcutaneously injected with ISO (150 mg/kg) for two days at an interval of 24 h. After the last treatment, all the rats were sacrificed and the activities of marker enzymes, lipid peroxides and antioxidant status were evaluated.

Results: The increased activities of marker enzymes and lipid peroxides and the deranged antioxidant status were brought back to near normal status with SAC pretreatment in ISO-induced rats.

Conclusion: This study reports the cardioprotective effect of SAC in ISO-induced MI in rats.

P-11

EFFECT OF BALSAMODENDRON MUKUL ON THE OXIDANT-ANTIOXIDANT STATUS IN HYPERTENSIVE PATIENTS

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Introduction Reactive oxygen species interfere with the mechanisms controlling blood pressure (BP), and play an important role in the development of hypertension and vascular damage. The aim of our study was to assess and compare the effect of Balsamodendron mukul (B.mukul) and nifedipine (a strandard antihypertensive drug) on lipid perioxidation, enzymic and non-enzymatic antioxidants in randomly selected patients with essential hypertension

Methods Fifty seven unrelated newly diagnosed hypertensive patients of both sexes (23 males and 34 females) aged 35-70 years with essential hypertension, participitated in this study. Hypertensive patients were randomly divided into 3 groups, they received either single-blind nifedipine (10mg/day) or single-blind *B.mukul* (1.5g/day) or double-blind therapy with nifedipine (10mg/day) and *B.mukul* (1.5g/day), for 6 weeks. All these groups were compared with control subjects. Fasting blood samples was analyzed for lipid peroxidation (TBARS), enzymic antioxidants (SOD, CAT and GPx) and non-enzymatic antioxidants (GSH, Vitamin C and Vitamin E).

Results In hypertension patients the levels of TBARS were elevated while the enzymic antioxidants (SOD, CAT and GPx) and non-

enzymatic antioxidants (GSH, Vitamin C and Vitamin E) levels were lowered as compared to control subjects. On treatment with *B.mukul* and/or nifedipine the TBARS level was significantly decreased ($p<0.05$) and the enzymic and non-enzymic antioxidants levels were significantly elevated as compared to untreated hypertensive patients ($p<0.05$).

Conclusion Thus our results demonstrate that treatment with *B.mukul* has a protective action against oxidative stress in hypertensive patients. Combined therapy with *B.mukul* and nifedipine was comparatively more beneficial than the treatment with *B.mukul* of nifedipine alone.

P-12

REDOX STATUS AND GLYCOPROTEIN COMPONENTS IN HYPERTENSIVE PATIENTS TREATED WITH MELOTHRIA MADERASPATANA LEAF EXTRACT

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Introduction: In India, different traditional medicine systems make use of a number of plants in the treatment of hypertension.. In this study, we have evaluated Melothria maderaspatana on lipid peroxidation, antioxidants status, and glycoprotein components in hypertensive patients.

Methods: Thirty patients with hypertension (SBP 159.4? 9.02 135.6?7.07 mmHg); (DBP 101.0?7.88 -93.5?5.87 mmHg) were selected from the Siddha division of Govt. Kamaraj Hospital, Chidambaram, Tamilnadu and were between 36 to 56 yrs and 25 healthy subjects served as control. Enzymic and nonenzymic antioxidants, lipid peroxidation and glycoprotein components measured before and after treatment with Melothria maderaspatana extract.

Results: The lipid peroxidation markers(thiobarbituric acid reactive substances and conjugated dienes), and glycoprotein components(fucose, sialic acid and protein-bound hexoses) increased while SOD, CAT and GPx activities and vitamin C & E ,and reduced glutathione levels decreased in hypertensive patients as compared with control. After 45 days of leaf extract consumption, reduction in lipid peroxidation markers, glycoprotein components and elevation in enzymatic and nonenzymatic antioxidants were observed in hypertensive patients.

Conclusion: Melothria maderaspatana aqueous extract reduced blood pressure and showed favorable effects on lipid peroxidation, enzymic, non enzymic antioxidants and glycoprotein components..

P-13

EFFECT OF AEGLE MARMELOS ON LIPID PEROXIDES AND LIPIDS ON ISOPROTERENOL-INDUCED MYOCARDIAL INFARCTION IN RATS

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Introduction: Cardiovascular disorders has become leading cause of death in many parts of the world. In our present study, the cardioprotective effect of Aegle marmelos leaf extract (AMLEt) in isoproterenol (ISO)-induced myocardial infarction in rats studied as an experimental model.

Methods: Rats were pretreated with AMLEt (50, 100, 200 mg/kg) for 35 days and then ISO (200 mg/kg) was administered to rats at an interval of 24 h for two days. AMLEt on cardiac marker enzymes, plasma lipid peroxides (TBARS and hydroperoxides) and lipid levels in ISO-induced MI rats were studied.

Results: Pretreatment with AMLEt for 35 days significantly decreased lipid peroxides and plasma TBARS and hydroperoxides in ISO-treated rats. AMLEt also decreased the levels of lipids in serum, heart and aorta in ISO-administered rats.

Conclusion: Our study shows that aqueous extract of Aegle marmelos exhibit cardioprotective effect in ISO-treated rats.

P-14

LIPID PEROXIDATION & GLUTATHIONE SYSTEM IN CARDIAC DISEASES

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Introduction: Cardiovascular disease is the largest cause of mortality in the general population. Ischaemia disrupts the handling of oxygen by the mitochondrial electron transport system and enzymes such as xanthine oxidase. Unless reperfusion to tissue is achieved, ischaemia will ultimately result in irreversible changes leading to cell death and tissue necrosis. When reperfused, this causes conversion of hypoxanthine to xanthine and superoxide anion. Taking this into account lipid peroxidation and glutathione system which plays an important role in scavenging oxygen free radicals and in the regeneration of antioxidants were studied using RBC as a model in cardiac patients.

Methods: Blood samples from patients suffering from cardiac disease (n=60) and age, sex matched controls (n=85) were collected. RBCs free from WBC and platelets were hemolysed and hemolysate was subjected to the analysis of glutathione peroxidase and glutathione reductase (Kinetic Method) MDA levels were measured (Stock J etal Method), glutathione levels were measured from whole blood by (Beutler) G6PD activity was also measured (Kinetic Method) as it regenerates reduced glutathione.

Results: There was fall in G6PD by 8.62% ($p<0.02$) Lipid peroxidation was higher by 93.25% ($p<0.001$) as expected, since there was fall in the GSH Px by 23.51% ($p<0.001$) and GR by 22.09% ($p<0.001$) activities so also fall in the levels of reduced Glutathione reductase by 18.96% ($p<0.001$).

Conclusions: The study shows that the availability of scavenging enzymes decreases leading to lipid peroxidation in cardiac injury.

P-15

EFFECT OF VITAMIN E ON HUMAN BLOOD XANTHINE OXIDASE IN ISCHEMIC MYOCARDIAL DISORDERS.

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Introduction: Free radicals are highly reactive species and detrimental to the tissues. These are involved in different diseases. Generation of oxygen free radicals increases upon reperfusion of ischemic myocardium.In the present report, we have assessed the effect of non-enzymatic anti-oxidant, vitamin E, on xanthine oxidase, a major source of free radicals in the patients reperfused after myocardial infarction.

Methods: The patients have been grouped as follows: Group 1 (n=15) patients receiving -blockers only, Group 2 (n=10) patients receiving 80 mg. aspirin along with -blockers and Group 3 (n=10) patients receiving 400 mg. vitamin E along with aspirin and -blockers for six days. Age and sex matched healthy persons (n=15) served as control.

Results: Our findings show that there is significant increase in the level of blood xanthine oxidase in the patients (p 0.0005). Upon administration of aspirin along with -blockers, the level of xanthine oxidase is lowered as compared to group 1 patients but less significant (p 0.005). Administration of vitamin E along with aspirin and -bockers results in highly significant decrease in the level of xanthine oxidase compared to Group 1 patients (p 0.0005).

Conclusions: Our findings suggest that administration of vitamin E reduces the level of free radical generation in the patients under investigation.

P-16

EFFECT OF ATORVASTATIN ON OXIDATIVE STRESS.

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Introduction: Insufficient antioxidant enzymes have been implicated in the pathogenesis of hypercholesterolemia (HC). Many antioxidant enzyme studies on HC have been reported but a very few studies have shown effect of statin tretment on antioxidant system in patients suffering from HC.

Methods: we have estimated serum Malondialdehyde (MDA), erythrocyte Superoxide Dismutase (SOD), Glutathione Reduced (GSH) and Glutathione Reductase (GRs) in 31 patients with mild HC, 27 patients with

severe HC and 31 healthy control subjects. Patients were undergone atorvastatin therapy (10mg/day) for 3 months.

Result: In both the HC group serum MDA and erythrocyte GRs level was significantly high ($p<0.05$) as compared to control. Erythrocyte SOD was significantly low ($p<0.05$) when compared with control. GSH was found insignificant as compared to control and even after statin treatment. Lipid profile, serum MDA and GRs were significantly reduced in both the HC group after statin treatment. SOD showed significant rise in both the HC group after statin treatment.

Conclusion: Atorvastatin may reduce free radical generation or may have ability to stimulate antioxidant enzyme.

P-17

HOMOCYSTEINE AND OXIDATIVE STATUS IN ISCHEMIC HEART DISEASE

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Introduction:- The mortality rate due to ischemic heart disease(IHD) in India rises exponentially as it occurs much more prematurely under 40 years of age. This cannot be explained by any conventional risk factors. Oxidative stress due to the production of reactive oxygen species may play vital role in the pathogenesis of IHD. Hence the present study was undertaken.

Methods:- Plasma homocysteine serum lipid peroxide, superoxide dismutase, erythrocyte gluthathione peroxidase and catalase activities were measuerd by standard methods in fasting samples collected from Myocardial infarction (n=30), chronic stable IHD (n =30) and normal healthy controls (n=30), having age group 20-65 years.

Results:- Plasma homocysteine was significantly elevated in IHD patients ($P<0.001$). Serum lipid peroxide was significantly elevated in myocardial infarction ($P<0.001$) and chromic stable IHD ($P<0.005$). Serum superoxide dismutase activity was significantly decreased in IHD ($P<0.001$) as compared to normal healthy controls. Erythrocyte glutathione peroxidase and catalase activities were significantly decreased in myocardial infarction ($P<0.001$), whereas no significant change was observed in chronic stable IHD ($P>0.05$).

Conclusion:- Increased serum lipid peroxide is the consequence of tissue ischemia as well as oxidation of PUFA. The decreased serum superoxide dismutase in IHD could be due to suppressed natural scavenging mechanism or enhanced free radical formation. The superoxide dismutase in chronic stable IHD suggests that the injured myocardiums are progressing towards recovery. Raised erythrocyte glutathione peroxidase and catalase activities in chronic stable IHD could be due to overload of toxic products of free radical metabolism during Post-reperfusion phase. Increased plasma homocysteine occurs due to excessive breakdown of methionine coupled with abnormal functioning of vitamin coenzymes.

FREE RADICALS AND ANTIOXIDANTS IN DIABETES MELLITUS

P-18

ANTIDIABETIC AND ANTIOXIDANT EFFECT OF PTEROSTILBENE ON STREPTOZOTOCIN INDUCED DIABETIC RATS

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Introduction: Chronic hyperglycemia is the primer of a series of cascade reactions causing the over production of free radicals and increasing evidences indicate that these contributes to the development of diabetic complications. In our present study, pterostilbene, an antioxidant was investigated for its anti-oxidative effect in streptozotocin (STZ) induced diabetes in rats.

Methods: Pterostilbene was administered orally for 6 weeks and different doses of the pterostilbene on blood glucose, plasma insulin, plasma lipid peroxidation markers (TBARS and hydroperoxides) and circulatory antioxidant levels in STZ-induced diabetic rats were studied.

Results: Oral administration of pterostilbene for 6 weeks resulted a significant reduction ($p<0.05$) of blood glucose and plasma insulin in dose dependent manner. Administration of pterostilbene significantly decreased ($p<0.05$) the lipid peroxidation markers with significant elevation ($p<0.05$) of circulatory antioxidant in diabetic rats.

Conclusion: The above observations suggest that pterostilbene play an antioxidant role in reducing the oxidative stress in diabetes..

P-19

ANTIOXIDATIVE AND HYPOLIPIDEMIC EFFECTS OF INDIAN HERBAL PREPARATIONS STREPTOZOTOCIN INDUCED DIABETIC RATS

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Introduction: Diabetes mellitus is a metabolic disorder of carbohydrate, fat and protein attributed to diminished production or mounting resistance to its action. Chronic hyperglycemia during diabetes causes glycation of proteins that in turn leads to secondary complications affecting eyes, kidneys, nerves and arteries. Diabetes is associated with profound alterations in the lipid and lipoprotein profile. The present study was carried out to investigate the effect of herbal hypoglycemic agents on lipid peroxidation and lipid profile in streptozotocin included diabetic rats.

Methods: Streptozotocin was administered as a single dose (65 mg/kg bw) to induce diabetes. A dose of 250 mg/kg/day of O.sanctum, 500 mg/kg/day of A.indica and 10ml/kg/day oa A sativum and M.Charantia were orally administrated to induced diabetic rats for four weeks. Simultaneous administration of insulin and glibenclamide was done to diabetic rats for four weeks. Blood glucose , plasma lipid peroxide and lipid profile including cholesterol, HDL-cholesterol and triglycerides were estimated in serum of diabetic rats.

Results: The levels of blood Glucose,lipid peroxide, Cholesterol and Triglycerides were found significantly elevated ($p<0.001$) in diabetic rats as compared to the control group. HDL-cholesterol levels were observed significantly reduced in diabetic rats. Daily dose of M.Charantia, A indica, O.santum and A. Sativum significantly decrease the glucose, lipid perioxide,cholesterol, and triglycerides to their levels and significantly elevated ($p<0.001$) the HDL-cholestrol levels in diabetic animals.

Conclusion: The results of the present study reveal that Indian herbal preparations under investigation exerted antioxidative and antihyperlipidemic effects and consequently may alleviate diabetes associated cardiovascular risk factors in streptozotocin induced diabetic rats.

P-20

EFFECT OF *DESMODIUM GANGETICUM* ON ANTIOXIDANT ENZYMES IN STREPTOZOTOCIN -INDUCED DIABETIC RATS

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Introduction: The elevated levels of blood glucose in diabetes produces oxygen free radicals, which cause membrane damage due to peroxidation of membrane damage due to peroxidation of membrane lipids and protein glycation. Desmodium gangeticum (L.) DC. (Family Leguminaceae) has been used in Indian system of medicine as a bitter tonic, febrifuge, digestive and in treatment of various other inflammatory conditions. Present study was undertaken to study the effect of Desmodium gangeticum on antioxidant enzymes in diabetic rats.

Methods: Streptozocin -induced diabetic rats were treated with D. gangeticum extract and its fractions and the levels of antioxidant enzymes were estimated. The effect was assessed on lipid peroxidation (LPO) and the antioxidant defense enzymes like GSH and SOD in rat tissues.

Results: Flavanoid fraction demonstrated hypoglycemic effect in the diabetic rats significantly at 25 mg/kg within three hours after administration whereas the alkaloid fraction did not have any significant reduction. Oral administration of the flavanoid fraction reduced the hepatic TBARS (1.83 nmoles/ mg protein as compared to 3.78 nmoles/ mg protein of control), GSH level (5.47 nmoles/ mg protein as compared to control of 3.86 nmoles/ mg protein) and SOD activity (7.56 units/ mg protein as compared to 13.97 of control).

Conclusions: The results indicate that the flavanoids fraction of D. gangeticum possess anti-oxidant properties in diabetic conditions.

P-21

OXIDATIVE PROTEIN & LIPID DAMAGE IN TYPE 2 DIABETES MELLITUS

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Introduction: Diabetes Mellitus is known to be a state of increased free radical activity leading to lipid peroxidation and oxidative damage to proteins in spite of protection by antioxidant defence mechanisms and protein repair and degradation systems. In order to evaluate the effect of oxidative stress in type 2 Diabetes Mellitus, a comparative study of the malondialdehyde (MDA - index of lipid peroxidation), protein carbonyl (marker of protein damage), fasting blood glucose, serum triglycerides and protein levels in type 2 diabetics and healthy controls were made.

Methods: 55 (31 male + 24 female) normotensive, non smoking type 2 diabetic patients free from other clinical complications and secondary causes of hyper glycemia and 50 (26 male + 24 female) age-matched healthy controls were chosen for the study. The patients were on only insulin treatment and no other medications including vitamins and antioxidants. Fasting blood samples were collected for the estimation of glucose, triglycerides, total protein, and MDA and protein carbonyl levels. MDA was measured as thiobarbutric acid reactive substances and protein carbonyl by the 2,4 dinitrophenyl hydrazine method.

Results: The diabetics showed a significant increase in glucose ($P<0.001$), triglyceride ($P<0.001$), MDA ($P<0.001$) and protein carbonyl ($P<0.001$) content when compared with controls. There was no significant difference in any parameter between the males and the females in each group.

Conclusion: The impaired glycemic control along with the increase in free radical enhanced lipid peroxidation and protein oxidative damage may be related to the underlying metabolic abnormalities and the development of further complications of diabetes.

P-22

ANTIDIABETIC ACTIVITY OF HYDRO-ALCOHOLIC EXTRACT OF *CRATEVA NURVALA BUCH.* IN ALLOXAN-INDUCED DIABTES IN RATS

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Introduction: *Crateva nurvala* Buch Ham Fam.: Capparaceae commonly called 'Varunha' is used in kidney and bladder disorders. Traditionally, it has been used in the treatment of diabetes by certain tribes of Vidarbha region. However, no scientific data are available about its antidiabetic activity of *C. nurvala*. Furthermore, it is reported to contain mainly saponins, flavonoids and glucosilinates that are components of many herbs possessing antidiabetic activity. In view of its traditional use in the treatment of diabetes, it was thought to investigate activity of hydroalcoholic extract of *C. nurvala* (HACN) in experimentally induced diabetes in rats.

Methods: Diabetes was induced in rats with single administration of alloxan monohydrate (120mg/kg, i.p.). The animals were divided into

four groups (n=6). Non-diabetic control, Diabetic control, Metformin treated and HACN treated. The HACN (300 mg/Kg, orally) was administered after taking initial blood glucose on 15th day of first administration of alloxan. The blood was withdrawn from retro-orbital plexus of rats at 0, 2, 4, 6 and 24 h of administration. The blood glucose was determined by GOD-POD method. In order to delineate antioxidant activity to antidiabetic activity, *in vitro* antioxidant activity of HACN was assessed by DPPH (1,1- Diphenyl Picryl Hydrazyl).

Results: Alloxan treatment induced significant hyperglycemia (>200 mg/dl). This hyperglycemia was reversed by oral treatment with HACN and Metformin 450mg/kg, orally. The antihyperglycemic activity of extract of *C. nurvala* was very much comparable to metformin. Furthermore, HACN showed significant *in vitro* antioxidant activity by scavenging DPPH radicals.

Conclusion: Thus, hydro alcoholic extract of *C. nurvala* exhibits antidiabetic activity in alloxan-induced diabetes in rats, which could be due to its free radical scavenging activity.

P-23

ANTIOXIDANTS ROLE IN THE CONTROL OF IN TYPE II DIABETES MELLITUS

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Introduction Diabetes is a dangerous disease than hypertension, affects multiple organ system. Even though it is a worldwide problem, in Indian cities is high and rising. Indians get diabetes at an average age of 35 years, the type 2 diabetes. Free radicals are found to be responsible for occurrence of most of the disease. So the present study was undertaken to evaluate the synergistic role of antioxidants as potential add on therapy along with Glibenclamide in type 2 DM.

Methods The study was carried out at out patient department in GHQH, Ooty, in 2 phases. The first phase of study was to asses the social habits and demographic data. In 2nd phase the patients were classified into two groups (i.e.) control and intervention group. Intervention group received Vit C 100mg, Vit E 100 IU once daily along with oral hypoglycemic therapy. Blood biochemical analysis was done on all study subjects like glucose, HBA1C, and SOD of base line and an interval of 1-month for three months.

Results The subjects were divided into two groups, the patients were sub-grouped as mild, moderate and severe based on their plasma glucose level .we found that 90% of the subjects were non vegetarian and also coming under obese in the age group of 50-70 years, their SOD levels was found to be very less in severe type 2 group. The urine and blood glucose values fluctuating through out the study in control group but in intervention group shown to maintained or reduced.

Conclusion The supplementation of antioxidants significant reduction in blood and urine glucose levels, elevation of SOD level and reduction in glycosylated hemoglobin HBA1C value in intervention group were observed.

P-24

LEVEL OF INCREASED METHYL GLYOXAL AND REDUCED ANTI OXIDANT STATUS ARE THE INDICATIONS OF SEVERITY OF COMPLICATIONS IN DIABETES MELLITUS.

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Introduction : Recently it has been reported that methyl glyoxal level increases in Diabetes mellitus. This is the prospective study of the co-relation between methyl glyoxal level and free radical damage as well as antioxidant status of Diabetes mellitus patients. In this study we want to establish the relation between the methyl glyoxal level and the severity of complications in the diabetic condition.

Materials and Methods : We selected 49 Diabetes mellitus patients attended in outpatient and inpatient department of Diabetology, Nilratan Sircar Medical College and Hospital, Kolkata and 40 normal healthy people were selected randomly as control. The Diabetic patients were divided into 3 groups . Group-I (n=32)consists of the patients having fasting blood sugar level <=250 mg /dl , group-II (n=11)consists of the patients having fasting sugar level 250 -350mg /dl , Group-III (n=6) consists of the patients having fasting sugar level >=350 mg /dl .The serum of patients and normal control were analyzed for methyl glyoxal , total antioxidant status, catalase activity , superoxide dismutase (SOD) activity , total reduced glutathione, NO , lipid peroxidation by malon dialdihyde level (MDA).

Result : We observed methyl glyoxal and malon dialdihyde (MDA) level increase significantly ($P<0.05$) with poor status of total antioxidant , catalase activity, SOD activity, reduced glutathione, NO level in group-II and group-III patients.

Conclusion : Our observation shows that increased cellular damage and methyl glyoxal level are accordingly to the blood glucose level and severity of complications in diabetic conditions.

P-25

IMPACT OF UMBELLIFERONE ON OXIDATIVE STRESS IN PLASMA AND LIVER OF STREPTOZOTOCIN DIABETIC RATS

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Introduction: Many plant drugs have been widely used in the treatment of diabetes mellitus. Umbelliferone is a derivative of coumarin which is benzopyrone in nature. The parent compound coumarin has been reported to reduce blood glucose level. In this study, we have evaluated the effect of umbelliferone on lipid peroxidation and antioxidants status in streptozotocin diabetic rats.

Methods: Male albino Wistar rats were induced diabetes mellitus by streptozotocin at a dose of 40 mg/kg b.wt. The animals were divided into five groups of six animals each. Group 1: normal control; group 2: normal rats treated with umbelliferone (30 mg/kg bwt.); group 3: diabetic control rats; group 4: diabetic rats treated with umbelliferone (30 mg/kg bwt.); group 5: diabetic rats treated with glibenclamide (600 µ g/kg bwt.). After 45 days of treatment, biochemical estimations were carried out in plasma and liver.

Results: Lipid peroxidation markers such as thiobarbituric acid reactive substances, lipid hydroperoxides and conjugated dienes increased and nonenzymic antioxidants (vitamin C, vitamin E and reduced glutathione) decreased significantly in plasma and liver of diabetic rats. Activities of superoxide dismutase, catalase and glutathione peroxidase decreased significantly in the liver of diabetic rats. Diabetic rats treated with umbelliferone brought them to near normal levels. A significant reduction in lipid peroxidation markers and significant elevation in both nonenzymic and enzymic antioxidants were found in normal rats treated with umbelliferone.

Conclusion: Our results indicate that treatment with umbelliferone has effectively reduced lipid peroxidation and elevated antioxidants status in diabetic rats.

P-26

POSTPRANDIAL LIPEMIA, OXIDATIVE STRESS AND NITRIC OXIDE END PRODUCTS IN TYPE 2 DIABETIC PATIENTS WITH MACROANGIOPATHY

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Introdution : Exaggerated postprandial lipemia (PPL) in type 2 diatetes mellitus (DM) may lead to increased production of lipid derived free radicals. This along with the impaired antioxidant defences has been implicated in endothelial dysfunction which is an initial event in atherosclerotic macrovascular complications. The present study has been carried out to address the relationship between postprandial hypertriglyceridemia & selected parameters of oxidative stress in Indian patients of type 2 DM with macroangiopathies.

Methods : 13 patients each of type 2 DM with (Group III) and without macrovascular complications (Group II) along with 13 age and sex matched healthy controls (Group I) were selected in this case-control study. Plasma glucose, lipid profile, malondialdehyde (MDA), nitric oxide end products, reduced glulathione (GSH) and superoxide dismutase (SOD), were measured in the fasting state and serially at 2, 4, 6 and 8 hours after a mixed meal.

Results : Diabetic patients (both groups) showed significantly higher levels ($p<0.05$) of plasma triglycerides (TG) and MDA post meal at all time points as compared to controls. Highest MDA levels were seen in Group III which corresponded with TG peak, further, MDA levels correlated positively ($r = 0.712$, $p<0.05$) with plasma TG in this group. Erythrocyte GSH and SOD activity was lower whereas level of plasma nitrate was higher in both groups of diabetics in the fasting as well as postprandial state, as compared to controls.

Conclusions : The magnitude of postprandial hypertriglyceridemia in type 2 DM is a major determinant of the oxidative stress which along with derangement of nitric oxide pathway may play an important role in development of macrovascular complications. Therefore, postprandial TG levels and oxidative stress should be taken into consideration for risk.

P-27

DEVELOPMENT OF A NOVEL MODEL FOR SCREENING ANTIDIABETIC ACTIVITY BY INDUCING HYPERGLYCEMIA WITH PYROGALLOL, A PROOXIDANT

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Introduction: Alloxan (ALX) and streptozotocin (STZ) are common diabetogenic agents employed in the screening of antidiabetic agents. The hyperglycemic effect of these agents is attributed to the free radicals generation. Though ALX produces reversible hyperglycemia, it is chemically unstable and produces high mortality. STZ induces irreversible hyperglycemia and making post experiment rehabilitation of animals difficult. Therefore, it was proposed to test pyrogallol (PGL), a known prooxidant, for hyperglycemia induction and to use this model to screen an antidiabetic agent.

Methods: The blood glucose levels were regularly estimated in rats who received different doses of PGL (i.p.) for different time periods. The effect of minimum dose of PGL that produced maximum hyperglycemia with minimum toxicity was studied on various parameters such as histology of pancreas, glucose tolerance, plasma insulin and antioxidant status of pancreas. The antidiabetic activity of metformin was screened in this model.

Results: Out of the various doses of PGL, 150 mg/kg, i.p. daily dose for seven days induced significant ($p<0.001$) hyperglycemia on day 3 that reached to maximum on day 7 and gradually returned to normal by 14th day. Though, this dose of PGL increased lipid peroxidation, reduced activities of superoxide dismutase and catalase in pancreas, elevated plasma insulin levels and exhibited histological damages to the beta cells, there was no mortality observed. Metformin (450mg/kg p.o. on day 7) reduced the pyrogallol-induced hyperglycemia. Vitamin C+ E treatment reversed the effect of pyrogallol on all above parameters. **Conclusion:** PGL-induces hyperglycemia by free radical generation and can be used as a preferable diabetogenic tool over ALX and STZ for screening an antidiabetic activity of any agent.

FREE RADICALS & ANTIOXIDANTS IN LIVER DISEASES

P-28

ANTIOXIDANT ACTIVITY OF VEDIC GUARD IN ANTI-TUBERCULAR DRUGS INDUCED HEPATOTOXICITY IN RATS

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Introduction: Chronic treatment of tuberculosis with Isoniazid (I) + Rifampicin (R) + Pyrazinamide (Z) has shown to induce hepatotoxicity mainly due to free radical generation. Vedic guard is a poly herbal formulation having natural antioxidant activity. Attempts have been made to evaluate hepatoprotective activity and free radical scavenging activity of Vedic guard in anti-tubercular drugs induced hepatotoxicity in rats.

Methods: Wistar rats were divided in 5 groups containing 6 each. Group 1: normal control. Group 2: treated with (I+R+Z) for 45 days. Group 3: treated with (I+R+Z) +Vedic guard (900mg/kg/day) for 45 days. Group 4: treated with (I+R+Z) for 45 days + no treatment from 45 to 65 days. Group 5: treated with (I+R+Z) for 45 days +Vedic guard (900mg/kg/day) from 45 to 65 days. Serum enzyme levels of ASAT, ALAT, ALP and total bilirubin and total protein levels were measured. Antioxidant enzymes in liver homogenates viz. SOD, catalase, TBARS and glutathione were estimated. Results: I + R + Z treated (group 2) animals showed elevated serum hepatic enzyme levels and decrease in antioxidant activity indicating liver damage ($P > 0.05$). Group 4 animals did not show recovery. Group 3 animals showed normal serum hepatic enzyme levels as well as normal antioxidant activity ($P > 0.05$). Group 5 animals showed recovery to normal in both serum hepatic enzyme levels and antioxidant activity ($P > 0.05$).

Conclusion: Simultaneous administration of Vedic guard prevented the anti-tubercular drug induced hepatotoxicity by its free radical scavenging activity. Administration of Vedic guard for twenty days after induction of hepatotoxicity showed recovery from hepatic damage.

P-29

ALTERATION OF LIVER LIPID PEROXIDATION AND ANTIOXIDANT ENZYMES IN EXPERIMENTAL DIABETES: ROLE OF N-BENZOYL-D-PHENYLALANINE AND METFORMIN

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Introduction: A new model of noninsulin dependent diabetes mellitus (NIDDM) is described, which exhibits more prominent defects in ?-cell function than the standard neonatal NIDDM model. The present study was carried to investigate the role of N-benzoyl-D-phenylalanine (NBDP) and metformin on oxidative stress and antioxidant enzyme status in type 2 diabetes.

Methods: To produce this model, 48 h old neonatal rats were injected with streptozotocin via ip route. After 10-12 weeks, male rats were selected for screening of NIDDM model. NBDP and metformin were

administered orally for six weeks to confirmed diabetic rats and the levels of blood glucose, lipid peroxidation in liver and the activities of antioxidant enzymes were studied.

Results: The diabetic control rats showed significant increase ($p<0.05$) in blood glucose and liver lipid peroxidation with significant decrease ($p<0.05$) in antioxidant enzymes. Both NBDP and metformin were significantly decreased ($P<0.05$) the blood glucose and restored the altered lipid peroxidation markers and antioxidant enzymes. Combination treatment was more effective than either drug alone.

Conclusion: From this study, it may be concluded that oxidative stress play a major role in type 2 diabetes. it was evident from significant inhibition of antioxidant defense mechanism in liver. Oral administration of NBDP and metformin exhibited significant decrease in blood glucose level along with *the amelioration of lipid peroxidation and antioxidant status.*

P-30

OXIDATIVE STRESS DURING LIVER CIRRHOSIS RESULTS IN MODIFICATION OF METAL BINDING CAPACITY OF SERUM ALBUMIN

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Chronic liver disease is a major problem in countries such as India, and oxidative stress has been implicated in the etiology of diseases such as liver cirrhosis. Albumin, synthesized in the liver, is the major protein in circulation, and this study examines the role of oxidative stress in modification of the metal binding activity of serum albumin. Serum was obtained from patients diagnosed with liver cirrhosis by liver function tests and clinical parameters. A significant increase in protein carbonyl content and a decrease in protein thiols were seen in serum from these patients when compared controls. Albumin binds a number of metals in circulation, and the binding of the protein to cobalt has been shown to be altered in conditions such as myocardial infarction. Cobalt binding activity of serum albumin can be measured by a spectrophotometric assay, and was found to be altered in patients with cirrhosis. In-vitro experiments demonstrated that exposure of serum to the xanthine-xanthine oxidase system (which generates superoxide) and hydrogen peroxide resulted in a significant increase in cobalt binding of albumin. This was accompanied by an increase in protein carbonyl content as well as a decrease in protein thiols- similar to the results from cirrhotic patients. These results indicate that during cirrhosis, oxidative stress causes modification of serum albumin, resulting in an altered cobalt binding capacity.

P-31

EFFECT OF ANTIOXIDANT (L-ASCORBIC ACID) ON NICKEL INDUCED ALTERATION OF NUCLEIC ACID CONCENTRATION IN RATS.

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Introduction : Nickel exhibit the ability to produce reactive oxygen species (ROS) or free radicals resulting in lipid peroxidation, DNA damage, depletion of sulfhydryl and altered calcium homeostasis. The present study was designed to elucidate the effect of L-ascorbic acid on nickel sulfate induced hepatic nucleic acids concentration in rats.

Methods : Adult male Wister strain rats (160 ± 5g) were divided into four groups (n=6). Group I served as an untreated control. Group II rats were administered nickel sulfate (2.0 mg / 100 g body weight ,i.p.) on alternate days until the tenth dose. Group III rats were treated orally with L-ascorbic acid (50mg / 100 g. b.wt.) and Group IV rats were given nickel sulfate and ascorbic acid simultaneously. Hepatic total protein, RNA and DNA concentration were determined by the standard methods.

Results: Nickel induced a significant decrease in hepatic DNA, RNA and protein content in the Group II rats in comparison to untreated control (Group I).Whereas simultaneous administration of L- ascorbic acid with nickel sulfate (Group IV) resulted in a remarkable improvement of hepatic nucleic acids and total protein concentration in comparison with rats treated with nickel sulfate alone (Group II).

Conclusions : Nickel sulfate appears to be a potential hepatotoxic heavy metal that affects adversely to the expression of genetic information by reducing DNA, RNA and protein concentrations in the liver of albino rats. But simultaneous treatment with L-ascorbic acid relatively prevents nickel induced alteration of nucleic acids concentration in the liver.

P-32

HEPATOPROTECTIVE ACTIVITY OF ARIEL ROOTS OF FICUS BENGALENSIS

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Introduction: Ficus bengalensis (Moraceae), commonly known as Banyan tree, Barh or Bargat is a remarkable tree of India and tropical Africa is well known to ancient Indian culture and medicine. The ethnobotanical uses of aerial roots of F. bengalensis are reported as styptic, aphrododisiac, useful in gonorrhoea, syphilis, biliousness, dysentery and inflammatory conditions of liver. These roots contain tannins(Ayurvedic Pharmacopoeia, 2001) Tannis being polyphenolic in nature are also known to possess antioxidant property. The present study was undertaken to observe the hepatoprotective potential of F. bengalensis aerial roots in the CCl4 induced hepatotoxicity in rats.

Methods: Plant materials and extraction: The aerial roots of F. bengalensis were collected from Barkatullah University campus, dried, coarsely powdered and extracted by maceration process by using water as a solvent (yield-5%). The extract was tested positive for presence of tannins. All the chemicals were of analytical grade. Albino rats of either sex (body wt range 250-300gm) were purchased from market and were maintained in a thermostatically controlled room at 24+/-20C. Animals were divided in four groups of five animals each. CCl4, mixed with liquid paraffin (1:1) was used as a hepatotoxic agent. The test drug was administered in the form of a suspension, made from CMC. Silymarin suspension was used as a standard hepatoprotective drug (Silybon 70). The first group (normal control) received neither any drug nor CCl4. Second group (toxic control) was injected with a single dose of CCl4 (IP, 1ml/kg) on day first only. Third group (silymarin treate) was given silymarin suspension (oral, 10mg/kg) for six days after CCl4 administration on day first. Fourth group was administered with test drug extract (oral, 100 mg/kg) for six days after CCl4 administration on day first. On the last day, animals were taken for biochemical evaluation for SGPT, SGOT, ALP & AP

Results and discussion: The toxic dose of CCl4 shown 199%, 89.1% increase in the levels of SGPT, SGOT respectively. The Silymarin shows 37.49% & 50.58% inhibition of increased levels of SGPT & SGOT. Being nonspecific enzyme of liver, ALP & AP levels are not considered significant. The Drug was found to lower the increased levels of all the four enzymes significantly which is comparable to the standard drug used in the study. The results were confirmed with histopathological studies. In test group, there was minimum mononuclear cell infiltration and normal staining nucleus. No periportal fibrotic bands were seen in test group.

Conclusion: The drug is shown to posess hepatoprotective potential.

P-33

INFLUENCE OF DIALLYL DISULFIDE ON OXIDATIVE STRESS IN N- NITROSODIETHYLAMINE INDUCED HEPATOCARCINOGENESIS

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Introduction: Hepatocellular carcinoma ranks fifth in frequency among all the malignancies in the world. In the present experiment, the possible antioxidant role of diallyl disulphide (DADS), an organosulphur compound in garlic on N-Nitrosodiethylamine (NDEA) induced hepatocarcinogenesis was studied.

Methods: Hepatocarcinoma was induced by single intraperitonial injection of NDEA (200mg/ kg body weight) and promoted by subcutaneous injection of CCl_4 (3 ml/ kg bodyweight) weekly once for 6 weeks. DADS (60 mg/kg bodyweight) was administered orally thrice in a week for 20 weeks along with carcinogenesis induction. At the end of experimental regimen, the level of thiobarbituric acid reactive substances (TBARS), reduced glutathione (GSH) and the activities of enzymatic antioxidants (catalase and superoxide dismutase) were assayed in liver of normal and experimental rats.

Results: In NDEA induced hepatocarcinogenesis, the significantly decreased ($p<0.05$) level of TBARS and significantly increased ($p<0.05$) level of GSH as well as enzymic antioxidant activities were observed. Upon treatment with DADS, all theses changes were significantly reversed ($p<0.05$) to near normal.

Conclusion: The above observation suggest that DADS play a antioxidant role by influencing the carcinogen metabolism in liver.

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DIALLYL TETRASULPHIDE ATTENUATES CADMIUM INDUCED OXIDATIVE DAMAGE IN RAT LIVER

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Introduction: Exposure to toxic metals has become an increasingly recognized source of ill ness worldwide. Cadmium(Cd) is known to be most toxic environment pollutant, which concerned with a variety of adverse effects. The present study was carried out to investigate the role of Diallyl tetrasulfide(DTS), the organosulfur compound found in garlic, in protection of toxic effects of cadmium on liver.

Methods: During the experiment, rats were injected with cd (3 mg/kg body weight) subcutaneously alone or with oral administration of DTS in different doses (10,20 and 40 mg/kg/day) for 3 weeks. The effect of different doses of DTS on hepatospecific markers(trasaminases, alkaline phosphatase and lactate dehydrogenase) in serum was assayed. In liver, the changes in the levels of lipid peroxidation indices (TBARS and lipid hydroperoxides) and antioxidant activities were also studied.

Results: In Cd treated rats, significantly increased ($p<0.05$) activities of serum hepatic markers with elevated levels of lipidperoxidation in liver were observed. Oral administration of DTS significantly decreased ($p<0.05$) the activities of hepatic markers in a dose related manner. In addition, DTS significantly decreased ($p<0.05$) the level of lipid peroxidation with restoration of depleted enzyme and non enzymic antioxidant levels in Cd treated rats. DTS at a dose of 40mg/kg/day was highly effective when compared to other doses.

Conclusion: The above observations suggest that the maintenance of liver antioxidant status with attenuation of lipid peroxidation may contribute to the protective role of Diallyl tetrasulphide in cadmium induced oxidative damage in liver.

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ANTIOXIDANT AND HEPATOPROTECTIVE ACTIVITY OF ARJUNOLIC ACID

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Introduction Arjunolic acid (AA) is the triterpenoid and major constitutent present in the bark of Terminalia arjuna (TA). This paper describes the hepatoprotective action of Arjunolic acid and its anti-oxidant acitivity against the DPPH and Nitric Oxide free radicals.

Method Arjunolic acid was isolated from stem bark of TA by column chromatographic method. 36 Albino rats of either sex (150-200G) were divided in to 5 groups. Group I served as solvent control and received only 1% Sodium Carboxy Methyl Cellose [SCMC] suspension, Group III and IV received Arjunolic acid (1%SCMC Suspension) 25 and 50mg/kg/po respectively, Group V received Silimarin (1%SCMC Suspension) 25mg/kg/po for seven days. All the groups except I, received CCl_4 in Olive oil (1:1) (3mg/kg/ip) on 3rd and 5th day. On 7th day all the animals were sacrificed and serum is separated for the estimation of biochemical parameters. Anti-oxidant activity was studied by invitro scavenging of DPPH and Nitric Oxide free radicals by graded concentrations of Arjunlic acid .

Result The levels of hepatitis marker enzymes such as SGOT, SGPT, Alkaline Phosphatase are elevated in groups treated only with CCl_4. Pretreatment with Silimarin, AA (25 & 50 mg) showed significant hepato protection. They also exhibit siginificant scavenging of DPPH and Nitric oxide free radicals.

Conclusion Arjunolic acid exhibited significant hepatoprotective action and it may be due its free radical scavenging activity.

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FREE RADICAL SCAVENGING AND HEPATOPROTECTIVE ACTIVITY OF BORRERIA HISPIDA

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Introduction Free radicals are implicated in the pathogenesis of many diseases like hepatitis, atherosclerosis, cancer, myocardial infarction. The present work describes the hepatoprotective activity of Borreria hispida [BH] and its in-vitro free radical scavenging activity against DPPH and Nitric oxide free radicals.

Methods Aerial parts of Borreia hispida was collected, dried, powedered and extracted with alcohol and concentrated. 36 Albino rats of either sex (150-200G) were divided in to 5 groups. Group I served as solvent control and received only 1% Sodium Carboxy Methyl Cellose [SCMC] suspension. Group III and IV received methanolic extract of BH (1%SCMC Suspension) 200 and 400mg/kg/po respectively, Group V received Silimarin (1%SCMC Suspension) 25mg/kg/po for seven days. All the groups except I, received CCl_4 in Olive oil (1:1) (3mg/kg/ip) on 3rd and 5th day. On 7th day all the animals were sacrificed and serum is separated for the estimation of biochemical parameters. Anti-oxidant activity was studied by in-vitro scavenging of DPPH and Nitric Oxide free radicals by graded concentrations of BH.

Result The levels of hepatitis marker enzymes such as SGOT, SGPT, Alkaline Phosphatase are elevated in groups treated only with CCl4. Pretreatment with Silimarin, BH (200 &400 mg) showed significant hepato protection. They also exhibit siginificant scavenging of DPPH and Nitric oxide free radicals.

Conclusion Arjunolic acid exhibited significant hepatoprotective action and it may be due its free radical scavenging activity.

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INFLUENCE OF A NOVEL SYNTHETIC CURCUMINOID ON FIBROTIC MARKERS IN ALCOHOL AND PUFA INDUCED TOXICITY.

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Introduction: Hepatic fibrosis is a result of an imbalance between enhanced matrix synthesis and diminished breakdown of connective tissue proteins, the net result of which is increased deposition of Extra cellular matrix (ECM). In this concept matrix metallo proteinases (MMPs) and Tissue inhibitors of matrix metallo proteinases (TIMPs) play an important role because their activity is largely responsible for ECM breakdown. In the present study, we have tested the influence of a novel curcuminoid (BDMC-A) on alcohol and thermally oxidized sunflower oil (PUFA) induced liver fibrosis.

Methods: Male albino Wistar rats were used for the study. The activities of MMPs, the levels of TIMPs and collagen were used as biomarkers to monitor the antifibrotic effects of BDMC-A.

Results: The levels of collagen and TIMPs were significantly increased in alcohol, PUFA and alcohol + PUFA groups, which were decreased significantly on treatment with BDMC-A. The activities of MMPs were significantly increased in alcohol and PUFA groups and significantly decreased in alcohol + PUFA group. Treatment with BDMC-A positively altered the activities of MMPs.

Conclusion: From the results obtained, we could conclude that BDMC-A influences hepatic fibrotic markers and effectively protects the liver against alcohol and PUFA induced toxicity.

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OXIDATIVE STRESS IN EXPERIMENTAL LIVER MICROVESICULAR STEATOSIS: ROLE OF MITOCHONDRIAAND PEROXISOMES

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Hepatic microvesicular steatosis is a clinical manifestation seen in a number of liver diseases. Though the role of mitochondrial ß oxidation in development of the disease has been well studied, information on peroxisomal function and the role of free radicals in this process is scarce. This study looked at oxidative stress in hepatic peroxisomes and microsomes during microvesicular steatosis, using an animal model of the disease. Rats were given intraperitoneal injection of sodium valproate (700 mg / kg body weight) to induce microvesicular steatosis, which was confirmed by histology. Oxidative stress was evident in liver homogenate after steatosis, accompanied by structural and functional alterations in hepatic mitochondria. Alterations in lipid composition, as well as increased lipid peroxidation were also evident in peroxisomes and microsomes from steatotic rats. All these changes were protected by administration of the peroxisome proliferator activator, clofibrate. These results suggest that in addition to impaired mitochondrial ß oxidation, oxidative stress in the peroxisomes and microsomes might play an important role in cellular damage during microvesicular steatosis.

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ANTI-OXIDANT ACTIVITY OF GLYCYNHIZA GLABRA LINN, ON CARBON TETRACHLORIDE INDUCED HEPATO-TOXICITY IN RAT

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Introduction: Glycynhiza glabra Linn of the family Fabaceae is a tall perennial undershurb used medicinally. In this study we present the antioxidant effect of G. glabra on CCl_4 induced hepatotoxicity in rats, supported by histopathological evidence.

Methods: Wistar rats of either sex weighing 200-250 gm were divided into three groups of six rats each (n=6) Group I served as control, which received the normal feed. Group II & III received CCl_4 0.3 ml/100 gm body weight s.c. in liquid paraffin (3:1v/v), twice a week for a period of 2 months. Group III rats, in addition to CCl_4 received a dose of 1000mg/kg body weight/day of G. glabra root powder mixed with the feed for 2 months. At the end 10% liver homogenate was for the prepared using tris-HCl buffer (0.1m pH 7..5) & used estimation of lipid peroxidation in turns of malondialdehyde & changes in anti-oxidant status by estimating the activities of catalase, superoxide dismutase & reduced glutathione.

Result: Significant increase ($P<0.05$) level of malondialdehyde during CCl_4 treatement as compared to control. Administration of G. glabra together with CCl_4 resulted in ($P<0.05$) decrease of malondialegyde in the liver compared with the corresponding CCl_4 treated rats compared to control. Administration of G. glabra along with CCl_4 restored the activities of the above antioxidant enzymes to near normal compared to the corresponding CCl_4 administrated rats. Histopathological studies demonstrated degeneration of hepatocytes by CCl_4liquid paraffin compared to controls. Administration of root powder of G. glabra showed significant improvement.

Conclusions: The herb is potential antioxidant & attenuates the hepatotoxic effect of CCl_4 by promoting the lipid per oxidation or by accelerating the scavening of free radicals.

P-40

HEPATOPROTECTIVE AND ANTI-OXIDANT POTENTIAL OF VENTILAGO MADRASPATANA ROOT BARK EXTRACTS IN RATS

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Introduction Indian medicinal plants and many herbal formulations belonging to the traditional system of medicines have been investigated as liver protective drugs. The protective effect is analyzed against carbon tetrachloride induced liver toxicity in rats. Anti-oxidant enzymes such as superoxide dismutase and catalase serve as a defence mechanism by converting the active molecules into non-toxic compounds thereby preventing the lipid peroxidation in body.

Methods Extracts (aqueous and methanolic) of root bark of ventilgo madraspatana (AEVM, EEVM) WERE prepared after defatting with petroleum ether. Wistar rats (150-200g) of either sex were used for the study of experimentally induced hepatitis. The rats were divided into 7groups. The group is treated accordingly I-solvent, II-liv-52 (1ml/kg), III-AEVM (200mg/kg), IV-AEVM (400mg/mg), V-EEVM (200mg/kg),

VI-EEVM (400mg/kg) for 6days. On the 3rd day and the 5th day CCl4 (3ml/kg). On the 7th day the blood is collected and liver is excised out. Biochemical parameters were seen in serum and liver. Total protein, reduced glutathione, super oxide dismutase, GPX, lipid peroxidation, vitamin C, vitamin E were estimated using liver, GOT, GPT, ALP, Bilurubin levels were seen in the serum.

Result On statistical evaluation all enzymatic and non-enzymatic anti oxidants showed significant activity at ($p< 0.01$) and the marker enzymes showed significant levels at ($p<0.001$).

Conclusion The extract possessed potent hepatoprotective activity and free radical scavenging property.

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FERULIC ACID, A NATURAL PROTECTOR AGAINST CARBON TETRACHLORIDE INDUCED LIVER TOXICITY

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Introduction: Liver fibrosis entails a common and difficult clinical challenge of worldwide importance. Chronic administration of CCl_4 causes liver fibrosis. CCl_4 is activated by cytochrome P-450, resulting in the formation of trichloromethyl free radical and trichloromethyl peroxyradical that initiate lipid peroxidation and protein oxidation. The present work is aimed at evaluating the protective effect of ferulic acid on CCl_4 induced liver fibrosis.

Methods: Female albino Wistar rats were used for the study. The degree of liver damage was measured by estimating the activities of liver marker enzymes. The extent of lipid peroxidation was measured by estimating the lipid peroxidative indices (TBARS and HP), the antioxidant status was measured by estimating the activities of enzymic and non-enzymic antioxidants in plasma, liver and kidney.

Results: The activities of liver marker enzymes [ALT, AST, ALP and GGT], the lipid peroxidative indices [TBARS, HP, NO and PCO] were increased and the antioxidant status [SOD, CAT, GPx and GSH] was decreased in CCl_4 treated groups when compare to normal. On treatment with ferulic acid there was a significant decrease in liver marker enzymes, lipid peroxidative indices and increase in the activities of enzymic and non-enzymic antioxidants in the plasma and tissues.

Conclusion: Our results showed that ferulic acid is an effective protective agent against CCl_4 induced toxicity.

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HEPATOPROTECTIVE EFFECT OF LUPEOL AND ITS ESTER DERIVATIVE ON EXPERIMENTAL HYPERCHOLESTEROLEMIA

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Introduction: Cholesterol feeding has often been used to elevate serum or tissue cholesterol levels to study the etiology of hypercholesterolemia-related metabolic disturbances. In exogenously produced hypercholesterolemic condition, the excessively accumulated tissue cholesterol in liver exerts oxidative stress. The present study was undertaken to evaluate the effects of lupeol and its ester, lupeol linoleate in hypercholesterolemic male albino Wistar rats.

Methods: Hypercholesterolemia was induced in rats by feeding them with atherogenic diet (4% cholesterol + 1% cholic acid) for 30 days. Lupeol and lupeol linoleate was supplemented (50mg/ kg body wt/day) for last 15 days. Lipid peroxidation, enzymic and non enzymic antioxidants, activities of membrane ATPase and functional marker enzymes (AST, ALT and ALP) were assessed by standard protocols.

Results: After the experimental period, we found decreased levels of hepatic enzymic and non enzymic antioxidants. Activities of membrane ATPase decreased with a concomitant increase in lipid peroxidation and serum aminotransferases and ALP activity. Treatment with lupeol and its ester decreased lipid peroxidation and brought back the activities of enzymic, non-enzymic antioxidants and marker enzymes to near normal values and also restored the membrane ATPase activities.

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ANTIINFLAMMATORY, ANALGESIC AND ANTIOXIDANT EFFICACY OF BARLERIA LUPULINA LINDL

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Introduction: Inflammatory diseases are common throughout the world. The disadvantages in synthetic drugs lie in their gastric toxicity and reappearance of symptoms. Therefore development of anti-inflammatory drugs is still in progress. Pain secondary to inflammation process is the manifestation of inflammatory disorder, its evaluation in anti-inflammatory agents are rational. The role of free radicals and free radical mediated lipid per oxidation as a mechanism of tissue damage in inflammation and ulcerogenosis is emphasized. So the present investigation aimed to study analgesic, anti-inflammatory and antiperoxidative effect of methanolic extract of Barleria lupulina (MEBL).

Methods: The anti-inflammatory activity of MEBL (200 and 300 mg/kg i.p) was studied by using the models of carrageenan, serotonin induced paw edema and cotton pellet granuloma pouch in rats for assessing the effect of acute and chronic inflammation respectively. The analgesic activity of MEBL (200 and 300 mg/kg i.p) was studied using acetic acid induced writhing test in mice for assessing peripheral analgesic effect. Invitro anti-oxidant studies were carried out to assess the efficacy as hydroxyl radical (OH.), hydrogen peroxide (H_2O_2), superoxide anion and lipid peroxide. The ulcerogenic study of the extract (300mg/kg) was also performed.

Results: MEBL treated rats showed significant inhibition of carrageenan and serotonin induced edema volume ($P<0.01$). It also exerted significant reduction in granuloma weight ($P<0.01$) when compared with indomethacin. The invitro results also showed significant scavenging of OH. ($P<0.01$) and decreased lipid peroxide formation ($P<0.01$). Acute administration of MEBL did not produce any gastric lesion in rats.

Conclusions: These results suggest that MEBL exerts analgesic and anti-inflammatory activity in acute and chronic inflammation without ulcerogenic activity. This effect may be probably released to its antioxidant activity. The present study establishes the analgesic and anti-inflammatory activity of the extract.

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HEPATOPROTECTIVE AND ANTITUMOR ACTIVITY OF SOY ISOFLAVONES

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Introduction: Chemoprevention of cancer by natural products is an emerging discipline due to its wider applicability and acceptance. In this study we assesses the protective effects of soy isoflavones (SFI), major active component in soybean, against carbon tetrachloride-induced oxidative hepatic damage and tumor response in male wistar rats.

Methods: Estimation of different antioxidant and antioxidant enzymes was carried out by standard methods. LPO was done by (Wright et al, 1981). Protein content in all samples was estimated by the method of (Lowry et al, 1951) using bovine serum albumin as standard. ODC was determined by method of O'Brien et al (1975). The isolation of renal DNA and incorporation of [^{3}H] thymidine was done by the method of Smart et al (1986).

Results: CCl_4 (1:1 v/v in corn oil was administered orally at dose of 1ml/kg bwt) causes oxidative stress, as shown by depletion in hepatic glutathione content, activities of hepatic anti-oxidant enzymes, with enhancement in thio barbituric acid reactive species. CCl_4 treatment also induced, SGPT, SGOT and LDH and tumor promotion markers, however pretreatment of rats with SFI (20 and 40mg/kg body weight, orally) resulted in a significant decrease in LPO, SGPT, SGOT and LDH hepatic ODC activity and DNA synthesis (P<0.001). There was also significant recovery of hepatic glutathione content (P<0.01), anti-oxidant enzymes and phase-II metabolizing enzymes (P< 0.001).

Conclusion: Thus, our results evaluate SFI's therapeutic potential against CCl_4-mediated hepatic oxidative stress, toxicity, tumor promotion and subsequent cell proliferation response in Wistar rats.

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ANTIOXIDANT TOLERANCE OF LIVER AFTER CADMIUM INDUCED HEPATIC INJURIES

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Introduction : Cadmium toxicity promotes formation of reactive oxygen species (ROS) such as hydrogen peroxide which may cause cell membrane damage. Liver, being primary site for biotransfor-mation of foreign compounds is vulnerable to various chemical assaults. Ginseng has wide range of pharmacological and therapeutical action. The pharmacological activity influence antioxidant enzymes and provide protection against free radical damage. In the present study an attempt has been made to study the cadmium chloride ($CdCl_2$) induced toxicity in liver and its possible protection by Panax ginseng.

Methods : Swiss albino mice were divided into various groups. Group I_A : Only DDW was given ($CdCl_2$ control). Group IB : Tween 80 was given orally as equal volume to Ginseng extract (Drug control). Group II : Ginseng root extract (10 mg/kg body wt.) was given orally. Group III : Cadmium chloride (1 mg/kg body wt.) was given i.p. Group IV: Ginseng root extract (10 mg/kg body wt.) was given before cadmium chloride treatment and continued upto 30 days. Histopathological study and liver function test in serum such as serum glutamate oxaloacetate transaminase (sGOT), serum glutamate pyruvate transaminase (sGPT) and alkaline phosphatase were done in liver.

Results : Histopathological damage was observed in liver such as necrosis, pyknosis, karyolysis, karyorhexis in animals of group III as compared to group I_A. Highly significant increase ($P < 0.001$) in the value of sGPT, sGOT and alkaline phosphatase have also been noticed. In combination group Ginseng maintained the liver histo architecture as normal with highly significant decrease ($p < 0.001$) in the value of sGOT, sGPT and alkaline phosphatase level.

Conclusion : Thus Ginseng is found to be protective against cadmium induced hepatic injury.

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INFLUENCE OF OXIDATIVE STRESS-INDUCED GASTROINTESTINAL ALTERATIONS ON PHARMACOKINETICS OF METFORMIN IN RATS

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Introduction: The gastric emptying, intestinal transit and transport are some of the determinants of absorption of any orally administered drug and oxidative stress has been reported to influence these determinants. Metformin is an oral antidiabetic agent and diabetes has been shown to generate oxidative stress. Hence, it is proposed to investigate influence of experimentally-induced oxidative stress on the pharmacokinetic profile of metformin.

Methods: The oxidative stress was induced in rats by co-joint administration of ferrous sulphate (FeSO4) and ascorbic acid (ASA) (250mg/kg i.g. each) for seven days. The Gastric emptying (GE) and intestinal transit (IT) were assessed by Non-nutrient meal and Charcoal meal methods, respectively. Vitamin E (100 mg/kg i.g.) was given simultaneously to substantiate the involvement of oxidative stress and to study the effect of antioxidant in the same. For pharmacokinetic studies, blood was withdrawn on different time intervals from 0 to 24 hours, plasma was separated and levels of metformin were determined by HPLC.

Results: Co-joint administration of FeSO4 and ASA generated significant oxidative stress in both stomach and intestine as indicated by the elevation in lipid peroxidation and reduction in superoxide dismutase and catalase activities. It has also significantly delayed GE and IT in rats. This was consistent with significant alteration in pharmacokinetic profile of metformin as compared to control. Tmax was shifted by 1 hour with significant reduction in Cmax and area under curve (AUC)0-24 compared to control. Vitamin E treatment attenuated all above alterations and attributes these alterations to oxidative stress.

Conclusion: Oxidative stress impairs functional abilities of organs like stomach and intestine leading to delayed emptying and transit that subsequently alters pharmacokinetic profile of metformin.

FREE RADICALS AND ANTIOXIDANTS IN RENAL DISEASES

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LIPIDS AND RENAL OXIDATIVE INJURY: ROLE OF EICOSAPENTAENOATE-LIPOATE (EPA-LA) DERIVATIVE

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Introduction: It is well known that dietary cholesterol plays an important role in development of atherogenesis and renal disease. The present study explores the lipemic-oxidative injury in the hypercholesterolemic atherogenic animals. Further the effects of eicosapentaenoic acid (EPA), DL â- lipoic acid (LA) and eicosapentaenoate-lipoate derivative (EPA-LA) have been tested for their efficacy in controlling the atherogenic oxidative stress.

Methods: Four groups of male Wistar rats were fed with a high cholesterol diet (rat chow supplemented with 4% cholesterol and 1% cholic acid; HCD) for 30 days. Of these groups, 3 groups of rats were treated with either EPA (oral gavage, 35 mg/kg body weight /day), LA (oral gavage, 20 mg/kg body weight /day) or EPA-LA derivative (oral gavage, 50 mg/kg body weight /day) from 16th day to 30th day of the experimental period. Lipid peroxidation, protein carbonylation and antioxidant status were assessed in renal tissue and their serum were assessed for activities of acid phosphatase, alkaline phosphatase and lactate dehydrogenase using standard procedures.

Results: HCD fed rat shows abnormal increase in renal lipid peroxidation, protein carbonylation as well as elevated activities of serum marker enzymes accompanied by a depressed renal enzymic and nonenzymic antioxidants defence system. These changes were partially restored to normalcy in the EPA and LA treated groups however, their combined derivative EPA-LA more effectively restored the altered parameters to near normalcy (P0.05).

Conclusion: The results of this study present the oxidative injury induced by hypercholesterolemic diet. Administration of the combination treatment of EPA-LA afforded sound protection against the lipemic-oxidative injury.

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NITRIC OXIDE LEVELS IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS

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Introduction:Nitric Oxide(NO), an L-arginine derivative, exerts a variety of renal and extra renal physiological and pathophysiological effects. NO regulates glomerular ultrafiltration, tubular reabsorption and intra renal renin secretion. Impaired NO synthetic pathway could have a keyrole in modulating the complex renal hemodynamic disorders associated with progression of renal diseases. This study was carried out to determine if there are any changes in the levels of NO in patients of chronic glomerulonephritis, as the disease progresses in conjunction with poor renal function.

Methods:30 patients of chronic glomerulonephritis who were on maintenance hemodialysis (MHD) with serum creatinine levels>2.5 mg/dl were included in the study. 30 healthy voluntary blood donors were taken as controls. NO was estimated by spectrophotometric method using cadmium reduction. Routine renal function tests like serum urea and creatinine were performed by standard clinical chemistry procedures.

Results:The serum NO levels were found to be significantly increased (P<0.001)in chronic glomerulonephritis patients on MHD (9935 mol/l) as compared to the controls (22 7mol/l).NO output correlated with serum creatinine and urea concentration (P<0.001).

Conclusion:In this study markedly enhanced NO level may be due to induction of NO synthase which is mainly derived from infilterating macrophages. Since NO output correlated with serum creatinine and urea concentration, the higher NO production may indicate insufficient blood purification. This effect most probably results from a common effect on their elimination pathway via the renal tract. Alterations of renal function that are reflected in changes of creatinine concentration will be accompanied by the changes in serum NO. Therefore, determination of NO levels in the peripheral blood may be useful in assessment of dialysis and as a marker in the follow up and prognosis of these patients.

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PROTECTIVE EFFICACY OF *MENTHA PIPERITA* AGAINST ARSENIC INDUCED RENAL DAMAGES IN SWISS ALBINO MICE

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Arsenic compounds are ubiquitously distributed natural toxicants and are considered to be mutagenic, teratogenic and carcinogenic in humans. Arsenic may be released into the environmental through industrial processes and through the generation of power from coal. It is also widely used in agriculture and was formerly used extensively in medicine. For the general population, exposure to arsenic occurs mainly through the ingestion of foodstuffs containing inorganic and organic arsenicals. Exposure of arsenic may induce the formation of reactive oxygen species (ROS) or free radicals in the body of animals. Excessive generation of ROS is implicated in many degenerative diseases. Hence phytochemicals, which have the propensity to scavenge free radicals, can effectively be employed to modulate oxidative damage. The present investigation reports protection against arsenic induced toxicity by *Mentha piperita* (commonly called, Peppermint; Family- Labiatae) leaves extract (ME) in Swiss albino mice. Activity of Alkaline phosphatase (ALP), Acid phosphatase (ACP), Lactate dehydrogenase (LDH), Lipid peroxidation (LPO), and Reduced glutathione (GSH) were measured in kidney homogenates. The results indicated that there was a significant increase in LPO content & ACP activity and decrease in GSH, LDH & ALP activity observed following sodium arsenite (4.0 mg/kg body weight) treatment. Whereas, in combined treatment of ME (1.0 gm/kg body weight) with sodium arsenite (4.0 mg/kg body weight), a significant decrease in LPO content & ACP activity and elevation in GSH, LDH & ALP activity was observed as compared to sodium arsenite treated group. ME extract was also effective in reducing the pathological alterations in the kidney. Thus the results from the present study suggest that pre and post treatment of *Mentha piperita* leaves extract can significantly protect the renal damage against sodium arsenite induced toxicity.

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ASSESSMENT OF ANTIOXIDATIVE POTENTIAL OF *TERMINALIA CHEBULA* AGAINST Fe-NTA INDUCED RENAL PROLIFERATIVE RESPONSE AND TOXICITY

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Introduction: Free radicals and reactive oxygen species have been associated with the etiology and or/progression of a number of renal diseases. Iron complexed nitrilotriacetate (Fe-NTA), which has been widely used as a polyphosphates in household detergent, is known to injure kidney through the activity of reactive oxygen species. This study explores the protective effect of *Terminalia chebula* in abating the toxic and hyperproliferative response of Fe-NTA in rat kidney.

Methods: Blood Urea Nitrogen (BUN) and Creatinine was estimated by method of Hare (1950) and Kanter (1975). ODC was determined by measuring the release of $^{14}CO_2$ from DL-[-^{14}C] ornithine by the method of O'Brien et al (1975). The isolation of renal DNA and incorporation of [^{3}H] thymidine was done by the method of Smart et al (1986).

Results: Single ip injection of Fe-NTA (9mg Fe/kg b.wt) in rats resulted in induction in ODC ($p<0.001$) and increase in [^{3}H] thymidine incorporation in renal DNA ($p<0.001$) as compared to saline treated control groups. Parallel to this a sharp increase in BUN ($p<0.001$) and serum Creatinine has been also observed ($p<0.001$) Pretreatment with *Terminalia Chebula* (5 & 10mg/kg b.wt) ameliorated the Fe-NTA mediated induction of ODC activity and [^{3}H] thymidine incorporation into DNA in a dose dependent manner. Also a sharp decrease in BUN and Serum Creatinine has been observed in a dose dependent manner.

Conclusion: The protective effect of *Terminalia chebula* against the toxic insult of Fe-NTA suggests that it is a potent chemopreventive agent and may suppress Fe-NTA induced early tumor promotion markers.

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IMPACT OF URSOLIC ACID ON ETHANOL-MEDIATED OXIDATIVE DAMAGE IN RAT KIDNEY

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Introduction: Oxidative stress play a vital role in the pathogenesis of ethanol associated tissue injury, supplementation of antioxidants may have a protective role in these conditions. Ursolic acid, a pentacyclic triterpenoid, is a natural antioxidant and its hepatoprotective effect against ethanol was already evaluated. The objective of this study was to determine the effect of ursolic acid on alcohol-mediated toxicity in rat kidney.

Methods: Adult albino Wistar rats'were used in this study. Ethanol and ursolic acid were administered (post oral) as aqueous solution using intragastric tube. At the end of the 60 days of experimental period, animals were sacrificed and the kidney was used for various estimations. Statistical analysis was done by one way analysis of variance followed by Duncan's multiple range test.

Results: Ethanol administered rats (7.9 g/kg/day for 60 days) exhibited significant ($p<0.05$) elevation of plasma urea, uric acid and creatinine and the lipid peroxidation products such as malondialdehyde and lipid hydroperoxides in plasma and kidney. The levels of reduced glutathione, ascorbic acid and ?-tocopherol and the activities of were decreased in the kidney of alcohol-administered rats. However, coadministration of ursolic acid (20 mg/kg for 30 days) along with the daily dose of ethanol reduced the levels of urea, uric acid, creatinine and lipid peroxidation markers. The levels/activities of antioxidants, which were reduced by alcohol administration, were raised by the coadministration of ursolic acid. Histological examinations also confirm the protective effect of ursolic acid on kidney of ethanol-administered rats.

Conclusion: Ursolic acid prevents the kidney damage in ethanol-administered rats by decreasing the lipid peroxidation and by enhancing the levels of endogenous antioxidants

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ROLE OF METHYL GLYOXAL IN ASSOCIATION WITH FREE RADICAL DAMAGE AND ANTIOXIDANT STATUS IN UREMIA.

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Introductin : Methyl glyoxal, an endogenus dicarbonyl compound, has been recently found to be accumulated by enzymatic or non-enzymic pathway in Diabetes mellitus. It is a common intermediate in Maillard reaction which reacts with protein to form advanced glycated end product (AGE) .AGE plays an important role to accelerate free radical mediated vascular damage . In our present study we wish to determine the methyl glyoxal concentration of blood level and total anti oxidant status in uremic patients as the disease is also associated with vascular tissue damage.

Materials and Methods : In the present study , 110 patients with high serum urea level and serum creatinine level above 7.0 mg/dl were identified from the out patient and inpatient dept. of Medicine , Nilratan Sircar Medical College and Hospital, Kolkata and 41 healthy normal people served as control over a period of 2 years. Serum of both patients and normal people were analyzed for methyl glyoxal level , total antioxidant status against trolox , NO level and lipid peroxidation by estimating malon dialdehyde (MDA) level by standard method .

Result : Methyl glyoxal level in uremic patients (creatinine > 7.0 mg /dl) were found to be highly significant ($p<0.01$) compared to normal control (creatinine < 1.2 mg / dl) . NO level as estimated by Griess reagent was significantly low . Lipid peroxidation , estimating the level of MDA was also significantly higher ($p<0.05$) associated with low level of reduced glutathione and low level of anti oxidant status of serum estimating against trolox as standard antioxidant.

Conclusion : Increased level of methyl glyoxal associated with poor level of NO, total antioxidant and glutathione can be correlated with vascular damage in uremia. Our hypothesis in this regard is increased level of methyl glyoxal in uremia possibly damage the protein part of nephrone interacting with it by neucleophilic attack and form glycated protein. Moreover it reduces the antioxidant defence mechanism utilizing glutathione by glyoxalase system.

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REVERSAL OF Fe-NTA INDUCED RENAL OXIDATIVE STRESS BY PLUCHEA LANCEOLATA (RASNA).

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Introduction: Fe-NTA is known to promote carcinogenesis; acts through induction of oxidative stress. Earlier investigations have proved an inverse correlation between the incidence of cancer and intake of dietary antioxidants and plant phenols. Here we have investigated the antioxidant properties of Pluchea Lanceolata (PL) against Fe-NTA induced renal oxidative stress and toxicity.

Methods: Estimation of different antioxidants and antioxidant enzymes was carried out by standard methods. Levels of MDA formation and Xanthine Oxidase (XO) was done by (Wright etal, 1981) and (Stripe and Della Corte, 1969). Protein content in all samples was estimated by the method of (Lowry et al, 1951) using bovine serum albumin as standard. The level of significance between different groups is based on ANOVA test, followed by the Dunnett's t test.

Results: Single i.p. injection of Fe-NTA (9mg Fe/kg b.wt) resulted in significant increase in MDA formation ($p<0.001$) and XO levels ($p<0.05$) with simultaneous depletion of renal catalase activity ($p<0.001$) and reduction in renal glutathione (GSH)($p<0.001$) and its dependent enzymes ($p<0.001$). Prophylactic treatment of PL extract at doses (100 & 200 mg\Kg bwt.) for seven consecutive days prior to Fe-NTA administration resulted in modulation of MDA ($p<0.001$) and XO levels ($p<0.10$ & 0.05) with concomitant attenuation of renal CAT activity ($p<0.001$) and restoration of other defence system that is GSH ($p<0.05$) and dependent enzymes ($p<0.001$) compared to treated control values.

Conclusion: Our data suggests that PL is a chemopreventive tool against Fe-NTA induced oxidative stress by increasing antioxidants level and by scavenging free radicals.

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PROTEIN THIOLS AND FREE IRON IN UREMIA

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Introduction: Uremia is generally associated with enhanced oxidative stress. The oxidative stress may be enhanced by hemodialysis. In the present study, oxidative stress marker i.e., protein thiols and serum free iron levels were estimated in patients with uremia on conservative management and on patients undergoing hemodialysis for atleast one year. The objective of the study was to correlate free iron levels with protein thiols and to establish whether the free iron was functioning as an oxidant and damaging the protein thiol groups.

Methods: The study was performed on controls (n=20), chronic renal failure (CRF) on conservative management (n=24) and on CRF patients on hemodialysis (HD) (n=32). The serum protein thiol was estimated using dithionitrobenzoic acid. Serum free iron (non transferrin bound iron) was estimated by the bathophenanthroline disulfonate assay.

Results: The free iron levels (ferrous, ferric and total) in HD were significantly higher than in normal controls and CRF. However, the free iron levels in CRF and controls were comparable. There was a significant decrease in protein thiols in the HD and CRF groups compared to controls. However, there was no significant difference in protein thiols between CRF and HD. The free iron levels correlated positively with serum creatinine whereas the protein thiols demonstrated a negative correlation with serum creatinine. There was a lack of correlation between free iron and protein thiols.

Conclusion: Iron is released from storage sites and transferrin in patients on hemodialysis and is present as NTBI in circulation. Free iron and protein thiols are indicators of extent of renal failure. A lack of correlation between free iron and protein thiols may indicate that free iron is not causing oxidative damage to protein thiol groups.

FREE RADICALS AND ANTIOXIDANTS IN NEUROLOGICAL DISORDERS

P-55

EFFECT OF CYCLOOXYGENASE-2 (COX-2) ON RESTRAINT STRESS INDUCED ALTERATIONS IN DIFFERENT BEHAVIORAL AND BIOCHEMICAL PARAMETERS

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Introduction: Chronic stress precipitates many neuropsychiatric disorders and alters the various oxidative stress parameters in brain. Cyclooxygenase is the rate-limiting enzyme in the metabolism of arachidonic acid into different prostanoids and recently it is known to express in different regions of brain. COX-2 is reported to play an important role in pathogenesis of various neurodegenerative disorders including stroke, seizures. With this background, the aim of the present study was to see the effect of COX-2 inhibitors in restraint stress.

Method: Male Laca mice, weighing 22-30 gm were used in the present study. Mice were immobilized for 6 hrs each day for total of seven days. COX-2 inhibitors were administered daily in respective groups before giving them restraint stress. On 8th day various behavioral and biochemical parameters were studied.

Results: Pretreatment with rofecoxib (2 mg/kg i.p.) and nimesulide (2.5 mg/kg, i.p.) showed significant protection in restraint stress. Biochemical analysis revealed that chronic restraint stress significantly increased lipid peroxidation, nitrite levels and decreased the reduced glutathione and adrenal ascorbic acid levels. Behavioral analysis revealed the hyperlocomotion activity and increased anxious response. Chronic treatment with COX-2 inhibitors significantly reversed the restraint stress induced behavioral and biochemical alterations ($p0.05$).

Conclusion: In conclusion, the result of the present study suggested that COX-2 plays an important role in chronic stress and the use of COX-2 inhibitors could be a useful neuroprotective strategy in the treatment of stress.

P-56

BRAIN OXIDATIVE STRESS AND COGNITIVE IMPAIRMENT IN ACUTE TREATMENT OF 3-NITROPROPIONIC ACID-INDUCED NEUROTOXICITY AS AN ANIMAL MODEL OF HUNTINGTON'S DISEASE

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Introduction: Huntington's disease (HD) is a progressive neurodegenerative disorder characterized by progressive dementia and involuntary abnormal movements. Oxidative stress and associated neurotoxicity has been implicated in the pathogenesis of neurodegenerative disorder, including HD. Chronic systemic administration of 3-nitropropionic acid (3-NPA) decreases the levels of the mitochondrial enzyme succinate dehydrogenase (SDH) and impairs the oxidative energy metabolism and cognitive functions, and is widely used as an animal model to study HD. Despite our increasing knowledge on the 3-NPA-induced neurotoxicity, the effects of acute administration 3-NPA on these parameters are not known.

Methodology: Therefore, the present study was undertaken to investigate the effect of single dose intraperitoneal injection of 40 mg/kg 3-NPA on oxidative energy metabolism, the role of free radicals mediated-neurotoxicity, involuntary movements, and cognitive decline in rats. Using Morris water-maze and elevated plus-maze paradigms assessed cognitive behavior and motor activity was also assessed 24h after 3-NPA administration. Rats were sacrificed on the same day (24h after 3-NPA administration) for estimation of succinate dehydrogenase (SDH) and oxidative stress parameters (malondialdehyde (MDA) and reduced glutathione) in the whole brain after completion of the behavioural task.

Results: A single intraperitoneal injection of 3-NPA in rats showed a significant increase in MDA levels, decrease in reduced glutathione and SDH level, and impaired cognitive functions ($P<0.05$). Besides, significant involuntary movements such as tremors and head wobbling, which resemble involuntary choreiform movements in HD patients, were also observed in rats.

Conclusion: The present findings suggest that acute 3-NPA-induced neurotoxicity may also be used as a valuable tool for studying pathogenesis of HD and to explore neuroprotective and antioxidant strategies in the prevention of oxidative stress as well as the cognitive deficits in this model. However further studies with neurochemical and morphological alterations in the brain are warranted.

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OXIDATIVE STRESS, VITAMIN E, ASCORBIC ACID AND REDUCED GLUTATHIONE STATUS IN SCHIZOPHRENICS

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A disturbance in the antioxidant defense system including vitamin E, ascorbic acid and reduced glutathione metabolism has been implicated in Schizophrenia, therefore the changes and role of vitamin E, ascorbic acid and reduced glutathione levels in blood and their correlation with oxidative stress were studied. Significantly lower levels of vitamin E ($P<0.01$), total ascorbic acid ($P<0.01$) and glutathione ($P<0.01$) were found in Schizophrenics compared to normal. A significant rise in dehydroascorbic acid ($P<0.02$) with concomitant fall in reduced ascorbic acid ($P<0.01$) suggests scavenging action of ascorbic acid and its utilization with increased oxidative stress as indicated by high blood malondialdehyde levels ($P<0.01$). Leucocyte ascorbic acid, the most stable index of ascorbic acid status, as it does not fluctuate with recent intake, was also found at a lower range in schizophrenia ($P<0.01$) suggesting depletion of body stores of ascorbic acid. Thus, supplementation of these vital antioxidants in schizophrenia may be beneficial to counteract oxidative stress.

P-58

ROLE OF HOMOCYSTEINE IN AETIOPATHOGENESIS AND CONTROL OF EPILEPSY

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Objectives: To find the association of hyperhomocysteinemia with i) risk of epilepsy, ii) control of epilepsy, iii) antiepileptic drugs (AED), iv) multivitamins.

Methods: 100 epilepsy patients aged <70 years, with normal CT scan / MRI brain were selected and divided into three groups according to AED given; Group I : 45 patients on phenytoin or carbamazepine; Group II : 45 patients on valproate; Group III : 10 patients on clobazam. Some patients were given vitamins (B_6, B_{12}, folate). Total plasma homocysteine (tHcy) levels were measured on the first visit and after 6 months therapy with AED.

Results: Group ^{2} patients (not on vitamins) showed significant increase in tHcy ($p<0.001$) which showed significant fall after adding vitamins ($p=0.017$). Group^{22} patients, (not on vitamins) showed significant decrease in tHcy ($p<0.001$) and showed further fall in tHcy after adding vitamins (% difference of tHcy $p=0.033$). Group ^{222} patients did not show any significant change in tHcy in patients with or without vitamins. Patients with different seizure types did not show any variation of tHcy with respect to one another. tHcy did not show any variation with number of seizure recurrence on follow-up or duration and recurrence of seizures in the past.

Conclusions: Plasma homocysteine levels increased in Group ^{2} (hepatic enzyme inducers) and decreased in Group ^{22} (hepatic enzyme inhibitors) patients. Vitamins significantly decreased tHcy in Groups ^{2} & ^{2} ^{2}. Group ^{222} patients did not show any change in tHcy with or without vitamins. The present study could not find any correlation of tHcy with type of seizures and past history of seizures. Addition of vitamins did not change the frequency of seizures.

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PROANTHOCYANIDIN SUPPLEMENTATION MODULATES CHOLINERGIC SYSTEM IN ADULT RAT BRAIN

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Introduction: It is a well known fact that food and health are closely related. Diet-derived antioxidants [AO] play an important role in prevention of human disease, especially polyphenols that have a significant role in disease prevention *in vivo*.

Methodology: Our investigation aimed at evaluating the changes, if any, in the cholinergic neurotransmitters as a response to oral supplementation of grape seed proanthocyanidin extract [PA], in the regions associated with cognition. The experimental design consisted of three supplementation groups [n=5], PA_1, PA_2 and PA_3 which received a daily oral PA of 25, 50 and 75 mg / kg body weight respectively, for a total period of 45 days. The controls were unsupplemented. Choline acetyl transferase [ChAT], acetyl choline [ACh] and choline esterase [AChE] activities were analyzed in the cerebral cortex [CC], hippocampus [HC], and cerebellum [CB].

Results: Significant [$p<0.05$] up-regulation in ChAT activity was evident in the PA_1 group as compared to PA_2 and PA_3. Regional changes were however insignificant. ACh, a neurotransmitter was found to be significantly higher [$p < 0.05$] in PA_1 animals than the controls and the other two supplementation groups. AChE activity was lowered in PA_1 animals in comparison with other supplemented groups and controls. Significant regional changes were noticed, with HC and CB exhibiting higher [$p < 0.05$] activity than CC

Conclusion: Collectively, our results focus on the neuromodulatory effects of PA when administered at a higher dose, wherein an increase in ACh synthesis was observed with a concomitant decrease in its hydrolyzing enzyme, AChE. Further, a parallel increase in ChAT signifies the probable implication of PA supplementation in enhancing the cognitive abilities with age.

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P-60

DOES REM SLEEP DEPRIVATION RESULT IN OXIDATIVE STRESS?

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Introduction: Free radicals and the resulting oxidative stress have been implicated as one of the causes for the effects of sleep deprivation like increased food intake and weight loss. Hence effect of REM sleep deprivation (REMSD) on brain oxidative stress was investigated in the current study.

Method: Wistar strain male rats weighing between 150-180g were deprived of REM sleep using the inverted flower pot technique. The animals were divided into four subgroups of six animals each based on the duration of REMSD 24,48,72 and 96 hours. Following the specified duration of REMSD animals were sacrificed and discrete regions of the brain, hypothalamus, midbrain, hindbrain and cerebral cortex, were dissected out for the study of lipid peroxidation, superoxide dismutase (SOD), catalase (CAT), total reduced glutathione (GSH) and glutathione peroxidase (GPX). All these results were compared with REM control animals as well as cage control animals. The effectiveness of restorative sleep in returning back these changes to baseline values were also investigated by allowing the animals to sleep in their home cages for 12,

18 and 24 hrs after depriving them of REM sleep for 96hrs. All the results obtained were analyzed using two way analysis of variance with time and group as main effects.

Results: REM sleep deprivation resulted in increase in lipid peroxidation and significant decrease in the levels of the antioxidant enzymes SOD, CAT and also GSH and GPX in all the regions studied. These changes were also time dependent. All these changes reverts back to baseline value gradually by 24 hours of restorative sleep

Conclusion: This study shows REM sleep deprivation (24h 96h) results in oxidative stress, which is reversible.

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POSSIBLE ROLE OF FREE RADICALS IN A MODEL OF NEUROPATHIC PAIN IN RATS WITH CHRONIC CONSTRICTION NERVE INJURY

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Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India**Introduction**: Neuropathic pain is a common and chronically debilitating condition characterized by persistent pain, dysthesia, hyperalgesia and allodynia. Peripheral nerve injury is associated with wallerian degeneration and significant neuroplastic changes in the spinal cord. It is well known that free radicals are released during tissue injury and cause oxidative stress. However, the role of free radicals and resultant oxidative stress is not known in nerve injury. Thus the present investigated the role of free radicals in nerve injury and to examine the effects of bioflavonoid, quercetin on chronic constriction injury to sciatic nerve in rats.

Methodology: The chronic constriction nerve injury was produced by placing 4 ligatures of chromic gut around the sciatic nerve with 1-mm intervals. Reduced glutathione and thiobarbituric acid reacting substances (TBARS), the markers of oxidative stress were measured in nerve homogenate. Allodynia (heightened response to normally non-noxious stimuli) and hyperalgesia (decreased threshold to noxious stimuli) were also evaluated in sham and sciatic nerve injured rats. Quercetin (10 and 20 mg/kg) was per orally administered 24 h before and 14 days following nerve injury.

Results: Sciatic nerve injury in rats significantly increased TBARS, a marker of tissue lipid peroxidation and decreased reduced glutathione as compared to sham-operation in rats. In addition, marked allodynia and hyperalgesia was also observed on day 14 following nerve injury in rats. Chronic quercetin treatment significantly decreased elevated TBARS levels and improved reduced glutathione levels. Further, quercetin treatment was also attenuated the maintenance of allodynia and hyperalgesia in nerve injured rats.

Conclusion: These results clearly demonstrate the pivotal role of free radicals and resultant oxidative stress in neuropathic pain following nerve injury in rats and suggest to explore antioxidant strategies in the prevention of oxidative stress as well as hypersensitivity following nerve injury.

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NICOTINE OXIDATIVE AND ANTIOXIDANT PROPERTIES IN CNS

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Introduction: Nicotine has been reported to be therapeutic in some patients with certain neurodegenerative diseases and to have neuroprotective effects in the central nervous system. However, nicotine administration may result in oxidative stress by inducing the generation of reactive oxygen species in the periphery and central nervous system. The possibility that nicotine might be used to treat certain neurodegenerative diseases underlies the necessity to determine whether nicotine has pro-oxidant, antioxidant or both. The present investigation addresses this issue.

Materials: The pro-oxidant activity of nicotine is evaluated by administering nicotine 1.6 mg/kg orally for 10 days. Animals were sacrificed at the end of the experimental period. The homogenates of liver, lung and brain was prepared and used for the estimation of lipid peroxide and antioxidant enzymes like superoxide dismutase, catalase and glutathione peroxidase. The anti-oxidant profile of nicotine is studied in-vitro model against generation of hydroxyl radical from hydrogen peroxide and chelation with iron.

Results: Nicotine at the tested dose level showed significant increase in lipid peroxide and decrease in antioxidant enzyme level ($P<0.01$). This indicates its oxidant nature of liver lungs and brain.

Results of in-vitro experiments showed significant metal chelating ($P<0.01$) and hydroxyl radical scavenging activity ($P<0.01$).

Conclusions: Our present investigation suggests that under certain circumstances nicotine induce oxidative stress. Though in-vitro studies showed antioxidant properties it was not found in-vivo. Therefore, it may be possible to suggest that the neuroprotective property of nicotine could be by another mechanism other than via. Antioxidant mechanism.

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ROLE OF NITRIC OXIDE IN THE EXPERIMENTAL MODELS OF PARKINSON'S DISEASE

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Parkinson's disease (PD), a severe and progressive neurodegenerative disorder is caused by the selective loss of dopaminergic neurons of nigrostriatal pathway. Recent studies attribute the cell loss in substantia nigra to oxidative stress, excitotoxicity and mitochondrial dysfunction. Nitric oxide (NO) a free radical, normally acts as a neuronal messenger, however, excessive production of NO cause neuronal death. nNOS positive neurons are found in the human and rat SN, while iNOS was found to be expressed in PD patients. NO thus seems to mediate an important role in neurodegeneration. Present study was undertaken to evaluate the role of O in 6-hydroxydopamine (6-OHDA) or lipopolysaccharide (LPS) inducedeurodegeneration, which was injected in the rat right striatum and substantia nigra. Involvement of NO was investigated by iNOS expression as well as by measuring NO metabolite, nitrite. Lesion positive animals exhibited amphetamine-induced rotations, increased iNOS expression and nitrite levels at 24, 48 and 72 hrs after LPS or 6-OHDA administration. While TH immunolabeling was reduced in a time dependent manner, which correlated inversely with the increase in iNOS staining. Rats pretreated with Nitro-L-arginine methyl ester (L-NAME, 30mg/kg) were protected from 6-OHDA or LPS induced neurodegeneration. Results obtained thus suggest that NO seems to have a detrimental role in 6-OHDA and LPS induced neurodegeneration.

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EFFECT OF CARVEDILOL ON OXIDATIVE STRESS-RELATED NEUROTOXICITY AND COGNITIVE IMPAIRMENT IN A RAT MODEL OF HUNTINGTON'S DISEASE

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Introduction: Huntington's disease (HD) is a neurodegenerative disorder characterized by abnormal movements and cognitive decline. 3-Nitropropionic acid (3-NPA) is known to induce cellular energy deficit and oxidative stress related-neurotoxicity via an irreversible inhibition of the mitochondrial enzyme succinate dehydrogenase (SDH). 3-NPA toxicity has gained as an animal model of HD. Therefore; the present study was designed to investigate effects of carvedilol (CVD), a third-generation beta-blocker with potent free radical-scavenging activity and curcumin (CMN) on 3-NPA-induced-oxidative stress and resultant cognitive impairment in a rat model of HD.

Methods: Male Wistar rats were intraperitoneally administered 3-NPA (40 mg/kg), four days after oral administration of CVD (5 and 10 mg/kg) and CMN (20 and 40 mg/kg). Cognitive behaviour tasks were assessed by using Morris water-maze and elevated plus-maze paradigms and motor activity by actophotometer 24h after 3-NPA administration. Rats were sacrificed on the same day (24h after 3-NPA administration) for estimation of succinate dehydrogenase (SDH) and oxidative stress parameters (Malondialdehyde (MDA), and reduced glutathione) in the whole brain immediately after completion of the behavioural tasks.

Results: Intraperitoneally administered 3-NPA caused a significant rise in MDA level and decrease in reduced glutathione and SDH. Unlike CMN (20 and 40 mg/kg), oral administration of carvedilol (5 and 10 mg/kg) significantly reversed the decrease in reduced glutathione level ($P<0.05$). However changes in lipid peroxidation levels were not significant in both the drugs (CVD and CMN) treatments as compared to control. Besides, both the drugs treatment significantly improved the cognitive performance tasks (moris water maze and plus maze) as well as motor activity in rats administered with 3-NPA. However, the decrease in SDH activity was unaltered by both CVD and CMN pretreatment.

Conclusion: The present findings indicate that pretreatment with carvedilol, but not curcumin, is effective in preventing 3-NPA induced oxidative stress as well as cognitive deficits in rats. Based on the above observations, further studies are warranted in chronic 3-NPA-induced

Date : 11th January 2005

Time : 1430-1600 H

Chairpersons: Rajni Agarwal India

Parameswaran Australia

FREE RADICALS AND ANTIOXIDANTS IN CANCER

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THERAPEUTIC EFFECT OF SEMECARPUS ANACARDIUM LINN NUT EXTRACT ON MITOCHONDRIAL TCA CYCLE AND RESPIRATORY CHAIN ENZYMES IN MAMMARY CARCINOMA RATS

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Introduction- Breast cancer is a life threatening disease confronting female population worldwide. Approximately 80% of the world's population rely on the use of traditional medicine which is predominantly based on plant materials. Semecarpus anacardium Linn of the family "anacardiaceae" has many applications in the Ayurvedic and Siddha systems of medicine

Materials and Methods- Mammary Carcinoma was induced with 7,12- dimethylbenz(a)anthracne (25 mg) dissolved in 1 ml of olive oil, into eight weeks old rats through gastric intubation for a period of three months. Treatment was started orally with Semecarpus anacardium nut extract (200 mg/kg body weight) dissolved in olive oil and continued for fourteen days daily. The activities of mitochondrial TCA cycle enzymes and respiratory chain enzymes in mammary carcinoma animals were studied..

Results- A significant decrease in the activities of the mitochondrial TCA cycle enzymes viz isocitrate dehydrogenase, ?- ketoglutarate dehydrogenase, succinate dehydrogenase and malate dehydrogenase ($p<0.001$)and respiratory chain enzymes such as NADH dehydrogenase and Cytochrome-c-oxidase ($p<0.01$)were observed in mammary carcinoma bearing (Group II) animals when compared to normal control animals (Group I). Semecarpus anacardium nut extract administration increased the activities of TCA cycle enzymes ($p<0.001$), Respiratory chain enzymes ($p<0.05$) when compared to diseased (Group II) animals. Non-significant variations were observed in drug control (Group IV) animals when compared to normal control animals (Group I).

Conclusion-In the present study, decreased activities of TCA cycle enzymes suggest a loss in mitochondrial function and integrity. Upon administration of Semecarpus anacardium nut extract the activity of mitochondrial enzymes were increased suggesting the role of Semecarpus anacardium in mitochondrial energy production and also shows the antitumour and anticancer effect of the drug.

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REGULATORY ROLE OF ROS AND RNS IN EXPRESSION OF TRANSCRIPTION FACTOR AP1 IN BREAST CANCER

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Background: Reactive oxygen species such as superoxide (O^{2}), hydrogen peroxide (H_2O_2), hydroxyl radical (OH) and reactive nitrogen species (RNS) like nitric oxide (NO), peroxynitrite ($ONOO^{-}$) have been shown to play a significant role in mutagenesis and tumorogenesis. AP1 is a composite transcription factor (activator protein). It is a homo or heterodimer DNA binding protein composed of either 2-jun family members (c-jun, jun-B, jun D) or one jun and one fos family protein (c-fos, fos B, fra 1, fra2). ROS and RNS have been shown to induce c-fos and c-jun oncoproteins, which can lead to carcinogenesis.

Aim: To study nitric oxide and scavenger enzymes in one hand and c-fos& c-jun expression on other hand in breast cancer patients.

Materials and Methods: 25 women with breast cancer were taken to evaluate the blood levels for oxidative damage markers and antioxidants (like MDA, NO, GSH, GPx and SOD) and cancerous breast tissue to evaluate the level of expression of transcription factors c-fos and c-jun.25 age and sex matched healthy women without any breast disease served as control for the study of blood parameters. Tumor free adjacent healthy breast tissue from mastectomised breast of 25 breast cancer patients of study group and healthy breast tissue from 5 benign breast disease patients served as control for the study of transcription factors c-fos and c-jun.

Results: The mean serum levels of NO were higher in study group than controls ($p=0.013$). A comparison between the study and control group showed higher levels of MDA in the study group ($p=0.064$). The difference between the mean values of GSH in the study group and the control group was also statistically significant ($p=0.042$). The SOD and GPx levels showed no statistically significant difference between the two groups. The expression of c-fos and c-jun in the cancer patients ranged from high to very high, whereas the expression of c-fos and c-jun in the control group ranged from nil to moderate ($p<0.001$).

Conclusion: The increased levels of nitric oxide and glutathione in the blood of patients and the high levels of expression of c-fos and c-jun may further lend credence to the fact that transcription factors are redox regulated. The mechanisms involved in the regulation of AP-1 needs to be defined before we can think of using redox status to study the expression of this transcription factor.

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LIPID PEROXIDATION IN CANCER

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Introduction In recent years, free radicals have been implicated in the cancer process and some cancer causing factors have been thought to involve a series of stages generating free radicals particularly those of molecular oxygen. Protection of cellular structures from damage by free radicals can be accomplished through enzymatic and non enzymatic defense mechanisms. An increase of activated forms of molecular oxygen such as super oxide , hydro peroxide, hydrogen peroxide etc., due to over production or inability to destroy them, may lead to severe damage to cellular structures. Highly reactive oxygen species and free radical nduced damage and are implicated in carcinogenic processes

Methods: In the present study 60 cancer patients (19 males and 41 females) of different organs, admitted in the cancer ward of Govt. General Hospital , Kakinada. Out of these,23 patients had cancer cervix, 13 had breast cancer, 19 had Oropharyngial cancer and 5 had genitourinary cancer. 30 healthy individuals served as controls. Plasma lipid peroxides estimated as malondialdehyde by using TBA method. Ascorbic acid was estimated by the Dinitro phenyl hydrazine method.

Results Table showing the SD and 'P' values of MDA and Vit. C in Controls vs various Cancer cases studied

STUDY GROUP	MDA (nmol/dl)	Vit.C (mg/dl)
Controls	265 ± 56.4 -	0.94 ± 0.2 -
Ca.cervix	522 ± 258 <0.001	1.0 ± 0.94NS
Ca.Breast	429 ± 148 <0.001	0.5 ± 0.29<0.001
Ca.Oropharyngeal	482 ± 166 <0.001	0.7 ± 0.3 <0.002

Conclusions: Lipid peroxidation has been implicated in the pathogenesis of various diseases and cancers in the present study the lipid peroxidation as expressed by serum Malondialdehyde (MDA) is significantly higher in Ca. Breast (P<0.001). in Ca Cervix (P<0.001) and in Oropharyngeal cancer (P<0.001) in comparison to the control group.

Vitamin C may protect cell against carcinogenesis through several mechanisms in addition to DNA oxidation. Lower Vit C levels were observed in Oropharyngeal cancers (P<0.002) and in Ca. Breast (P<0.001) in comparison with control group.

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CHEMOPREVENTIVE EFFECT OF GINGER ON CIRCULATORY LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN 1,2- DIMETHYLHYDRAZINE INDUCED COLON CANCER.

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Introduction: The present study was designed to investigate the chemopreventive efficacy of ginger (*Zingiber officinale* Rosc), a naturally occuring dietary component with antioxidant and anticarcinogenic properties, during the initiation and promotion/progression stages of 1,2-dimethyl hydrazine (DMH) induced colon carcinogenesis in male wistar rats.

Materials and methods: Rats were given a weekly subcutaneous injection of DMH (20 mg/kg body weight) a known colon carcinogen. in the groin for 15 weeks. Ginger (50 mg/kg body weight) was given at the initiation and also the promotion/progression stages of carcinogenesis to DMH treated rats. The animals were sacrificed at the end of 30 weeks.

Results: The incidence of cancer as well as the number of tumors in the colon was significantly reduced on treatment with ginger as compared to the unsupplemented DMH treated rats. In the presence of DMH the levels of lipid peroxidation (thiobarbutiric acid reactive substances, lipid hydroperoxides and conjugated dienes were significantly increased whereas enzymic (superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase and glutathione reductase) and non-enzymic antioxidants (reduced glutathione, vitamin C, vitamin E, and -carotene) were significantly decreased as compared to control rats. On treatment with ginger (50 mg/kg body weight) at the initiation stage and also at the promotion/progression stages of carcinogenesis a significantly reduced circulating lipid peroxidation and significantly elevated the enzymic and non-enzymic antioxidants were observed in the circulation of DMH treated rats as compared to unsupplemented DMH-treated rats.

Conclusion: Our results show that ginger supplementation significantly inhibits colon carcinogenesis induced by the procarcinogen DMH.

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.SERUM GLUTATHIONE-S-TRANSFERASE IN ORAL CANCER

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Introduction: Free radical induced damage and the role of free radical scavenging enzymes have been linked with various epithelial malignancies including oral cancer. We estimated serum total glutathione-s-transferase (GST) in various stages of oral cancer and followed up these cases for two years to ascertain whether GST can indicate the severity of disease and chances of recurrence.

Methods: 27 biopsy proven cases of cancer of oral cavity in various stages were chosen as cases and 10 healthy age and sex matched persons were taken as controls. Blood was taken after obtaining informed consent using aseptic precautions. Serum GST was estimated before the start of any definitive treatment by the method of Habig et al. The cases (n=18) were followed up for two years after the completion of treatment to assess recurrence. GST values were expressed in international units/liter.

Results: GST level between case and control group did not show any significant change. However among the cases there was a direct correlation between GST level and severity of cases. The increase of GST from stage 2 to stage 4 was highly significant (p 0.001). Out of the cases which were followed up for two years, 13 cases had recurrence of disease within two years.

Conclusion: Serum GST level was proportional to severity of oral cancer. However the relationship between GST level and recurrence could not be commented upon because sample size was small.

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ACTIVITIES OF ENZYMES OF RESPIRATORY BURST IN THE NEUTROPHILS FROM ORAL CANCER PATIENTS SUBJECTED TO RADIOTHERAPY

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Normal neutrophils respond to foreign stimulus by undergoing 'respiratory burst' which involves a several fold increase in the activities of enzymes related to O_2^- generation.. Cancer is a pathological condition wherein neutropenia remains the factor most frequently predisposing to infections,caused due to myelosuppressive radiotherapy.Enhancement of superoxide anion production and protein levels in granulocytes leading to haemopoietic injury has been reported with a single dose of (5 grays) total body irradiation of mice.However little data is available regarding relevant studies in the granulocytes of cancer patients.Therefore we sought to determine the possible occurrence of alterations in the activities of respiratory burst enzymes in cancer patients who were on radiation treatment.17 hospitalised patients with cancers of oral cavity and oropharynx were selected for the study.

The neutrophils of these patients were analysed for the activities of NADPHoxidase,Myeloperoxidase(MPO),Glutathioneperoxidase(GSH PX),Glucose 6phosphate,dehydrogenase(G6PD),Superoxidedismutase (SOD),andGlutathione (GSH) in the baseline as well as 2 follow up samples following radiotherapy, at 15 days and 30 days respectively. 25 age and sex matched normal persons served as controls. An apparent decrease was observed in the activity of NADPH oxidase in baseline samples as well as samples obtained following radiotherapy,,compared to controls. No significant changes were observed with regard to other enzyme activities . However a significant increase in SOD was observed in the second follow up obtained after radiation,compared to baeline values.A suppression of superoxide producing enzyme in cancer suggests a very poor immune response of neutrophils in cancer patients which is in agreement with the literature. An increase in SOD activity following radiation is suggestive of an induction of this enzyme by radiation to detoxify the superoxide, targeted towards the cancer cells by way of radiation.

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MODULATORY EFFECT OF TERMINALIA ARJUNA ON GLYCOPROTEIN LEVELS ON DIETHYLNIROSAMINE INDUCED LIVER CANCER IN RATS

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Introduction: Hepatocellular carcinoma (HCC) is one of the most frequently occurring malignancy in developing countries. Even though chemotherapeutic agents like mitomycin, adriamycin and cisplatinum are effective against liver cancer, most of them are produce cytotoxic and side effects. Therefore, there is a need of alternatives for the cure of hepatic cancer. In this context, many research work have been carried out from the natural sources for cure of human diseases, particularly to cancer. Therefore we studied the efficacy of Terminalia arjuna on glycoprotein levels on DEN induced liver cancer in rats.

Methods: Single intraperitoneal injection of N-nitrosodiethylamine (200 mg/kg body weight) followed by Phenobarbitol (0.05%) were administrated to induce liver cancer. After the induction period animals were treated with ethanolic extract of T.arjuna orally at a concentration of 400mg/kg body weight for 28 days. Serum, liver and kidney samples were collected. Glycoproteins such as Hexose, Hexosamine and Sialic acids were assyed by standard methods.

Result: A significant increase in the level of Hexose, Hexosamine and Sialic acids were observed in serum and liver of cancer bearing animals ($P<0.001$). In kidney of cancer bearing animals the levels of glycoproteins were increased (Hexose $P<0.001$; Hexosamine and Sialic acids $P<0.01$) were increased. These enzymes levels were normalized in T.arjuna treated animals.

Conclusion: The reversal of glycoprotein levels to almost normal in the T.arjuna treated animals may be due to the alteration in cell membrane glycoprotein synthesis and leads to regression of cancer.

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MODULATORY EFFECT OF RESVERATROL ON COLONIC MUCOSAL LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN 1,2-DIMETHYLHYDRAZINE INDUCED COLON CARCINOGENESIS

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Introduction Colon cancer is the second most frequent cause of cancer mortality in the United States and the third most common cancer worldwide. Recently, the progressive spread of western dietary habits has been paralleled by an increase in colon cancer in developing countries. Plant phytochemicals (biological active, non nutritive compounds) are receiving considerable attention for their potential role in reducing cancer risk. This study examines the modulatory effect of resveratrol on colonic mucosal lipid peroxidation and antioxidant status in 1,2-dimethylhydrazine (DMH) induced colon carcinogenesis.

Methods Rats were divided into 4 groups at six weeks of age. Group 1 (CON)-served as control, Group 2 (CON+RES)-received resveratrol (8mg/kg body weight orally everyday) for 30 weeks. Group 3 (DMH)-received DMH injections (20mg/kg body weight s.c., once a week for 15 consecutive weeks). Group 4 (DMH+RES)-received resveratrol (8mg/kg body weight orally) after the last injection and continued till the end of the experiment. At the end of 30 weeks the animals were sacrificed and the proximal and distal colonic mucosal lipid peroxidation and antioxidants were analysed.

Results DMH induction reduces the levels of colonic mucosal lipid peroxidation markers (TBARS, lipid hydroperoxides and conjugated dienes), enzymic antioxidants (SOD, CAT) and non-enzymic antioxidants (GSH, -tocopherol, ascorbic acid) as compared to control and resveratrol alone supplemented animals ($P<0.005$). Resveratrol supplementation in the promotion/progression period restores the levels of TBARS and antioxidant levels to near those of the control rats.

Conclusion Administration of resveratrol to rats prevented the adverse effects of DMH on colonic mucosal cells by optimizing lipid peroxidation and the antioxidant status.

P-73

LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN PATIENTS WITH PAPILLARY THYROID CARCINOMA

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Introduction : Thyroid cancer, the most common endocrine cancer, is a cancerous tumour or growth located within the thyroid gland. The annual incidance rate of thyroid carcinoma varies from 0.5 to 10 cases per 100,000 in different parts of the world, papillary carcinoma and follicular carcinoma are the most common types respectively accounting for about 70% and 15% of cases.

Method : The levels of lipid peroxidation products (TBARS) non-enzymatic antioxidants and enzymatic antioxidants activity were investigated in plasma and erythrocytes of twenty clinically diagnosed stage III papillary thyroid cancer patients and an equal number of age and sex matched healthy subjects, using specific colorimetric methods.

Results : An increase in the levels of lipid peroxidation products, decrease in non-enzymatic antioxidants levels and enzymatic antioxidant activities in plasma and erythrocytes were detected in papillary thyroid cancer patients as compared to healthy subjects.

Conclusion : Impairment in antioxidant defense mechanisms are responsible for enhanced lipid peroxidation observed in plasma and erythrocytes of papillary thyroid cancer patients.

P-74

CHEMOPREVENTIVE EFFICACY OF MENTHOL

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Several studies suggest that naturally occurring nutritive and non nutritive components of the diet are important dietary constituents playing a significant role in the inhibition of tumor induction. Menthol, a major constituent of peppermint oil, is being used as an stimulant, tonic, vermifuge, antispasmodic, diaphoretic, stomachic, carminative, antiviral, antifungal, antibactericidal.

In the present study we have studied the chemopreventive activity of menthol, in two stage skin papilloma model using 7 12, Dimethyl benz (a) anthracene (DMBA) and croton oil. For forestomach cancer model we have used Benzo (a) pyrene for the induction of tumor.

In the the skin papilloma model, menthol (600 mg/kg body weight) treated mice during pre, peri and post initiation phases showed significant reduction in number, incidence and size of tumor

(papilloma). There was increase in the latency period in menthol treated group. Menthol treated animals showed a significant increase in the hepatic level of Reduced Glutathione (GSH) and decrease in hepatic level of Lipid Peroxidation (LPO) as compared to control group. In conclusion, our results provide evidence that the menthol exhibits a chemopreventive action by stimulating antioxidant potential of the cell. Studies on Forestomach tumor model is in progress.

P-75

ETIOLOGY, PREVENTION AND CLINICAL TREATMENT OF CERVICAL CANCER IN RAJASTHAN

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Introduction: Gynecological malignancies represent approximately 13% cancer in women and accounts for 9.8% of all cancer deaths. Work has already been done to prove the chemo preventive efficacy of *spirulina* in oral cancer patients, as well as to chemo prevent chemically induced skin papillomagenesis in mice. We sought to determine the treatment of pre-invasive cervical cancer patients with *spirulina* by screening them with papnicolaou smear, before the onset of invasive cervical carcinoma.

Methods: 78 females above the age of 35, with eroded cervix were identified with pre-cancerous lesions in Zanana hospital who were questioned about their habits, habitat, dietary habits, economic status, reproductive history and other related conditions. The females were divided into 2 groups, the first group with eroded cervix was treated with *spirulina* and the patients of both the groups were screened at 4 to 6 month intervals for 2 years annually thereafter.

Results: The sensitivity or probability of detection as well as the predictive value positive is found to be 13.33%. High positive predictive value (i.e., >10%) is likely to result when the Pap smear yields a high proportion of true positives or is associated with high prevalence of pre-clinical disease. It was

also observed that no dysplastic changes occurred in the group treated with *spirulina* than as found in the other untreated group

Conclusions: It is a public health procedure intended to identify women with CIN before invasive cervical cancer develops. In addition, the procedure may identify women in whom invasive cervical cancer has already developed as well as certain diseases also to reduce the morbidity and mortality from a particular cancer among the person.

P-76

BERBERINE CHLORIDE ENHANCES RADIATION RESPONSE IN MICE BEARING EHRLICH ASCITES CARCINOMA

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Introduction: The purpose of this study was to assess the radiation sensitizing effect of berberine chloride (BCl) an isoquinoline alkaloid, in mice transplanted with Ehrlich ascites carcinoma (EAC).

Methods: EAC mice were given 0, 2, 4, 6, 8, 10 or 12 mg/kg b. wt. BCl intraperitoneally before exposure to 0, 2, 4, 6 or 8 Gy Co^{60} gamma radiation to select the optimum dose. EAC mice were administered 6 mg/kg b. wt. BCl using various treatment modalities. The animals were monitored up to 120 days post-irradiation and survival was assessed using median survival time (MST) and average survival time (AST). Glutathione, glutathione-s-transferase and lipid peroxidation were assessed in EAC cells treated with 6 mg/kg BCl before exposure to 6 Gy radiation.

Results: The highest radiosensitizing activity of BCl was observed at 6 mg/kg b. wt. Treatment of animals with 6 mg/kg b. wt. BCl, before exposure to 6 Gy of hemi-body gamma irradiation and then once daily for another six consecutive days post-irradiation increased the life span of EAC mice as is evident by more number of long term survivors (LTS) as well as survivors beyond 120 days when compared to double distilled water treated irradiation group. BCl treatment caused a decline in the glutathione and glutathione-S-transferase contents accompanied by an elevation in lipid peroxidation.

Conclusions: The radiosensitization by BCl may be due to depletion of glutathione and glutathione S- transferase, accompanied by elevated levels of lipid peroxidation and induction of DNA damage in tumor cells.

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EFFECT OF GALLIUM NITRATE ON TAMOXIFEN TREATED BREAST CANCER RELATED HYPERCALCEMIA WITH REFERENCE TO CALCIUM AND MAGNESIUM IN RATS

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Introduction In breast cancer related hypercalcemia, serum calcium, urinary calcium, the index of bone resorption alkaline phosphatase and magnesium levels were tremendously elevated in their blood due to its metastatic bone destruction. It is also one among the side effects of tamoxifen, a nonsteroidal antiestrogen, been approved for use in advanced breast cancer. We sought to nullify the tamoxifen-induced hypercalcemia using gallium nitrate.

Methods Experimental groups I: Control, II. Hypercalcemia rats from tumour, (induced with 7,12 dimethyl benzanthracene (25mg/ml) dissolved in sesame oil and given by gastric intubation), III. Hypercalcemia rat treated with Tamoxifen, [(10mg/kg) in ethanol subcutaneously for 30 days] IV. Group III treated with gallium nitrate [(2.5mg/kg) by intravenous infusion for 7 days]. V.Control with gallium nitrate. Calcium level, alkaline phosphatase and magnesium levels were analysed in serum, kidney and liver (homogenates) using Calcium kit from Menarini Diagnosis-Italy, King (1965) using a Photochem colorimeter and Magnesium kit from Menarini Diagnosis-Italy, respectively.

Result Group II animals showed increase in calcium, alkaline phosphatase and magnesium levels ($p<0.001$). After treatment with tamoxifen (Group III), there was a significant rise in the calcium where as, alkaline phosphatase and magnesium levels were reduced. On administration of gallium nitrate in-group IV animals, the levels of calcium, alkaline phosphatase and magnesium were reverted to near normal and no marked changes were observed in drug control group when compared to control animals.

Conclusion Upon treatment with gallium nitrate, the calcium; alkaline phosphatase and magnesium levels were normalised. From the above observation, it can be accepted that gallium nitrate is a very potent and effective drug for hypercalcemia and it is found to nullify the iatrogenic effects of tamoxifen.

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EFFECT OF KALPAAMRUTHAA ON LIPID PEROXIDATION AND ENZYMIC ANTIOXIDANTS IN DMBA INDUCED MAMMARY CARCINOMA

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Introduction: Free radicals are known to be involved in carcinogenesis. There are potentially different types of chemical changes in DNA resulting from reactive oxygen species (ROS) that could be mutagenic and involved in the etiology of cancer. The antioxidants (ROS scavengers) require the activation of specific metabolic pathways and investment of energy. The effect of Kalpaamruthaa (KA), a herbal formulation on breast cancer was studied for gaining insight into the intrigue disease in relation to lipid peroxidation (LPO) and enzymic antioxidant enzymes.

Methods: Mammary carcinoma was induced by administration of 25mg of 7,12-dimethylbenz(a)anthracene to Sprague-Dawley rats by gastric intubation. After 90 days, KA was administered at 300mg/kg body weight/day for 14 days. After the treatment, the levels of LPO and enzymic antioxidants (superoxide dismutase, Catalase, Glutathione peroxidase, Glutathione-S-transferase) in liver, kidney, breast tissue and erythrocytes of control and experimental animals were measured.

Results: The level of LPO in mammary carcinoma bearing animals was found to be significantly ($p<0.05$) increased and the levels of all the enzymic antioxidants were significantly ($p<0.05$) decreased when compared to control animals. On drug administration, the above pathological changes were reverted to near normal levels. No significant changes were observed in drug control animals when compared to control animals.

Conclusion: The results of this study indicate that KA possesses a strong antioxidant property and could be considered a good therapeutic agent for mammary carcinoma.

FREE RADICALS AND ANTIOXIDANTS INFECTIOUS DISEASES AND IMMUNITY

P-79

MEASUREMENT AND SIGNIFICANCE OF 3-NITROTYROSINE IN SLE PATIENTS

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Introduction: Humans are exposed to a whole range of reactive nitrogen intermediates (RNS) such as nitric oxide, nitrates, nitrites, peroxynitrite and nitrogen oxides. 3-Nitrotyrosine has been identified as a stable end product and marker of inflammation and increased NO production. Elevated nitrotyrosine levels have been detected in many disease conditions including systemic lupus erythematosus (SLE) which is a prototype autoimmune disease characterized by the presence of autoantibodies to a variety of nuclear antigens as well as protein antigens and protein-nucleic acid complexes. In this study we show that the level of 3-nitrotyrosine, which can be produced by nitric oxide dependent oxidative damage is elevated in patients with SLE and that there is a possible role of nitric oxide modified epitopes in the etiology of the disease.

Methods: Commercially available poly L-tyrosine was exposed to nitric oxide generated by sodium nitrite in acidic medium. The nitrated product was then analyzed by various physico-chemical techniques. Sera from 24 SLE patients were studied for their recognition of native and nitrated poly L-tyrosine by direct binding and inhibition ELISA. 3-nitrotyrosine was also detected by western blot analysis, separation of 3-nitrotyrosine was achieved by HPLC, and the concentration was calculated in SLE patients.

Results: The UV absorption spectra of nitrated poly L-tyrosine showed a peak shift and hypochromicity of 25% at 280 nm. Another peak was observed at a wavelength of 419 nm, which is a characteristic of 3-nitrotyrosine. Fluorescence studies confirmed the modification to thearomatic ring of tyrosine. The possible role of nitric oxide in SLE was probed by evaluating the binding of 24 SLE sera to native and nitrated poly L-tyrosine. All the twenty-four SLE sera showed stronger binding to nitrated poly L-tyrosine as compared to native form. Elevated levels of 3-nitrotyrosine was seen in all the cases of SLE patients tested, whereas no nitrotyrosine was detected in the case of normal human serum pool. The average concentration of 3-nitrotyrosine in SLE patients was found to be 1.02 ± 0.59.

Conclusions: Poly L-tyrosine exposed to nitric oxide resulted in the formation of 3-nitrotyrosine. Elevated level of 3-nitrotyrosine was seen in SLE patients when compared to healthy subjects This data confirms the overproduction of NO in the pathogenesis of human SLE and highlight serum 3-nitrotyrosine as a new tool for studying the role of nitric oxide in SLE.

P-80

EFFECT OF VITAMIN C ON ANTIOXIDANTS IN PULMONARY TUBERCULOSIS

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Introduction : Tuberculosis is one of the major causes of public health problem. It is associated with increased oxidative stress. Functional deficiency of some antioxidant enzymes (GSH-Px, G6PD) is reported in neutrophils & increase in activity of SOD, GSH-Px & GR is reported in blood. Little data is available on the effect of Vitamin C supplementation on the antioxidants in blood. We studied the effect of Vit. C on whole blood glutathione, total thiols & plasma glutathione S transeferase activity.

Methods : 40 patients of pulmonary tuberculosis & 30 age and sex matched normal controls were included in the study. The patients were divided into two groups for follow up. One group received standard ATT(n=20), the other received Vit. C along with the standard ATT (n=20). Whole blood GSH, t. thiols, plasma Vit C & GS-T activity was measured at the time of admission and after one month & two months of therapy.

Results : Whole blood GSH, t. thiols & Vit. C levels were significantly decreased whereas GS-T activity was significantly higher in patients than in controls. A progressive rise in first 3 parameters following ATT was observed whereas GS-T activity decreased. Changes were more marked in group supplemented with vitamin C.

Conclusion : The observations suggest that antioxidant defence is compromised in pulmonary tuberculosis.This status showed improvement with treatment more so with Vit C supplementation. This study suggests that antioxidants may play an important role in enhancing the recovery of these patients.

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ROLE OF FLAVONOIDS IN THE ALLEVIATION OF ANEMIA ASSOCIATED WITH VISCERAL LEISHMANIASIS

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Flavonoids are a broad class of plant poly phenolic compound that display a wide spectrum of clinical properties .The prevalence of visceral leishmaniasis (VL) in Indian subcontinent has been reported to have an

increasing trend in recent years. VL is associated with severe anemia, which accounts for formidable volume of suffering in the diseased condition. The anemia is multifactorial, early hemolysis being one of the important factors leading to the shortened lifespan of erythrocytes. Oxidative damages of erythrocytes have been implicated in the reduced survival of erythrocytes during leishmanial infection. Considering the antioxidant potential, we investigated the ability of the flavonoids in the protection of the degradative process in the red cells .This study reveals the efficacy of five naturally occurring flavonoids in arresting the development of anemia during post infection period. Amongst the compounds studied, quercetin was most successful in inhibiting the oxidation of proteins and lipids on the red cell membranes of infected animals. Apart from its anti-anemic property, quercetin also appeared to be highly potent in lowering the parasite load in the spleen. Combination therapy of quercetin with the antileishmanial drug stibanate resulted in an aversion from early lysis of red cells compared to that induced by quercetin or drug treatment alone. Subsequent studies demonstrated the therapeutic efficacy of the combination treatment in the abatement of both anemia and parasitemia under the diseased condition.

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ANTIOXIDANT VITAMINS AND IMMUNE FUNCTION IN LEPROSY.

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Introduction : Leprosy is a chronic infectious disease caused by Mycobacterium leprae (Hansen,1875) affecting mainly the immune system. Oxidant-mediated tissue injury is a particular hazard to the immune system, since phagocytic cells produce reactive oxygen species as part of the body's defence against infection. Adequate amounts of neutralizing antioxidants are required to prevent damage to the immune cells themselves. Vitamin E, C, and beta-carotene (provitamin A) are essential nutrients that the human organism cannot synthesize and which act as antioxidants by stabilizing highly reactive and potentially harmful molecules, as are the free radicals.

Method: To assess the severity of oxidant stresses all subjects and controls were studied for plasma lipid peroxide levels .The plasma levels of vitamin C, vitamin E and vitamin A (carotene) were measured to know the status of antioxidant vitamins.

Results :- Plasma lipid peroxide level measured as Malondialdehyde level was significantly increased ($p<0.05$) while the plasma levels of vitamin C, vitamin E and vitamin A were significantly decreased ($p<0.05$) as compared to controls.

Conclusion: -The increased levels of lipid peroxide gave an idea about the possibility of oxidant mediated tissue damage, while the decreased levels of antioxidant vitamins indicated that these vitamins are essential in controlling lipid peroxidation which otherwise lower cell mediated immune responses causing immunosuppression in lepromatous leprosy.

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OXIDATIVE STRESS AND THE ROLE OF ANTIOXIDANTS IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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Introduction: Plit ML(1998) reported that even after six months of apparently successful antimicrobial chemotherapy, pulmonary tuberculosis is associated with increased oxidative stress. The present study was undertaken to evaluate whether reduction in oxidative stress by addition of a chain breaking antioxidant to first line antituberculosis agents will improve the clinical outcome

Methods: Randomized control clinical trial approved by institutional ethical committee was undertaken in newly diagnosed cases of pulmonary tuberculosis (PTB), of either sexes exhibiting sputum AFB. Control group A (n=50) was treated with routine 2EHRZ regime daily for initial phase of two months while study group B received Vit E and Vit C concurrently daily along with 2EHRZregime. Lipid peroxidation levels were used as markers of cellular damages.

Results: Statistical significant reduction in LPO, augmentation of Sputum AFB negativity, and Radiological improvement was noted in study group receiving antioxidants.

Conclusion: Better clinical improved in cases of pulmonary tuberculosis, receiving concurrent antioxidants, as evidenced by early sputum AFB

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ELEVATION OF METHYL GLYOXAL IN ASSOCIATION WITH FREE RADICAL MEDIATED DAMAGE IN RHEUMATOID ARTHRITIS.

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Introduction : Recently, oxygen free radicals have been implicated as mediators of tissue damage in patients with Rheumatoid Arthritis (RA). Poor anti-oxidant status, actually serves as risk factors for developing RA. However, very little information is known about causation of these free radicals in blood and synovial fluid of RA patients.Here we report that Methyl Glyoxal , a keto-aldehyde compound is significantly elevated in association with increased level of free reactive iron , poor anti oxidant status , high lipid peroxidation and poor level of NO in RA patients.

Materials and Method : Normal healthy volunteers (n = 40) were selected randomly and Rheumatoid patients (n=85) were selected from indoor / outdoor department of Medicine , Rheumatology Unit , Nilratan Sircar Medical College and Hospital , Kolkata. Blood (and Synovial fluid) were collected aseptically from patients and Volunteers. Sample were analyzed for superoxide dismutase (SOD) activity, catalase activity, total reduced glutathione level, total antioxidant status (TAS) against Trolox, serum methyl glyoxal level and lipid peroxidation by malon dialdehyde (MDA) level using standard method. Free reactive iron was estimated by Ferrozine reaction and NO by Griess reagent.

Results : Both serum and synovial fluid level of SOD , Catalase ,reduced Glutathione and Total Antioxidant Status of patients were found to be significantly low level ($p<0.01$) where as methyl Glyoxal , Lipid peroxidation (as measured by MDA) and Ferrozine detected free reactive iron were found to be significantly high. Moreover a significantly poor NO level($p< 0.01$) compared to normal control were observed.

Conclusion: Poor Antioxidant status , elevated methyl glyoxal level and free reactive iron in both Blood and Synovial fluid suggest that accumulation of methyl glyoxal, a toxic metabolite may be an important precursor of free radicals which in association with iron mediated Fenton reaction produce dreadly damaging ÓH radicals. The mechanism and significance of the phenomenon, elevation of Methyl Glyoxal in Rheumatoid Arthritis pathology remain to be established.

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TUBERCULOSIS PATIENTS EXPRESSING HIGH LEVELS OF ANTI-INDUCIBLE NITRIC OXIDE SYNTHASE (INOS) ACTIVITY EXHIBITED CIRCULATING MYCOBACTERIUM ANTIGEN 85B COUPLED TO IGG IN SERUM

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Introduction: Tuberculosis (TB) is a global public health problem. A third of the world's population is estimated to be infected with Mycobacterium tuberculosis, and tuberculosis is the most common cause of death of adults from infectious disease throughout the world. The role of nitric oxide has been implicated in the pathogenesis of the disease.

Methods: In the present study, determination of proteins of varying molecular weights expressed in serum of TB patients falling under all the three categories as designated by World Health organization (WHO) undertaken in this study were analyzed by PAGE. A total of 40 serum samples from category I, 35 serum samples from category II and 26 serum samples from category III were subjected to PAGE analysis. Immunological investigations were carried out by employing ELISA.

Results: Category I and II patients exhibited a 200 kDa band, whereas category III patients did not. It appears that the 200kDa band is that of antigen 85B conjugated to IgG, due to non- clearance of secretory 85B protein antigen in urine of tuberculosis patients. The presence of circulating 85B antigen conjugated to IgG in serum as being indicated by electrophoretic results is substantiated by ELISA results where highly specific anti-Ag85 monoclonal antibody was used to confirm the above. Thus, probably, it is suggested that Ag85 circulated as complexes with plasma proteins due to lack of urinary Ag85 in patients with active tuberculosis. Furthermore, ELISA with anti-iNOS antibodies exhibited recognition in category 1 and 2 patients respectively whereas category 3 patients did not show any binding with anti-iNOS Ab.

Conclusion: Thus, in conclusion, it appears that, tuberculosis patients exhibiting circulating mycobacterium antigen 85B coupled to IgG in serum expressed high levels of anti-inducible nitric oxide synthase (iNOS) activity.

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COMPARITIVE STUDY OF VITAMIN E, A AND C LEVELS IN LEPROSY SUBTYPES

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Introduction : Oxidative damage caused by Reactive Oxygen Species(ROS) is known to be involved in the disease pathology of leprosy. Continuing macrophage function,immune complex mediated damage are potential sources of ROS in leprosy infection.Antioxidants like vitamins E, A and C provide protection against the deleterious effects of ROS.

Methods : The subjects for this study were normal human controls (n=50), paucibacillary leprosy patients (n=50) and lepromatous leprosy patients (n=50). Plasma levels of Vitamin E, A and C levels were estimated by standard spectroscopic methods. Statistical analysis was done by student 't' test.

Results : The result showed a statistically significant decrease in Vitamin E ($p<0.01, p<0.001$); Vitamin A ($p<0.01, p<0.001$) and Vitamin C ($p<0.001$) levels in paucibacillary and multibacillary leprosy respectively as compared to control group. The decrease was found to be significantly pronounced in multibacillary leprosy as compared to paucibacillary leprosy.

Conclusion : The low plasma antioxidant vitamin levels indicate the involvement of oxidative stress in leprosy. Treatment approaches involving supplementation of antioxidant vitamins may find beneficial in the management of oxidative stress in leprosy.

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ENDOTHELIAL FUNCTION AND CARDIOVASCULAR DISEASE

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Introduction: Endothelium is a dynamic, multifaceted, organ system intimately involved in regulation of vascular tone and hemostasis. EC dysfunction is defined by blunting of the vasodilatory response to acetylcholine or hyperemia, both of which are known to produce NO-dependent vasodilatation. Many drugs have been to shown to have improvement on endothelial dysfunction in patents like ACE inhibitors, Statins, Calcium Channel blockers, Estrogens, L-Arginine, Anti-oxidants.

Methodology: There are various ways to asses endothelial function including Flow mediated dilation; Brachial artery diameter and flow; Veno-occlusive plethysmography; lazer blood flow neter; Digital pulse plethysmography. We have used shear stress and Albuterol induced change in DPG (digital Pulse Plethysmography) has been used as one of the alternative methods for endothelial dependent vasodilatation in patients with CAD, PVD, DM and compared with healthy subjects.

Results: Shear stress and salbutamol showed endothelial dysfunction with patients compared to healthy subjects as evidenced by change in b/a ratio. In healthy subjects before shear the b/a was 0.29, which increased by 16% to 0.32 after shear stress. In patients with CAD, PVD, DM b/a ratio was 0.36, 0.30 and 0.38 respectively before shear and the same became 0.35, 0.27 and 0.36 respectively after shear. Quinalapril was used as an intervention drug. Quinalapril produced significant alteration in % RI index compared to baseline and control subjects.

Conclusion: Endothelial function plays a pivotal role in cardiovascular health. Diabetes, hypertension, dyslipidemia and heart failure contribute to endothelial dysfunction. Appropriate therapy for each of these disorders should address the endothelial path9logy. Quinalapril, a new ACE inhibitor showed significant improvement in endothelial dysfunction.

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PEROXYNITRITE INDUCED MODIFICATION OF HUMAN DNA: IMPLICATIONS IN ETIOPATHOGENESIS OF SLE

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Introduction: Systemic Lupus Erythematosus (SLE), a multisystem autoimmune disease, is characterized by the production of a variety of autoantibodies against nuclear, cytoplasmic and cell surface antigens. The cellular and molecular mechanisms that are responsible for the production of anti-nuclear antibodies in this disease and the way these antibodies participate in tissue destruction remain highly debated. The primary autoantigen is believed to be DNA modified or complexed in some form rather than the naked analogue. Modification in DNA can take place through interaction with various radicals, radiations or chemicals leading to B-helix conformational alteration or generation of single stranded regions. One such species is peroxynitrite, which causes oxidative DNA damage.

Methods: We have characterized peroxynitrite radical damaged human DNA through spectroscopic and fluorometric analysis, nuclease S1 studies, alkaline agarose and thermal denaturation profile assays. ELISA was used to probe the binding of SLE autoantibodies to native and

modified DNA.

Results: The modified DNA was found to be highly unstable having appreciably high percentage of SS regions with the damage to backbone and disruption in base stacking. It exhibited 29.4% hyperchromicity at 260 nm and a decrease of 6..0 °C in Tm. Binding of naturally occurring SLE autoantibodies to the native and modified DNA shows higher recognition of the modified conformer by the SLE autoantibodies in direct binding and completion ELISA experiments as well as in gel-retardation assays.

Conclusions: DNA was substantially modified by the peroxynitrite species rendering it quite unstable. Higher recognition of human SLE autoantibodies clearly indicates that the modified DNA presents better epitopes for the SLE autoantibodies. Role of peroxynitrite radical in the induction of SLE anti-DNA autoantibodies has been discussed.

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OXIDATIVE STRESS IN RHEUMATOID ARTHRITIS

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Introduction : Rheumatoid Arthritis is a chronic multisystem disease of unknown origin. The characteristic feature of RA is persistent inflammatory synovitis, usually involving peripheral joints in a symmetrical distribution. It is seen throughout the world and affects all races. There has been accumulating evidence of the role of oxidative damage in RA. However there have been few comprehensive studies. The objective of the present study was to evaluate in a comprehensive manner certain important parameters of oxidative stress in patients of RA and normal controls, and thus to determine whether there was any significant difference between the two groups.

Methods : The study included 40 patients of RA (n=40), and 20 age and sex matched controls (n=20). Serum from patients and controls was analysed for nitrite levels (Griess Reaction), protein carbonyl levels (Reznick and Packer 1994), level of malondialdehyde (TBA test), and ceruloplasmin levels (Ravin 1961).

Results : Free radical oxidation products in serum were significantly elevated in patients of RA compared to that of controls. Serum nitrite ($p < .001$), serum protein carbonyls ($p < .001$), serum MDA ($p < .001$), and serum ceruloplasmin ($p < .001$) levels were all significantly elevated.

Conclusions : There is significantly increased nitric oxide generation in patients of RA, along with significantly increased protein carbonyls and lipid peroxides in serum. Serum levels of antioxidant ceruloplasmin is significantly increased possibly as a compensatory mechanism. These markers of oxidative stress may play an important role in diagnosis and prognosis of RA and may also guide antioxidant therapy for this yet incurable disease. **PROTECTIVE EFFICACY OF *MENTHA PIPERITA* AGAINST ARSENIC INDUCED RENAL DAMAGES IN SWISS ALBINO MICE**

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FREE RADICALS AND ANTIOXIDANTS IN ENVIRONMENTAL BIOLOGY

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OXIDATIVE STRESS IN COPD. IS CHULLA SMOKE MORE DANGEROUS THAN TOBACCO SMOKE?

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Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a global problem. There exists a relationship between COPD and increased oxidative stress. Females exposed to indoor pollution from biomass fuel (Chulla smoke) are equally at risk similar to proven risk factor in male tobacco smokers. In view of above facts we analyzed Oxidant: Antioxidant in male ex-smokers and females exposed to Chulla smoke, both suffering from COPD.

Methods: 39 patients of COPD diagnosed clinically and supported by lung function tests (as per GOLD guide lines) were studied from private Chest Hospital over 2 months period and were divided into 2 groups. Group I comprised of male ex- smokers (n= 19) and group II females with history of prolonged exposure to Chulla smoke (n=20). Serum Malondialdehyde(MDA), Superoxide Dismuatse (SOD), Plasma Vitamin C were estimated.

Results: The levels of MDA in Gr.I were 7.58±2.68 and in Gr.II 7.69±2.1 are comparable but within normal range. But on other hand Antioxidants like SOD levels in Gr.I were 1.8± 0.474 and in Gr.II, 1.78± 0.76 and plasma vitamin C in Gr.I 0.346±0.35 and in Gr.II, 0.278±0.34 respectively. Both these parameters were comparable but significantly lower than normal values.

Conclusion: Lung damage because of chronic exposure to domestic biomass fuel in female COPD patients seems equally detrimental to lungs as ex-smokers in males COPD patients. This is documented in our study by increased oxidative stress in the form of decreased SOD and Vitamin C in both groups. WHO goals are to increase awareness of COPD and decrease morbidity and mortality. To support this goal along with smoking cessation in males, avoiding chronic exposure to Chulla smoke in females is equally important in preventing this chronic debilitating disease.

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NUTRITIONAL INTERVENTION IN REDUCING THE ALTERATIONS IN ANTIOXIDANT ENZYMES CAUSED BY LEAD

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Introduction: Lead (Pb) is a non-essential toxic heavy metal. It has been used by mankind for over 6000 years and is today one of the most widely distributed metal in the environment. The possibility of lead exposure in human is therefore of great significance from the health point of view. Lead affects many system in the body including the antioxidant system.This study was carried out to investigate the effect of Pb on the antioxidant enzymes, and to evaluate the nutritional intervention

Materials and Methods: Adult male Wistar albino rats were used for the experiments. The rats were divided into two groups; **'well nourished' (WN)** and the **'under nourished' (UN).** The WN and UN subjects were given 500 ppm Pb as lead acetate in the drinking water and their controls had no lead supplements in their drinking water. Blood lead levels were estimated using ESA Lead Analyzer as per as C.D.C approved protocol. Reduced Glutathione(GSH) was estimated by DTNB reagent method and Super oxide dismutase(SOD) by Nitro blue tetrazolium (NBT)

method

Findings: The blood lead levels of the under nourished group had increased drastically compared with the well-nourished group. Decreased GSH levels and SOD activities were seen in the undernourished rats suggesting lead induced oxidative stress.

Conclusion: Nutritional intervention help in reducing the lead induced oxidative stress

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ANTI-RADICAL ACTIVITY OF TEA POLYPHENOLS

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Introduction: Fruits and vegetables are rich in phenolics and flavonoids, possessing health benefits. So also tea, in the form of green / oolong / black tea provides ample polyphenols. Fermentation of tea leaves results in larger polyphenolics (thearubigins). In the present investigation, we have studied the total radical and superoxide radical ($O_2^{\cdot}$) scavenging activity of these polymeric black tea polyphenols extracted from popular brands of black tea..

Methods: The total radical scavenging activity was determined by 2,2'-azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid (ABTS) method. The results expressed as Trolox Equivalent Antioxidant Capacity (TEAC). The copper complexes (CuL) of these extracts were used as superoxide dismutase mimetics and the scavenging of $O_2^{\cdot}$ was determined by using pulse radiolysis technique. Total phenols / flavonoids were determined spectrophotometrically.

Results: From the variation in the total phenolics and total flavonoid content of tea extracts it was evident that fermentation procedures and species variation affect the composition / contents of these compounds. Samples having higher ABTS radical scavenging ability were the ones where the phenolic content was higher compared to the rest. The decay rates of the ABTS radical in the presence of extracts was determined pulse radiolytically and the bimolecular rate constants determined. Using ideal Cu:L ratios the scavenging rate constants were determined. All the above results are compared with some monomeric phenols present in unfermented teas.

Conclusions: Due to variation in the active principles of different tea extracts their antiradical activities differ. The radical scavenging antioxidant activity of tea polyphenols was lesser than that of standards used. Copper complexes of these tea extracts scavenge $O_2^{\cdot}$.

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FREE RADICAL REACTIONS AND ANTIOXIDANT ACTIVITIES OF SESAMOL: PULSE RADIOLYTIC AND BIOCHEMICAL STUDIES

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Introduction: Sesamol (S-OH), 5-hydroxy-1,3-benzodioxole or 3,4-methylenedioxyphenol, is a constituent of sesame seed (*sesamum indicum*) oil, and is responsible for the high resistance of this oil to oxidative deterioration. Sesame seed as well as its oil are used for human consumption worldwide in various forms. Free radical scavenging reactions and antioxidant activity of this non-toxic, thermally stable dietary compound have been studied. Methods: Pulse radiolysis technique has been used for in-situ generation and observation of radicals. Transient UV-visible absorption of the transients have been monitored to follow the reactions. Lipid peroxidation has been studied using brain homogenate of Albino Charles-Foster rats. Hydroxyl radical induced deoxyribose degradation and plasmid DNA degradation have also been studied.

Results: Sesamol efficiently scavenges hydroxyl, superoxide, organo-haloperoxyl, various oxidizing and reducing radicals, lipid peroxyl and tryptophanyl radicals. SOH reacted with oxidizing radicals to produce phenoxyl radical whereas with reducing radicals adduct as well as cyclohexaienyl radical are produced. Sesamol alone did not break DNA but protected DNA in the super coiled and nicked circular forms against hydroxyl radical. S-OH has not been found to react with Fe(II) but reduces Fe(III) into Fe(II) at pH 7.4. Lipid peroxidation and deoxyribose degradation by hydroxyl radicals was inhibited by sesamol in a dose-dependent manner. Its antioxidant activity has also been evaluated with cyclic voltammetry.

Conclusions: Dietary compound sesamol, water and lipid soluble, has been found to be an efficient antioxidant in chemical and biochemical studies.

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FREE RADICAL SCAVENGING AND RADIATION PROTECTION BY TOCOPHEROL MONOGLUCOSIDE

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Objective: Tocopherol monoglucoside (TMG), a water soluble derivative of vitamin E has been shown to protect against ionizing radiation-induced damage to DNA under *in vitro* and *in vivo* conditions. The present work aims to examine the efficacy of TMG to scavenge free radicals and to protect membrane lipids *in vivo* and cellular DNA in human peripheral blood leucocytes *ex vivo*, exposed to gamma radiation.

Methods: Free radical scavenging property of TMG was studied by DPPH assay and quenching of hydroxyl radical. Protection of membrane lipids from radiation induced peroxidation was investigated in rat liver microsomes *in vitro*. For *in vivo* studies TMG was administered to mice prior to whole body radiation and peroxidative damage in lipids of various tissues was analyzed in terms of thiobarbituric acid reacting substances. Protection of human blood leucocytes against gamma radiation induced DNA strand breaks was studied by alkaline single cell gel electrophoresis (comet assay).

Results: TMG reduced the stable free radical 1,1-diphenyl-2-picryl hydrazyl in a dose dependent manner. It inhibited the hydroxyl radical induced degradation of deoxyribose. Exposure of rat liver microsomes to 500 Gy gamma radiation resulted in peroxidation of lipids equivalent to 13 n moles of malonaldehyde per mg protein. TMG inhibited the radiation-induced lipid peroxidation in a concentration dependent manner, 100 µM TMG inhibited 90% and 25µ M TMG inhibited 30% of the lipid peroxidation. In TMG administered animals exposed to whole body gamma irradiation (3Gy), there was significant reduction in lipid peroxidation in various tissues such as liver, spleen and intestinal crypt compared to irradiated controls. Studies using comet assay revealed that exposure of human blood peripheral leucocytes to gamma radiation resulted in increase of comet parameters due to radiation-induced strand breaks in DNA. The comet parameters were significantly reduced when TMG was present along with the cells during irradiation; thus indicating protection of cellular DNA under ex vivo conditions.

Conclusion: The results reveal that TMG can protect cells and bio-molecules from ionizing radiation induced damages under *in vitro*, *in vivo* and *ex vivo* conditions. TMG is a good free radical scavenger. It protects biological membranes under in vitro and in vivo conditions of irradiation. TMG protects cellular DNA against gamma radiation-induced strand breaks.

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ROLE OF ANTIOXIDANTS IN THE TREATMENT OF IRON DEFICIENCY ANAEMIA

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Introduction:

Iron deficiency anemia is the most common disorder mostly effecting women and children all over the world and has attracted attention on a global scale. Amongst all ion compounds being used as supplements to treat anemia ferrous sulphate has found to have better haematinic effect but it also has shown to increase oxidative stress because of generation of free radicals due to conversion of Fe^{++} to Fe^{+++} during its absorption.

A combination of ferric ion combined with maltose, Iron Polymaltose Complex (IPC) are also available but these have not shown much efficacy. The present study is designed to compare the efficacy of Ferrous sulphate when administered along with antioxidants like Vitamin C and Vitamin E in anemic rats. Efforts are also made to compare the efficacy of Ferrous sulphate with IPC in anemic rats.

Method: Anemia was induced by administering 15 mg/kg Cadmium Chloride in health y rats weighing 200 to 250 gms. Anemic rats were divided into different groups (n= 6) and each group was treated with I) Ferrous sulphate II) Ferrous sulphate with Vitamin C & Vitamin E III) IPC alone IV) IPC with Vitamin C & Vitamin E.

After 4 weeks of treatment blood sample were collected in dry EDTA bulbs and following biochemical parameter were studied.

i) Hemoglobin.

ii) Reduced glutathione.

iii) Lipid peroxide

iv) Super Oxide Dismutase (SOD)

v) Catalase.

Result: Ferrous sulphate along with Vitamin C & Vitamin E produces significant (P<0.01) increase in hemoglobin in anemic rats as compared to Ferrous sulphate alone. Treatment with IPC also produce increase in hemoglobin levels but less significant than the above treatment. Lipid peraoxidation was significantly decreased, reduced glutathione and catalyase activity was significantly increased in animals treated with Ferrous sulphate with Vitamin C and Vitamin E. However no change was observed in SOD.

Conclusion: Improved efficacy of ferrous sulphate in presence of Vitamin C and Vitamin E accounts for the antioxidant activity of Vitamin C and Vitamin E which decrease the oxidative stress and facilitate iron absorption.

FREE RADICALS AND ANTIOXIDANTS IN HUMAN REPRODUCTION AND INFERTILITY

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SIGNIFICANCE OF CHANGES IN LIPID PEROXIDATION AND ANTIOXIDANT STATUS AFTER SUPPLEMENTATION OF VITAMIN-E AND C IN WOMEN AT RISK OF PRE-ECLAMPSIA.

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Introduction: Increased Lipid peroxidation and decreased antioxidant activity may contribute to the development of complications of pregnancy.

Methods: In the present study we measured lipid peroxidation products by TBARS methods and counteracting antioxidant functions before and after supplementation with Vitamin-E and C in third trimester pre-eclamptic women by spectrophotometer. The subjects for the study were third trimester normal pregnancy (n=25) as controls and Pre-eclamptic patients (n=25) of the same trimester.

Results: In the pre-eclamptic group MDA, a lipid peroxidation product was significantly increased (P<0.001) while the enzymatic antioxidants like SOD (P<0.001), catalase P<0.01) and GSH.Px (0.001) and non enzymatic antioxidants like reduced glutathione (p<0.001), Vitamin-E (P<0.001) and Vitamin-C (P<0.001) were reduced significantly as compared to normal pregnancy.

A Significant negative correlation was detected between Lipid peroxidation and antioxidant levels. Further study with supplementation of non-enzymatic antioxidants like vitamin-E and Vitamin-C to the pre-eclamptic patients for four weeks, shows significant decreased levels of MDA (P<0.001) and increased levels of enzymatic and non-enzymatic antioxidants like GSHPx (P<0.001), catalase (P<0.01), Reduced Glutathione, Vitamin-.E, Vitamin- C (P<0.001), while SOD is decreased but not significantly

Conclusion: Supplementation of antioxidants like Vitamin-E and C during pregnancy may prevent impeding complications of PIH.

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FREE RADICALS MEDIATED TESTICULAR LESIONS BY CADMIUM CHLORIDE AND MODULATION BY PANAX GINSENG

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Introduction : Cadmium is one of the cumulative toxic heavy metal and an important environmental pollutant that causes tissue damage. Panax ginseng is one of the most highly recognized medicinal herb in the orient. It has wide range of pharmacological and therapeutical action. Thus promotes the functioning of immune system and antioxidant potential of cells. In the present study an attempt has been made to investigate free radical induced testicular damage by cadmium chloride ($CdCl_2$) and its possible protection by Panax ginseng.

Methods : For the present study, male Swiss albino mice were divided into various groups : Group I : Control group, Group II : Ginseng root extract (10 mg/kg b. wt.) orally. Group III : $CdCl_2$ (1mg/kg b.wt.) i.p. Group IV : Ginseng root extract was given 10 days before $CdCl_2$ treatment and continued upto 30 days. Histopathological analysis, total protein content, lipid peroxidation (LPO) and glutathione (GSH) level was estimated to find out the toxicity damage).

Results : Histopathological damage was observed in testis such as shrinkage of tubules, karyolysis, pyknosis, depletion of germ cells, oedematous fluid in interstitium in animals of group III as compared to control. A marked increase ($P < 0.001$) in the value of LPO and a significant decrease ($P < 0.001$) in the total protein content and GSH level were also noticed. The combination group (Group IV) Ginseng maintained the testis histoarchitecture to near normal with decreased ($P < 0.001$) LPO level and significant increase ($P < 0.001$) in total protein content and GSH level.

Conclusion : Thus Ginseng is found protective against cadmium induced oxidative damage by way of enhanced synthesis of GSH.

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MALONDIALDEHYDE FOR PREDICTION OF PRE-ECLAMPSIA

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Introduction: In modern obstetrics hypertensive disorders of pregnancy encompass a clinical spectrum of abnormalities ranging from minimal elevation in blood pressure to severe hypertension with multiorgan dysfunction. Pre-eclampsia is the development of hypertension with proteinuria or oedema or both induced by pregnancy after 20th week of gestation. Vasospasm is basic to pathophysiology of pre-eclampsia. Free radicals have emerged as likely promoters of vascular malfunction. Lipid peroxidation is the source of free radicals. Malondialdehyde is the most abundant individual aldehyde resulting form lipid peroxidation

Methods: In the present study, 52 primi gravid women and 48 multi gravid women with past history of pre-eclampsia , IUGR and growth retardation between 16 to 20 weeks of pregnancy were selected. Serum malondialdehyde levels were estimated using Valipasha and Sadasivudu method . These women were prospectively followed up for development of pre-eclampsia.

Results: Of these 19 women developed pre-eclampsia, 81 remained normotensive. Malondialdehyde levels were significantly ($p = 0.001$) elevated in those who developed pre-eclampsia. Whether malondialdehyde levels estimated in 16-20 weeks of gestation can be used to predict pre-eclampsia later in pregnancy was noted using logistic regression technique. It was found that 1 unit elevation in malondialdehyde levels in serum between 16-20 weeks of gestation account for 1.098 times increased risk for development of pre-eclampsia later in pregnancy.

Conclusion: Malondialdehyde levels estimated between 16-20 weeks of gestation can be used as a predictive parameter in development of pre-eclampsia later in pregnancy.

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LIPID PEROXIDATION AND ANTIOXIDANTS STATUS IN PATIENTS WITH PERIODONTITIS

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Introduction : Periodontitis, an inflammatory disorder of periodontium, damages the bone and connective tissue that supports the teeth. In recent years more attention has focused on the role of reactive oxygen species, lipid peroxidation products and antioxidants system in the pathological phenomenon of periodontitis. Our aim was to assess the oxidative stress in periodontitis patients and periodontitis patients treated with taurine, from Rajah Muthiah Dental College and Hospital Annamalai University, by measuring the levels of thiobarbituric acid reactive substances (TBARS) and antioxidants.

Methods : This study has been conducted on 25 newly diagnosed periodontitis patients, admitted to treatment for their periodontitis. Periodontitis patients were received 500 mg/day taurine orally for thirty days. The levels of TBARS and antioxidants in plasma, erythrocytes and gingival tissues were assayed using specific colorimetric methods.

Results : Elevated lipid peroxidation and disturbed antioxidants status were noticed in patients with periodontitis as compared to healthy subjects. However, the status of lipid peroxidation and antioxidants was revert back to near normal level after treatment with taurine for 30 days in periodontitis patients.

Conclusion : The impairment in endogenous antioxidant defense system due to over production of lipid peroxidation products at inflammatory sites make periodontitis patients more prone to oxidative stress.

FREE RADICALS AND ANTIOXIDANTS IN TOXICOLOGY

P-100

PROTECTIVE EFFECTS OF CURCUMIN AGAINST NICOTINE-INDUCED PULMONARY FIBROSIS IN WISTAR RATS.

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Aim: Nicotine, a major pharmacologically active substance in tobacco is generally regarded to be a primary risk factor in the development of cardiovascular disorders, pulmonary disease and lung cancer. In the present study, we evaluated the protective effects of curcumin on lipid peroxidation and antioxidants status in bronchoalveolar lavage fluid (BALF) and bronchoalveolar lavage (BAL) during nicotine-induced toxicity in rats.

Methods: The male Albino rats of Wistar strain were used for the experiment and were divided into 4 groups (Normal, nicotine, nicotine+curcumin, curcumin). Lung toxicity was induced by subcutaneous injection of nicotine at a dose of 2.5 mg/kg body weight (5 days a week, for 22 weeks) and curcumin (80 mg/kg body weight) was given simultaneously by intragastric intubation for 22 weeks. Measurement of biochemical marker enzymes: alkaline phosphatase, lactate dehydrogenase, lipid peroxidation and antioxidants were used to monitor the antiperoxidative effects of curcumin.

Results: The increased biochemical marker enzymes as well as lipid peroxides in BALF and BAL of nicotine treated rats was accompanied by a significant decrease in the levels of glutathione, glutathione peroxidase, superoxide dismutase and catalase. Administration of curcumin significantly lowered the biochemical marker enzymes, lipid peroxidation and enhanced the antioxidant status.

Conclusion: The results of the present study suggest that curcumin exert its protective effect against nicotine-induced lung toxicity by modulating the biochemical marker enzymes, lipid peroxidation and augmenting antioxidant defense system.

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COMPARATIVE EFFECTS OF CURCUMIN AND ITS ANALOG IN CARBON TETRACHLORIDE INDUCED HEPATOTOXICITY IN RATS

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Introduction: Liver diseases constitute a major problem of worldwide proportions. Carbon tetrachloride is a well known hepatotoxin that is widely used to induce toxic liver injury in a range of laboratory animals. Damage by CCl_4 is regarded as the analog of liver damage caused by a variety of hepatotoxins in humans.

Methods: Rats were administered with CCl_4 (3 ml/kg/week) for a period of three months. Curcumin (80 mg/kg) and its analog (CA) (80 mg/kg) were orally administered to rats for three months. In CCl_4-treated rats, the levels of aspartate transaminase, alkaline phosphatase and g-glutamyl transferase increased in plasma. The levels of thiobarbituric acid reactive substances and hydroperoxides were increased in plasma and tissues (liver and kidney). There was a decrease in the levels of vitamin C, vitamin E and glutathione in plasma. In tissues, the levels of glutathione and the activities of superoxide dismutase, catalase and glutathione

peroxidase increased

Results: Rats treated with curcumin and CA significantly decreased the levels of marker enzymes, lipid peroxides and improved the antioxidant status.

Conclusion: Our study shows that curcumin and CA exhibit antioxidant effect and the effect exerted by CA was more effective than curcumin.

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IRON AND ZINC INTERACTIONS AT THE SITE OF ABSORPTION IN RATS: RELEVANCE TO INTESTINAL PEROXIDATIVE DAMAGE

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Introduction: Iron deficiency remains a major public health problem. Recent clinical studies raised concerns about co-existence of a sub-clinical zinc deficiency in vulnerable segments of our population. Iron and zinc share absorptive pathways and exhibit mutual antagonism. Further, dietary zinc deficiency or excess iron is known to enhance oxidative stress. The present studies were undertaken with the objective of understanding the biochemical consequences of interactions of iron and zinc at the site of absorption, especially on oxidant-antioxidant balance.

Methods: Three separate depletion-repletion experiments using 24 weanling WKY female rats per experiment were carried. The design of the study involved either depleting iron and/or zinc for 4 wk, followed by repletion (n=8) with 8 mg iron and/or 6.6 mg zinc for 2 wk. Indicators of iron and zinc status were monitored in addition to assessing intestinal TBARS, protein carbonyls, antioxidant enzyme activities, functional integrity using marker enzymes and aconitase activity. Further, localization of ^{59}Fe, ^{65}Zn, ferritin and metallothionein induction was studied at the site of absorption. The extent and type of free radical species produced was studied using ESR spectroscopy.

Results: Iron repletion induced intestinal TBARS, protein carbonyls and depletion of GSH in iron and/or zinc deficiency suggesting overt oxidative stress. Combined repletion of Fe and Zn though marginally reduced their status, resulted in reduced localization of ^{59}Fe, ferritin and ^{65}Zn, metallothionein at the site of absorption. Inclusion of zinc was found to reduce the signals associated with OH. The impact of interactions was greater when iron and zinc deficiencies coexisted.

Conclusions: Co-administration of zinc along with iron reduced iron induced peroxidative damage and is beneficial in optimizing the intestinal antioxidant defense.

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PROTECTIVE EFFECT OF FERULIC ACID AGAINST NICOTINE INDUCED OXIDATIVE STRESS IN BRONCHOALVEOLAR LAVAGE (BAL)

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Introduction: Currently 1.2 billion people worldwide smoke tobacco despite clear evidence that smoking is a leading "preventable" cause of death. The addiction liability and pharmacological effects of smoking are primarily mediated by the major tobacco alkaloid "nicotine"Nicotine is known to induce oxidative stress in bronchoalveolar lavage (BAL), there by decreasing the level of antioxidants, a condition which occurs in numerous pulmonary diseases. Natural antioxidants have been receiving a lot of attention as chemopreventive agents. Hence, ferulic acid (FA), a naturally occurring monophenolic compound was tested against nicotine induced changes in BAL of Wistar rats.

Methods: Female Albino Wistar rats were used for the study. Membrane integrity of BAL cells was tested by analyzing the activities of alkaline phosphatase (ALP) and lactate dehydrogenase (LDH). BAL cytology was measured by BAL cell count and viability. Extent of lipid peroxidation was measured by thiobarbituric acid reactive substances, hydroperoxides and nitric oxide. Antioxidant effect of ferulic acid was analysed by measuring antioxidant levels in both BAL fluid and cells.

Results: Activities of ALP & LDH were significantly increased during nicotine treatment which was effectively brought back by FA. Positive modulation of BAL cytology was observed during FA treatment. The increased lipid peroxidative indices and decreased antioxidant status during nicotine toxicity were positively modulated by FA treatment.

Conclusion: From the results obtained, we could conclude that FA effectively protect the lung against nicotine induced toxicity and can be a gain for the current search of effective lung protective agent in future.

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EFFECT OF LUPEOL AND ITS ESTER ON CYCLOPHOSPHAMIDE INDUCED LIPEMIC-OXIDATIVE STRESS

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Introduction: Cyclophosphamide (CP), an alkylating agent widely used in cancer chemotherapy causes fatal cardiotoxicity. Lupeol is a pentacyclic triterpene isolated from Crataeva nurvala stem bark. Linoleic acid is a ω-6 fatty acid. The aim of the present study was to evaluate the hypocholesterolemic property of lupeol and its ester, lupeol linoleate in experimental cardiotoxicity induced in rat model by CP.

Methods: Group I served as control. Group II, Group V and Group VI animals were injected intraperitoneally with a single dose of CP (200mg/kg body weight) dissolved in saline. Group III and Group V animals received lupeol (50 mg/kg body weight) dissolved in olive oil for 10 days by oral gavage. Group IV and Group VI animals received lupeol linoleate (50 mg/kg body weight) dissolved in olive oil for 10 days by oral gavage. The levels of reactive oxygen species such as superoxide and hydroxyl radical levels in heart tissue were estimated. Serum lipids and lipoprotein fractions and cardiac lipid metabolizing enzymes were assayed.

Results: Superoxide and hydroxyl radical levels were significantly increased in CP administered rats. Significant alterations ($p < 0.05$) in serum lipid profile and activities of lipid metabolizing enzymes were also observed. Lupeol and its ester; lupeol linoleate caused significant reversal of the above alterations induced by CP.

Conclusion: The results of this study present the decreased activity of lipoprotein lipase and hypercholesterolemia associated with CP induced oxidative stress. Supplementation of the pentacyclic triterpenes highlight the hypocholesterolemic property against CP induced lipemic-oxidative stress.

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ALCOHOL AND THERMALLY OXIDIZED PUFA INDUCED OXIDATIVE STRESS: ROLE OF N-ACETYL CYSTEINE

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Introduction: Alcohol related disabilities are one of the world's major

public health concerns. The effects of alcohol intake include alteration of redox state, acetaldehyde and free radical production, which lead to membrane damage. The damage caused by alcohol is enhanced by polyunsaturated fatty acid ingestion. When alcohol is taken along with thermally oxidized sunflower oil, the toxicity is still more pronounced due to toxic metabolities produced during heating. In our study, we have analysed the effects of a thiol supplier N-acetyl cysteine on alcohol and thermally oxidized sunflower oil induced toxicity.

Methods: Male albino Wistar rats were used for the study. The degree of liver damage was assessed by estimating the activities of liver marker enzymes (ALP & GGT). The extent of lipid peroxidation was measured by estimating the lipid peroxidative indices (TBARS and hydroperoxides). The antioxidant status was measured by estimating the enzymic and non-enzymic antioxidants.

Results: The activities of liver marker enzymes (ALP & GGT) and the lipid peroxidative indices (TBARS & hydroperoxides) were increased in alcohol & PUFA groups when compared to normal and were decreased inN-acetyl cysteine treated groups. The antioxidant status (SOD, CAT, GPx & GSH) was decreased in tissues of alcohol & PUFA groups, which were found to be improved in N-acetyl cysteine treated groups.

Conclusion: Our results showed that N-acetyl cysteine regresses the oxidative damage induced by alcohol and thermally oxidized sunflower oil.

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OXIDANTS AND ANTIOXIDANTS IN MYOCARDIAL INFARACTION AND REPERFUSION

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Introduction: Free radicals have been implicated in the pathogenesis of both acute myocardial infaraction (AMI) and reperfusion injury leading to deleterious effects. There is inadequate data regarding levels of antioxidants and oxidants as markers of oxidative stress in these conditions. The present study aimed to determine reliable, non-invasive biochemical markers of oxidative stress.

Method: the study group comprised of 52 patients who satisfied defined criteria for AMI. These were further divided into reperfused and non-reperfused categories based on clinical and other criteria for reperfusion. 20 healthy individuals comprised the control group levels of Malondialdehyde (MDA), Glutathione peroxidase (Gpx), Ascorbic acid, Alpha Tocopherol and Ceruloplasmin were assessed in both study and patient groups at 0,2 and 4 hours after thrombolysis with Streptokinase using standard techniques of test methods.

Results: All patients of AMI showed significant elevated levels of MDA ($p<0.001$) and Gpx ($p<0.001$). However, ascorbate levels were significantly lower ($p<0.05$). Analysis of the two study groups showed a significant decline of alpha-tocopherol levels from 0.4 hours in reperfused compared to non-reperfused group. Other markers showed no significant deference in the two groups ($p>0.05$).

Conclusion: The study concludes that Gpx and MDA are good markers of AMI while alpha-tocopherol can be proposed as a simple, non-invasive biochemical marker for myocardial reperfusion.

P-107

FREE RADICALS AND ANTIOXIDANTS IN AGING

AGE RELATED CHANGES IN LIPID PEROXIDATION AND ANTIOXIDANTS IN ELDERLY PEOPLE

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Introduction: Advancing age is associated with an accumulation of low level free radical damage, which leads to the physiological and clinical modifications. Age related changes resulting from free radical reactions include increasing levels of lipoperoxides, alteration in enzyme activities and greater osmotic fragility. The objective of the present study was to estimate the level of lipid peroxidation product and antioxidants Catalase (CAT), Glutathione (G-SH), Vitamin E and percent hemolysis in elderly people.

Methods: The study group consisted of 34 elderly people between 60-75 years of both sexes. They were divided into four groups: 1.Normal elderly group (n=13), 2.With diabetes (n=8), 3.With hypertension (n=7) and 4. With diabetes hypertension (n=6). The control group included 15 healthy individuals of both sexes between 20-32 years. Malondialdehyde (MDA), Vitamin E, G-SH, CAT and % hemolysis was measured by standard methods.

Results: The increase in MDA is highly significant ($p<0.0001$) in elderly diabetic and elderly diabetic-hypertensive patients when compared to controls. The vitamin E concentration decreased significantly in normal elderly group ($p<0.0001$). The decrease in G-SH is highly significant in elderly diabetic and elderly diabetic-hypertensive patients. Catalase activity is highly decreased in normal elderly group ($p<0.0001$). % hemolysis is highly decreased in normal elderly people when compared to controls. A negative correlation was obtained between MDA and the antioxidants and Vitamin E and G-SH.

Conclusion: We found an increase in lipid peroxidation and decrease in antioxidants in normal elderly people. Highly significant increase in MDA and decrease in antioxidants was observed in elderly people when complicated with diabetes and hypertension. Supplementation of antioxidants may prevent further oxidative injury in elderly people.

P-108

FREE RADICALS AND ANTIOXIDANTS IN AGEING

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Free radicals (FR's) are chemical species as atoms or molecules with singlet, i.e. unpaired electron which makes them highly unstable, and causing them to react almost instantaneously with any substance in its vicinity and also leads to cascade of new free radicals in multiplying (chain reaction) effect. All free radicals are extremely reactive and will seek out and acquire an electron in any way possible, causing themselves to attack another molecule and there by modifying it biochemically. When FR's activity is taking place damage to cell occurs, protein synthesis becomes impaired, tissues become less pliable, arteries incur damage, age pigments accumulate which literally drown the cells in lipofuscin, preventing them from functioning and generally all signs and indications of ageing are promoted.

Ageing is the seemingly inevitable decline in physiologic function that occurs over time for all living creature, the ultimate terminus of ageing is the same: death. The free radical theory of ageing (FRTA) was first published by Dr. Denham Harman in 1956 and subsequently major review of FRTA done by Beckman & Ames provides varying degree of support to FRTA. The rate of ageing is directly related with the level of oxidative stress. Free radicals are involved in some of the disease of ageing of eyes such as cataracts, light and drug induced retinopathy and ocular siderosis. Investigation had shown that cataract formation is due to radical damaged to lens tissues. Antioxidant eliminates the consequences of free radicals disastrous effect at cellular and biomolecular levels, which was proved by Dr. Harman that life span increases by using artificial antioxidants such as Butylated hydroxy toluene. The major antioxidant effect is obtained from nutrients such as vitamin C & E, selenium, C0Q10, lipoic acid, quercetine. The pineal hormone 'melatonin' also plays as antioxidant. Vit. C & Vit. E are found to have synergistic antioxidant activities. There can be very little doubt that antioxidants in the diet offer protection from many of the diseases as well as from many signs of ageing.

FREE RADICALS AND ANTIOXIDANTS IN RADIATION BIOLOGY

P-109

RADIATION- AND FREE RADICAL-EXPOSURE AND REGULATION OF PROTEIN SYNTHESIS BY HEME REGULATED EUKARYOTIC INITIATION FACTOR 2 KINASE

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Introduction: Heme regulated Inhibitor (HRI) is a member of the eIF-2 kinase family and is a potent regulator of initiation of translation. During a variety of cytoplasmic stresses such as, heme deficiency, heat shock and lead toxicity, HRI undergoes activation through autophosphorylation, and inhibits global protein synthesis. Investigations from this lab have earlier demonstrated that during drug-induced anemia in rabbit, there is a 2-3-fold increase in HRI mRNA level while a 24-fold increase in the protein level. Over expression and activation of HRI is reported in lead acetate toxicity and heat shock in human cells *in vitro*. However nothing is known about HRI mediated regulation of protein synthesis during exposure to radiation and oxidative stress.

Materials and Methods: In the present investigation, radiation, and hydrogen peroxide and hydroxyl radicals have been used to induce oxidative stress in human K562 cells as a model. The parameters estimated are cell proliferation, HRI expression at mRNA level and HRI activity as measured by eIF-2 phosphorylation.

Result: -Our data suggest that hydrogen peroxide inhibits cell proliferation in a concentration dependent manner in K562 cells. Under an optimum dose of 150M of H_2O_2, concurrent with decreased cell proliferation, there is an induced HRI kinase activity indicating inhibition of protein synthesis. Further, under such exposure, determination of modulation in transcription of HRI and its contribution to regulation of protein synthesis is in progress. Experiments on the radiation exposure and regulation of protein synthesis are currently being standardized.

Conclusion: -The detailed data, which tend to indicate the possibility of using HRI as a molecular marker for free radical-and radiation-exposure will be presented and discussed.

P-110

RADIOPROTECTION OF SWISS ALBINO MOUSE BY TINOSPORA CORDIFOLIA

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Introduction : Radioprotection of normal healthy animals is a serious problem which has yet to be solved. There is no remedy of accidental / medical or exposure at the time of war. Amifostine is the only chemical available in the market which is with a lot of side effects and is very costly. The present study is an attempt to find out a nontoxic remedy of plant origin.

Methods : The experiments were conducted on adult healthy swiss albino mice. They were irradiated with a lethal dose (8Gy) of gamma rays with and without Tinospora cordifolia (TC) aqueous extract orally 1 hr. before irradiation. The optimum dose of TC was selected on the basis of survival. The animals were sacrificed at 1/4, 1, 3, 5, 7, 10, 14 and 28 days after treatment. Their body weight was recorded daily. Weight of liver, spleen and thymus were recorded. The data were analysed statistically by using students 't' test.

Result : It was observed that irradiation to a lethal dose decreases body weight of the mice. All the animals which were irradiated without plant extract pretreatment died after 10 days. But those which were irradiated with the same dose of irradiation and given plant extract one hour before irradiation survived more than 30 days (i.e. experimental period). Their body weight was significantly more than which were irradiated without plant extract. Not only this,their body weight recorded to increase to a significant extent during the experimental period. Weight of the liver, spleen and thymus also decreased after irradiation and was significantly more in the plant extract pretreated group. The plant extract treated group showed recovery in the weight of various organs significantly.

Conclusion : On the basis of above results it concluded that TC significantly protects Swiss albino mouse against radiation injury. This plant which is being termed as "Tridosh shamak" or cure for all diseases protects against radiation injury. It's well known immunomodulatory,

P-111

TREATMENT OF ASCORBIC ACID IMPROVES HEALING OF EXCISION WOUNDS IN MICE EXPOSED TO DIFFERENT DOSES OF g-RADIATION

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Introduction: Due to the crucial practical importance of acute radiation exposure associated with combined injuries, it is necessary to investigate the efficacy of cost-effective nutritional factors in the reconstruction of irradiated wounds. Therefore, effect of pretreatment of ascorbic acid was studied on the healing of excision wound in mice exposed to 2, 4, 6 or 8 Gy whole-body g radiation.

Methods: A full-thickness wound was created on the dorsum of the irradiated mice and the progression of wound contraction was monitored by capturing video images of the wound at various post-irradiation days.

Results: Irradiation caused a dose dependent delay in wound contraction and wound healing time, while ascorbic acid pretreatment resulted in a significant elevation in the rate of wound contraction and a decrease in the mean wound healing time. To understand the mechanism of healing, collagen,and hexosamine contents of wounds were measured after exposure to 6 Gy, treated or untreated with ascorbic acid. Treatment with ascorbic acid prior to irradiation enhanced the synthesis of collagen and hexosamine , while histological assessment of wound biopsy revealed an improved collagen deposition, fibroblast and vascular densities.

Conclusion: The present study demonstrates that ascorbic acid pretreatment has a conducive effect on the irradiated wound and could be an substantial therapeutic strategy to ameliorate radiation-induced delay in wound repair in the case of combined injury situations.

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RADIO-PROTECTION OF DNA BY FERULIC ACID

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Introduction: Ferulic acid is a monophenolic phenylpropanoid occurring in plant products such as rice, green tea and coffee beans is very good free radical scavenger. In the present work effect of ferulic acid was studies on plasmid relaxation and DNA strand breaks in peripheral blood leukocytes and bone marrow cells of mice exposed to whole body ã-radiation.

Methods: Plasmid DNA (300-350ng) was exposed to different doses of radiation in presence and absence of ferulic acid. Concentration dependent protection of mice blood leukocytes and bone marrow cell was studies by intraperitoneal administration of different amounts (50, 75 and 100 mg/kg body weight) of ferulic acid 1 hour prior to 4Gy ã -radiation exposure. Alkaline single cell gel electrophoresis (comet

assay) was carried out to study radiation-induced damage to mice blood leukocytes and bone marrow cells as well as DNA repair study.

Results: Presence of 0.5mM ferulic acid significantly inhibited the disappearance of super-coiled (CCC) plasmid pBR322 with a reduction factor (DRF) of 2.0. Intraperitoneal administration of different amounts of ferulic acid 1 hour prior to radiation exposure showed dose dependent decrease in the yield of DNA strands breaks in mice peripheral blood leukocytes and bone marrow cells. The dose dependent protection was more pronounced in bone marrow cells than in the blood leukocytes. Administration of 50 mg/kg body weight of ferulic acid after whole body irradiation of mice showed enhancement in the DNA repair.

Conclusions: Thus ferulic acid is having good radio-protective property both in vitro and in vivo condition. The possible mechanism of the radioprotection is free radical scavenging and enhanced DNA repair.

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TITLE: A NOVEL METHOD OF TESTING RADIOPROTECTIVE EFFECT OF OCIMUM SANCTUM IN PATIENTS UNDERGOING HEMI BODY IRRADIATION (HBI).

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Objectives: -. Flavinoids- Orientin and Vicenin from Ocimum sanctum (OS, Tulasi) extract have shown very promising radioprotector activity in animal experiments. We have developed a novel clinical model for testing these agents in vitro. The aim of the current study was to test the radioprotective (RP) effect of Tulasi.

Materials and methods: In this ICMR funded DBRCT, patients undergoing HBI for disseminated cancers are randomised to receive a placebo or an aqueous extract of OS. HBI provides a unique chance of testing the RP effects of single high dose RT on the two most radiosensitive organs (salivary glands & bone marrow) using objective laboratory endpoints which is not possible with fractionated RT to smaller areas of the body. The patients were evaluated pre and post HBI for salivary amylase, Super oxide dysmutase (SOD), Glutathione reductase (GR) and glutathione peroxidase (GP) and haemogram.

Results: In this trial, 95 patients have been enrolled and biochemical data for 71 patients is available for analysis. The radiation salivary tissue injury manifested in marked increase in the serum salivary amylase levels, peaking 24 hours after upper HBI. The peak salivary amylase levels were significantly higher in the arm A (46 x base line) as compared to arm B (27 x base line) of the study (p=0.056). This indicates a possible radioprotective effect on the salivary glands by the Drug in arm B. No significant variations were noticed in the mean serum levels of the SOD, GR and GP or haematological parameters between the two arms of the study. None of the patients in the trial had any serious adverse even due to the investigational drug.

Conclusions: The effect of Tulasi on the salivary tissue is encouraging and merits further investigations. We will have to wait for the completion of accrual and breaking the code to confirm that Tulasi has indeed radioprotective effect.

P-114

RADIOPROTECTIVE EFFECT OF SESAMOL ON ?-RADIATION INDUCED CELLULAR CHANGES IN CULTURED HUMAN BLOOD LYMPHOCYTES

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Introduction: The development of radiation protectors is important not only to enhance the effectiveness of cancer treatment, but also for the study of the underlying mechanisms of radiation cytotoxicity. Available radio protective substances possess unacceptable toxicity limiting its clinical usefulness. Therefore, it is necessary to develop protectors that will minimize toxicity while maintaining efficacy.

Methods: Cultured lymphocytes were divided into fourteen groups. Thirty minutes prior to irradiation three test doses (1, 5 and 10 ? g/ml) of sesamol were added to the grouped normal lymphocytes. Lymphocytes dispersed in 35 mm Petri dishes covered with a membrane (transpire surgical tape ? 1527-3) were irradiated. The cobalt teletherapy unit (Phonex,60Co) was used for in vitro irradiation(1,2 and 4 Gy). DCaberration, micronuclei, TBARS, GSH, SOD, CAT and GPx were studied.

Results: Our results show that there is a dose dependent increase in the MN, DC frequencies and lipid peroxidation levels and decrease in GSH levels and SOD, CAT and GPx activities in ? -irradiated lymphocytes. On the other hand pretreatment of sesamol decreased the frequencies of MN, DC and TBARS levels and increased the levels of GSH, SOD, CAT, and GPx to normal levels in a concentration dependent manner.

Discussion: The radio protective effect of sesamol can be explained by the scavenging of free radicals before they cause damage to cellular macromolecules because sesamol is a potent antioxidant with the capacity for free radical trapping.

Conclusion: Even at very low concentration sesamol exhibited radio protective effect and hence sesamol may be useful in the protection of normal cells during ionizing radiation exposure

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RADIO PROTECTIVE EFFECTS OF *SPINACIA OLERACEA* ON BIOCHEMICAL ACTIVITY IN BRAIN OF SWISS ALBINO MICE AFTER GAMMA EXPOSURE

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Introduction : Present study is an attempt to investigate the protective effect of *Spinacia oleracea* extract (SE) against radiation induced oxidative stress, which is evaluated in term of biochemical parameters of lipid peroxidation, cholesterol, protein and glycogen concentrations. *Spinacia oleracea* L. is rich in antioxidant compounds like carotenoids (-carotene, lutein and zeaxanthine), ascorbic acid, flavonoids and protein, which is easily available and affordable throughout the year it could be recommend in dietary course for the personnels working with radiation in laboratories as well as to the population residing in areas where they are continuously exposed to background radiation.

Methods : Swiss albino mice of 6 weeks weighing 22±3 gm were selected and divided into four groups. One group which did not receive any treatment (normal) and two groups were supplemented orally with SE at a dose of 1100 mg/kg.b.wt./day dissolved in double distal water (DDW) for 15 consecutive days. Fourth group was given orally the DDW. Then two groups, one with drug treated and another DDW treated, were exposed to 5 Gy of gamma radiation. The animals were autopsied at 1,3,7,15 and 30 days post-exposure and brain was removed for estimation of biochemical parameter.

Results: The radiation-induced augmentation in LPO, cholesterol and glycogen content of brain was significantly ameliorated by the drug. The radiation-induced depletion in protein was also significantly protected by the drug treatment.

Conclusions: Results evaluated from this study clearly indicate the antioxidative property of SE against gamma radiation, which is suggestive of free radicals scavenging and singlet oxygen quenching

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RADIOMODULATORY INFLUENCE OF NUTMEG (*MYRISTICA FRAGRANS*) EXTRACT IN SWISS ALBINO MICE AFTER WHOLE BODY EXPOSURE TO GAMMA RADIATION

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Introduction : In recent years, an extensive research work has been carried out in the field of radioprotection. Several synthetic compounds have been tested against radiation but their practical applicability is limited due to toxicity at effective dose levels. Myristica fragrans (Family : Myristicaceae) has been widely used as a spice and herbal medicine.

Methods : To determine its possible radioprotective role, animals were divided into four groups. I Control : Animals were administered 0.9% NaCl orally. II Myristica fragrans (MF) treated group : The animals were administered 10 mg/kg body weight MF seed extract orally in 0.9% NaCl. III Radiation treated group : The animals were exposed to 8 Gy gamma radiation. IV Combination group : Animals were administered MF seed extract continuously for three days and on 3rd day, they were irradiated to 8Gy gamma radiation after 30 minutes of extract administration. Animals were autopsied at 48 hours and testis were taken to analyse LPO, GSH level and histopathological studies.

Results : A highly significant increase in TBARS ($P < 0.001$) and decreased GSH ($P < 0.001$) level was observed in irradiated (Group III) animals. Irradiated testis revealed shrinkage of tubules, broken germinal epithelium, pycnotic nuclei, germ cell depletion specially spermatogonia and spermatocytes. All above pathological symptoms were reduced in MF pretreated irradiated animals. A significant reduction in TBARS ($P < 0.001$) and increased GSH ($P < 0.001$) content was also noticed. No significant alteration was observed in MF treated group as compared to control (normal).

Conclusion : Present result suggest that radioprotection afforded by MF might be possible due to its free radical scavenging activity generated by ionizing radiation.

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RADIO PROTECTIVE ROLE OF ACTONE EXTRACT OF *CENTELLA ASIATICA* AGAINST GAMMA RADIATION INDUCED LESIONS IN PERIPHERAL BLOOD OF MICE.

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Introduction : Hematopoietic tissues are the most radiosensitive tissues of the body. After whole body exposure, the manifestations of injury to mammalian tissues are well reflected in peripheral blood. Ionizing radiation causes severe damage in to blood cells. Irradiation to 6 and 8 Gy gamma irradiation leads to the destruction of circulating blood cells. For this purpose we have tested a medicinal plant ***Centella asiatica***. It belongs to the family Apiaceae. It has been used around the world to treat leprosy, cancer, skin disorders, arthritis, hemorrhoides and tuberculosis. It is known as brain tonic. It improves learning, memory and strengthen central nervous system.

Methods : The experiments were conducted on Swiss albino mice 6-8 week old, weighing 25 (±2) gm. The whole body of the animals were exposed to 6 and 8 Gy gamma radiation. The animals were pretreated with acetone extract of *Centella asiatica*, orally at the dose rate of 25 mg/kg b.w., one hour prior to irradiation. Animals were divided in 3 groups. I group served as normal group. Group II was irradiated with 8 Gy of gamma rays and served as control group. Group III was pretreated with Acetone extract of *Centella asiatica* and exposed to 8 Gy of gamma radiation. This group served as experimental group.

Results : Hemoglobin content, hematocrit value, RBC and WBC count showed severe decline in their number after irradiation while MCV, MCH and platelets started to increase up to significant level after few hours of irradiation,in 8 Gy irradiated Group in comparison to normal animals (< 0.001). Experimental animals also showed same trend but this damage was significant lesser (< 0.05 to < 0.001) at each autopsy interval, in comparison to control animals. Hemoglobin content, hematocrit value and number of RBC and WBC count showed lesser decline, while MCV, MCH and platelets count showed lesser increase in their number. We did not observe any significant change in MCHC value in both control and experimental values.

Conclusion : From these finding it is proved that acetone extract of *Centella asiatica* protected peripheral blood against gamma radiation induced damage.

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MODULATION OF RADIATION INDUCED ALTERATION IN THE ANTIOXIDANT STATUS OF MICE BY NARINGIN.

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Introduction: The alteration in the antioxidant status and lipid peroxidation was investigated in Swiss albino mice treated with 2 mg/kg b.wt. naringin a citrus flavoglycoside, before exposure to 0.5, 1, 2, 3, and 4 Gy gamma radiation.

Methods: Lipid peroxidation, glutathione, glutathione peroxidase, catalase and superoxide dismutase were determined in the liver and small intestine of mice treated or not with naringin at 0.5, 1, 2, 4 and 8 h post-irradiation.

Results: Whole-body irradiation of mice caused a dose dependent elevation in the lipid peroxidation while a dose dependent depletion was observed for glutathione, glutathione peroxidase, superoxide dismutase and catalase in both liver as well as small intestine. Treatment of mice with 2 mg/kg b. wt. naringin inhibited the radiation induced elevation in the lipid peroxidation as well as depletion of glutathione, glutathione peroxidase, superoxide dismutase and catalase in liver and small intestine. Radiation-induced lipid peroxidation increased with time, which was greatest at 2 h post-irradiation and declined therafter in the liver and small intestine. Similarly a maximum decline in the glutathione glutathione peroxidase, and superoxide dismutase was observed at 1 h, while catalase showed a maximum decline at 2 h post-irradation.

Conclusions: Our study demonstrates that naringin protects mouse liver and intestine against the radiation-induced damage by elevating the antioxidant status and reducing the lipid peroxidation.

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ELISA TO MONITOR AMPLIFIED HEMOLYSIS BY THE COMBINED ACTION OF OSMOTIC STRESS AND RADIATION : APPLICATIONS IN MONITORING RADIOPROTECTORS AND MEMBRANE STABILIZERS.

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A new assay has been developed to study the osmotic fragility of red blood cells (RBC's) and the involvement of oxygen-derived free radicals and other oxidant species in causing human red blood cell hemolysis (RBCH). The amount of hemoglobin released into the supernatant, which is a measure of RBCH, is monitored using an ELISA reader, which significantly reduced the assay time for hemoglobin measurements and

blood volume required to obtain the desired number of RBCs. This ELISA based osmotic fragility test (OFT) compared well with the established OFT, with the added advantage of significantly reduced time and the requirement of only 60 l of blood, to analyze 192 samples, present in two 96 well ELISA plates. This small amount of blood was collected fresh, by finger puncture, and diluted 50 times immediately afterwards with PBS, thus eliminating the use of anticoagulants and the subsequent washings. Since exposure of RBCs to 400 Gy -radiation caused less than 5% hemolysis 24 h after radiation, the new method amplified the RBCH induced by radiation by irradiating the cell in hypotonic saline. Exposure of RBC suspension to 400 Gy radiation in the presence of 0.09% NaCl, significantly increased the RBCH, compared to the RBCH, observed in 0.09% NaCl solution alone. The method was validated by examining the protective effect of Trolox, an analog of vitamin E and reduced glutathione(GSH) , a well known radioprotector against RBCH caused by the combined action of radiation and osmotic stress. Trolox, a known membrane stabilizer and an antioxidant and GSH, offered significant protection against RBCH, induced by the combined action of osmotic stress and 400Gy irradiation. Thus this new method, which is simple, needs significantly less time and RBCs, offers the scope, to study the effect of various antioxidants and membrane stabilizers, in modifying the RBCH induced by various stressors including radiation and other oxidative stresses. This method also offers scope to assess the osmotic fragility of erythrocytes, in various laboratory and clinical studies.

Date : 12th January 2005

Time : 1430-1600 H

Chairpersons: Sucheta Dhandekar India
Epe B Germany

FREE RADICALS AND ANTIOXIDANTS IN APOPTOSIS

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INHIBITION OF CELL PROLIFERATION AND INDUCTION OF APOPTOSIS BY GENISTEIN IN EXPERIMENTAL HEPATOCELLULAR CARCINOMA

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Hepatocellular Carcinoma (HCC) is one of the major cancers with highest mortality in the world. The isoflavonoid in soyabean, genistein has been proposed to contribute anticancer effect. So the present study was aimed to test the anticancer potential of the isoflavone genistein in N-nitrosodiethylamine (DEN) induced and Phenobarbital promoted experimental HCC in Wistar albino rats using the measurement of proliferating cell nuclear antigen (PCNA) by immunohistochemistry and apoptosis (DNA Fragmentation) by agarose gel electrophoresis. The results showed the inhibition of the expression of PCNA by genistein and induced apoptosis too. The present study reveals that the isoflavone genistein has anticancer activities by inhibiting tumor cell growth and also inducing apoptosis in experimental hepatoma bearing animals.

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ANTIOXIDANT AND IMMUNOMODULATORY PROPERTIES OF CHLOROPHYLLIN IN *VITRO* AND *IN VIVO*

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Introduction: Chlorophyllin (CHL), a water soluble salt of green plant pigment chlorophyll has been reported to be antimutagenic and anticarcinogenic against a wide variety of mutagens and carcinogens. Recently, it was successfully used as a chemopreventive agent in humans who are at high risk of exposure to liver carcinogen aflatoxin B1 in certain parts of China. Our previous reports have shown the antioxidant and radioprotective activities of this non-sulfhydryl compound in cell free systems. In the present studies, antioxidant and immunomodulatory properties of CHL were explored *in vitro* and *in vivo* in spleen cells from BALB/c mice.

Methods: Entry of CHL in cells was estimated spectrophotometrically. Gamma radiation and 2,2'-azobis(2- propionimidinedihydrochloride) were used to induce oxidative stress in cells. Intracellular free radicals were measured by labeling the cells with dichlorodihydrofluorescein diacetate (DCF-DA) using flow cytometry. Apoptotic cells were measured by propidium iodide staining. Cell proliferation was estimated by carboxyfluorescein diacetate succinimidyl ester (CFSE) dye dilution followed by flow cytometry. Phagocytic activity of peritoneal macrophages was assessed flow cytometrically using fluorescein isothiocyanate (FITC) labeled bacteria. Nitric oxide generation by splenic adherent cells was estimated using Griess reagent. *In vivo* B and T cell responses following sheep red blood cell (SRBC) immunization were measured by plaque forming cell assay and increase in footpad thickness respectively.

Results: CHL was found to enter spleen cells and also scavenged radiation and AAPH-derived free radicals significantly. CHL administration to mice protected against whole body irradiation (WBI) induced apoptosis and lipid peroxidation. About 50 % inhibition was observed after 24 hr of CHL (200 g / gbw) administration. It also augmented nitric oxide generation, phagocytic activity and humoral and cell mediated immune responses in mice.

Conclusions: Our studies demonstrated the antioxidant / radioprotective and immunomodulatory properties of CHL in cellular and animal models.

NITRIC OXIDE

P-122

ALTERATIONS OF ARGINASE ACTIVITY IN SWISS MICE AS A RESPONSE TO WHOLE BODY HYPERTHERMIA (WBH)

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The objective of this study is to find the role of arginase in thermoregulation of mice exposed to heat stress caused by whole body hyperthermia treatment. Arginase catalyses the hydrolysis of arginine to urea and ornithine. It is a key enzyme taking part in several pathways of intermediary metabolism. In mammalian cells, L-arginine is used as a substrate by both nitric oxide synthases (NOSs) and Arginase. Arginase and NOS share a common substrate. NO production is likely to be linked to the regulation of arginase activity. WBH treatment stimulates NO production which causes thermoregulatory vasodilation. In present studies the effect of WBH on arginase activity in hepatic and extrahepatic tissue has been studied under different conditions, to find out the role of arginase in heat stress condition. It was observed that reduced activity in liver of WBH treated mice as compared to normal mice liver. However in extra hepatic tissue like kidney , arginase shows increase in activity as compared to normal mice kidney. Administration of arginine to mice treated with WBH showed arginase activity to normal level. Thus arginase shows alteration in its activity due to thermal stress.

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IRRADIATION INDUCED NITRIC OXIDE PRODUCTION, iNOS ACTIVATION AND INHIBITION BY CURCUMIN AND NICOTINAMIDE.

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Introduction: Nitric oxide is produced endogenously by a family of nitric oxide synthases and has a wide range of physiological and pathophysiological actions. Increased iNOS expression/activation is

reported in breast, CNS and nervous system tumors. Nitration, the consequence of NO production also has been found to be increased in many inflammatory conditions. These inflammatory conditions can be alleviated by curcumin. Curcumin and nicotinamide are both known to be anticarcinogenic. Their mechanism of action is not known and seems to be multi-pronged. In this study we have examined the effects of irradiation on NO production, iNOS activation and the subsequent nitration of proteins, their modulation by curcumin, nicotinamide and JNK inhibitor.

Methods: Peritoneal macrophages were activated with LPS followed by irradiation in presence or absence of modulators. NO production in culture supernatants was estimated by Greiss reaction. Expression profiles of iNOS and total nitrated proteins were estimated by western blot and dot blot assay respectively.

Results: Increase in NO production after irradiation was due to increase in iNOS expression. Inhibition by curcumin, nicotinamide and JNK inhibitor was more profound at the level of NO production and nitration

rather than iNOS expression. Curcumin and the JNK inhibitor together did not show synergistic effect on the inhibition of NO, iNOS activation and nitration.

Conclusion: Induction of iNOS is not the only mechanism that controls the NO production. Nitration is also regulated at various steps.

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SYNTHESIS AND EVALUATION OF ANTI-OXIDANT ACTIVITY OF DERIVATIVES OF GALLIC ACID

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Introduction: Gallic Acid is found to have various pharmacological activities like anti- bacterial , analgesics , vaso constrictor , anti cancer ,chemoprotective, antifungal, anti-inflammatory , anti-oxidant. The present paper deals with synthesis of 4 derivatives of gallic acid and evaluation of their anti-oxidant activites.

Method: 4 compounds have been synthesized from prpyl gallate. 4 different heterocylic ring namely indole, spirothiazoline, oxadiazine and pthalazine hav e been incorporated in propyl gallate .Their anti-oxidant activity have been evaluated by Nitric -oxide scavenging method.

Result: All the 4 compounds showed good anti-oxidant activity than that of the parent compound propyl gallate. The anti-oxidant activity for various compounds are

propyl gallate	= 508µg/ml
propyl gallate containing indole IC50	= 358µg/ml
propyl gallate containing spirothiazoline	= 322µg/ml
propyl gallate containing oxadiazine	= 384µg/ml
propyl gallate containing pthalazine	= 372µg/ml

Conclusion: It is concluded that the nitrogen containing heterocycles , when they are attached to gallic acid ,increases anti-oxidant activity of gallic acid.

RECENT ADVANCES IN MARKERS OF OXIDATIVE STRESS

P-125

GLUTATHIONE REDOX PARADIGM IN BLOOD, A BIOMARKER OF OXIDATIVE STRESS IN EPIDEMIC DROPSY PATIENTS

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Introduction: Epidemic dropsy is an acute food adulterant toxic syndrome caused by the consumption of edible oils contaminated with argemone oil (AO). Interconvertible sanguinarine and dihydrosanguinarine alkaloids are the toxic etiological agents present in AO. Our prior in vitro studies have demonstrated that the toxicity of AO is due to the production of reactive oxygen species (ROS). Since, normocytic anemia is the characteristic feature of dropsy, the present study was designed to investigate the role of oxidative stress and prooxidative environment in the RBC's of dropsy patients.

Methods: Blood of 21 dropsy patients and 7 healthy volunteers were collected. Erythrocyte stability to 2,2'-azobis (2-amidinopropane) dihydrochloride (AAPH) induced peroxidative stress, glutathione reduced (GSH) and oxidized (GSSG) content, GSH redox potential including GSH related enzymatic antioxidants were measured in the blood of dropsy patients and compared with healthy control subjects.

Results: Erythrocytes of the patients were found to be more susceptible to AAPH induced peroxidative stress. Significant decrease ($p<0.05$) in GSH (40%) and increase in GSSG (196%) levels were found in dropsy patients when compared to control. Further, significant decrease ($p<0.05$) of glutathione reductase (47%), glutathioneS-transferase (54%) and glucose-6-phosphate dehydrogenase (51%) activities were observed in dropsy patients. The glutathione redox potential was found to have more oxidative environment in the erythrocytes of the patients (-178 mV) than controls (-213 mV).

Conclusions: These finding suggests that the over production of ROS leads to an increase in erythrocyte susceptibility along with pro-oxidant environment in the erythrocytes of the patients which may be associated with the development of anemia.

USE OF NATURAL PRODUCTS IN HUMAN HEALTH

P-126

PROTECTIVE EFFECT OF *EMBLICA OFFICINALIS* WITH SPECIAL REFERENCE TO ARSENIC INDUCED MICRONUCLEI FORMATION IN MOUSE BONE MARROW

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The environmental contaminant arsenic (As) causes cancer, developmental retardation and other degenerative diseases and thus is a serious health concern worldwide. Effect of *Emblica officinalis* fruit extract (EO) against arsenic induced genotoxicity was studied. In order to investigate the protective efficacy of EO extract against arsenic induced genotoxicity, Swiss albino mice were divided into 4 groups. Group I:- No treatment was given. Group II:- Sodium arsenite 4.0mg/kg body weight was given. Group III:- *Emblica officinalis* extract (500mg/kg body weight) was given. Group IV:- *Emblica officinalis* (500 mg/kg body weight) was given 10 days before sodium arsenite treatment and continued upto 30 days after treatment. The bone marrow cells were collected at different time intervals following various treatments and processed for scoring micronuclei (MN). Arsenic intoxication caused highly significant ($P<0.001$) enhancement in MN frequency. Pre and post treatment of EO extract with arsenic showed highly significant reduction ($P<0.001$) in MN frequency. In order to know the mechanism of arsenic induced genotoxicty, reduced glutathione (GSH) and lipid peroxidation (LPO) in blood were also measured. A significant decrease in GSH content and increase in LPO was observed in blood of arsenic intoxicated mice. Whereas, in combined treatment of EO with arsenic, showed a highly significant elevation in GSH level and a highly significant decline in LPO level in blood of Swiss albino mice. Thus in our present study, results strongly suggest that As-induced genotoxicity in bone marrow of Swiss albino mice can be alleviated/protected by *Emblica officinalis* fruit extract.

P-127

KINETICS OF OXIDATION OF CURCUMIN BY T-BUTOXYL RADICALS IN WATERACETONITRILE MEDIUM.

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Introduction: Curcumin is a biologically active phenolic compound from the plant Curcuma longa (turmeric), a natural yellow pigment. Curcumin, exhibits bactericidal action and may minimize oxidative damage through free radical scavenging. In this context, the study of

kinetics of oxidation of curcumin by t-BuO has been undertaken.

Methods: The kinetics of oxidation of curcumin by t-BuO in water acetonitrile medium was followed at its $_{max}$ 422 nm on a Chemito 2100 UV-vis spectrophotometer. t-BuOOH is activated to radical reactions at 254 nm and hence, light intensity at 254 nm is measured using peroxydisulphate chemical actinometry to calculate quantum yields.

Results: The initial rates of oxidation of curcumin by t-BuO were found to increase with increase in [curcumin], [t-BuOOH] as well as light intensity. Also in the absence of t-BuOOH, there is no change in the concentration of curcumin on shining the light. This indicates that curcumin might be acting as sensitizer and transfer energy to t-BuOOH which homolytically cleaves to give radicals. The fractional order dependence of rates on [curcumin] as well as [t-BuOOH] indicates a pre-equilibrium step involving curcumin and the t-BuO radical which subsequently undergoes oxidation process leading to the formation of curcumin which on further oxidation by t-BuO radical gives final product. At pH=7 the keto form predominates and the heptadienone linkage between the two-methoxy phenol rings contains a highly activated carbon atom. We propose that H-atom donation may take place from this CH_2 due to weak C-H bond and delocalisation of unpaired electron on the adjacent oxygens.

P-128

QUERCETIN A BIOFLAVONOID, ATTENUATES LIPOSACCHARIDES INDUCED HEPATOTOXICITY AND OXIDATIVE STRESS IN RAT LIVER

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Introduction: Septicaemia caused by G-negative pathogen is a dangerous complication and is associated with high incidence of liver dysfunction. Beside other factors the direct effect of endotoxin to a variety of organs is probably due to increase in production of reactive oxygen intermediates such as O2.-, peroxides and nitric oxide. Quercetin (QT) and its sugar conjugates are the most abundantly distributed biofalvonoids in plant kingdom and has potent antioxidant properties. Thus the present study is aimed at investigating the effect of QT in salvaging endotoxin-induced hepatic dysfunction and oxidative stress in rat liver.

Methods: Male wistar rats (150-200g) bred in central animal house of Panjab University, Chandigarh, India were used. Hepatotoxicity was induced by administering lipopolysaccharide (LPS), in a single dose of 1 mg/kg intraperitoneally to the rats, which were being administered QT daily for 14 days. Liver enzymes (AST, ALT), total bilirubin and total protein were estimated in serum. Oxidative stress in liver tissue homogenates was estimated by measuring thiobarbituric acid reactive substances (TBARS), glutathione (GSH) content and superoxide dismutase (SOD).

Result: LPS induced a marked hepatic dysfunction evident by rise in serum levels of ALT, AST and total bilirubin ($P<0.05$). TBARS levels were significantly increased whereas GSH and SOD levels decreased in the liver homogenates of LPS treated rats. Chronic treatment of QT successfully attenuated these effects of LPS.

P-129

INFLUENCE OF *Terminalia bellarica* ON THE RESPONSE OF *Saccharomyces cerevisiae*

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Introduction : The interest in the study of the biological activities of medicinal plants is growing rapidly because of their natural origin and minimal side effects. *Terminalia bellerica* is a medicinal plant whose extract is widely used in certain ayurvedic formulations. The extract of this plant was tested for its potential antioxidant activity *in Saccharomyces cerevisiae* and various invitro tests were also conducted.

Methods : Colony forming assay was performed to determine the influence of the extract on the survival response of Saccharomyces cerevisiae. For this purpose YEPD agar medium was used for growing the cells. Initially the cells were grown as a lawn culture and then the cells from the lawn were used for inoculation and liquid culturing was carried out and the cells were grown to saturation. Phenolic content of the extract was determined. pBR322 assay , DPPH and superoxide scavenging assays were also performed. The extract was tested for its activity in wild type X2180 strain of yeast.

Results : The extract was found to be a good antioxidant. In S. cells, it significantly reduced the damage caused by radiation as evidenced by the survival response of the yeast cells. The growth of the yeast cells revealed the potential role of the extract as a good radioprotector against damage by ionizing radiation. Further, the extract was found to effectively inhibit radiation induced strand breaks in plasmid DNA. Studies also showed that radiation induced lipid peroxidation in rat liver microsomes was inhibited by the extract and IC_{50} value was found to be 13 µg/ml. The extract was found to scavenge free radicals as demonstrated by DPPH and superoxide scavenging assays.

Conclusion : Results indicate that phenolic compounds present in the extract were probably responsible for the protective ability against radiation damage.

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ANTI-OXIDANT ACTIVITY OF EXRACTS OF BALIOSPERMUM MONTATUM

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Introduction: Anti- oxidants often referred to as free radical scavengers. Plants are potential source of anti oxidants, these have strong tendency to neutralize free radicals and thus prevent cell damage to the biological systems. Here we attempt to evaluate the anti oxidant activity of ethanolic and water extracts of baliospermum montanum

Methods: The invitro antioxidant potential of ethanol and water extracts (25-800?g) were evaluated for the following parameters using spectrophotometer. Nitric oxide scavenging was measured using sodiumnitroprusside/Griess reagent.

The degree of lipid peroxidation was assayed by estimating thiobarbituric acid substances using ferrous sulphate in liver homogenate while reduced glutathione assay was determined by method of Ellman using trichloroacetic acid in EDTA in liver homogenate. DPPH method was also performed.

Results: Both the extracts of BM (ethanol and water) showed free radical scavenging activity. It also inhibits lipid peroxidation the ethanolic extract showed significantly higher percentage inhibition in the above-mentioned parameters. The ethanolic and ethyl acetate extract showed IC50 at the 512?g, 867?g concentration in NO, DPPH(606?g , 598?g)and lipid per oxidation (564?g, 598?g)and glutathione reduced assay (765?g, 567?g) respectively.

Conclusion: Reactive oxygen species (ROS) scavenging and lipid per oxidation inhibition \indicates that baliospermum montanum might be a valuable natural anti oxidative source.

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IN VITRO INHIBITION OF LIPID PEROXIDATION IN FISH BY TURMERIC (CURCUMA LONGA)

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The beneficial effects of ù-3 fatty acids on human health have been well documented. Fish and fish oils are the richest sources of ù -3 fatty acids, which are highly susceptible to lipid peroxidation. Regular consumption of cooked fish may be a risk factor for the induction and development of atherosclerosis due to the lipid peroxidation. In the present study, the antioxidant effects of turmeric on fish during standard cooking practices and on time-dependant changes in the peroxidation of fish homogenate was investigated. The antioxidant effects of â -tocopherol were studied to confirm the relevance of the used test method. Thiobarbituric acid (TBA) reactivity in the homogenate was determined by following the method of Luotola. The amount of lipid peroxidation was determined using the molar extinction coefficient of MDA as 1.55×10^{5} and expressed as nmoles TBARS as MDA equivalent /gm of tissue. Peroxides formed in each groups with control were measured by thiobarbituric acid reactivity method at different time intervals and expressed as MDA equivalent/gm of tissue.

Homogenate treated with turmeric in cooking medium showed significantly decrease ($p<0.01$) in peroxide level as compared to control. The effects of TBARS with turmeric at different time intervals as hourly for 4 hours showed 2.7%, 15.8%, 15.8%, 18.7% respectively as compared to controls.

The results indicate a significant protective action of turmeric against lipid peroxidation in the cooked fish and fish homogenate as compared to that of â- tocopherol. Based on these findings, turmeric may be considered as a safe, cheap and easy to use antioxidant for food preaparation.

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ANTI-OXIDANT ACTIVITY OF POLYPHENOLICS ENRICHED ETHANOLIC EXTRACT OF *POLYGALA CHINENSIS* LINN.

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Introduction: Oxidative damage has been implicated in enzymes, DNA, carbohydrates etc. and provoke chain reactions like uncontrolled lipid peroxidation/auto-oxidation, resulting in the manifestation of diseases. Polygala chinensis Linn (Indian senega), family Polygalaceae, is widely used for the treatment of fever, dizziness, asthma, chronic bronchitis and cataract in Indian systems of medicine. The ethanolic extract of the root, rich in polyphenolics viz. xanthones, flavonoids, phenolic acids and their glycosides has been used to evaluate the anti-oxidant potential both in in vitro and in vivo experimental models.

Method: The estimation of lipid peroxidation was done by thiobarbutric acid (TBA) assay method. TBA forms a colored adduct with malondialdehyde (MDA), which is one of the major peroxidation products of rat brain phospholipid and has been measured colorimetrically at ë 532 nm. In in vitro study, ferric ion /ascorbic acid was used as inducer of hydroxyl radical. While in in vivo the animals were divided into four groups (six animals in each). One group was intoxicated with CCl_4 the control group received only vehicle (1% PEG), other two groups were treated with the sample and Vitamin-E used as standard.

Results: In in vitro study, the ethanolic extract of the plant showed high degree of protection on rat brain lipid peroxidation up to 76.93 ± 0.28%. The inhibitory effect was also found to be dose dependent up to 800 mcg/37.5mg of brain tissue. In in vivo study, CCl_4, used as inducer of free radical, elevated the MDA contents from 18.8 ± 1.96% to 85.65 ± 1.64%. The extract of the plant showed significant inhibition of CCl_4 induced lipid peroxidation up to 33.99%, which was comparable with the vitamin-E (41.17%), used as standard.

Conclusions: Both the in vitro and in vivo study showed that the ethanolic extract of the roots of Polygala chinensis rich in polyphenolics has significant anti-oxidant property.

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FREE RADICAL- INDUCED MEMBRANE DAMAGE AND ANTIOXIDATIVE/RADIOPROTECTIVE ROLE OF HERBAL PRODUCTS

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Introduction : Oxidative stress and its adverse effects are inevitable to living cells and are being highly implicated in many diseases. Therefore, intake of natural antioxidants credited with phytochemicals/micronutrients is of paramount importance. To this end, we have extensively investigated the antioxidative/radioprotective role of aqueous extracts of two indigenous medicinal plants, *Andrographis* paniculata (Ap) and *Swertia* chirata (Sc) in cellular system.

Methods: Using rat liver mitochondria as a model system, oxidative damage-induced by -radiation, photosensitization and physiological oxidants was monitored against membrane constituents, lipids, proteins, antioxidant defenses as well as detoxication system. Degradation of mitochondrial protein was measured employing SDS-PAGE technique. To under stand the possible mechanism, scavenging capacity of these extracts against superoxide, hydroxyl and other stable radicals was also investigated.

Results: Exposure of rat liver mitochondria to ROS generating agents, in presence of *Andrographis paniculata* (Ap) and *Swertia chirata* (Sc)(50g/ml) independently demonstrated significant depletion ($P<0.001$) in oxidative damage as exemplified by reduced levels of peroxides, carbonyl formation, and restoration to detoxication /antioxidant defenses. Both the extracts could prevent degradation of mitochondrial proteins. Extracts have high scavenging reactivity with superoxide/ hydroxyl radicals, high reducing activity and considerable amounts of phenolic contents. The *exvivo* studies significantly demonstrated antioxidative effects of the extracts. In view of these observation, *Andrographis paniculata* and *Swertia chirata* may emerge as an effective radioprotective /antioxidative agents. Possible mechanism with relevance to antioxidative potential will be discussed.

Conclusion: In conclusion, the extracts of *Andrographis paniculata* and *Swertia chirata* exhibit antioxidative and radioprotective effects and may thus have potential therapeutic applications in radiobiology and chemotherapy to protect normal tissues from radiation and drugs respectively.

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ANTIOXIDANT ACTIVITY OF SOME COMMON PLANTS OF MEDICINAL VALUE : A COMPARATIVE STUDY

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Introduction : Some common Indian medicinal plants used in traditional Ayurveda sysem have antioxidant activities. They contain plenty of polyphenols , coumarines and antioxidant vitamins like A,E,C etc. .In the present study we estimated antioxidant potency of following plants viz. : fenugreek or methi (*Trigonella foenumgraecum*), pudina (*Menthe piperita*), tulsi (*Ocimum sanctum*), beetel (*Piper beette*), neem (*Azadirachta indicus*), Turmeric (*Curcuma longa*), Jashtimadhu (*Glycyrrhiza glabra*), anantmul (*Hemidesmus indicus*), bhuiamla (*Phylanthus nirurri*)and sajina (*Moringa oleifera*).

Materials and Methods : The aqueous extract of the aerial part of *Phylanthus nirurri* , green leaves of *Menthe piperita, Ocimum sanctum, Piper beette, Azadirachta indicus, Moringa oleifera, the seeds of Trigonella foenumgraecum* , root of *Curcuma longa* and root bark of *Glycyrrhiza glabra, Hemidesmus indicus* were taken for the in vitro examination. The anti oxidant potential of these plant extracts were determined by estimating superoxide dismutse (SOD) activity , catalase activity, total reduced glutathione & total anti oxidant status against Trolox. SOD activity was estimated by using NBT system. The catalase activity was estimated by estimating rate of change of H_2O_2 degradation by using Ammonium molybdate,. Reduced GSH is measured bu DTNB system and total antioxidant status , based on the TRAP assay against Trolox.

Result : While evaluating comparative total anti oxidant activity of the experimental herbal samples , significant total anti oxidant activity against known antioxidant Trolox are observed in decreasing order in the following samples *Phylanthus nirurri, Glycyrrhiza glabra , Trigonella foenumgraaecum , Ocimum sanctum, Menthe piperita, Azadirachta indicus, Hemidesmus indicus. Curcuma longa, Piper beette, and Moringa oleifera* .

Conclusion : The encouraging anti oxidant properties of those plants extracts can be valuable candidates for the treatment of free radical mediated disease conditions.

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ANTARTH, A POLYHERBAL PREPARATION PROTECTS AGAINST THE DOXORUBICIN-INDUCED TOXICITY WITHOUT COMPROMISING ITS ANTINEOPLASTIC ACTIVITY

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Introduction: Doxorubicin (DOX), an anthracycline drug widely used for the treatment of various cancers, causes a cumulative dose-dependent cardiac toxicity that is characterized by an irreversible dilated cardiomyopathy and congestive heart failure. Antarth (ANT) a polyherbal preparation was evaluated for its cardioprotective properties against the doxorubicin induced cardiotoxicity in mice.

Methods: Mice were treated with 25 mg/kg ANT orally once daily for 5 consecutive days before single intraperitoneal injection of 15 mg/kg doxorubicin. The animals were killed 30 h after DOX treatment.

Results: DOX induced a significant elevation in the serum levels of glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT), creatine kinase (CK-MB) and lactate dehydrogenase (LDH), indicating its acute cardiotoxicity. The treatment of mice with ANT before DOX administration significantly reduced the serum levels of GPT, GOT, CK-MB and LDH indicating that ANT protected against the DOX induced cardiotoxicity. Pretreatment of mice with 25 mg/kg ANT inhibited the DOX-induced decline in the antioxidant status. Intraperitoneal injection of 1.25 mg/kg DOX once daily for 9 consecutive days, significantly improved the survival of mice bearing Ehrlich ascites carcinoma (EAC). Treatment of EAC with 25 mg/kg ANT alone did not affect the anticancer activity of DOX since ANT did not alter the tumor cell growth, median survival time and average survival time of tumor bearing mice.

Conclusion: The present study demonstrates that ANT, protects mice against the DOX-induced cardiotoxicity, without compromising with the antineoplastic activity of DOX.

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CHEMOPREVENTIVE & ANTIMUTAGENIC PROPERTIES OF *ACACIA NILOTICA* (LINN.) ON 7,12-DIMETHYLBENZ(A) ANTHRACENE INDUCED SKIN PAPILLOMAGENESIS IN SWISS ALBINO MICE

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Introduction : Acacia nilotica Linn. (Babul), Family-Leguminosae, widely distributed in Rajasthan, has been subjected to long term clinical trials in folk medicine. The present investigation is an attempt to evaluate the chemopreventive & antimutagenic effects of Acacia nilotica (AN) aqueous extracts on DMBA / croton oil induced skin papillomagenesis in Swiss albino mice.

Methods : For this purpose, male Swiss albino mice were divided into two groups. Group I (Control)-In which animals were given DMBA and croton oil, no extract was given. In group II (treatment) animals were treated with AN gum (Group II-a) (800 mg/kg body weight /day), AN flower (Group II-b), AN leaf (Group II-c) during peri and post initiation periods of DMBA and croton oil application. Animals were observed to 16 weeks for the presence of papillomas.

Results : AN Gum, flower and leaf extracts treated mice showed a significant reduction in tumor burden, tumor incidence, cumulative number of papillomas and showed a marked increase in letency period as compared to control. We also reported a significant reduction in chromosomal aberrations and number of micronuclei in all treated groups as compared to control. For antioxidative properties, animals treated orally with AN flower (Group II-b) and leaf (Group II-c) extract for 15 days showed a highly significant decrease in the hepatic lipid peroxidation (LPO) levels, whereas AN gum (Group II-a) treated animals showed a marked reduction in LPO as compared to control. Conversely, a significant increase in the hepatic reduced glutathione (GSH) content was observed in AN flower (Group II-b), leaf (Group II-c) and non-significant elevation observed in AN gum (Group II-a) as compared to control.

Conclusions : The chemoprevention and antimutagenicity of Acacia nilotica can be attributed to its antioxidant and antiperoxidant porperties.

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FREE RADICAL SCAVENGING POTENTIAL OF HELICTERES ISORA.L

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Introduction: The concern over free radicals and reactive oxygen species (ROS) is of growing interest It plays a significant role in pathological conditions like cancer, inflammation, and ischemia. Antioxidants react with free radicals and prevent the damage by chelating the catalytic metals and acting as oxygen scavengers. Humans have an inbuilt antioxidant defense system to prevent free radical mediated injury in form of enzymatic and non-enzymatic systems. An insufficiency in these defense systems requires administration of antioxidants. So the present investigation is to assess the free radical scavenging potential of Methanolic extract of Helicteres isora L (Sterculiaceae) (MEHI)

Methods: The degree of lipid peroxidation was assayed by estimating the Thiobarbituric acid-reactive substances (TBARS) initiated by FeSO4 in rat liver. Reducing power is determined by treating with trichloroacetic acid and FeCl3 (Oyaizu). Free radical scavenging activity by DPPH method and NO scavenging is done by standard methods. Reduced Glutathione was determined by Ellman method. Hydrogen peroxide scavenging is done by hemolysis of RBC induced by H2O2 systems. OH scavenging is done by EDTA/H2O2 method.

Results: MEHI inhibited FeSO4 induced lipid peroxidation in a dose dependent manner. The IC50 of MEHI was found to be 528 ?g/ ml. The oxidation of reduced glutathione was inhibited by MEHI and the IC50 is 572?g/ml. It also showed marked significant ($P<0.01$) activity against OH radicals generated by EDTA/H2O2 systems. Hemolysis of RBC is significantly ($P<0.01$) inhibited by MEHI when compared to control. Reduction of the DPPH radicals by MEHI is found from the percentage inhibition of 85.85%. The reducing power of MEHI increased with increase in concentration and showed significant level at ($P<0.01$) when compared to control.

Conclusion: The present study indicates that MEHI shows good antioxidant property.

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BIOACTIVITY GUIDED FRACTOINATION OF CORONOPUS DIDYMUS: A FREE RADICAL SCAVENGING PERSPECTIVE

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Introduction: Earlier studies by us on an aqueous extract of Coronopus didymus [CD], Linn. (Brasicaceas) had indicated a potent free radical scavenging and possible radioprotective actions. To locate the bioactive fraction/ compound, a bioactivity-guided fractionation of CD was undertaken with a free radical scavenging perspective.

Methodology: Fractionation of CD was done by column chromatography on silicagel G by gradient elution from chloroform to methanol. All the fractions were pooled based on TLC into fractions designated as CDF-1, CDF-2, CDF-3 CDF-4. All fractions were subjected to [1] dose dependent scavenging of DPPH, ABTS.-, and hydroxyl radicals. [2] Protection from Fenton reagent induced calf thymus DNA damage. For further confirmation, nanosecond pulse radiolysis and stop-flow spectrophotometry was carried out.

Results and discussion: CDF-1 was found to be more active compared to other fraction in scavenging DPPH and ABTS.-. Stop-flowspectrometric studies indicated the reaction with DPPH in a time scale of 100 seconds, 58.13% inhibition at 15 g/ml and a concentration of 300 g/ml scavenged 32.31% ABTS.- in100 seconds. However all the fractions showed reactivity towards hydroxyl radical by pulse radiolysis. Competition kinetics of CDF-1 with potassium isocyanate by pulse radiolysis also revealed 13.6% reactivity towards hydroxyl radical in comparison to potassium isocyanate. Fenton reagent induced calf thymus DNA protection by CDF-1 at 400 g/ml indicates it to be a most potent fraction of all. Isolation and In-vivo radioprotection studies of CDF-1 consists of our future research perspective.

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IN VITRO ANTIOXIDANT ACTIVITY OF METHANOL EXTRACT OF CITRUS AURANTIFOLIA FRUITS

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Introduction: Many plants are consumed not only as vegetables or used in food preparations, but they are also utilized for medicinal purposes. Citrus aurantifolia (CA) (christm.) Swingle (Family Rutaceae) is used widely in the traditional medicine. Some experiments provide evidences of anti-cancer, anti-inflammatory, analgesic and anti-bacterial properties. In this study the in vitro antioxidant activity of C.aurantifolia fruits is evaluated.

Methods: C.A. Fruits were cut into small pieces, shade dried and coarsely powdered. Then methanol extract (MeCA) was prepared using soxhlet, and its in vitro antioxidant activity has been evaluated by (i) Ferric thiocyanate (FTC) and (ii) Thiobarbituric acid (TBA) method. In vitro antioxidant activity of MeCA was compared with vitamin E.

Results: MeCA showed low absorbance value in both FTC and TBA methods similar to that of Vitamin E. Lower absorbance value can be interpreted as higher antioxidant activity. During the oxidant process, peroxide is gradually decomposed to lower molecular compounds that are measured by FTC and TBA methods. FTC method is used to measure the amount of peroxide at the primary stage of linoleic acid peroxidation, whereas TBA method used for evaluating the completion of LPO. MeCA extract produced significant in vitro antioxidant activity and this might be due to the presence of flavonoid compounds in it.

Conclusion: Methanolic extract of C.aurantifolia fruits possess antioxidant activity which is comparable to that of vitamin E. The antioxidant activity may be attributed to the presence of flavonoids in the MeCA.

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ANTIOXIDANT PROPERTIES OF GERMINATED FENUGREEK SEEDS

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Introduction: Fenugreek (*Trigonella foenum-graecum*-known as *'Methi'* in Hindi) is an important spice used in India and various other Asian, African and European countries. It is also one of the oldest medicinal plants being used in many Asian and African countries and has

beneficial therapeutic properties such as antidiabetic effects. Germinated fenugreek seeds are being used as vegetable and health food, and are also considered to be more beneficial than dried seeds. Since antioxidant properties have been linked to health benefits of natural products, we have assessed antioxidant potential of germinated fenugreek seeds.

Methods: In the present study, we have examined the antioxidant activities of different fractions and extracts from the powder of germinated seeds of fenugreek and two of its active chemical constituents namely trigonelline and diosgenin, at different levels of their action. The assays employed were ferric reducing antioxidant power (FRAP), radical scavenging by 1,1-diphenyl-2-picrylhydrazyl, ferrylmyoglobin/2,2'-azobis-3-ethylbenzthiazoline-6-sulfonic acid (ABTS), pulse radiolysis, oxygen radical absorbance capacity (ORAC) and inhibition of lipid peroxidation. Chemical composition was determined by HPTLC.

Results: Aqueous fraction of fenugreek exhibited the highest antioxidant activity as compared to other fractions. As quantity of phenolic and flavonoid compounds can be related to antioxidant activity, their contents from these extracts were measured. HPLC analysis was carried out to detect polyphenols, flavonoids and other components.

Conclusion: Our study reveals significant antioxidant activities in germinated fenugreek seeds and these proved to be more potent than other antioxidant rich foods. This may be partly due to the presence of flavonoids and polyphenols and mainly due to water-soluble components such as gallic acid. The antioxidant activities observed can possibly explain its health benefits.

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ANTIOXIDANT EFFECT OF GREEN LEAFY VEGETABLES

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Introduction: Sabasigi (*Anthem graveolens*), Fenugreek (*Trigonella Foenum Gracecum* Linn) Drumstick leaves (*Moringa Olifera*) are commonly used green leafy vegetables in India, which contains several flavonoids and phenolic acids. In view of the pharmacological interest the antioxidants present in the vegetables/fruits are given importance, as they are non-toxic natural antioxidants.

Methods: 0.2g of fresh leaves of vegetables were extracted in 10ml of water and alcohol separately, centrifuged, clear supernatant (extract) were used for further study. Antioxidant effects of aqueous and ethanol extracts were assessed by means of inhibition ferrous sulphate/ ascorbate (non enzymatic) and lipoxygenase induced linoleic acid peroxidation. Free radical scavenging properties using DPPH radical was also evaluated.

Results: Water extracts of Fenugreek, Drumstick and Anthem sowa showed maximum inhibition against ferrous sulphate/ascorbate induced linoleic acid peroxidation dose dependently at 100l extract in 0.5ml of reaction mixture. Antioxidant activity of aqueous extract was found to be in the order of Fenugreek>Drumstick>Anthem sowa. (753.2, 702.3, 602.1%) where as methanol extract showed moderate inhibition which is in the order of Fenugreek>Drumstick>Anthem sowa (551.2, 482.2, 421.8%) respectively. Aqueous extracts of Fenugreek, Drumstick and Anthem sowa showed inhibition against lipoxygenase induced linoleic acid peroxidation dose dependently at 500l extract in 3.0ml assay mixture by 82.43.2, 65.92.2, 62.61.8% respectively. The aqueous extracts of Fenugreek, Drumstick and Anthem sowa showed highest percent of DPPH scavenging activity which is about 881.2, 862.8, 841.6% respectively.

Conclusion: In the light of above antioxidative effects it presumable that consumption of natural antioxidants from food stuffs can protect the human body from attack of free radicals and subsequent to that it could have beneficial effect in terms of disease prevention.

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ANTI-INFLAMMATORY AND ANTIOXIDANT ACTIVITIES OF CASSIA FISTULA LINN BARK EXTRACTS

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Introduction Cassia fistula linn (Caesalpinaceae) tree is one of the most widespread in the forests of India, usually occurring in deciduous forests The whole plant possesses medicinal properties useful in the treatment of skin and inflammatory diseases, rheumatism, anorexia and jaundice. The present study reports the anti-inflammatory and antioxidant activity of Cassia fistula stem bark extracts in rats.

Methods The aqueous (CFA) and methanolic(CFM) extracts of stem bark were prepared by soxhlet extractor after defatting with petroleum ether. Wistar albino rats of either sex (120-180g) were used for the study of acute (carrageenan induced inflammation) and chronic (cotton pellet granuloma) models of inflammation. Both extracts were administered at the dose of (500 mg / kg / po) and the results were compared with standard NSAID drug diclofenac sodium (5 mg / kg / po). The antioxidant activity of extracts was studied by DPPH, Nitric oxide, Lineolic acid and Hydroxyl radical induced invitro assay methods. The Lipid peroxidation level was evaluated in rat liver and kidney homogenates initiated by CCl4 and FeSO4.

Results The aqueous(CFA) & methanolic(CFM) extracts found to possess significant($p<0.001$) anti-inflammatory effect in both acute and chronic models. Cassia fistula stem bark extracts showed significant radical scavenging activity by inhibiting lipid peroxidation in rat liver and kidney homogenates. Both extracts exhibited significant antioxidant activity in DPPH, Nitric oxide, Lineolic acid and Hydroxyl radical induced in-vitro assay methods.

Conclusion The present study indicates that cassia fistula stem bark extracts (CFA & CFM) posses significant anti-inflammatory and anti oxidant properties.

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ANTIARTHRITIC AND FREE RADICAL SCAVENGING ACTIVITY OF RICINUS CUMMUNIS ROOT EXTRACT

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Introduction Rheumatoid arthritis(RA) is a painful and crippling systemic disease for which there is no cure. It is an autoimmune disorder. In Indian system of medicine many plants are used as cure for many inflammatory disorders. In the present study aqueous(RCA) and methanolic (RCM) extracts of ricinus cummunis(root) were evaluated for antiarthritic and invitro free radical scavenging activities.

Method The aqueous and methanolic extracts of root bark of RC was prepared by soxhlet extractor after defatting with petroleum ether. Wistar rats (150-200g) of either sex were used for the study. Arthritis was induced by complete freund's adjuvant-carrageen induced inflammation 0.1ml CFA was inoculated intradermally at the base of tail to all group of animals. 10 days later 0.1ml of (2% w/v of carrageen in saline) was

injected to sub plantar apo neurosis of right hind paw. The edema volume was determined by using plethysmograph. RCA & RCM (500mg/kg/po) and diclofenac sodium (5mg/kg/po) were administred from day 10 to day 21st after the establishment of arthritis. On 22nd day blood were collected by retro orbital puncture. Liver was homogenized in tris buffer and subjected to biochemical studies SOD, GPX, LPO, RedGlutathione, vitamin C, vitamin E were estimated.

Result Both RCA & RCM significantly ($p< 0.001$) reduced the edema volume of arthritic rats when compared to untreated control. Simultaneously the levels of enzymatic & non enzymatic anti oxidants showed significant ($p< 0.01$) increase in RCA & RCM treated animals when compared to untreated control.

Conclusion Both RCA & RCM possessed anti arthritic and antioxidant activities in experimental induced arthritis.

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ANTIINFLAMMATORY, ANALGESIC AND ANTIOXIDANT EFFICACY OF BARLERIA LUPULINA LINDL

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Introduction: Inflammatory diseases are common throughout the world. The disadvantages in synthetic drugs lie in their gastric toxicity and reappearance of symptoms. Therefore development of anti-inflammatory drugs is still in progress. Pain secondary to inflammation process is the manifestation of inflammatory disorder, its evaluation in anti-inflammatory agents are rational. The role of free radicals and free radical mediated lipid per oxidation as a mechanism of tissue damage in inflammation and ulcerogenosis is emphasized. So the present investigation aimed to study analgesic, anti-inflammatory and antiperoxidative effect of methanolic extract of Barleria lupulina (MEBL).

Methods: The anti-inflammatory activity of MEBL (200 and 300 mg/kg i.p) was studied by using the models of carrageenan, serotonin induced paw edema and cotton pellet granuloma pouch in rats for assessing the effect of acute and chronic inflammation respectively. The analgesic activity of MEBL (200 and 300 mg/kg i.p) was studied using acetic acid induced writhing test in mice for assessing peripheral analgesic effect. Invitro anti-oxidant studies were carried out to assess the efficacy as hydroxyl radical (OH.), hydrogen peroxide (H2O2), superoxide anion and lipid peroxide. The ulcerogenic study of the extract (300mg/kg) was also performed.

Results: MEBL treated rats showed significant inhibition of carrageenan and serotonin induced edema volume ($P<0.01$). It also exerted significant reduction in granuloma weight ($P<0.01$) when compared with indomethacin. The invitro results also showed significant scavenging of OH. ($P<0.01$) and decreased lipid peroxide formation ($P<0.01$). Acute administration of MEBL did not produce any gastric lesion in rats.

Conclusions: These results suggest that MEBL exerts analgesic and anti-inflammatory activity in acute and chronic inflammation without ulcerogenic activity. This effect may be probably released to its antioxidant activity. The present study establishes the analgesic and anti-inflammatory activity of the extract.

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FREE RADICAL QUENCHING EFFECT OF SEMECARPUS ANACARDIUM LINN. NUT EXTRACT AGAINST ADJUVANT ARTHRITIS.

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Introduction: Oxidative stress mechanisms are known to play a significant role in the development of various diseases like rheumatoid arthritis (RA) an auto immune disease with a chronic joint inflammation, which cripples the activity of human beings. Reactive oxygen species (ROS) are highly reactive transient chemical species, which play an important role in the etiology of tissue injury in rheumatoid arthritis. The effects of milk extract of Semecarpus anacardium Linn. nut (SA) was studied on adjuvant arthritis in rats against reactive oxygen species.

Methods: Arthritis was induced by injecting 0.1 ml of heat killed Mycobacterium tuberculosis (10mg/ml of paraffin oil) intradermally into the left hind paw of the rats. After 14 days, Semecarpus anacardium Linn. nut extract was administered at 150mg/kg body weight/day for 14 days. After the experimental period, ROS, such as superoxide radical; hydroxyl radical; H2O2 were measured in erythrocytes, lymphocytes and bone.

Results: ROS (superoxide radical; hydroxyl radical and H2O2) in adjuvant arthritic animals were found to be significantly increased ($p<0.05$). Treatment with SA recouped the altered ROS components to near normal levels. No significant changes were observed in drug control animals when compared with control animals.

Conclusion: These evidences suggest that the free radical mediated damage during arthritis was controlled by SA by its free radical quenching and antioxidative potential.

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ORAL ADMINISTRATION OF GINGER (ZINGIBER OFFICINALE ROSC.), PROTECTS AGAINST THE RADIATION-INDUCED MORTALITY

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Introduction: The rhizome of Zingiber officinale, commonly known as ginger, is consumed daily worldwide as a spice and flavoring agent. The rhizome of ginger has been reported to possess diverse medicinal properties in the traditional Indian system of medicine. Therefore radioprotective effect of hydroalcoholic extract of ginger rhizome, Zingiber officinale (ZOE) was studied in mice administered ZOE before exposure to various doses of gamma radiation.

Methods: The animals were administered with 250 mg/kg ZOE orally using oral gavage once daily for five consecutive days before exposure to 6, 7, 8, 9, 10 or 11 Gy of â-radiation. The animals were monitored daily up to thirty days post-irradiation for the development of symptoms of radiation sickness and mortality.

Results: Pretreatment of mice with ZOE reduced the severity of symptoms of radiation sickness and mortality at all the exposure doses, and also increased the number of survivors in the ZOE + irradiation group when compared with the concurrent DDW + irradiation group. The ZOE treatment protected mice against the GI death as well as bone marrow deaths. The dose reduction factor (DRF) was found to be 1.2. The administration of ZOE after exposure to irradiation was not effective as no survivors could be reported up to 30 days post-irradiation. Reducing the administration schedule to three or increasing the schedule

to seven days was not as effective when compared to five consecutive days schedule. The irradiation of animals resulted in a dose dependent elevation in the lipid peroxidation, while depletion in the GSH contents on day 31 post-irradiation. Treatment of mice with ZOE before irradiation caused a significant depletion in the lipid peroxidation followed by a significant elevation in the GSH concentration in the liver of mice at 31 days post-irradiation. The mechanism of action of ZOE was determined by evaluating its free radical scavenging capability. The ginger was found to scavenge ?OH , O2?- and ABTS?+ radicals in a dose dependent manner in vitro. The drug was non-toxic up to a dose of 1500 mg/kg b. wt., the highest drug dose that could be tested for acute toxicity.

Conclusions: The oral administration of ginger provided protection against the radiation-induced sickness and mortality in mice by protecting against the GI as well bone marrow deaths. The free radical scavenging, elevation in antioxidant status and reduction in lipid peroxidation seem to be the important mechanisms of radioprotective action by ginger.

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HERBAL RELEIF FROM FREE RADICAL STRESS.

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Introduction : Free radicals are atoms or molecules that are highly reactive with other cellular structure because of their unpaired electron They are natural byproducts of ongoing biochemical reactionsin the body including ordinary metabolic processes & immunesystem responses. Since free radical creation is part of our bodies'natural metabolic process, we have built in mechanism to neutralize andscavenge free radicals.Our

bodies produce enzymes such as Glutathione Peroxides,SOD. & Catalase that bind to free radicalsand inactivate them. However modern life has enormously increased the number of free radicals sometimes even harmful introduced in our body, and our bodies are struggling to cope with their relentless onslaught. Fortunately nature has provided an abundance of natural antioxidant food nutrients and botanicals that actually scavenge free radicals in the body, as well as enhance the body's own product of antioxidant enzymes. Efforts have been made in this

paper to summarize the free radical scavenging activity of various herbs which probably account for their vital actions like Antiaging , anticancer, Hepatoprotective,Immunomodulatory etc.

Methods-A literature survey was done on the herbal drugs that are recognized for the excellent antioxidant activity, and were summarized under following titles. And were categorized under following titles-

I) Immune Antioxidants; Licorice Root. Nutmeg. Burdock Root Salem Panja. Guduchi. Tulsi, Ashwagandha AmlaEchinacea purpurea. Reishi & ShiitakeMushrooms

II) Nutritive Antioxidants: Soy Beta Carotene.Carrots Vit.C Broccoli Vit.E Chlorella Laminatia digitata Grape seeds

III) Digestive Antioxidants. Turmeric Rosemary Fennel Thyme. Sage Ginger Clove Cinnamon

IV) Cardiovascular Antioxidnts Garlic Onions Fenugreek Asragalus Shizandra

Results -The above summary gives an impressive reference to actually explore various mechanisms through which the drug acts as antioxidants and how effectively & economically they can be used to treat oxidative stress generated due to various environmental pollutants.

Conclusion: Herbal antioxidants due to their remarkable free radical scavenging activity can be further explored to treat diseases like Alzheimers', Epilepsy, Parkinsonism of which no certain mechanism and cure is known as yet.& neuronal damage caused due to generation of free radicals might be one of the causes of these diseases.

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STUDY ON FREE RADICAL SCAVENGING &PROTECTIVE EFFECT OF Hybanthus enneaspermus UPON ISOLATED HEPATOCYTES

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Introduction: Role of free radical is highly indicated in several liver dysfunctions. The different hepatotoxicants inducing liver cirrhosis are known to cause the damage by the free radical mediation. In this study we investigated the whole aqueous extract of the plant Hybanthus enneaspermus in regard to its antioxidant and protection to the hepatocytes against five hepatotoxicants.

Methods: Hepatocytes (chicken) were isolated following the procedure of Snell and Evans (1987). They were exposed to five hepatotoxicants such as CCl4, allyl alcohol, paracetamol, diazepam and tetracycline in their toxic dose under five different groups. Each group was again subdivided into five subgroups representing a control; hepatotoxicants-induced; drug alone; drug pretreated+ hepatotoxicants; hepatotoxicants and post-treated with extract for three consecutive days. In drug-treated group again five different concentrations of the drug were investigated. The cell viability was studied by the Trypan blue exclusion method. The extent of lipid peroxidation was carried out by modified method of Stock and Dormandy (1971) taking the liver homogenate.

Results: From the results significant ($p<0.005$) increase in cell viability was observed because of the treatment of extract in pre-treated groups where the drug was administered once. In post-treated groups the extent of protection of cells was dose-dependent and similar when it was administered for three days twice daily. In both cases, the response was dose-dependent but the dose dependency was more in post-treated groups. A similar trend was observed in all hepatotoxicants. The drug could significantly reduce the extent of lipid peroxidation proving its antioxidant capability.

Conclusions: It is concluded from the study that the extract of Hybanthus enneaspermus showed good hepatoprotective and antioxidant activity.

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A NOVEL BIOACTIVE ANTIOXIDANT MOLECULE THAT PROTECTS CELLS AGAINST XENOBIOTIC-INDUCED CELL INJURY

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Introduction : Xenobioticinduced cell injury is a critical event in the expression of toxico-pathological effects in animals. There is a great deal of interest in molecules that attenuate the xenobiotic-induced cellular injury and theses molecules could serve as health-promoting nutraceuticals. We have isolated a bioactive molecule from the aqueous extract of the edible tubers of *Decalepis hamiltonii*, having high antioxidant activity. Further, the molecule showed cytoprotective effect against xenobiotic induced cell injury in EAT cells.

Materials and Methods: Purification of the bioactive molecule was achieved by fractionation on silica column followed by preparative TLC. The purity was confirmed by RP- HPLC. Molecular characterization was done using GC-MS and NMR spectroscopy. DPPH, hydroxyl and superoxide radical scavenging and inhibition of lipid peroxidation (LPO) were used to check antioxidant activity. Cytoprotective action of the molecule against cell injury by the xenobiotics HCH, CCl, and CHP in EAT cells was done.

Results: The molecule was identified as 14-aminotetradecanoic acid. The molecule exhibited potent DPPH, hydroxyl and superoxide radical scavenging activity with IC_{50} values 15.6mM, 3.23mM and 1.35mM respectively and inhibited microsomal LPO (IC_{50} 1.26mM). The molecule significantly prevented cell death, LDH leakage, reactive oxygen species (ROS) production and LPO induced by xenobiotics.

Conclusion: The natural bioactive molecule isolated is being reported for the first time. 14-aminotetradecanoic acid showed high antioxidant activity and prevented xenobiotic-induced cell death hence could serve as a novel health promoting nutraceutical.

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ANTIOXIDANT PROPERTIES OF WHEATGRASS (*TRITICUM AESTIVUM* L.) EXTRACTS AS A FUNCTION OF THEIR GROWTH

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Introduction - Wheatgrass (*Triticum aestivum* L.) juice is a herbal drink extracted from tender wheatgrass of 6-15 days old. In some Western countries as well as in India, fresh wheatgrass in the form of juice or tablets is commercially available. It is believed that the wheatgrass is a rich source of vitamins, antioxidant compounds such as vitamins C and E, -carotene, ferulic acid and vanillic acid, and the minerals are in the bioavailable form. It is known to possess antimutagenic and DNA-protective effects. However, its antioxidant effects, as a function of its growth, at different levels of action, are not available in literature.

Methods - We have examined the antioxidant effects at different levels of action of aqueous and ethanolic wheatgrass extracts at 6,7,8,10 and 15 days of germination. The assays employed were radical scavenging using DPPH (1,1-diphenyl-2-picryl hydrazyl), ferrylmyoglobin/ ABTS (2,2'-azobis-3-ethylbenzthiazoline-6-sulfonic acid), FRAP (ferric reducing/ antioxidant power), ORAC (oxygen radical absorbance capacity) and lipid peroxidation. Total phenolic and flavonoid contents were also determined to explain the possible antioxidant effects observed. The studies were also carried out using a commercial tablet preparation of wheatgrass for comparing the results.

Results - In all the assays ethanolic extracts were more effective than the aqueous ones. The antioxidant potential as obtained by various assays and phenolic and flavonoid contents of the extracts increase as a function of the growth. ORAC values for 10^{th} day ethanolic and aqueous extracts were 48.2 and 39.9, respectively, which is significantly higher than many other food ingredients. Studies on ascorbate-Fe^{2+}-induced lipid peroxidation in rat liver mitochondria showed that 10^{th} day ethanolic extract was very effective. Commercial wheatgrass preparation has higher antioxidant effects than the extracts. However, the composition and method of preparation of commercial tablet is not known.

Conclusions - Our results show that wheatgrass extracts on 10^{th} day of growth have significant antioxidant activities probably due to their radical scavenging and damage preventive properties and the observed effects may possibly explain the beneficial properties being ascribed to wheatgrass juice or tablets.

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EFFECT OF NARINGIN ON FERRIC IRON INDUCED OXIDATIVE DAMAGE IN VITRO

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Introduction: Iron is essential for oxygen transport and a variety of cellular processes like respiration and DNA synthesis. It may become toxic when not handled carefully by cellular proteins and shielded from surrounding media. Naringin treatment may help to overcome the iron induced toxic effects in vitro.

Methods: HepG2 cells were treated with 0.5, 1, 2.5 & 5 mM/L naringin 1 h before exposure to 0.1, 0.25, 0.5 & 1 mM/L ferric iron. The effect of iron or naringin or combination treatment was studied on cell survival, DNA double strand break induction, DNA oxidation, lipid peroxidation and various antioxidants.

Results: The exposure of cells to iron caused a dose dependent decline in their clonogenic potential, while naringin pretreatment resulted in a significant elevation in the cell survival. Exposure of cells to iron resulted in a time dependent elevation in DNA strand breaks and a peak level of DNA strand breaks was observed at 24 h, while naringin pretreatment inhibited the DNA double strand breaks accompanied by an early repair. Similarly, treatment of HepG2 cells with iron caused increased DNA oxidation, that showed reduction when cells were pretreated with naringin. The iron overload caused a significant elevation in the lipid peroxidation accompanied by depletion in GSH (glutathione) concentration, while naringin inhibited lipid peroxidation and arrested the iron-induced depletion in the GSH concentration. Iron treatment also reduced various antioxidant enzymes like glutathione peroxidase (GSHPx), catalase and superoxide dismutase (SOD). Pretreatment of HepG2 cells with naringin resulted in an elevation in all the antioxidant enzymes.

Conclusions: Enhanced antioxidant status by naringin could compensate the oxidative stress, and may facilitate an early recovery from iron induced genomic insult in vitro.

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STUDIES ON ANTIDIABETIC AND ANTIOXIDANT ACTIVITIES OF CAESALPINIA CRISTA

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Introduction: In the Indian subcontinent diabetes and the accompanying secondary complications pose major health problem. There are many plants being used traditionally for specific cause, but not mentioned in texts for the said medication. One such plant is Caesalpinia crista, the roasted seeds of which are being used as antidiabetics in West Indies whereas the kernel and its decoction in certain region of Gujarat and Orissa. Though there are several indications like antimalarial, tonic, astringent, anti-inflammatory and diuretic, but its antidiabetic property is not mentioned. In our study we investigated antioxidant (in vitro and in vivo), glycemic and lipidaemic status of diabetic rats treated with the drug for 90 days.

Methods: After getting approval from IAEC, Inbred rats of Wister strain (100-140g) comprising an equal number of male and female were randomized into three groups (n=10). Group-I, II and III were served as control, diabetic-control and diabetic+drug treated group respectively. Alloxan (150mg/kg) was used for the induction of diabetes. Biochemical and antioxidant evaluation were carried out using standard methods. Separate three groups (n=6) of rats were used for the oral glucose tolerance test.

Results: The results showed significant ($p<0.005$) reduction in the levels of blood glucose and liver TBARS; and also showed improvement in

different biochemical parameters like liver (glycogen, protein) and serum (triglyceride, cholesterol, creatinine, uric acid). Histopathological study revealed significant change in the altered pancreatic architecture (in diabetic rats) than that of the treated diabetic animals, suggesting possible regeneration. After treatment, the animals successfully withstood the oral glucose tolerance test. The extract showed good antioxidant activity in different in vitro systems.

Conclusions: It can be concluded that Caesalpinia crista possesses good antidiabetic and antioxidant activities.

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FREE RADICAL SCAVENGING ACTIVITY OF EXRACTS OF LUFFA ACUTANGULA VAR AMARA

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Introduction: There is increasing evidence that reactive oxygen species and their promoted oxidative damage are involved in large number of pathologies as well as in ageing process the oxidative stress experienced by a tissue, organelle or organ results from the balance between the production and removal of potentially damaging reactive oxygen species. In this paper we have reported the anti oxidant activity of ethanolic and ethyl acetate extracts of leaves of Luffa acutangula var. amara.

Methods: The invitro antioxidant potential of ethanol and ethyl acetate extracts (25-800?g)were evaluvated for the following parameters using spectrophotometer. Nitricoxide scavenging was measured using sodiumnitroprusside/Griess reagent.

The degree of lipid peroxidation was assayed by estimating thiobarbituric acid substances using ferrous sulphate in liver homogenate while reduced glutathione assay was determined by method of Ellman using trichloroacetic acid in edta in liver homogenate. DPPH method was also performed.

Results: Both the extracts of LA (ethanol and ethyl acetate) showed free radical scavenging activity.it also inhibits lipid peroxidation the ethanolic extract showed significantly higher percentage inhibition in the above mentioned parameters. The ethanolic and ethyl acetate extract showed percentage inhibition at the 800?g concentration in NO (59.6?0.104,45.68?0.143), DPPH(62.56?0.101,44.69?0.114), and high inhibitory activity on lipid per oxidation (60.95?0.409,45.10?0.106)and glutathione reduced assay (51.09?.2279,38.41?.038) respectively.

Conclusion: Reactive oxygen species (ROS) scavenging and lipid per oxidation inhibition activites indicate that luffa acutangula might be a valuable natural anti oxidative source.

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ALTERATIONS IN THE INTESTINAL GLYCOCALYX AND BACTERIAL FLORA IN RESPONSE TO ORAL INDOMETHACIN

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Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs), used extensively in clinical medicine, tend to cause adverse effects in the gastrointestinal tract. Earlier work has shown that indomethacin produced oxidative damage and attenuation of the glycocalyx layer in the rat small intestine.

Objectives: The aim of this study was to assess indomethacin-induced changes in the composition of the glycocalyx of the rat small intestinal mucosa, with specific reference to surfactant-like particles (SLP) and brush border membranes (BBM) of the mucosa. Changes in gut flora in response to the drug were also to be studied.

Methods: Rats were dosed orally with 40 mg/kg of indomethacin. SLP and BBM were isolated 12 and 24 hours later and their content of sugars and lipids estimated. Intestinal bacterial counts and their adherence to mucosa were also determined.

Results: The content of various sugars was increased in SLP and decreased in the BBM following indomethacin treatment, at both time periods studied ($p = <0.05$ in all cases). The composition of lipids in the SLP was also found to be significantly altered. There was an increase in the number of E.coli in the luminal contents of the small intestine and caecum in these animals, as compared with controls ($p = <0.05$). The number of bacteria adherent to the intestinal mucosa was also significantly higher in the drug-treated group. In vitro studies revealed that there was an increased tendency for bacteria to adhere to SLP isolated from indomethacin-treated rats ($p = <0.05$).

Conclusions: These results suggest that alterations in glycosylation of the small intestinal SLP and BBM, in response to indomethacin-induced oxidative stress, are associated with a quantitative increase in intestinal bacterial flora and an increased tendency of bacteria to adhere to the mucosa. We postulate that these factors may facilitate translocation of luminal bacteria into the intestinal mucosa and contribute to damage produced by NSAIDs.

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LIPID PEROXIDATION AND ANTIOXIDANT STATUS IN SICKLE CELL ANAEMIA.

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Sickle erythrocytes and their membranes are susceptible to endogenous free-radical-mediated oxidative damage which correlates with the proportion of irreversibly sickled cells. Nevertheless discrepancy in the status of various antioxidants is observed in different studies. In view of these contradictory reports, the present study was undertaken to assess the oxidative stress in sickle cell anaemic cases and also to find out whether any correlation exists between the free radical activity and the percentage of Haemoglobin-S in blood. Eighty-three sickle cell anaemic cases were studied, of which, 26 were homozygous for the sickle cell disease and 57 were heterozygous (Traits) as confirmed by hemoglobin electrophoresis and also by variant hemoglobin percentage testing. Fifty-two age and sex matched apparently healthy non-sickler subjects were taken as controls for this study. All the subjects (cases and controls) were analyzed for the concentrations of Malondialdehyde (MDA), Ascorbic acid, alpha - Tocopherol and beta- Carotene in plasma. Observations suggested a significant increase in the free radical activity (reflected by increased plasma MDA concentration) and decrease in the antioxidant status (reflected by decreased plasma concentrations of antioxidant vitamins). A significant positive correlation was also observed between the malondialdehyde concentration in plasma and the percentage of Haemoglobin-S variant in blood.

P-156

OXIDATIVE STRESS AND ENZYMATIC ANTIOXIDANT RESPONSE IN NEONATES SUFFERING FROM RESPIRATORY DISORDERS.

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Introduction:- Respiratory disorders like Birth asphyxia and Respiratory distress syndromes (RDS)are the two most common cause of neonatal morbidity and mortality. Postnatal changes from relative hypoxic to hyperoxic environments during artificial ventilation increases the risk of ROS formation

Material & method :-Present study was carried out to evaluate oxidative stress and antioxidant defense in neonates with respiratory disorder who received oxygen therapy. Total 100 subjects were included in the study .out which 50 neonates were suffering from respiratory disorder and 50 served as control.Blood samples were collected before and after oxygen supplementation for estimation of LPO by method of K.Satoh, Hemoglobin by cynmethemoglobin method ,activity of SOD by using RANSOD kit and catalase activity by method of L.Goth.

Results:- Levels of Lipid peroxidation (in terms of MDA-molondialdehyde)increased sgnificanly before as well as after oxygen therapy than control (P<0.0001).Hb before therapy has no significant difference from control but after therapy concentration of Hb decreased significantly than control (P<0.0001).Activities of super oxide dismutase and catalase decreased significantly(P<0.0001) before therapy while increased significantly (P<0.0001)after oxygen therapy.

Conclusion:-The ability of neonate to response to oxygen therapy by augmented enzyme activities seems to be mandatory for its surviral, facing the confront of oxidative stress. When these defencive mechanisms fail the victim get succumbed to oxidative challenge.

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OXIDATIVE STRESS AND NONENZYMATIC ANTIOXIDANTS IN NEONATAL HYPERBILIRUBINEMIA

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Introduction:- Hyperbilirubinemia is the most common and certainly one of the most vexing problems in newborn period. Precipitation of bilirubin inside the brain at low pH may have toxic effects. Neurons undergoing differentiation are particularly susceptible to injury from bilirubin. Unconjugataed bilirubin can induce a loss of neurons and atrophy of involved fibers system. Thus NNH may end into bilirubin encephalopathy.Phototherapy is effective in prolonged reduction of bilirubin levels in infants with NNH.

Material and method :- The study undertaken was carried out to evaluate the oxidant status and antioxidant response in neonates with NNH before and after phototherapy. Number of subjects included were 80,out of which 30 were suffering from Neonatal hyperbilirubinemia(NNH) and 50 were controls. Blood samples were analysed for LPO (in terms of MDA)by method of K.Satoh, hemoglobin concentration. by cynmethemoglobins, ascorbic acid concentration by method of Ayekyaw and concentration. of uric acid by enzymatic kit method .

Results:- Concentration .of LPO elevated before as well as after phototherapy significantly(P<0.0001),concentration of Hb decrased significantly (P<0.0001) before and after phototherapy. Ascorbic acid and uric acid decreased significantly(P<0.0001) before therapy and increased after therapy significantly (P<0.0001) but not more than control.

Conclusion:- Estimation of routine biochemical parameters can help to monitor oxidant and antioxidant status in NNH before as well as after phototherapy.

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OXIDATIVE STRESS AND ANTIOXIDANT STATUS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Introduction : COPD comprises of chronic bronchitis and emphysema which although pathologically distinct diseases, are usually co-existent. All the tissues of our body are vulnerable to oxidative stress but most prone is the respiratory system being in direct contact with the environment. The oxidants/free radicals may cause (1) direct oxidative damage to airspace epithelial cells or (2) indirect injury via oxidative inactivation of antiproteases leading to emphysema. Inhaled pollutants activate hemocytes to produce oxidants. The PUFA's in cell membranes are highly susceptible to pathological free radical damage.

Methods : In our study, we have estimated (1) Oxidative stress (lipid peroxidation):by Serum Malonyldialdehyde(MDA) levels. (2) Antioxidant status by: (i) Blood Glutathione (GSH), (ii) Serum Ascorbic acid levels. The study group comprised of 70 diagnosed patients of COPD subdivided into two groups depending upon severity of the disease (i) Acute COPD (n=40); (ii) Stable (clinically) COPD (n=30). The Control group consisted of 40 healthy age and sex-matched individuals.

Results : (1) Mean levels of MDA in patients of acute COPD were signficantly increased vs control group and stable COPD group. In stable group the increase was non-significant versus controls. (2) Mean levels of GSH and Ascorbic Acid in acute COPD were significantly decreased vs. control and stable COPD groups. In the clinically stable group the decrease was not significant vs control group. (3) We observed a positive correlation between serum MDA levels and the severity of COPD.

Conclusion : There was an inverse relationship between both GSH and Ascorbic acid levels vs MDA levels. This concludes an enhanced oxidative stress and depleted antioxidant status in patients with COPD. This oxidant/anti-oxidant imbalance in favour of oxidants results in oxidative lung injury. Thus a therapeutic trial of antioxidants may be worth pursuing in the management of COPD.

P-159

EFFECT OF ROS AND PROTEINASE INHIBITOR IN RHEUMATOID ARTHRITIS

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Introduction: Free radicals are known to play important role in the disease "Arthritis". The correlation of reactive oxygen species (ROS) and protease inhibitor activity namely Alpha-2-Antitrypsin is an area of immense interest in arthritis.

Methods: The serum trypsin inhibitory activity was determined by the method of Waheed & Salahuddin (1975) using BAPNA as substrate. A total of 50 cases of Rheumatoid arthritis were investigated out of the above 50 cases, 23 were males whereas 27 females **Results:** In comparison to control enhanced level of alpha-1-antitrypsin activity was found in the females (age group : 20-35 yrs), while decreased level

of alpha-1-antitrypsin activity was found in the age group of 36-80 years. In case of males, deficient alpha-1-antitrypsin activity was observed in all the age groups except in the age group of 51-65 years which showed slightly enhanced levels. Furthermore, attempt was also made to probe the binding of serum alpha-1-antitrypsin in rheumatoid arthritis by ELISA. A maximum titer of 1:6400 was observed in patients of the age group of 20-35 years. Moreover, antibodies in serum of patients with rheumatoid arthritis exhibited an appreciable degree of immuno-interaction with H2O2 modified DNA. Similar results were observed on plates coated with H2O2 modified DNA and alpha-1-antitrypsin as inhibitor.

Conclusion: Deficient cases of alpha-1-antitrypsin represented chronic illness of rheumatoid arthritis, while elevated levels were indicative for acute phase of the disease.

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GLUTATHIONE PEROXIDASE (GPx)-LIKE ANTIOXIDANT ACTIVITY OF ANTITHYROID DRUGS.

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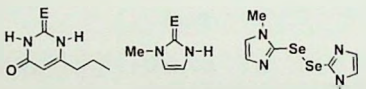
Thyroxine (**T4**) is the main secretory product of the thyroid gland, and the deiodination of this prohormone to the biologically active hormone, 3,5,3'-triiodothyronine (**T3**), is the first step in thyroid hormone action. It is well known that type I iodothyronine deiodinase (ID-1), a selenocysteine-containing enzyme, is responsible for most of this conversion. The activation of thyroid stimulating hormone (TSH) receptor by autoantibodies leads to an overproduction of thyroid hormones, which can be controlled by specific inhibitors such as 6-*n*-propyl-2-thiouracil (**1**, **PTU**) and methimazole (**3**, **MMI**) that either block the thyroid hormone biosynthesis or reduce the conversion of **T4** to **T3**.



3, E = S (PTU) 5, E = S (MMI)
4, E = Se (PSeU) 6, E = Se (MSel)

7 ($MSel_{ox}$)

Recent studies on thyroid hormone metabolism suggest that glutathione peroxidase (GPx), present in the thyroid gland, degrades intracellular H_2O_2 and thereby inhibits the iodination reactions. These observations indicate the possibility that some of the anti-thyroid drugs may inhibit the thyroid hormone biosynthesis by reducing H_2O_2 (GPx-like activity), because the oxidation of iron center in TPO by H_2O_2 is the first step in thyroid hormone synthesis. Therefore, we focused our attention on the GPx activity of **MSelox** and some related compounds.[1] Interestingly, **MSelox** exhibited high GPx activity, providing a novel mechanism for its inhibitory action. The activity of **MSelox** was found to be comparable to that of ebselen, a well-known GPx mimic. On the other hand, the sulfur analogue, **MMI**, did not show any noticeable activity under identical experimental conditions. The high GPx activity of **5**-**7** suggests that the selenium analogues of the anti-thyroid drugs and other GPx mimics inhibit the LPO activity by reducing H_2O_2 and these compounds may also act as antioxidants and protect cells from oxidative damage. These results reveal that the selenium analogues of the anti-thyroid drugs, together with GPx, may constitute a defense system against reactive oxygen species in the thyroid gland. The LPO inhibition activity of some other sulfur-containing compounds will also be discussed.

(1) G. Roy, M. Nethaji and G. Mugesh *J. Am. Chem. Soc*, **2004**, *126*, 2712.

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A STUDY ON THE ROLE OF RNI AND ROI IN SLE

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Introduction: Systemic lupus erythematosus (SLE) is marked by hyperproduction of antibody and injury of multiple organs and tissues. A population of anti-DNA Abs have been found in serum of SLE patients and their titer correlates with disease activity. DNA, to which most of the antibodies are directed in SLE is no longer regarded as the inciting antigens because immunization with native DNA does not induce SLE like disease and the resultant formed were exclusively directed towards modified structures.

Methods: Human monocytes (MN) from PBMC were cultured for 120 hrs with or without reactive oxygen intermediate (ROI) and reactive nitrogen intermediates (RNI) inhibitors, namely NAC and L-NMMA respectively. The concentration of each inhibitor used was 10 mM. DNA from treated/untreated human monocytes were isolated and used in competitive ELISA.

Results: In comparison to native DNA from untreated monocytes, the inhibitors treated DNA exhibited a decreased recognition by immunoaffinity purified anti-DNA SLE autoantibodies. Inhibition ELISA showed a maximum of 84.3% inhibition in the anti-DNA activity with native DNA. Fifty percent inhibition was achieved at 2 ? g/ml of native DNA inhibitor. However, on the other hand NAC and L-NMMA treated human DNA exhibited a maximum inhibition of 54.6% and 43.7% respectively. Fifty percent inhibition was achieved at 2.7 ?g/ml and 3.1 ?g/ml for NAC and L-NMMA treated DNA respectively. Furthermore DNA was also isolated from monocytes of SLE patients as a positive control. Anti-iNOS antibodies exhibited a remarkable recognition of DNA from SLE patients (maximum inhibition = 73.1%), in comparison to DNA from NAC treated monocytes (23.2%) and DNA from L-NMMA treated monocytes (31.24%) respectively.

Conclusion: The results are suggestive for the strong involvement of RNI followed by ROI in the pathogenesis of SLE.

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ANTIOXIDANT MECHANISM OF HYDROXY CINNAMIC ACIDS

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Introduction: Antioxidants are known to show protection from free radical damage and other reactive oxygen species by scavenging them involving several mechanisms. In principle, compounds possessing multiple double bonds and especially with active methylene group can act as radical scavengers via addition to double bonds and / or abstraction of hydrogen atom from the allylic position. As an antioxidant hydroxy cinnamic acids prevent cell damage caused by free radical reactions. We have assessed the mechanism of the antioxidant activity of these compounds, in which in addition to phenolic groups a vinyl moiety if present at the position with respect to one of the phenyl ring can play a predominant role.

Methods: Pulse radiolysis technique has been used to study the mechanism involved in the antioxidant activity of Rosmarinic acid (RMA), Caffeic acid (CA) and Dihydrocaffeic acid (HCA) against deleterious free radicals like GS$^{\bullet}$, ROO$^{\bullet}$, $O_2^{\bullet-}$, NO$^{\bullet}$, $NO_2^{\bullet}$. The dosimetry was carried out using an air-saturated aqueous solution containing 5 x 10^{-2} mol dm^{-3} KSCN assuming G for $(SCN)_2^{\bullet-}$ = 23,889 $dm^3 mol^{-1} cm^{-1}$ per 100 eV at 500 nm. The kinetic spectrophotometric detection system covered the wavelength range from 250 to 800 nm.

Result: Pulse radiolysis studies have shown that RMA scavenges GS radical to form a transient showing strong absorption at 380 nm. With progress of time absorption due to the transient decreased while the absorption intensity due to another species increases at 500 nm. Formation of the transient at 380 nm was very fast showing a bimolecular rate constant of 7.5×10^{-6} dm3 mol^{-1} s^{-1} and is ascribed to GS radical adduct. The absorption at 500 nm is due to phenoxyl radical. The decay of adduct and the formation of the phenoxyl radical were concomitant showing that formation of the phenoxyl radical takes place via the adduct having a rate constant of 1.1×10^{-5} s^{-1}. However DHCA, which does not show the presence of double bond, leads to the formation of only phenoxl radical. This clearly proves that initially there is formation of very fast adduct at the double bond followed by intramolecular rearrangement furnishing phenoxyl radical in the case of RMA and CA. Other radicals like CCl_3OO, NO, NO_2 also react in a similar manner with RMA, CA and DHCA. Theoretical evidences are in agreement with the experimental data.

Conclusions: Optical pulse radiolysis studies and quantum chemical calculations reveal that the presence of double bond in addition to phenolic groups plays important role in the antioxidant efficacy of hydroxy cinnamic acids concerning bio- relevant radicals at physiological pH.

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BINDING OF BILIRUBIN TO ERYTHROCYTES FROM CANCER PATIENTS

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Introduction : Cancer is one of the leading causes of death being second only to coronary artery disease. Erythrocytes are the elements of peripheral blood most affected by the free radical activity in the pathogenesis of cancer. Cancer patients show significant biochemical changes in the erythrocytes membrane. Any change in the physicochemical properties of erythrocytes membrane is expected to cause changes in the bilirubin binding behaviour of erythrocytes. Thus erythrocytes serve as a model to study the bilirubin uptake mechanism by other cell types. In view of these consideration the present study was carried out to evaluate bilirubin binding capacity of erythrocytes from cancer patient.

Methods: Binding of bilirubin to erythrocytes was studied by incubating erythrocytes with bilirubin solution containing varying amounts of bilirubin in a defined range. Cells were washed erythrocytes bound bilirubin was eluted with 2.5 ml of 2.5% albumin solution. Amount of biliruin in eluate was determined by method of Fog.

Results: Binding of bilirubin to erythrocytes from healthy individuals and cancers patients was studied at a given amount of bilirubin in the incubate in the range of 100-900 nmoles. When 100, 200..... 900 nmoles of bilirubin was present in the incubate the percentage increased in the amount of bilirubin bound was 13,13,8,11,11,1,3,7 and 6% respectively.

Conclusion: Thus it can be concluded that the erythrocytes from cancer patents are capable of binding more bilirubin as compared erythrocytes from healthy individuals. This can be attributed to erythrocytes membrane changes in cancer patients.

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OXIDATIVE STRESS IN THYROTOXICOSIS

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Introduction: Thyrotoxicosis is one of the most common afflictions involving the endocrine system. The most common causes of thyrotoxicosis include Graves' disease, toxic multinodular goiter and toxic solitary nodule. Clinical features include heat intolerance, weight loss, anxiety, tachycardia, atrial fibrillation, proximal myopathy and ophthalmopathy. Oxygen derived free radicals is implicated in the causation of myocardial insufficiency and myopathy in thyrotoxicosis.

Objective: To study the oxidative change in thyrotoxicosis by measuring blood levels of lipid peroxidation product - malondialdehyde(MDA) and the activity of antioxidant enzyme-superoxide dismutase (SOD) against healthy euthyroid controls.

Methods: 18 hyperthyroid patients due to grave's disease, toxic multinodular goiter and toxic solitary nodule confirmed by the thyroid function tests formed the study group. 22 healthy euthyroid controls were taken. Patients clinically proven to have diabetes mellitus, coronary artery disease, renal disease and hypertension which can alter MDA levels were excluded from the study. MDA was measured in serum based on Valipasha and Sadasivadu's procedure. SerumSOD activity was measured by the method suggested by Marklund and Marklund 1974.

Results: In thyrotoxic patients compared to control group -MDA level is significantly elevated (p value < 0.05) -Serum SOD activity is decreased significantly (p value < 0.01)

Conclusion:

The present study confirms the presence of oxidative stress in thyrotoxicosis. This warrants nutritional support with antioxidant

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INFLUENCE OF BEEDI SMOKING ON LIPIDPEROXIDATION STATUS

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Introduction : An endogenous free radical load is generated during aerobic oxidation. Circulating erythrocytes are particularly susceptible to oxidative damage as they have membrane rich in polyunsaturated fatty acids and contain large amounts of iron that can potentiate free radical reaction. Smoking increases this free radical load. Cigarette smokers are generally reported to have increased lipid peroxidation. However, not much have been reported in case of beedi smokers. The present work analyses the effect of beedi smoking on erythrocyte lipid peroxidation.

Methods : Status of lipid peroxidation in 25 beedi smokers and 25 age and sex matched non-smokers were analyzed. Fasting blood samples were collected and erythrocyte lipid peroxidation level was measured by the thiobarbituric acid assay and results were expressed as nmoles of MDA (malondialdehyde) formed.

Results : MDA level was found to be more in beedi smokers compared to nonsmokers. The mean + SD in smokers was found to be 231.04+ 76.49 while in non-smokers it was 122.82+51.27. Statistical analysis of MDA level of smokers with non-smokers was found to be highly significant ($P<0.001$).

Conclusion : The Present study has analyzed the effect of beedi smoking on erythrocyte lipid peroxidation. Erythrocyte lipid peroxidation was markedly increased. Hence the present study highlights the occurrence of lipid peroxidation in beedi smokers.

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ANTIOXIDANT ACTIVITY OF COLEUS AROMATICUS

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Introduction: Medicinal plants are one of the sources of effective antioxidant drugs to combat oxidative stress induced diseases such as diabetes, cardiovascular diseases, cancer, inflammation and related degenerative disorders. The present study demonstrates the antioxidant activity of *Coleus aromaticus* in *in vitro* model systems.

Methods: 1g of fresh leaves of Coleus aromaticus was extracted in 10ml distilled water and methanol separately, centrifuged and the clear supernatant of each extract were used for the further study. Anti-lipid peroxidation assay of mice liver homogenate was assessed by TBA method. DPPH radical scavenging activity was done by standard method.

Results: The result of the study indicated that Coleus aromaticus extract exhibits good antioxidant activity against ferrous sulphate: ascorbate induced lipid peroxidation. The water extract inhibited lipid peroxidation by 74±3.8% dose dependently at 100µl, which is effective than the methanol extract that offered maximum inhibition of 51±3.4:% at 300µl. The DPPH radical scavenging activity of water and methanol extract of Coleus aromaticus was 87±4.5% and 5 4 ± 2.8% inhibition respectively in a dose dependent manner at 100µl. The a tocopherol and BHA at 0.4mM were used as positive controls which showed inhibition of lipid peroxidation and free radical scavenging activity to the extent of 90%.

Conclusions: The above study represents that the water and methanol extracts of Coleus aromaticus exhibit good antioxidant and free radical scavenging activities suggesting that it may be a natural antioxidant in combating oxidative stress implicated during physiological processes and oxidative stress related disorder

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OXIDATIVE STRESS AND ANTIOXIDANT SYSTEM IN CEREBROVASCULAR ACCIDENTS.

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Introduction: Cerebrovascular accidents (CVA) are one of the major causes of mortality and morbidity worldwide. There is free radical generation during acute ischemic episode and subsequent reperfusion. The present study is undertaken to evaluate correlation between malondialdehyde (MDA) (a marker of oxidative stress) and glutathione (important intracellular antioxidant) in CVA.

Methods: 30 cases of CVA who were admitted in Medicine Department of Rajindra Hospital, Patiala were studied and age and sex matched 30 normal healthy controls were enrolled. MDA was estimated in serum using method of Ohkawa et al (1979). Blood glutathione was estimated by photometric method adapted by Beutler (1963).

Results: The study showed that maximum number of cases were in age group of 61-70 years, 16.7% of total cases died in hospital. The mean value of MDA was 44.43±10.84 imol/L in study group while in control group it was 9.54±3.61imol/L and this elevation of MDA in cases was statistically highly significant. On statistical analysis there was insignificant difference in values of serum MDA in different types of CVA (43.31imol/L in infarct; 44.76imol/L in intracerebral hemorrhage; 50.66imol/L in subarachnoid hemorrhage). Serum MDA was significantly elevated in those who died of CVA (58.95imol/L) as compared to those who survived (41.53imol/L). Glutathione levels in study group were significantly decreased as compared to those of control group (28.35±6.73 mg% vs 43.84±4.76 mg%). There was trnd towads negative correlation between serum MDA and blood glutathione levels ir study group (r = -0.27) but this was statistically insignificant.

Conclusion: The present study demonstrates significant elevation of MDA and reduction of glutathione in cases of CVA suggesting involvement of free radical injury in pathogenesis and prognosis of CVA.

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MELATONIN IMPROVES CIRCULATORY ANTIOXIDANT LEVELS DURING N-NITROSODIETHYLAMINE -INDUCED HEPATOCARCINOGENESIS IN RATS

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Introduction: Melatonin, a pineal gland hormone has multiple biological roles. It is well known as an indirect antioxidant and a direct free radical scavenger. We analyzed the effect of melatonin on circulatory lipid peroxides; thiobarbituric acid reactive substances (TBARS) and antioxidants [superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and reduced glutathione (GSH)] during N-nitrosodiethylamine (NDEA) induced hepatocarcinogenesis in Wistar rats.

Methods: Male albino Wistar rats (150-170 g) were divided into 4 groups of six animals each. Group I rats served as controls. Group II animals received signal intraperitoneal injection of NDEA (200 mg/kg b.w) followed by weekly subcutaneous injection of CCl_4 (3 ml/kg b.w). Group III animals received NDEA + CCl_4 at the same dose as Group II animals. In addition melatonin (5 mg/kg b.w) was administered intraperitoneally throughout the experimental period of 20 weeks. Group IV rats received melatonin above at the same dose as Group III rats.

Results: Higher levels of TBARS accompanied by a decrease in the antioxidant levels were observed in NDEA treated rats when compared with control animals. A significant decrease in the levels of TBARS and an increase in antioxidant levels were observed in the animals treated with NDEA as well as melatonin.

Conclusion: These findings reveal that melatonin exerts a chemopreventive effect by enhancing the antioxidant status during hepatocarcinogenesis.

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RADIO PROTECTION OF SWISS ALBINO MICE BY SEED EXTRACT OF BRASSICA COMPESTRIS (VAR SARASON)

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Brassica compestris var. sarason is a traditional edible plant. Our earlier study has shown that the ethanolic extract of seed of *Brassica compestris* significantly inhibits the induction of skin papillomas in Swiss albino mice (Qiblawi and Kumar, 1999).The present study reports the effect of *Brassica compestris* seed extract on radiation induced hematological and biochemical changes in Swiss albino mice. Animal of Group-I (Control, radiation alone) were exposed to gamma radiation (3.6 Gy), while, animals of Group-II (Experimental, Radiation+*Brassica*),

received *Brassica* seed extract (800 mg/kg body weight) and were exposed to gamma radiation(as in Group-I).*Brassica compestris* seed extract was given orally for seven consecutive days prior to radiation exposure. Hematological parameters were assessed at different intervals of post-irradiation from day 1 to 14. The average hemoglobin (Hb), total erythrocyte count (TEC) and total leucocyte count (TLC) in experimental group were significantly elevated as compared to the control group of animals. Also, *Brassica compestris* seed extract treatment significantly elevated reduced glutathione (GSH) level in blood against radiation-induced depletion. Treatment with *Brassica* seed extract also caused a significant decrease in Malondialdehyde (MDA) formation, suggesting its role in protection against radiation induced membrane and cellular damage. The results of the present study suggest that *Brassica compestris* seed extract modulate the radiation induced hematological and biochemical alteration in Swiss albino mice.

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RADIO PROTECTIVE EFFECT OF ALCOHOLIC EXTRACT OF MENTHA PIPERITA LINN IN SWISS ALBINO MICE

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Mentha piperita (Linn.) Family-Labiatae, Commonly called peppermint, is considered as aromatic stimulant and carminative. It is used for allaying nausea, flatulence and vomiting.

Alcoholic extract of Mentha piperita leaves (Al.M) has been analysed for its radioprotective effect against 8Gy gamma radiation. The optimum dose of Al.M which exhibited maximum radioprotection was found to be 100 mg/kg body weight /day for three consecutive days before irradiation (8Gy). The animals pretreated with 50,100, 200, 400 (mg/kg body weight /day) showed 37.50, 75, 50, 62.50%. Survival respectively against 8Gy gamma radiation after 30 days. A regression analysis of survival data yielded LD 50/30 as 8.052?0.04 and 5.598? 0.12 Gy for radiation and Al.M combined group and radiation alone, respectively and produced a dose reduction factor (DRF) of 1.43. Optimum dose of Al.M (100 mg/kg body weight /day) was given for three consecutive days to the experimental group. The experimental and control groups were irradiated at 8Gy gamma radiation on the 3rd day. Hematological and biochemical parameters were assessed at 3, 7, 30 day intervals post irradiation. The average hemoglobin (Hb), total erythrocyte count (TEC) and total leucocyte count (TLC) in experimental group were significantly elevated as compared to the control group of animals. Also, Mentha piperita (Linn.) extract treatment significantly elevated reduced glutathione (GSH) level in blood against radiation-induced depletion. Treatment with Mentha piperita (Linn.) extract also caused a significant decrease in Malondialdehyde (MDA) formation, suggesting its role in protection against radiation induced membrane and cellular damage. The results of the present study suggest that Mentha piperita (Linn.) extract modulate the radiation induced hematological and biochemical alteration in Swiss albino mice. The radioprotection of Mentha piperita (Linn.) can be attributed to its antioxidant and antiperoxidants property because of the presence of eugenol, caffeic acid, rosmarinic acid and ?-tocopherol.

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EVALUATION OF CHEMOPREVENTIVE ACTION AND ANTIMUTAGENIC EFFECT OF THE STANDARDIZED PANAX GINSENG EXTRACT, EFLA400, IN SWISS ALBINO MICE

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In the present investigation the chemopreventive action and antimutagenic effect of the Standardized Panax Ginseng Extract (EFLA400, processed Panax ginseng extract containing high titer of ginsenoside Rg3 (>3.0% w/w) known as Phoenix ginseng) in Swiss albino mice have been evaluated. The oral administration of EFLA400 at 1, 3 and 10 mg/kg body weight at pre, peri and post-initiational phases, showed significant reduction in number, size and weight of the papillomas induced by 7, 12 - dimethylbenz (a) anthracene (DMBA) and croton oil. A significant reduction in tumor incidence (71. 41± 6.73, 72.19 ± 4.54 and 70.46 ± 0.38% at 1, 3 and 10 mg/kg body weight, respectively) was observed in animals EFLA400 treated group as compared to the 100% tumor incidence in control group. The cumulative number of papillomas during observation period of 16 weeks was significantly reduced in EFLA400 treated group (24±0.94, 16 ± 1.41 and 11 ± 1.41 at 1, 3 and 10 mg/kg body weight, respectively). However, average latent period was significantly increased from 10.81± 0.1 weeks in control group to 12.39 ± 0.28 weeks in treated group (10 mg/kg body weight). The average tumor weight was recorded as 128.55 ± 8.48, 116.00 ± 8.48 and 57.5 ± 3.29 mg in 1, 3 and 10 mg/kg body weight EFLA400 treated group respectively. Chromosomal aberrations and micronuclei induction was also evaluated in bone marrow cells. These genotoxicity end-points were compared with papilloma occurrence at the same dose levels of carcinogen and ginseng. In EFLA400 treated groups significantly reduced frequencies of chromosomal aberrations and micronuclei induced by DMBA and croton oil were observed. However, maximum decrease in the frequencies of chromosomal aberrations and micronuclei were recorded in 10 mg/kg body weight EFLA400 treated group than that of 1 and 3 mg/kg body weight EFLA400 treated animals. The results from the present study suggest the dose dependent effectiveness of EFLA400 in chemoprevention and antimutagenicity in Swiss albino mice.

Key words: DMBA; croton oil; chemoprevention; Standardized Extract of Panax ginseng (EFLA400); chromosomal aberrations; micronuclei; papilloma; mouse bone marrow.

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ANTI-OXIDANT ACTIVITY OF *HYGROPHILA AURICULATA* IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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Introduction: The increase in oxygen free radicals (OFR) in diabetes could be due to increase in blood glucose levels. An important Ayurvedic medicinal plant, *Hygrophila auriculata* (K. Sheum) (Fam. Acanthaceae) has been shown to possess hypoglycaemic activity in human subjects and hepatoprotective activity in experimental animals. The hypoglycemic and anti-oxidant activities of the dried leaves of *H. auriculata* in streptozotocin-induced diabetic rats were evaluated in different single doses of hydroalcoholic extracts in diabetic rats.

Methods: Streptozotocin -induced diabetic rats were treated with hydroalcoholic extract of *H. auriculata* in three different single doses (100, 150 and 250 mg/kg body weight) for three weeks. The effects of extract on the fasting blood glucose, reduced glutathione (GSH), hepatic superoxide dismutase (SOD) activity along with thiobarbituric acid reactive substances (TBARS) were monitored.

Results: Extract demonstrated a significant reduction in elevated fasting blood glucose levels in diabetic rats at 250 mg/kg. Oral administration of the extract reduced the fasting blood glucose (136 mg/dl), hepatic TBARS (2.245 nmoles/mg of protein) and GSH level (1.84 nmoles/mg of protein) and significantly increased the hepatic SOD.

Conclusions: The results obtained suggest that *H. auriculata* possesses potent antidiabetic and antioxidant activity suggesting that ethnopharmacological approach in selecting the plant for study may be useful. The report of the efficacy of this plant as hypoglycaemic may be due to its antioxidant property.

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TOXICITY OF PENTACHLOROPHENOL METABOLITES TO HEPG2 CELLS IN CULTURE

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Department of Cellular Biochemistry and Human Genetic, Hebrew University, Jerusalem, Israel Pentachlorophenol (PCP) is a pesticide used worldwide in industrial and domestic applications, including as a general biocide and wood preservative. Metabolic studies carried out in rodents and human hepatoma cells have indicated that PCP undergoes oxidative de-chlorination to form tetrachlorohydro-quinone (TCHQ) and tetrachlorocatechol (TCC).

The present study was designed to investigate the cytotoxic effects of TCC alone and in combination with other pollutants, with special reference to the toxicity of its analog the TCHQ.

The effects of TCC on Human hepatoma cell line (HepG2) were studied in order to verify certain mechanistic aspects of their toxicity.

It was clearly indicated that TCC is more toxic than TCHQ. The effect was time and dose dependent. Intracellular ATP content was depleted (> 70%) following exposure to TCC, indicating that it is strong uncoupler of mitochondrial respiration.

Mitochondrial membrane potentials ($\Delta\Psi'_m$) were evaluated using Mito-Tracker (red) fluorescent probes. TCC reduced the membrane potential (by 60%), already within first 4 h of exposure. Reduced number of viable cells following the first day of exposure was observed and accompanied by growth arrest at the G1 cell cycle phase. No Sub-G1 fraction was apparent following TCC exposure, ruling out the possibility that TCC induced apoptotic cell death.

In contrast to TCC, TCHQ caused a markedly smaller mitochondrial membrane depolarization, as well as a smaller reduction in cellular ATP level. During exposure to TCHQ, the corresponding semi-quinone radical (TCSQ) has been formed, and ROS have apparently been involved. H_2O_2, Ascorbate, DFO and metal chelators shed light on the toxicity of these polychlorophenols, and yielded a better understanding of the mechanism of their action on mammalian cells, in culture.

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DYSLIPIDEMIA, OXIDATIVE STRESS AND ANTIOXIDANT STATUS IN PREGNANCY INDUCED HYPERTENSION

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Introduction: Hypertension is the most common medical problem of pregnancy and is associated with increased incidence of maternal and foetal morbidity and mortality. Uncontrolled lipid peroxidation may contribute via disruption of membrane lipids and other cells components to the pathogenesis. The theme of endothelial dysfunction emphasizes the role of oxidative stress (an imbalance of oxidant and antioxidant status) in understanding pregnancy induced hypertension (PIH).

Materials and methods: Fifty patients of PIH and fifteen patients of eclampsia were age matched with normal non pregnant females (10) and normotensive pregnant females (25) as controls. Lipid parameters relating to Cholesterol, Triglycerides, High Density Lipoprotein and Low Density Lipoprotein were analysed by conventional methods. Malondialdehyde (MDA) was measured by thiobarbituric acid reaction as a marker of lipid peroxidation. The antioxidant status was measured by vitamins, uric acid and ceruloplasmin.

Results: An increase of lipid fractions were seen in normal pregnancy but dyslipidemia was significant in PIH and eclampsia. Triglyceride was markedly increased & the MDA level increase, was of statistical significance in these two classes of patients. The antioxidant status measured by different parameters was variable. The postpartum results show a significant decrease in lipids and MDA, but to attain the near normal range, these patients had to be followed for a period of six months to one year. Each parameter of the antioxidant system either increase or decrease, has different theories.

Conclusion: Free radical reactions promoted by cross talk between the diseased placenta and maternal dislipidemia promote a vicious cycle of events that make cause an effect difficult to distinguish but likely to contribute to the pathogenesis of PIH. The knowledge of such markers makes therapeutic trials easier and earlier in prevention and progress till term.

[This analysis was carried out (for M.D, Post Graduate students of Institute of Obstetrics & Gynecology, Osmania Medical College, Hyderabad), in the Department of Biochemistry, Nizam's Institute of Medical Sciences, Hyderabad].

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GINSENG EXTRACT EXHIBITS ANTIMUTAGENIC ACTIVITY AGAINST MUTAGENESIS IN VARIOUS STRAINS OF SALMONELLA TYPHIMURIUM

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Oxidative stress resulting from toxic effects of free radicals on tissues plays an important role in the aetiology or pathogenesis of various degenerative diseases of aging such as cancer. The inhibition of such free radical-mediated pathophysiology has become a central focus for research efforts designed to prevent or ameliorate malignancy, and, a number of studies have been performed to discover antioxidants from natural products or medicinal plants for prevention of free radical induced carcinogenesis. Recent studies have reported that ginseng saponins exhibit antioxidant action in vitro and in vivo. Ginseng extract has also been reported to act as an antimutagen by increasing the rate of DNA excision repair synthesis in V79 cells in response to treatment with UV radiation or methyl methane sulphonate. Root extract of Panax ginseng has also been reported to possess antimutagenic activity in Chinese hamster lung cells and the same has been proposed to be due to its involvement in biochemical reactions such as DNA repair synthesis. We further felt that this antimutagenic effect could also be because of the oxygen radical scavenging and inhibition of lipid peroxidation, thus in the present study we proposed to test ginseng extract in the Salmonella typhimurium test system (Ames test) using oxidative mutagens. There are no reports in literature regarding the antimutagenic action of ginseng in the different strains of Salmonella typhimurium employing Ames test. We evaluated Ginseng extract I (Helios Pharmaceuticals, Ahmedabad) and Ginseng extract II (Ranbaxy Laboratories ltd., Gurgaon) for their ability to decrease mutagenicity of ter-butylhydroperoxide in Ames tester strain TA102, and sodium azide and 4-nitroquinoline-N-oxide in TA100 strains. Further, we evaluated and compared the in vitro scavenging activity of these two samples of ginseng extract against superoxide anions, hydrogen peroxide and DPPH radicals, to corroborate the postulation that ginseng extract is antimutagenic because

of its capacity to scavenge ROS. Ginseng extract I showed a better DPPH free radical scavenging (IC50=289.06 ig), superoxide anion scavenging (IC50=80.19) and hydrogen peroxide scavenging activity (IC50=119.41 ig). Both ginseng extract I and II were examined for their antimutagenic activity in the dose range of 1000-4000 ig/plate. Ginseng extract I is having better antimutagenic activity than that of Ginseng extract II with ginseng extract I showing almost 80% inhibition at a dose level of 4000 ig/plate. Despite the known antioxidant activity of Ginseng, it did not show any antimutagenic action towards tBOOH in TA102 strain and the fact could not be explained.

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PROTECTIVE EFFECT OF GINGER EXTRACT AND ITS FORMULATION IN OXIDATIVE STRESS (ETHANOL)- INDUCED GASTRIC MUCOSAL LESIONS IN EXPERIMENTAL RATS

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The etiology of gastroduodenal ulcers is influenced by various aggressive and defensive factors such as acid-pepsin secretion, mucosal barrier, mucus secretion, blood flow, cellular regeneration and endogenous protective factors (prostaglandin and epidermic growth factors). The reactive oxygen species generated by the metabolism of arachidonic acid, platelets, macrophages and smooth muscle cells may contribute to mucosal damage. Therefore, scavenging free radicals can be one of the useful options for protecting the gastric mucosa from oxidative damage. Ginger (Zingiber officinale), a fascinating herb, has been used in folk medicine for the relief of a variety of illness, especially nausea, motion sickness and several other gastrointestinal ailments. Recently it has been claimed as an effective antioxidant and also an anti ulcer agent. In the present study we confirm the purported antioxidant activity of the ginger extract in different in-vitro test systems (DPPH assay, .OH scavenging, H2O2 scavenging, .O2 scavenging and nitric oxide scavenging). Considering that a more effective ulcer healing can be achieved by a localized therapeutic action with a long duration, floating beads of ginger extract were prepared and evaluated along with ginger extract in ethanol induced gastric ulcers in rats. The latter is a well established model for oxidative stress induced gastric ulcers. Ginger extract and its formulations were found to be 50-75% effective in countering the ethanol induced oxidative stress which was evaluated in terms of induction of lipid peroxidation and catalase, glutathione and superoxide dismutase levels of the stomach homogenates. The number and severity of ulcers expressed in terms of ulcer index and also the length of haemorrhagic streaks was significantly reduced both by ginger extract and its floating beads.

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EVALUATION OF ROLE OF OXIDANTS STRESS IN REHEUMATOID ARTHRITIS

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Introduction: Rhemumatooid arthritis (RA) follows a chronic course, with unsatisfactory outcome despite treatment. Its actiology and pathogenesis is yet to be fully elucidated. It is proposed that, movement-induced hypoxia-reperfusion triggers generation and release of reactive oxygen species and oxygen-derived free radicals into synovial joints, leading to persistence of chronic synovitis. We examined whether oxidant stress has any correlation with disease activity in RA by comparing blood levels of Malondialdehyde (MDA). Superoxide dismutase (SOD). Catalase and Glucose-6-Phosphate-Dehydrogenase (G6PD) in health and disease.

Methods: This study was conducted on patients attending the Rheumatology clinic of medical College, Calicut, Kerala between December 2000 and November 2001. cases were grouped into two: clinically active (6) and inactive (44, in remission) with 50 age- matched controls. RA overlapping with other connective tissue disorders, acute infections and co-existing diseases were excluded. We chemically estimated lvels of serum MDA, activities of SOD and Catalase in RBCs and G6PD activity in serum.

Results: In active cases, compared to control the MDA levels were significantly high ($p<0.01$) and in inactive cases, significantly low ($p<0.05$). This decrease could be due to the effect of steroids, NSAIDs and other drugs used for treatment. G6PD activity of bother active and inactive cases was elevated (p-0.05, $p<0.01$ respectively). This could be due to dis-inhibition of G6PD, a regulatory pathway of HMP pathway. SOD and Catalase did not show statistically significant difference in activity between cases and control.

Conclusions: MDA level in RA could be used as a biochemical marker of disease activity and to monitor treatment response. There is not definite correlation between enzyme levels of SOD Catalase and G6PD and disease activity.

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OVEREXPRESSION OF CONNEXIN 43 ATTENUATES NITRIC OXIDE PRODUCTION IN ENDOTHELIAL CELLS: AN EPIPHENOMENON OF CELL DENSITY DEPENDENT ENOS DISTRIBUTION IN ENDOTHELIAL CELLS

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Co-translational and post-translation modifications of endothelial nitric oxide sysnthase (eNOS) control nitric oxide (NO) production. Agonist mediated sub-cellular trafficking of eNOS implicates in the activity of eNOS. Recent publications suggest that a significantly larger population of eNOS localizes at the cell-cell interfaces. This information prompts us to hypothesize that the overexpression of connexin 43 (cx43), a gap junction protein, intrigue in the bio-availability of nitric oxide (NO) by interfering with the eNOS activity.

ECV 304, a human endothelial cell line is used for the experiments. Griess assay, a spectrophotometric method, is employed to measure NO generation by the cells. Expression of cx43 is verified by using the electrophysiology techniques. Localization, co-localization and trafficking of eNOS and cx43 are studied by immunofluorescence confocal microscopy.

Results of our experiments show that bradykinin promotes sub-cellular eNOS-GFP trafficking with the simultaneous production of nitric oxide. Next, confocal microscopy experiments prove that the population of eNOS-GFP proteins localized at the cell-cell interface in highly confluenced cell population by 30% more in comparison to individual non-attached cells. Further, overexpression of Cx43 in high density ECV304 cells attenuates NO production by 80%.

Present studies show that sub-cellular trafficking of eNOS is a cell density dependent phenomenon and overexpression of cx43, which co-localizes with eNOS, attenuates the production of NO in high density cell population. These results direct us to dissect the mechanism of cx43 dependent NO production in EC.

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FLY ASH LEACHATE INDUCES CYTOTOXIC EFFECT IN CLUTURED HEPATOCYTES OF FRESH WATER FISH *CHANNA PUNCTATA* (BLOCH) AN IN-VITRO ASSESSMENT.

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Introduction: Fly ash is a complex mixture of heavy Metals, dioxins and diffurans, PCBs, PCDs, PAHs and PHAH produced by combustion of coal. Recently we reported its effect on antioxidant level of fresh water fish *Channa punctata* (Bloch) (Ali et al. 2004). Recently we investigated the effect of fly ash leachate on cultured hepatocytes of fish water fish *Channa punctata* (Bloch).

Methodology: Liver cells, were isolated and maintained by method of Klauring (1985). Cells were treated with different concentration of FAL (10, 20 50 and 100%) for 24 and 48 hrs. The LDH, H2O2 and Superoxide generation and Apoptosis were estimated by standard protocols. LPO and Protein were measured according to Mihara and Uchiyama (1978) and Lowry et al (1951).

Results: Cultured hepatocytes of fresh water fish *Channa Punctata* (Bloch) was used to assess cytotoxicity of Fly ash Leachate (FAL). The production of H2O2, superoxide and level of Lipid Peroxidation (LPD) increased significantly ($p<0.01$, 0.001) with concentration but at highest concentration (100%) a significantly ($p<0.001$) decrease reported. Leachate dehydrogenase (LDH) release and percentage of apoptotic cells were increased significantly ($p<0.01$, 0.001) with concentration of FAL.

Conclusion: It may be concluded that 10, 20, 50% FAL causes LPO by producing ROS such as H2O2, superoxide while 100% FAL may lead to cell death and decrease in levels of all three parameters studied. Moreover, LDH release and induction of apoptosis in the cells may also be due to ROS.

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PROTECTIVE ROLE OF *Piper betle* (L) ON CCl_4 INDUCED OXIDATIVE STRESS *IN VITRO*

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The aqueous and methanolic extracts of *Piper betle* leaves were studied for its hepatoprotective and antioxidant activity in CCl_4 induced hepatic damage in goat liver slices. Hepatic dysfunction was evaluated by measuring the concentrations of lipid peroxidation, enzymic and non-enzymic antioxidants. The aqueous and methanolic extracts at 500 mg/kg reduced the elevated lipid peroxidation. There was also a significant increase in the levels of Superoxide dismutase (SOD), Catalase (CAT), Glucose-6-phosphate dehydrogenase (G6PD), Glutathione related enzymes [glutathione peroxidase (GPX), glutathione reductase (GR) and glutathione-S-transferase (GST)], Vitamin A, Vitamin C, Vitamin E, Total thiols and GSH. Both aqueous and methanolic extracts exerted protective effects but the antioxidant effect of the latter was more pronounced and was comparable with a standard hepatoprotective agent, silymarin. Our findings suggest that the probable mechanism of hepatoprotection by *Piper betle* against CCl_4 induced hepatic injury could be due to its antioxidant and free radical scavenging property.

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ANTIOXIDANT STATUS OF TWO VARIETIES OF *Solanum nigrum* (L)

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A majority of diseases or disorders are mainly due to the imbalance between pro-oxidant and antioxidant homeostatic phenomenon in the body. Antioxidant principles from the natural resources possess multifacetedness in their multitude and magnitude of activities and provide enormous scope in correcting the imbalance. Therefore much attention is being directed to harvest the antioxidant principles from the natural resources like plants. The objective of the present investigation was to assess the activities of the enzymic antioxidants (SOD, CAT, Px, GPx, G6PD, PPO and Ascorbic acid oxidase), and the levels of non-enzymic antioxidants (â-carotene, Vitamin C, Vitamin E, GSH, Total phenols and chlorophyll) and the minerals (Mn, Zn, Fe, Cu and Se) in the leaves of two varieties of *Solanum nigrum* (L), one bearing the black berries and the other bearing the red berries. The extent of inhibition of Lipid peroxidation, Superoxide and Nitric oxide radical generation were also studied. The results showed that the leaves of both varieties were rich in antioxidants.

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PROTECTIVE EFFECT OF *Moringa oleifera* ON ETHANOLAND CCl_4 INDUCED OXIDATIVE STRESS IN RATS

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In recent years, there is an upsurge in the interest in issues related to human health and in the possible role of nutrition in the prevention of disease. Scientific interest in reactive oxygen species (ROS) and oxidative stress is growing very rapidly. The field of ROS and antioxidants now ramifies into all areas of biology and medicine. Oxidative stress mechanisms are known to play a significant role in the development of various diseases. Phytochemicals, which have the propensity to scavenge free radicals can be effectively employed to prevent or reduce oxidative damage.

Moringa oleifera is a traditional medicinal plant of Moringaceae family. The *in vivo* antioxidant and hepatoprotective activities of aqueous extracts of *Moringa oleifera* was evaluated against ethanol CCl_4 induced oxidative stress in rats. The ethanol CCl_4 induced rats simultaneously received aqueous extract of *Moringa oleifera*. The lipid peroxidation, enzymic and non-enzymic antioxidants were assessed in the liver. Ethanol CCl_4 intoxication resulted in significantly elevated levels of hepatic LPO products such as conjugated dienes and and hydroperoxides, TBARS and lowered the activities of the antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and glutathione-S-transferase when compared to control rats. Decreased levels of non-enzymic antioxidants Vitamin A, Vitamin C, Vitamin E, and reduced glutathione were observed in ethanol CCl_4 induced rats when compared to controls. The concurrent administration of *Moringa oleifera* extract resulted in significant reduction of TBARS, conjugated dienes, hydroperoxides and elevated the levels of enzymic and non-enzymic antioxidants when compared with ethanol-CCl_4 treated rats. The levels were also comparable to those induced by the standard hepatoprotective agent, silymarin. These observations clearly suggest the antioxidant and hepatoprotective potential of *Moringa oleifera* in experimentally induced oxidative stress in rats.

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MOLECULAR STUDIES ON THE EFFECT OF *Withania somnifera* USING Hep 2 CELL LINE.

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Ayurveda emphasizes a holistic lifestyle that has many components, which can reduce free radical damage due to ROS. Traditionally, different parts of *Withania somnifera* are used in the treatment of a variety of disorders. This attracted us to this plant and the antioxidant potential of different parts of the plant namely leaves, roots, stem, fresh and dry tubers was confirmed. The present study was undertaken to see if the antioxidants present in the plant offered protection against oxidant assault to *in vitro* system namely Hep 2 cell line. The leaves, fresh and dry tuber extracts were tested for their ability to protect blood cells and Hep 2 cell line against DNA damage induced by H_2O_2 and subsequent repair. The extent of cytotoxicity of the extracts were also analysed. The leaf and fresh tuber extracts decreased the damage to a greater extent followed by dry tuber extract. Effective repair of the damaged DNA took place in the presence of the leaves and tuber extracts. The cytotoxicity test showed a decrease in the fraction of viable cells upon H_2O_2 treatment. Co-treatment with the extracts improved viability. The extracts themselves caused Hep 2 cells to die, implying that they may possess anticancer principles.

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COMPARATIVE STUDY OF SELECTED ANTIOXIDANTS IN FLOWERS AND LEAVES OF WHITE AND VIOLET VARIETY OF *Clitoria ternateae* (SANGU PUSHPAM)

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Plants are one of the most important sources of medicine. Herbal products are being used as drug from time immemorial in all parts of the world. The use of plants or parts of plants such as root, bark, flowers and seeds are remedies for diseases. Most evidence suggest that plant derived products are protective against several diseases. The present study was carried out in *Clitoria ternateae* (Linn) leaves and flowers (white and violet). The enzymic antioxidants (catalase, peroxidase, superoxide dismutase, glutathione-S-transferase and glutathione reductase) and total carotenoids were analyzed in the leaves and flowers. Chlorophyll was also estimated in the leaf samples. The results showed that all the plant parts analyzed possessed considerable antioxidant content, albeit differences in the levels of individual components. The extracts of these plant parts were also effective in inhibiting the lipid peroxidation induced *in vitro*. Our results indicate that the plants of *Clitoria ternateae* are rich sources of antioxidants and can be exploited for combating oxidant-induced diseases after further studies.

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PREVENTIVE EFFECTS OF *Artemisia vulgaris* LEAVES AGAINST DNA DAMAGE INDUCED *IN VITRO* BY OXIDANTS

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The objective laid out for the study was to compare the efficiency of the extracts in the *Artemisia vulgaris* leaves extracted into solvents of differing polarities and to judge the extent of DNA damage in various DNA sources induced by H_2O_2 in the presence and absence of the leaf extracts *in vitro*. The observations suggested that the leaves of *Artemisia vulgaris* contain polar and non polar components that decreased DNA damage significantly and the extent of protection offered was dependent on the nature of DNA. Another candidate in the investigation of reversal of DNA damage was cultured Hep 2 cells. The three extracts of the leaves significantly decreased the number of comet bearing cells and increased the viability of the H_2O_2 assaulted Hep 2 cells. The extent of damage to deoxyribose was studied and the leaves were found to possess hydroxyl radical scavenging activity and can thus protect the sugar moiety of DNA. The antioxidant properties of *Artemisia vulgaris*, as revealed by this study, makes it an ideal candidate for the search of antioxidant and anticancer drugs.

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EVALUATION OF THE PROTECTIVE EFFECTS OF *Triticum aestivum* AGAINST OXIDATIVE STRESS IN SELECTED *IN VITRO* MODELS

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Medicinal plants have always had an important place in the therapeutic armoury of mankind. Both cancer-inducing and cancer-reducing properties have been attributed to a large number of plants in folklore and in systems of traditional medicine all over the world. Some plant products may increase the repair of DNA damage thus reducing the chances of carcinogenesis and this is mainly rendered by the antioxidants present in the plants. The aim of the present study was to assess the extent of oxidative stress, the activities and the levels of antioxidants, *in vitro* inhibition of LPO, SO, NO generation by the *Triticum aestivum* leaf (Wheat grass) extracts *in vitro* at three different time periods of growth (4 days, 8 days and 12 days after sowing) in the presence and absence of oxidative stress. The *in vitro* models used were goat liver slices and human peripheral blood cells as a means to replace or minimize the live animals in experiments. Our results showed that the leaves of the 4th day plant exhibited good antioxidant effect.

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EFFECT OF THYROID STATE ON HYDROPEROXIDE METABOLISING ENZYMES OF RAT TESTES

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Introduction: Thyroid hormones are considered to be one of the most important biological modulators of metabolism which ultimately affect many physiological processes in general and male reproduction in particular. The effect of thyroid hormone on male reproduction is well reported in the past but the information on the effect of thyroid hormone

on antioxidant defence system of testes is scanty. In the present study, we observed the effect of triiodothyronine (T_3) on the activities of the hydroperoxide metabolizing enzymes namely, catalase and glutathione peroxidase (GPx) with respect to different durations of treatment.

Methods: Male Wistar rats were given a daily intraperitoneal injection of 20 g T_3/ 100g body weight for 1 day, 3 days and 5 days (n=5 for each set). The control rats for each experimental set were given vehicle for the three respective periods as mentioned above (n=5 for each set). Catalase and GPx activites were assayed in the post-mitochondrial fraction of testes.

Results: The results of the present study showed that T_3 treatment for 1 day failed to induce any significant alteration in catalase activity whereas the enzyme activity significantly increased following T_3 treatment for 3 days when compared to the control ($P < 0.05$). On the other hand, the enzyme activity decreased significantly from control in response to 5 days of T_3 treatment ($P < 0.05$). No significant change was observed in the activity of GPx in any of the three durations of treatment.

Conclusions: These results suggest that hyperthyroidism induced by T_3 hormone plays a crucial role in regulating the expression of catalase whereas it did not influence the glutathione peroxidase activity in the testes of rats.

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INVITRO ANTIOXIDANT ACTIVITY OF FICUS GLOMERATA

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Introduction: ***Ficus glomerata*** Roxb. (Family: ***Moraceae***) is an evergreen tree found through out India and Sri Lanka.Almost all parts possess medicinal properties. The root is useful in dysentery and a fluid obtained from it by incision is administered as a powerful tonic. The root is also useful in hydrophobia. The bark is cooling, acrid, galactagogue, good for the gravid uterus, asthma and piles. It is given as an astringent and as a wash for wounds. The antidiabetic and antidiarrheal activity of its bark and antipyretic activity of its root is reported in the literature. Several triterpenes and steroids have been isolated. Except these studies no other activities have been carried out. Many plants of genus ficus are used in medicine for the treatment of skin diseases, ulcer, gonorrhoea etc. Several of these diseases are do to the involvement of free radicals in our body. Hence, in the present study, methanol extract of the bark and roots of ***ficus glomerata*** were screened for ***in vitro*** antioxidant activity using standard methods.

Methods: The bark and root of ficus glomerata were collected authenticated and extracted with methanol by maceration. The extracts after concentration and drying under vacuum were screened for antioxidant activity using DPPH, ABTS, hydroxyl radical scavenging by p-NDA, hydrogen peroxide, nitric oxide and superoxide radicals scavenging methods.

Results: Methanol extract of bark shows potent scavenging activity of DPPH, ABTS, hydroxyl and hydrogen peroxide radicals with IC_{50} values of 1.62±0.054, 0.913±0.04, 25.83±0.36 and 27.16±0.166 µg/ml respectively. Methanolic extract of root also showed strong activity on ABTS with IC_{50} value 6.48±0.15 µg/ml. In the other method moderate to low activity was observed by both the extracts. The bark extract was found to be more potent when compare to the root extract.

Conclusions: The plant merits further in in-vivo models and identification of its active constituents.

P-189

MODULATION OF RADIOSENSITIVITY OF BREAST CANCER CELL LINE MCF-7 BY TOCHOPHEROL SUCCINATE

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Introduction: -Tocopherol succinate (TOS) is an esterified analogue of -tocopherol (vitamin E) lacking the antioxidant property of parent molecule. TOS has been shown to preferentially kill the malignant cell through apoptosis without showing significant toxicity to normal cells (Neuzil 2000). In the present investigation, Radiation induced membrane oxidative damage and apoptotic cell death and their modification by TOS has been investigated in breast cancer cell line MCF-7 *in vitro*.

Methods: After harvesting the tumor cells from culture condition, they were suspended either in PBS or in isotonic sucrose solution (272 mM, pH: 7.4). The cells were irradiated for desired radiation dose at room temperature (dose rate: 0.5 Gy/min.) with -rays (Junior Theratron, MDS Nordian, Canada). Gamma radiation and TOS induced membrane changes were measured by DPH fluorescence polarization method. Cell viability was determined by trypan blue and per cent apoptosis was measured by annexin V and MC-540 fluorescence.

Results: It was observed that tumor cells treated with increasing concentration of TOS (10-100 M) yielded dual response to alterations in membrane fluidity. A decrease in viability and increase in per cent cellular apoptosis was observed in TOS treated cells depending on the concentration of TOS. Results showed that TOS induced apoptosis maximally after 24 hr of treatment of MCF-7 cells. The results suggest that treatment of tumor cells with TOS increased the per cent apoptosis by irradiation. In addition, a significant increase in apoptosis was observed when tumor cells were immediately irradiated after TOS treatment.

Conclusion: The combined effect of TOS and radiation on tumor cells showed synergistic action on tumor cells which possibly was mediated through lysosomal destabilization. It is further shown that TOS induced apoptosis in tumor cells suggesting that may provide an approach to develop more effective clinical outcome in cancer radiotherapy.

P-190

AMELIORATIVE EFFECT OF IRRADIATED CURCUMIN AND FERULIC ACID IN EXPERIMENTAL DIABETES

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Introduction: Diabetes mellitus, a metabolic disorder is a major health problem. Although there are a number of drugs available in the market, long time use of these may cause a number of side effects. Hence a large number of studies are in progress to find natural sources which are effective in reducing the intensity of diabetes. We have studied the effect of irradiated curcumin and ferulic acid on experimental diabetes in order to evaluate the antidiabetic and antioxidant properties of these compounds on streptozotocin (40 mg/kg b.w) induced diabetes.

Methods: Irradiated curcumin was given at a dose of 10, 30 and 80 mg/kg body weight and ferulic acid at 10 and 40 mg/kg body weight. The level of glucose, activities of glucose metabolizing enzymes hexokinase and glucose-6-phosphatase and antioxidant enzymes superoxide dismutase, catalase and glutathione peroxidase were altered in diabetic condition.

Results: The levels of thiobarbituric acid reactive substances, hydroperoxides and free fatty acids were also elevated in diabetic

animals. Oral administration of both ferulic acid and irradiated curcumin for 45 days resulted in a significant decrease in the levels of blood glucose along with near normalizing the enzymic activities and the levels of lipid peroxidative markers. The most effective results were obtained on treatment with 30 mg irradiated curcumin and 10 mg ferulic acid.

Conclusion: Our results indicate that both the drugs are effective in controlling the blood sugar and maintaining the antioxidant status even at much lower levels.

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ANTI-OXIDANT ACTIVITY OF MURRAYA KOENIGII IN ALLOXAN-INDUCED DIABETIC RATS

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Introduction: The increase in oxygen free radicals (OFR) in diabetes could be due to increase in blood glucose levels. An important Ayurvedic medicinal plant, Murraya koenigii (spreng) (Fam. Rutaceae) has been shown to possess hypoglycaemic activity in human subjects and hepatoprotective activity in experimental animals. The hypoglycemic and anti-oxidant activities of the dried leaves of M. koenigii in Alloxan-induced diabetic rats were evaluated in different single doses of hydroalcoholic extracts in diabetic rats.

Methods: Alloxan -induced diabetic rats were treated with hydroalcoholic extract of M. koenigii in three different single doses (50, 100 and 200 mg/kg body weight) for one week. The effects of extract on the fasting blood glucose, reduced glutathione (GSH), hepatic superoxide dismutase (SOD) activity along with thiobarbituric acid reactive substances (TBARS) were monitored.

Results: Extract demonstrated a significant reduction in elevated fasting blood glucose levels in diabetic rats at 200 mg/kg. Oral administration of the extract reduced the fasting blood glucose (115 mg/dl), hepatic TBARS (2.015 nmoles/mg of protein) and GSH level (1.75 nmoles/mg of protein) and significantly increased the hepatic SOD.

Conclusions: The results obtained suggest that M. koenigii possesses potent antidiabetic and antioxidant activity suggesting that ethnopharmacological approach in selecting the plant for study may be useful. The report of the efficacy of this plant as hypoglycaemic may be due to its antioxidant property.

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INFLAMMATORY MARKERS IN CORONARY ARTERY DISEASE

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Introduction: Pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumour necrosis factor (TNF-) are important in vascular endothelial dysfunction and the initiation and progression of atherosclerosis and type 2 diabetes mellitus (DM2). Cytokine expression could increase the redox state and activate oxidant-sensitive inflammatory signals. Carotid intimal-medial thickness (IMT) is also an early index of inflammation in the development of atherosclerotic lesion. This study is being undertaken to investigate the interplay between cytokine expression and redox state in Indians.

Methods: The study included 67 controls and 84 cases of CAD-DM or CAD. IL-6 and TNF- levels were analysed in the serum of the subjects by enzyme-linked immunosorbent assay using kits from Cytimmune Sciences Inc., USA. Carotid IMT was measured using high-resolution Sonos 5500 (Hewlett Packard, Inc., Anaheim, CA, USA) with a duplex B-mode scanner and a linear phased array transducer of 7.5 MHz frequency, in a fasting state.

Results: Significant increases were noted in the serum concentrations of IL-6 (mean SD for controls vs cases, 0.796 0.519 ng/ml vs 0.969 1.18 ng/ml ; $P < 0.0001$) and TNF- (1.558 0.392 ng/ml vs 2.323 0.978 ng/ml; $P < 0.0001$). Carotid IMT was increased in the cases (mean SD, 0.716 0.185 mm).

Conclusion: Concentrations of the pro-inflammatory cytokines IL-6 and TNF- are significantly elevated in CAD and type 2 DM which might reflect the emergence of inflammation as a conceivable unifying etiologic mechanism for both. Increased IMT in the cases also supports the role of inflammation in atherosclerosis, though at present its elevation is not significant. Thus both CAD and type 2 DM are possibly associated with endothelial dysfunction and elevated oxidative state.

P-193

TOTAL ANTIOXIDANTS AND OXIDATIVE STRESS IN LIVER CIRRHOTICS

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Background: Oxidative stress is an important pathophysiological mechanism in alcoholic liver cirrhosis (ALC).

Objective: To assess oxidative stress and antioxidant enzymes in the development of ALC. We assess the oxidative stress by measuring malondialdehyde (MDA) and antioxidant status by measuring glutathione peroxidase (Gpx), superoxide dismutase (SOD), and total antioxidant capacity (TAC).

Method: 40 patients (mean age 52? 16.8 years) and 20 healthy volunteers (mean age 35? 18.0 years) from OPD of the department of Gastroenterology, AIIMS, New Delhi were included in the study. In the etiology of alcoholic liver cirrhosis, traditional liver function profile was abnormal and intake of alcohol was upto 60 gram/day. Serum levels of MDA, Gpx, SOD and TAC were determined by Spectrophotometric methods.

Results: Serum levels of MDA (4.68? 1.25 vs. 2.56? 1.52 nM/ml, $p<0.002$) were increased in patients with ALC vs. controls. The levels of Gpx (875? 112 vs. 806? 106 U/L) were not significantly different in the patients vs. controls. However, serum level of SOD (1.28? 0.32 vs. 2.28? 0.67 U/ml, $p< 0.002$) and TAC (1.60? 0.42 vs. 2.46?0.56 nM/ml, $p <0.000$) were significantly decreased in patients with ALC.

Conclusion: The presence of MDA in-patients with alcoholic liver cirrhosis suggests the oxidative stress in this process. This finding suggest that impaired antioxidant defense mechanisms may be an important factor in the pathogenesis of ALC and treatment approaches that affect the antioxidant enzymes may be beneficial in patients with ALC.

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EFFECT OF VITAMIN E ADMINISTRATION ON ALCOHOL LEAD INTERACTIVE NEUROTOXICITY

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Introduction: Lead is an environmental toxicant and alcohol abuse is associated with deleterious effects on brain. Recently, alcohol has been reported to enhance neurotoxic effects of lead. But the mechanisms and mediators of alcohol-lead interactive toxicity and modes of treatment of neurotoxicity remains largely unknown.

Methods: Eight groups of rats were used for study, Group I: control, Group II: lead acetate (160 mg of lead acetate per liter in water). Group III: 10% of alcohol in drinking water. Group IV: lead and alcohol. Group V, VI, VII AND VIII: same treatment as mentioned for Group I to IV but diet containing of 500 mg of vitamin E per kilogram of diet for 8 weeks. Lipid peroxidation was assessed by thiobarbituric acid reactive species. The protein content was determined by Lowry's method. Protein carbonyl content was determined by colorimetric method. The cerebral cortex was used for determination

Results: In rats coexposed to lead and alcohol, the increase in MDA levels and protein carbonyl content was more marked compared to rats treated with alcohol or lead alone. The decrease in protein content was more significant in alcohol-lead coexposed rats. Vitamin E was effective in suppressing MDA levels and proteins carbonyl content. Protein content was decreased significantly after vitamin E treatment.

Conclusions: Lead and alcohol interaction results in more pronounced neurotoxicity Vitamin E suppression of lead alcohol interactive toxicity indicate the role of oxidative stress in lead alcohol interactive neurotoxicity. However, oxidative stress independent mechanism may also contribute to neurotoxic effects of lead and alcohol.

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EFFECTS OF VITAMIN E ADMINISTRATION ON ALCOHOL LEAD INTERACTIVE HEPATOTOXICITY

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Introduction: Liver, kidneys and brain have been considered as the target organs for the toxic effects of lead. Alcohol abuse is associated with deleterious effects on several organs in the body particularly liver and brain. Alcohol has been shown to potentiate lead induced cytotoxic effects but the molecular mechanisms and mediators of alcohol-lead interactive toxicity and modes of prevention and treatment of hepatotoxicity are not clearly known.

Methods: The study consisted of SD rats and the animals were treated with lead, alcohol and vitamin-E for eight weeks, Group I:control, Group II Lead acetate (160mg of lead acetate per litre in water), Group III: 10% alcohol in drinking water, Group IV: lead and alcohol. Group V, VI, VII, VIII: same treatment as mentioned for I to IV but diet consists of 500 mg of Vitamin E per Kg of diet. Lipid-peroxidation was assessed by TBARS, the protein content was determined by Lowry's method, Vitamin C, and Vitamin E was determined by colorimetric method.

Results: In rats coexposed to lead and alcohol, the increase in Lipid-peroxidation was more marked, compared to rats treated with alcohol or lead alone. The Vitamin C and protein content was markedly decreased in alcohol lead coexposed rats. Vitamin E was partially effective in suppressing MDA levels. Both protein and Vitamin C content was marginally increased after Vitamin E supplementation.*Conclusions:* Lead and alcohol interaction results in more pronounced hepatotoxicity. Vitamin E suppression of toxic effects of these chemicals indicates the role of Oxidative Stress in lead plus alcohol interactive hepatotoxicity. However, mechanism independent of Oxidative stress may also contribute to hepatotoxic effects of lead and alcohol.

P-196

OXIDATIVE STRESS AND PRE-ECLAMPSIA

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Introduction: The etiology and pathogenesis of pre-eclampsia, a frequent complication of pregnancy, remain obscure. Although free radical mediated endothelial cell injury might be an etiologic factor, the role of oxidative stress in pre-eclampsia are not clearly known. The present study was aimed to address the role of oxidative stress in pre-eclampsia.

Methods: The study was carried out on thirty normotensive non-pregnant women and thirty normotensive pregnant women as controls and thirty established cases of pre-eclampsia as cases. Serum was analysed for malonaldehyde, ceruloplasmin, glucose, urea, creative and uric acid. Urine samples were analysed for protein, creatinine and glucose.

Results: Malonaldehyde levels were moderately increased in pregnant controls, but markedly increased in pre-eclamptic women. In the pre-eclamptic group, malonaldehyde levels showed significant correlation to urine protein to creatinine ratios ($p<0.05$). Serum ceruloplasmin levels were significantly increased in pre-eclamptic women ($p<0.01$). In the postpartum samples, although blood pressure returned to normal after delivery, proteinuria and oxidative stress remained at higher levels after delivery.

Conclusions: Pre-eclampsia is associated with increased oxidative stress that may be the cause for renal injury in this condition. Enhanced oxidative stress is not dependent on compromised ceruloplasmin function.

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PARAOXONASE ACTIVITY AND OXIDATIVE STRESS IN NON INSULIN DEPENDENT DIABETES MELLITUS WITH AND WITHOUT MICROALBUMINURIA

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Introduction: Recently, protective effect of HDL against oxidative modification of LDL by enzymatic hydrolysis of phospholipid hydroperoxides by paraoxonase has been reported. Low serum paraoxonase activity independent of genotype has been reported in diabetes mellitus, but the effect of hyperglycemic control and oxidative stress has not been examined. In the present study, we have evaluatedthe changes of paraoxonase activity in non insulin independent diabetes mellitus(NIDDM) and modulation of paraoxonase activity by oxidative stress

Methods: The study was carried out on 21 NIDDM cases with microalbuminuria, 40 cases of NIDDM without microalbuminuria and thirty six controls. Serum was analyzed for malonaldehyde levels, paraoxonase activity, HDL-cholesterol levels and apolipoprotein A-I levels Urine samples were analyzed for albumin and creatinine

Results: Serum paraoxonase activity was decreased in diabetes mellitus. The activity was significantly low in NIDDM cases with microalbuminuria compared to NIDDM cases without microalbuminuria

as compared to well-controlled diabetes mellitus. The correlation between paroxonase activity and microalbuminuria was significant

Malonaldehyde levels were moderately increased in NIDDM cases with or without microalbuminuria. Decreased paraoxonase activity was associated with decrease in HDL-cholesterol and apolipoprotein A-I levels in plasma.

Conclusions: Decreased paraoxonase activity in diabetes mellitus may reflect impaired HDL function resulting from glomerular injury.

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TOTAL ANTIOXIDANT STATUS IN CHRONIC RENAL FAILURE (CRF) PATIENTS ON HEMODIALYSIS (HD) AND CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD).

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Enhanced oxidative stress has been implicated as one of the co morbid factors in the premature cardiovascular complications in chronic renal failure (CRF) patients on hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD). The present study was taken up to evaluate the antioxidant status in the above category of patients.30 HD and 20 PD patients with age/sex-matched controls were enrolled in the study. Materials and methods: The parameters evaluated were total antioxidant activity and reduced glutathione-GSH by spectrophotometric methods. Fasting serum samples were assayed for total antioxidant capacity by the method of Koracevic et al. The assay measures the capacity of biological fluids to inhibit the production of thiobarbituric acid reacting substances (TBARS) from sodium benzoate under the influence of the free oxygen radicals (ROS) derived from Fenton's reaction.GSH from whole blood was measured by the modified method of Beutler et al. The method involves the reacation of sulphydryl compounds with Ellman's reagent (DTNB) to form yellow colored compound measured at 412 nm. Total antioxidant status in serum and GSH in rbc's were significantly reduced in the HD and CAPD patients than the control gp. However the antioxidant status and GSH activity was slightly on the higher side in the CAPD patients than the HD gp showing the CAPD patients had better compliance and tolerance than HD patients. This is attributed to loss of blood, and soluble antioxidants like ascorbic acid in the HD gp during dialysis than found in the CAPD gp. Also high doses of IV iron therapy to maintain adequate iron stores for hematopoiesis to counter anemia may aggravate the oxidative stress in HD gp. Thus enhanced oxidative stress with low antioxidants levels as shown above to counter the ROS generated during dialysis, coupled with oxidatively modified lipid components like oxidized LDL, malnutrition and accumulation of uremic toxins may be contributing to the high mortality rate due to cardiovascular diseases in the above category of patients.

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ANTIOXIDANT ENZYMES AS BIOMARKERS FOR LEAD TOXICITY

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Lead is a widely prevalent environmental contaminant. Although lead is not biologically required, but it enters the biological systems through inhalation, dermal or oral routes and causes toxic effect in adults and more severe effects in children. Besides nephropathy, hematological, gastrointestinal and neurological dysfunctions, it is reported to cause oxidative stress. Hence the aim of this investigation has been to estimate the antioxidant activity of lead treated samples invitro, using peripheral blood samples from healthy donors .Two controls and three sets of treatments like: Pb treated, Pb + UV radiation treated and UV radiation treated lymphocytes from peripheral blood samples were set up for experimental purposes. Total antioxidants in these 5 sets of experiments were determined by ABTS assay. Our results reveal that the toxic effect of Pb is enhanced in the presence of UV radiation, since the total antioxidant enzymes were inhibited. The endogenous antioxidant enzymes with their sulfhydryl groups serve as targets of divalent cationic lead which may form a closed ring complex thus inhibiting its action. The antioxidant status can thus be used as a biomarker for Pb toxicity..

P-200

AN EVALUATIN OF ANTIOXIDANT AND NUTRITIONAL STATUS OF NON-INSULIN DEPENDENT DIABETES MELLITUS SUBJECTS

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Studies have reported that elevated levels of lipid per-oxidation in diabetic patients especially in poorly controlled compared with well-controlled diabetic patients increased Reactive Oxidative Stress (ROS) mediated lipid per-oxidation in diabetes may result from disturbances in antioxidant defense. The present study was carried out in NIDDM subjects (n=300) and healthy control subjects (n=100 and assessed the nutritional intake of the subjects and their antioxidant status. Biochemical parameters like mean of glucose (350mg/dl), lipids such as total Cholesterol (228mg/dl), Triglycerides (199mg/dl), HDL cholesterol (38mg/dl), LDL cholesterol (151mg/dl) were analyzed for diabetic subjects. Normal subjects mean values of glucose, Cholesterol, Triglycerides, HDL and LDL cholesterol were 125 mg%, 178mg%, 108mg%, 48mg%, 96mg% respectively. All the values are found to be above the optimal level. The mean antioxidants values such as Vitamin 'E' (1.9mg%) Glutathione (0.29mmol/ml), SOD (982 U/g Hb), Mg 91.45 mg%) were analyzed in Diabetic and healthy subjects antioxidants are found 2.24mg%, 0.42mmol/ml, 1512 U/gHb, 2.1mg% respectively. The dietary intake/pattern was obtained from each subject by 24 hr recall method and the nutrient intake was calculated. It was found that all the DM subjects were >40 years age majority had developed complications like neuropathy. Food intake data revealed a less frequent and inadequate intake of antioxidant-rich vegetables and fruits by DM subjects. The study indicates that increased ROS-mediated lipid per oxidation in diabetes may result from disturbances in antioxidant defenses.

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EVALUATION OF TOTAL ANTIOXIDANT STATUS IN THYROID DYSFUCTION

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Introduction: Cell damage caused by free radicals is a major contributor to many diseases. In Thyroid dysfunction, free radicals have been implicated as one of the causative factors. Antioxidant vitamins and enzymes serve as scavengers to these free radicals. When the availability of antioxidants and free radical scavengers become limited in the body, damage can be cumulative and debilitating. Various free radicals are controlled or neutralized by different groups of antioxidants.

Material and Methods: In this prospective study, 25 proven cases of hypothyroidism and hyperthyroidism each were chosen for evaluation of Total Antioxidant Status. 25 healthy subjects with normal thyroid function were chosen as controls.

Results: The total antioxidant capacity was found to be significantly decreased (<0.01) in patients with thyroid dysfunction in comparison to healthy subjects.

Conclusion: The decrease in total antioxidant status suggests that an adequate intake of antioxidant or modulation of free radical generation can lead to protection from free radical damage of the thyroid gland.

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THE TOTAL ANTIOXIDANT CAPACITY IN TYPE II DIABETIC PATIENTS

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Introduction: Diabetes is one of the most common endocrine disorders characterized by the development of micro and macrovascular complications. Good glycaemic control has been found to delay or prevent the development of such complications. Oxidative stress is suggested as one of the mechanisms underlying Diabetes Mellitus. The aim of our study was to evaluate the total antioxidant capacity (TAC) in the type II diabetic patients and its relation to glycaemic control.

Materials and Methods: In this prospective study, 50 subjects with type II uncontrolled diabetes mellitus were evaluated for total antioxidant capacity, fasting Blood sugar, glycated hemoglobin. 50 subjects with type II controlled diabetes mellitus were chosen as the control group.

Results: Compared with the controls TAC was significantly decreased in uncontrolled diabetics ($p< 0.01$).

Conclusion: The present study suggests that measurement of TAC may have a role in the evaluation of glycaemic control and development of diabetic complication in type II diabetes. Improving the antioxidant status thus may have a protective role in type II diabetes.

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OXIDATIVE STRESS, PROTEIN GLYCATION AND DYSLIPIDEMIA IN ESSENTIAL HYPERTENSION

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Background: Essential Hypertension is a multifactorial disease. Genetic factors and environmental factors have been implicated as etiological factors. Coronary Heart disease is the most common complication of essential hypertension. However, the factors, which lead to this complication, are unknown. Based on this background the present study evaluates Oxidative stress, Protein glycation and plasma lipid levels in patients with Essential Hypertension.

Materials and Methods: 10 Hypertensive cases (B.P > 140/90), 17 prehypertensive cases (B.P 120-139 / 80-89) and 13 controls (B.P < 120/80) were included in the study. Reduced glutathione, glutathione peroxidase, glutathione transferase and catalase were estimated in erythrocytes by using standard protocol. Plasma lipid levels were estimated by enzymatic methods. Plasma CRP, APO-B, Direct LDL, Fructosamine and whole blood Glycated Hemoglobin were estimated by kit methods.

Results: Reduced glutathione ($p < 0.005$), glutathione transferase ($p < 0.005$) catalase ($p < 0.05$) and HDL-Cholesterol ($p < 0.05$) were significantly decreased in prehypertensive and hypertensive cases compared to controls. Glutathione peroxidase ($p < 0.05$), glycated hemoglobin ($p < 0.001$), fructosamine ($p < 0.05$) and triglycerides ($p < 0.05$) were significantly increased in prehypertensive and hypertensive cases compared to controls. There was no significant difference in CRP, APO-B, direct LDL and total cholesterol levels between cases and controls.

Conclusion: Based on the results the present study concludes that oxidative stress, Protein glycation and Dyslipidemia are the risk factors leading to complications of essential hypertension.

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EVALUATION OF SERUM MARKERS IN ALCOHOLICS

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Introduction: Liver disease due to alcoholism is a common medical problem associated with mortality and morbidity. The objective of the present study was to correlate the parameters routinely asessed for diagnosis of liver disease with the marker enzyme Gama glutamyl transferase (GGT) and find out the best combination that would be useful in detecting liver injury in alcoholics.

Methods: 25 alcoholic subjects, consuming alcohol regularly, since five years were chosen for the study. 25 subjects who were non alcoholics and non smokers and without any debilitating disease served as the controls. Serum was analysed for GGT, ALT, ceruloplasmin, albumin and uric acid by standard methods.

Results: A significant increase in the serum levels of GGT ($p=.002$), ALT ($p=.022$), ceruloplasmin ($p=.000$) and decrease in the uric acid ($p=0.00$) were observed in alcoholics. Serum albumin levels remained unaltered. Correlation of GGT showed a positive association with ALT and uric acid and negative association with ceruloplasmin in the alcoholics. Correlation of ALT with ceruloplasmin was also negative.

Conclusions: Measurement of ceruloplasmin, an important plasma antioxidant and uric acid along with GGT or ALT would be ideal in identifying habitual alcoholics. Diagnostic and treatment measures taken at an early stage may help prevent the progress to liver cirrhosis.

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REFERENCE INTERVALS FOR SERUM APOLIPOPROTEINS A-I, A-II, B, C-II, C-III, E IN HEALTHY INDIAN

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Introduction: Study of lipoproteins & apolipoproteins in ethnic Indians vis a vis other ethnic groups have been a matter of study for long. In the present study however, it is an attempt to study the same in Indian population. There are number of methods of estimation of serum apolipoproteins, out of which currently immunoturbidimetric assay method is found to be more adaptable for routine automated laboratory estimation & is adapted for the present study also. 82 healthy individuals were selected after screening them for normal lipid profile, x-ray chest, TMT, ECG and for diabetes. The age & sex difference, effect of drinking & smoking on all the parameters were studied.

Observation & Results: The mean serum value for apoA-I was 111.61 ± 19.06 mg/dl, apoA-II was 27.12 ± 4.33 mg/dl, apoB was 82.55 ± 16.47 mg/dl, apoC-II was 2.82 ± 2.07 mg/dl, apoC-III was 6.90 ± 2.18 mg/dl, apoE was 2.97 ± 0.92 mg/dl and lp(a) was 16.91 ± 10.91 mg/dl. Effect of smoking & drinking was found to be non-significant. A two-tailed Pearson correlation coefficient & test of significance was worked out.

Conclusion: The reference intervals of apolipoproteins & lipoproteins determined in this interim analysis which is a part of more expanded study undertaken. The values and results were compared with those of other workers. There was age & sex difference in most of the serum apolipoproteins & lipoproteins levels.

The establishment of reference interval for apolipoproteins using commercially available reagent kit for automated analyzers will help in a long way in assessing coronary heart disease particularly with hyperlipidemia.

Key words: Apolipoproteins; Immunoturbidimetric assay; Treadmill test (TMT); Lp (a).

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GLUCOSE CATALYSED OXIDATION OF AMINO ACIDS IMPLICATIONS IN ATHEROSCLEROSIS

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Glucose catalysed protein modification is attributed to the onset of diabetic complications. Formation of Amadori product and its rearrangement to give Advanced Glycation End products is well characterized.

In addition to lysine and aminogroup modification amino acids like tyrosine can undergo oxidative dimerization forming dityrosine. We have shown the formation of dityrosine in vitro catalysed by glucose. The dityrosine was isolated by thin layer chromatography and characterized by its fluorescence properties. The presence of dityrosine was also confirmed by ESI-Mass spectrometry.

ApoA1 was isolated from oxidatively modified HDL. It showed a molecular mass twice that of ApoA1 by SDS PAGE and MALDI TOF. Our results suggest that dityrosine formation may be a possible mechanesim of oxidative modification of serum lipoproteins.

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COMPARATIVE *IN VITRO* STUDY OF WATER- AND LIPID-SOLUBLE FREE RADICAL INITIATORS IN RAT ERYTHROCYTES

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Lab. Gerontology, Department of Zoology, Bangalore University, Bangalore-560 056, India.

Introduction: The survival of aerobic organisms in an oxygen environment involves a complicated interplay between the biological generation of very reactive chemical species called free radicals and the ability of organism to control these substances.

Methodology: The study was designed to investigate the effects of free radical-inducers, water-soluble 2, 2' azobis (amidinopropane) dihydrochloride [AAPH] and lipid-soluble 2, 2' azobis (2,4-dimethylvaleronitrile) [ADVN] on erythrocyte and its membrane. The samples were incubated at concentrations of 10 mM and 50 mM. Oxidative stress (OS) indices- hemolysis, malondialdehyde (MDA), lipofuscin (LF), protein carbonyls and osmotic fragility were analyzed.

Results: 50 mM concentration of AAPH and ADVN caused greater OS to the cells when compared to 10 mM concentration. Hemolysis increased significantly in 50 mM concentration of both AAPH ($p < 0.02$) and ADVN ($p < 0.005$). Whole cells showed significant increase in MDA in response to both concentrations of 10 and 50 mM of AAPH ($p < 0.002$, $p < 0.001$) and ADVN ($p < 0.001$, $p < 0.005$), while membrane MDA and LF increased significantly only at 50 mM AAPH ($p < 0.01$) and ADVN ($p < 0.05$). Protein carbonyls significantly increased in the erythrocyte membrane at both concentrations of AAPH and ADVN ($p < 0.01$). Cells were more fragile osmotically at 50 mM AAPH and at 10 and 50 mM ADVN.

Conclusion: Hemolysis and membrane fluidity are greatly affected by ADVN than AAPH. ADVN, a lipid-soluble free radical-inducer causes more damage to the erythrocyte membrane than AAPH, a water-soluble compound.

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PLASMA CERULOPLASMIN LEVELS IN PREGNANCY WITH PRE-ECLAMPSIA

Sukanya Shetty and Vivian D'Souza

Department of Biochemistry, KSHEMA, Mangalore. Department of Biochemistry, KMC, Mangalore.

Introduction : Pre-eclampsia is a pregnancy specific disorder complicating 5 to 7% of pregnancies and characterized by elevated blood pressure, proteinuria, edema and activation of haemostatic system. The cause of pre-eclampsia is unknown although several factors have been shown to contribute. Pre-eclampsia is more common in women during their first pregnancy, who have diabetes, gestational hypertension. In the present study plasma ceruloplasmin levels have been evaluated in pregnancy with pre-eclampsia and compared with normal pregnancy.

Methods : 15 normal subjects, 15 pregnant women and 15 pre-eclamptic patients were selected for the study. The blood samples were analyzed for plasma ceruloplasmin by ortho - Dianisidine method.

Results : Plasma ceruloplasmin level in pregnant women was significantly higher ($P < 0.001$) than the normal subjects. A highly significant increase ($P < 0.05$) is also found in pregnancy with pre-eclampsia when compared to normal pregnancy.

Conclusion : Ceruloplasmin is an acute phase protein in normal pregnancy.It is said to have oxidase activity towards polyamine and polyphenol substrates and also acts as a copper donor for monoamine oxidase and diamine oxidase enzymes. Because of antioxidant property of ceruloplasmin, which prevents peroxidation and free radical formation, increased ceruloplasmin level is found in pregnancy with pre-eclampsia

INDEX ORAL

INDEX ORAL

INDEX POSTERS

INDEX POSTERS

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(A division of Aurobindo Pharma Ltd.)

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AUROBINDO PHARMA LTD

Corporate Profile

Aurobindo Pharma Ltd (APL) India is a vertically integrated global Pharmaceuticals company based at Hyderabad, India. APL is the largest Active Pharmaceutical Ingredient(API) company among top 5 Phrma companies from India with an annual sales turnover of more than **USD 308** million and with Export over **USD 147 million** to over 100 countries for the year ended 2003-2004.

Aurobindo Pharma is among the top in Cephalosporins and Semi Synthetic Penicillins and Anti- HIV Drugs globally.

Aurobindo Pharma is equipped with modern and mega facilities, for the manufacturing of API's and formulations. With the cost efficient mega manufacturing infrastructure of 4 Formulation and 10 API manufacturing location that are USFDA and E.U. complaint, Aurobindo Pharma Ltd has successfully broadened the operations base to more than 100 countries, to cater to the global clientele. APL has warehouses in various strategic locations like in Hongkong, USA, Moscow, Montevideo.

Aurobindo Pharma's facilities have been inspected and approved by various regulatory agencies like MHRA of UK, MCC of South Africa, ANVISA of Brazil to name a few.

APL is equipped with world class Research and Development(R&D) centre and a Bio-Equivalence centre with more than 500 scientists, developing a broad portfolio of products in the area of Non- Infringing Process, filing patent and supporting DMFs/ ANDA's for US and E.U. Markets.

Aurobindo is a ISO certified company and is also a receipt of several awards as the best API company. Aurobindo is rated among the top 20 candidates from India across all sectors to emerge as a Global Champion.

DEPARTMENT OF LABORATORY MEDICINE
CARE HOSPITAL
THE INSTITUTE OF MEDICAL SCIENCES
BANJARA HILLS,
HYDERABAD

A. CARE GROUP OF HOSPITALS :

"CARE" was born in 1997 with a motto "Practicing medicine as it should be". Within a span of 7 years CARE has grown to 1,000 beds and emerged as leading name in health care.

BRIEF MILE STONES OF CARE HOSPITAL:

- The Heart Institute of CARE Hospital was established in 1997 with 200 beds.
- 50 bedded cardiac centre was established in Sec-bad in 1998.
- Heart Institute at Vishakhapatnam with 100 beds was set up in 1999.
- CARE Foundation received Defence Technology Spin-off award from the Prime Minister in 1999.
- Institute of Neurosciences was set up in Hyderabad in 2000.
- Institute of Medical Sciences with Multi Specialty Services with 350 beds at Banjara Hills at Hyderabad was set up in 2000.
- Dr.B.Soma Raju and Dr.D.Prasada Rao founders of CARE were awarded Padmashri in 2001.
- Bharath Ratna Dr.A.P.J.Abdul Kalam joined the board in 2001.
- India's first V-SAT based Public-Private Telemedicine System was launched by the then Chief Minister of A.P. in 2001.
- Telemedicine network was extended to Orissa and to Tripura in 2002.
- Mr. Sachin Tendulkar, associated with CARE group as Chief Patron in 2003.
- Robotic Surgery was introduced for the first time in India outside New Delhi in 2004.

B. DEPARTMENT OF LABORATORY MEDICINE :

The department has six divisions namely Biochemistry, Haematology, Clinical Pathology, Histopathology & Cytology, Microbiology and Blood Bank. The department does about 1000 tests per day both for In-patients and Out-patients.

FACILITIES AVAILABLE:

a. BIOCHEMISTRY :

(i) EQUIPMENTS:

* CX9 Clinical chemistry Auto analyzer (Beckman)
* Chemiluminescence immunoassay analyzers
  1. Elycsys (Roche) 2. Access (Beckman)
* Beckman Electrophoresis unit and Densitometer
* Coagulometers (Stago/Pacific Haemostasis/Transasia)
* ELISA equipment (Ark Diagnostics)
* Blood gas analyzer (Nova)
* Electrolyte analyzer (Nova)
* Semi autoanalyser (PLD)
* Nephelometer (Dade Behring)
* Turbitimer (Dade Behring)

(ii) TESTS AVAILABLE:

* All routine clinical biochemistry including blood gas and electrolyte analysis.
* Coagulation studies including factor assays and thrombophilia work up.
* Protein Elctrophoresis in all fluids and Immunofixation Electrophoresis.
* All Immuno assays covering hormones, tumor markers and vitamins.
* Pro BNP, GFR by MDRD and some drug assays.

b. HISTOPATHOLOGY :

* Provided with state of art equipment for histopathology and cytopathology with Cytospin.
* Immunoflourescence techniques available.
* Immunohistochemistry

c. HAEMATOLOGY & CLINICAL PATHOLOGY :

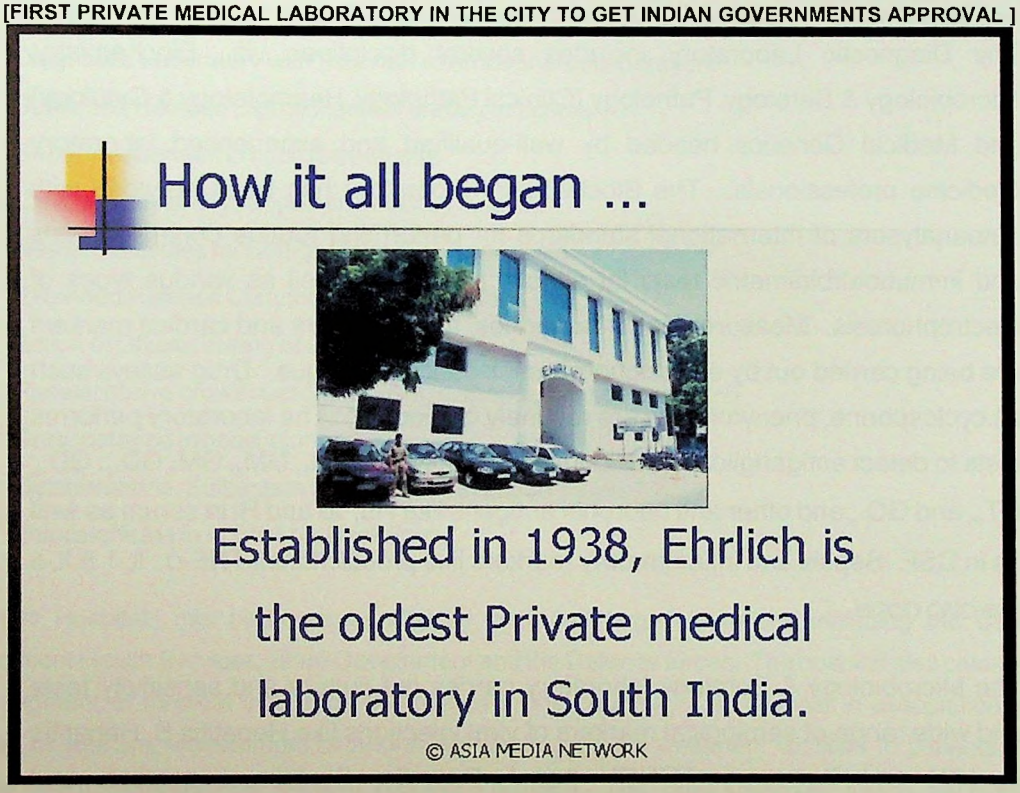
* Cell counters are available (Beckman, Sysmax, Roche)

EHRLICH LABORATORY PVT LTD

INTRODUCTION

Ehrlich Laboratory was started in 1938 and was a pioneer in the diagnostics arena. Nearly 70 years later, it is still renowned for its quality and its expertise, catering to generations of patients, organizations and research institutions. Ehrlich Lab takes its promise of quality very seriously, and is consistently accredited by independent organizations. It was the first Laboratory in South India to obtain ISO certification by DNV- Netherlands, and one of the first to obtain International Accreditation from ILAC and APLAC. We were visited by a Brazilian Pharmaceutical Company recently. In addition, Ehrlich is now in the process of applying for CAP accreditation .

[FIRST PRIVATE MEDICAL LABORATORY IN THE CITY TO GET INDIAN GOVERNMENTS APPROVAL]



Ehrlich's Gold Standard/Quality policy is "Ehrlich is committed to offer contemporary medical diagnostic service, investigative and preventive. Every member of the team will strive to achieve "Excellence in Reliability". Amongst other quality programs, Ehrlich has the External Quality Assurance System (EQAS) with Biorad, US /RIQAS/Randox-U K .

KAMINENI HOSPITALS - HYDERABAD

Kamineni Hospitals at Hyderabad, a 300-bed hospital spread over a sprawling 450,000 sft., over the last decade has grown to be among the country's finest Super Specialty Healthcare facility with several clinical departments recognized for post-graduate, DNB courses. The Diagnostic Laboratory being the highlight of this venture, which has been accredited by the **National Accreditation Board of Testing and Calibration Laboratories (NABL),** is also the key referral laboratory to many other hospitals, nursing homes and physicians in the city and the state of Andhra Pradesh. Kamineni Hospitals, Hyderabad is one of several institutions belonging to Kamineni Groups, which includes a 500-bed hospital attached to medical, dental and nursing colleges, and another corporate hospital.

The Diagnostic Laboratory includes several disciplines viz., Biochemistry, Microbiology & Serology, Pathology (Clinical Pathology, Heamotology & Cytology) and Medical Genetics headed by well-qualified and experienced laboratory medicine professionals. The Biochemistry laboratory has been provided with autoanalysers of international standards for performing routine chemistry tests and immunoturbidimetric tests for special proteins as well as various types of electrophoresis. Measurement of hormones, tumor makers and cardiac markers are being carried out by electrochemiluminiscence technique. Drug assays such as cyclosporine, phenytoin, etc are routinely carried out. The laboratory performs tests to detect antiganglioside antibodies (IgG, IgM) for GM_1, GM_2, GM_3, GD_{1a}, GD_{1b}, GT_{1b} and GQ_{1b} and other anti neuronal antigens like Hu, Yo and Ri in serum as well as in CSF. Sepsis and inflammatory markers like procalcitonin, TNF-á , IL-1 & IL-6 are also done.

The Microbiology & Serology laboratory carries out culture and sensitivity tests and wide range of serological markers of viral infections like Hepatitis B, Hepatitis C, HIV and Dengue. TORCH panel, Brucella, Syphilis, Leptospira and Tuberculosis serology are routinely carried out. PCR techniques are employed for the detection of tuberculosis, Hepatitis B, Hepatitis C, cytomegalo virus and HLA-B27 marker. The laboratory also conducts investigations for autoimmune diseases

which are some times induced by drug reaction. Further to routine investigations, the Pathology laboratory carries out immunofloscence technique for renal and skin biopsies. Frozen section studies and squash preparations are done for rapid interpretation. Routine histopathology and immunohistochemistry techniques are available. Bone marrow aspiration and bone marrow biopsy are being done. The Genetics laboratory performs Karyotyping, cytogenetic analysis for patients with mental retardation, cancer, bad obstetrics history, primary and secondary sterility. Molecular mutation and mitochondrial gene mutation are being analysed using PCR in patients with ambiguous genitalia, neurodegenerative disorders, MR (fragile X syndrome), cardiomyopathies and endocrinal abnormalities. The laboratory is engaged in research projects to understand the role of nuclear/mitochondrial gene mutations and polymorphisms in the aetiology of a number of diseases pertaining to neurology, cardiology, nephrology and endocrinology.

- At present the following clinical studies are undertaken by various departments of Kamineni
- Diagnostic Laboratory with national / international collaboration:
- Sustained Release Ciprofloxacin in urinary infections
- Renal involvement in fluorosis patients
- Clinical study of Erythropoietin in kidney disease
- Newer molecules for Benign Prostatic Hyperplasia
- Extended Release Clarythromicin in infections
- Action of Ofloxacin long acting preparation
- Platelet derive growth factor in healing diabetic ulcers of lower limb
- Corticosteriod in head injuries
- Cefaperazone Sulbactam in abnominal infection
- Thiocolchicide in Acute Low Back Pain

Kamineni Hospitals has been empanelled by over 140 large institutions including the Central Government Health Services, State Government and the Defence forces. The hospital also caters to a large segment of medical insurance companies in the country. The hospital in association with Ministry of Tourism, Government of Andhra Pradesh, provides treatment facilities to patients from various countries under the Medical Tourism Program. The Diagnostic Laboratory services at Kamineni Hospitals focuses on keeping up with the technological advances in basic and applied research in order to provide the latest state-of-the-art services for better patient care.

NPIL & DR.PHADKE'S PATHOLOGY LABORATORY :

Modern medicine relies on the combined medical and scientific skills of the pathology laboratory to assist in the investigation and management of a patient's illness.

At the heart of pathology is the care of the patient. The pathology laboratory must produce accurate and reliable results quickly in response to their colleagues' requests. The modern pathology laboratory is a complex operation that relies on the skills and teamwork of many people to ensure that each patient and doctor receives the best service possible.

The pathologists, with their blend of medical training and specialist training in the science and discipline of pathology supervise the laboratory investigations as well as consulting with the patient's doctor. The modern pathology laboratory also requires the skills of highly trained professional scientists and technicians, as well as various equally skilled support staff to ensure that investigations are performed efficiently and accurately.

Any pathology investigation starts with one or more specimens obtained from the patient. Doctors may collect some specimens, the laboratory can collect others. Pathology laboratories can examine a wide range of specimens including blood, urine and tissue specimens.

Once the specimen has arrived in the laboratory, depending on the tests requested, various expert departments might be involved in the investigation. Some tests are simple and can be performed rapidly, more complex tests can take days. Some tests can only be performed by highly specialised laboratories and the specimens may need to be sent interstate or even internationally to the appropriate laboratory. Once the tests are completed and checked for accuracy, a report is sent to the patient's doctor

.

NPIL & Dr.Phadke's Pathology Laboratory & Infertility Centre Pvt.Ltd. prides itself in being at the forefront of modern medical pathology practice. Every aspect of our investigations is performed under an umbrella of strict quality control using the most advanced accurate and reliable equipment. The laboratory is organised into departments that can be called upon to contribute their specialist skills and knowledge to any investigation.

Our laboratory has the prestigious NABL Accredittion from the Govt.of India.Some of the parameters in Haematology,Biochemistry,Clinical Pathology and Immunology are accredited.

d. MICROBIOLOGY:

* Automated blood culture system (BacT/Alert (Biomeriux) available for fascilitating fast reporting of blood cultures.
* Routine and special serological work.

A. BLOOD BANK :

* All facilities are available for grouping, cross matching and donor bleeding.

The Department of Laboratory Medicine is accredited by National Acreditation Board for Testing & Calibration Laboratories (NABL) in the areas of Biochemistry, Histopathology & Cytology, Haematology, Clinical Pathology and Microbiology.

The Department of Laboratory Medicine is participating in the following Drug trials in collaboration with Clinical departments of CARE Hospital.

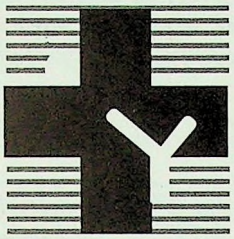
S. No	Name of Study	National/ International	Principal Investigator
1.	FG-463-210 : A Randomised, comparitive, Double-Blinded study of Micafungin (FK463) versus Liposomal Amphotericin B (AMBISOME)	International	Dr.N.Krishna Reddy
2.	A randomized double blind, double dummy parallel group, multinational, clinical study to evaluate the efficacy and safety of enoxaparin versus unfractionated heparin in patients with acute ST-segment elevation myocardial infarction receiving fibrinolytic therapy "EXTRACT-TIMI-25" study.	International	Dr.N.Krishna Reddy
3.	A Randomized, Double-Blind, Placebo Controlled, Dose Ranging, Parallel Group Study of Oral Sildenafil in the treatment of Children, Aged 1-16 years, with Pulmonary Arterial Hypertension.	International	Dr.B.K.S.Sastry
4.	Action in Diabetes and Vascular disease preterax and Diamicron MR controlled Evaluation – ADVANCE study	International	Dr.P.Krishnam Raju
5.	Hyperglycemia and its effects after Acute Myocardial Infarction on Cardiovascular Outcomes in Patients with Type-2 diabetes (HEART-2D).	International	Dr.Bipin K Sethi
6.	A multi-centre, International, Randomized, 2x2 factorial design study to evaluate the effects of LANTUS® (Insulin Glargine) versus standard care, and of OMEGA-3 fatty acids versus placebo, in reducing Cardiovascular Morbidity and Mortality in high risk people with Impaired Fasting Glucose (IFG), Impaired Glucose Tolerance (IGT) or early type 2 Diabetes Mellitus : The origin trial (outcome reduction with initial Glargine Intervention) ORIGIN study.	International	Dr.Bipin K Sethi
7.	E2E/DRL/03-N1 Ezetimide : Efficacy and safety in treatment of dyslipidaemia in an Indian population	International	Dr.Bipin K Sethi (Finished study)

QUALITY CONTROL PROGRAMMES:

The department of laboratory medicine is participating in external quality assurance programme.

* Clinical chemistry (Biorad, Randox, Transasia, Christian Medical College (CMC),Vellore,India.
* Immunoassays (Biorad)
* Coagulation (Christian Medical College, Vellore)
* Haematology (Biorad, Randox, All India Institute of Medical Sciences, India)
* Microbiology (Christian Medical College, Vellore)

Interlaboratory Proficiency testing programme in Clinical chemistry is being run with a few corporate hospitals in the city of Hyderabad.



Central Lab

9, Ground Floor Dhodusa Complex
Richmond Circle Junction (Opp. Petrol Bunk)
Bangalore - 560 025 Tel/Fax : 22237370
Mobile : 98440 37371 Pager : 9624 510944
e-mail centralab@rediffmail.com

A Brief Note on Central Lab

We are a premier specialty lab operating from Richmond Circle, Bangalore. We introduced the concept of testing and reporting of higher chemistry parameters on day-to-day basis in the city. Today, we are positioned as a quality conscious reliable team of professionals for high-end lab investigations. Medical centers of different specialties in and around Bangalore refer samples of body fluids to our lab for testing. We enjoy goodwill and reference from a good number of super-specialists.

In our quest for quality, we have subscribed for NABL Accreditation a Board under Central Government of India for accreditation of laboratories. It follows global standards i.e. ISO IEC 17025 guidelines for its programs. We have already completed final assessment and are awaiting recommendation for certification. In addition, we are also participating in external QC Programs run by Biorad - USA, AIMS Delhi, CMC Vellore.

We have provided support directly to a few globally positioned pharma companies in their research projects and worked with a number of pharma companies through a reputed CRO in Bangalore continuously for over a year. In the absence of other modalities of diagnosis such as Radiology & Imaging, Cardiology, Neurology etc, we give all our time and attention to different dimensions of laboratory services. Our customers experience fine assistance because of this.

ANAND DIAGNOSTIC LABORATORY

(Anand Institute of Laboratory Medicine)

Timings: 8 AM to 5 PM. Monday to Saturday

Client facility:
No. 512, 4th 'A' Cross, 15th Main, 3rd Block, Koramangala
Bangalore-560034 Tel: 51102058

NABL accredited

No. 11, Blue Cross Chambers. Infantry Road Cross. BANGALORE 560001.
Ph.25591947, 25599895, Telefax 5591925. Email: info@anandlab.com
Website:www.anandlab.com

About us..

Anand Diagnostic Laboratory (Anand Institute of Laboratory Medicine) came into existence in the year 1974 with the primary intention of providing quality service in the field of laboratory medicine. Over the years it has grown to provide wide-ranging laboratory investigations with state of the art equipment under the expertise of senior and qualified Pathologists. It has pioneered the use of many investigations with the distinction of being first in the state of Karnataka for many of them.

The laboratory also has additional facility for X-ray, ultrasound scan, Doppler, ECHO cardiogram, Tread Mill test and Pulmonary Function Test.

Qualified Medical Personnel.

The laboratory is owned and run by three qualified Pathologists - Dr.A.V.Ramaprasad. MD, Dr.N.Jayaram. MD, and Dr.Sujay Prasad. MD, DNB. In addition, two pathologists, a radiologist and a physician are on the panel of consultants.

Laboratory.

The laboratory is situated in the heart of the city of Bangalore, located in the central Shivajinagar area, off Infantry road, at Blue Cross Chambers. The total floor area is about 7000 sft including a separate spacious waiting area, which can seat at least fifty persons at any given moment of time. Technical procedures and various related equipment are housed in separate areas of the laboratory located adjacent to the waiting area. The registration counters are designed in such a way that waiting time is minimal.

Staff Pattern.

The laboratory has been functionally divided into the following departments: Clinical pathology, Clinical biochemistry, Histopathology and Cytology, Microbiology and Serology, and Hematology. A minimum of three qualified and experienced technicians man each section of the laboratory.

Quality control and assurance programme :

In any given set up, errors can occur at three stages namely pre-analytical (sample collection and identification), analytical (sample testing) and post analytical (printing / transcription and proper dispatch of report). Though it must be admitted that it is not possible for any laboratory to consistently achieve "zero error" status day after day and year after year, it has been our constant endeavor to minimize these errors. The steps taken to achieve a "minimum error" status are listed below:

1) Laboratory Information System. The information flow into and from the laboratory is managed by custom-built windows based software, which operates on a local area network (LAN). All the equipment with provision for RS232 interface are linked to the laboratory information system, thereby eliminating human transcriptional errors. Retrieval of data is fast and simple.

2) Pre-analytical stage: Patient registration is computerized and each individual is assigned a unique lab identification number. A bar code label bearing the patient's name and unique patient number identifies the request form as well as the samples. By this we have minimized errors resulting from wrong labelling of patients sample.

3) Analytical stage: Most of our machines are equipped with facility to read bar codes, hence chances of feeding wrong samples into the machine is minimized. At the start of each day, as well as at periodic intervals during the day, controls are run to check whether the machines and reagents are functioning well. All data pertaining to quality control testing is filed for periodic review.

4) Post-analytical stage: Most of our machines are interfaced to the LAN and hence reports, which are passed, are directly downloaded to the patient's database. This has minimized transcriptional errors, which could result from manual entry of report.

Accreditation status:

Anand Diagnostic Laboratory has been accredited by NABL for Departments of Clinical Biochemistry, Clinical Pathology, Hematology, Microbiology & Serology, Histopathology & Cytopathology from 15-09-2001 with current validity till 27-10-2007 (Certificate Nos. T-0348, 0349, 0350, 0351, and 0352).

We have the distinction of being the first clinical diagnostic lab in South India to acquire NABL accreditation.

Major equipment:

1. *Bayer Centaur Automated Chemiluminiscence based immunoassay system*
2. *VIDAS Fluoroimmunoassay systems*
3. *Stratec 300 automated RIA*
4. *Chemwell automated ELISA system*
5. *Olympus AU-400 automated chemistry analyzer*
6. *Konelab 30 automated chemistry analyzer*
7. *Cobas mira plus automated chemistry analyzer*
8. *REP automated Rapid electrophoresis*
9. *SEBIA Hydrasys automated electrophoresis*
10. *Ion selective electrolyte analyzers*
11. *Pentra 60 and Pentra 60 C+ automated 5 part particle blood cell counters*
12. *Semi-automated coagulation analyzer*
13. *Automated ESR*
14. *API automated microbiology analyzer*
15. *Automated tissue processor*
16. *Semi-motorized rotary microtome*
17. *Paraffin station*
18. *Cryostat*
19. *Cyto-centrifuge*
20. *Semi-automated urine analyzer*
21. *Semi-automated semen quality analyzer*
22. *State of the art Laboratory informatics with hardware.*

Name : Mr. Anil Jaswant Thakur **Date of Birth : October 2, 1954**

Founder & Managing Director of Accurex Biomedical Pvt. Ltd.

After graduating from the University of Mumbai with principal subject as Chemistry in 1976, he joined Bayer Diagnostics India Ltd. (formerly known as Miles India Ltd.). His tenure with Bayer was from 1976 through 1984 during which he held various important posts in the organization. His last designation was as the Product Manager for all Biochemistry Kits and Reagent Strips for Urinalysis. The 8 years working provided him rich experience in the field of Diagnostics.

He founded the company ***Accurex Biomedical Pvt. Ltd.*** in 1984 with manufacturing facilities at the factory located at Tarapur (100 kms. from Mumbai). It started with a production of small range of 4 biochemistry kits. Today, the products have expanded to a huge product range and the company is a leading Indian manufacturer of diagnostic products. Due to his continuous efforts, today Accurex Biomedical Pvt. Ltd. enjoys a stable growth on a wide base of expertise in this business in Indian and overseas market.

Mr. A. J. Thakur always inspired his employees to look forward for developing new ideas. He always believed in constant research and self up gradation. His ideas and vision were dynamic. He also participated in many international seminars and conferences.

Thus, Mr. A. J. Thakur has given his major contribution in the field of Diagnostics. He will always be remembered as the pioneer of Indian Diagnostic Company.

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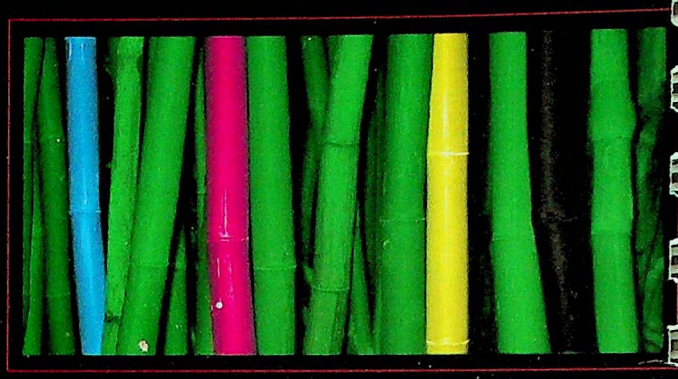
Rediscover



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REDISCOVER THE PERFECTION

CALELNDER-2005

JANUARY-2005

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MAY-2005

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JUNE-2005

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JULY-2005

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24	25	26	27	28	29	30

AUGUST-2005

SUN	MON	TUE	WED	THU	FRI	SAT
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

SEPTEMBER-2005

SUN	MON	TUE	WED	THU	FRI	SAT
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	

OCTOBER-2005

SUN	MON	TUE	WED	THU	FRI	SAT
30	31					1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29

NOVEMBER-2005

SUN	MON	TUE	WED	THU	FRI	SAT
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30			

DECEMBER-2005

SUN	MON	TUE	WED	THU	FRI	SAT
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

A RADICAL VIEW OF ANTIOXIDANTS - DESTINATION INDIA

INTERNATIONAL CONFERENCE

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