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Inside

CSIR-Indian Institute of Toxicology Research
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EVENTS

संस्थान में हिंदी सप्ताह, 14 से 20 सितंबर, 2012 का आयोजन किया गया

सी.एस.आई.आर. भारतीय विषविज्ञान अनुसंधान संस्थान (आई. आई.टी.आर) लखनऊ के प्रेक्षागृह में दिनांक 14.9.2012 को प्रातः 11:00 बजे, हिंदी सप्ताह, 14 से 20 सितंबर, 2012 के उद्घाटन समारोह का आयोजन किया गया। इस अवसर पर मुख्य अतिथि श्री गोपाल चतुर्वेदी, सेवानिवृत्त, आई.आर.ए.एस थे। मुख्य अतिथि को संस्थान के निदेशक, डॉ. के.सी. गुप्ता ने शाल और स्मृति चिन्ह भेंट किया। श्री प्रदीप कुमार, अनुभाग अधिकारी और कार्यक्रम के

निदेशक महोदय मुख्य अतिथि को स्मृति चिन्ह भेंट करते हुये

संयोजक ने मुख्य अतिथि का औपचारिक परिचय दिया। मुख्य अतिथि ने अपने संदेश में कहा कि राजभाषा में कार्य करना हमारा संवैधानिक दायित्व है। भाषा से स्वाभिमान जुड़ा होता है। भाषा से चिंतन जुड़ जाता है। भाषा का जीवन में महत्वपूर्ण स्थान है। मुझे संस्थान ने आमंत्रित कर गौरव प्रदान किया है। मैं आपका आभारी हूँ। अपने अध्यक्षीय संबोधन में संस्थान के निदेशक, डॉ. के.सी. गुप्ता ने मुख्य अतिथि श्री गोपाल चतुर्वेदी, सेवानिवृत्त, आई.आर.ए. एस. का संस्थान में आने हेतु आभार व्यक्त किया। उन्होंने कहा कि हमें विचार करना है कि हिंदी की प्रगति कैसे बढ़ाई जाए। हम भाषा की उन्नति के लिए प्रयासरत रहें। आशा करता हूँ कि सभी हिंदी सप्ताह के कार्यक्रमों में उत्साह से भाग लेंगे। उन्होंने हिंदी सप्ताह के दौरान आयोजित होने वाली विभिन्न प्रतियोगिताओं में सभी से

क्विज प्रतियोगिता में भाग लेते प्रतिभागी

प्रतिभागिता हेतु अनुरोध किया। श्री मुकुन्द सहाय, प्रशासनिक अधिकारी ने कार्यक्रम के अन्त में सभी को धन्यवाद दिया। दिनांक 20.9.2012 को हिंदी सप्ताह के पुरस्कार वितरण एवं समापन समारोह का आयोजन हुआ। इस अवसर पर संस्थान के निदेशक, डॉ. के.सी. गुप्ता ने कहा कि संस्थान में राजभाषा कार्यान्वयन की प्रगति अच्छी है और लगातार इसमें वृद्धि होती रहनी चाहिए। यह हर्ष का विषय है कि संस्थान से प्रकाशित राजभाषा 'विषविज्ञान संदेश' को नगर राजभाषा कार्यान्वयन समिति, लखनऊ द्वारा प्रथम पुरस्कार प्रदान किया गया। इसमें वैज्ञानिकों को हिंदी लेखन में ज्यादा योगदान करना चाहिए ताकि इसकी गुणवत्ता में नियमित वृद्धि होती रहे। सप्ताह के दौरान आयोजित वाद-विवाद, आशुभाषण, लेख, टिप्पण व मसौदा लेखन, हिंदीतर भाषी का हिंदी ज्ञान, हिंदी टंकण, अनुवाद एवं क्विज प्रतियोगिताओं में विजयी प्रतिभागियों को प्रथम, द्वितीय व तृतीय पुरस्कार एवं प्रमाण पत्र प्रदान किया। इसके अलावा हिंदी में कार्य करने की प्रोत्साहन योजना के अन्तर्गत विजयी प्रतियोगियों को दो प्रथम, तीन द्वितीय और पाँच तृतीय पुरस्कार और प्रमाण पत्र भी प्रदान किए गए। श्री मुकुन्द सहाय, प्रशासनिक अधिकारी ने धन्यवाद प्रस्ताव दिया। कार्यक्रम का आयोजन श्री प्रदीप कुमार, अनुभाग अधिकारी ने किया।

CSIR Foundation Day Celebrated

The seventieth CSIR Foundation Day function was held in the auditorium of CSIR-Indian Institute of Toxicology Research, Lucknow on September 25, 2012. Dr. K.C. Gupta, Director, CSIR-IITR while welcoming the chief guest on the occasion, Prof. R. K. Sharma, Director, SGPGIMS, Lucknow, and the Guest of Honor, Prof. M.K. Mishra, Vice-Chancellor, University of Lucknow; guests and members of IITR family said that CSIR with its 37 laboratories spread all over the country is one of the largest public funded organization in the world. CSIR has decided to celebrate the foundation day in a big way at New Delhi. President of CSIR-The Prime Minister is expected to inaugurate and address CSIR family. CSIR labs have contributed significantly but common people are not very aware of the accomplishments of CSIR. CSIR is number one in filing patents and has to its credit the SARAS aircraft, TKDL database, SWARAJ tractor among noteworthy technology and products. In drug sector 11 of the 16 drugs developed in India are from CSIR-CDRI. There are several herbal products from CSIR-CIMAP and CSIR-NBRI. CSIR-IITR works in five major areas including regulatory toxicology and was involved in the safety study of BT-cotton. IITR has other noteworthy products such as water analysis kit, mobile van for water quality analysis and argemone detection kit.

CSIR Foundation Day celebrations:
Dr P Kakkar introducing the chief guest

Dr. R.K. Sharma, Director of Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow spoke on "Are your kidneys OK?" In his talk Dr. Sharma gave an idea about Chronic Kidney Disease (CKD) and discussed about recommended clinical actions to treat CKD. Chronic Kidney Disease is progressive loss of renal function with time. Different stages of kidney malfunction eventually leads to Kidney failure which ultimately necessitates organ transplant. Chronic Kidney Disease can be caused from diabetes, hypertension, glomerulonephritis but some people are genetically pre disposed to this disease. In India the Chronic Kidney Failure (CKF) prevalence is 7572/ million and the reported incidence is around 757/ million according to study report of Indian Council of Medical research (ICMR). The indicators to predict the risk of kidney disease need to be monitored as symptoms appears late. The simplest tests are determination of serum creatinine and presence of albumin in urine. In India due to large population community based screening of high risk groups such as high blood pressure and diabetes has been found to be a useful strategy proven by studies carried out by AIIMS. It is now understood that there could be a fetal origin of adult disease, such as kidney disease, is associated with low birth weight babies and malnourished mothers. The key interventions to delay diabetic renal disease are to control blood sugar level, blood pressure/hypertension, quit smoking. SGPGIMS, Lucknow, has carried out more than 2000 renal transplants in the last several years. Dr. Sharma elaborated extensively the Chronic Kidney Failure (CKF) risk factors and prevention strategies. He concluded that

Group photograph with the staff completed 25 years of service

Group photograph with the winners of essay competition

intense community awareness is required to help people understand and manage Chronic Kidney Failure. Dr. Poonam Kakkar, Convener, CSIR Foundation Day introduced the Guest of Honor, Prof. M.K. Mishra, Vice-Chancellor, University of Lucknow. Prof. M.K. Mishra in his presidential address congratulated CSIR and CSIR-IITR for the rich contribution made for the welfare of society.

On this occasion six members of staff who had superannuated during the last one year were felicitated by Director. They were Dr. Deepa Agarwal, Dr. Virendra Mishra, and Dr. Pramod Kumar, Sri. Kailash Chandra, Sri. P.S. Shukla, Sri. Swami Nath. Director also presented mementos to twelve members of IITR who had completed 25 years of service. They were Dr. Mukul Das, Dr. Poonam Kakkar, Dr. A.K. Srivastava, Dr. V.P. Sharma, Dr. Devendra Parmar, Dr. B.S. Khangroot, Dr. Pradeep Kumar, Smt. C.K. Takroo, Sri. Kamta Prasad, Sri. Mohamad Aslam, Smt. Balbeer Kaur, Sri. A.K. Srivastav.

A view of the audience

On this occasion a cash prize was given to Km. Kanak Parmar, daughter of Dr. Devendra Parmer and Sri. Kaushik Barman, son of Dr. S.C. Barman for securing above 90% marks in three science subjects. Earlier an essay competition was organized for the wards of CSIR staff. The winners were awarded certificates. The winners from junior group (class V to class VIII) were Mr. Divyansh Sing (1st prize), Mr. Aryn Karla (2nd prize) and Miss. Samiah Siddiqui (3rd prize). The winners from senior group (class IX to XII) were Miss. Priya Awasthi (1st prize), Mr. Addya Shukla (2nd prize), Miss. Sakshi Yadav (3rd prize). Dr. Mukul Das, Chairman, CSIR Foundation Day Organizing Committee proposed the vote of thanks.

सतर्कता जागरूकता सप्ताह

संस्थान में सतर्कता जागरूकता सप्ताह-2012 के अवसर पर सप्ताह के दौरान विभिन्न कार्यक्रम आयोजित किये गये। कार्यक्रमों का आरम्भ संस्थान में कार्यरत वैज्ञानिकों एवं कर्मचारियों को दिनांक 29 अक्टूबर, 2012 प्रातः 11:00 बजे निदेशक द्वारा प्रतिज्ञा दिला कर किया गया। सतर्कता जागरूकता सप्ताह-2012 के दौरान संस्थान में कार्यरत कर्मचारियों हेतु सतर्कता जागरूकता विषयों पर वाद-विवाद प्रतियोगिता एवं व्याख्यान प्रतियोगिता दिनांक 30.10.2012 को क्रमशः प्रातः 11.30 बजे एवं उपरान्ह 3.30 बजे आई.आई.टी.आर. के गोष्ठीकक्ष में आयोजित की गयी। साथ ही दिनांक 31.10.2012 को अपरान्ह 3.30 बजे विभिन्न स्कूल/कालेज के छात्र/छात्राओं एवं आई.आई.टी.आर. के कर्मचारियों के बच्चों हेतु जूनियर ग्रुप कक्षा 5 से 8 तक एवं सीनियर ग्रुप कक्षा 9 से 12 तक के लिये निबन्ध प्रतियोगिता का आयोजन किया गया।

डॉ. मुकुल दास मुख्य अतिथि को स्मृति चिन्ह भेंट करते हुये।

अतिथि व्याख्यान एवं पुरस्कार वितरण समारोह का शुभारम्भ करते हुए संस्थान के प्रशासनिक अधिकारी श्री मुकुन्द सहाय ने सतर्कता जागरूकता सप्ताह 2012 पर संक्षिप्त विवरण प्रस्तुत किया। संस्थान के निदेशक डा. के.सी. गुप्ता ने अपने अध्यक्षीय भाषण में सतर्कता विषयों पर प्रकाश डाला। डा. मुकुल दास, वरिष्ठ वैज्ञानिक ने मुख्य अतिथि का संक्षिप्त परिचय दिया। सतर्कता जागरूकता सप्ताह-2012 के अन्तर्गत संस्थान में दिनांक 2 नवम्बर, 2012 को अपरान्ह 4:00 बजे आई.आई.टी.आर. के प्रेक्षागृह में एक अतिथि व्याख्यान का आयोजन किया गया। यह व्याख्यान मुख्य अतिथि जनरल पी आर गंगाधरन, सशस्त्र बल न्यायधिकरण, लखनऊ ने व्याख्यान में सतर्कता एवं भ्रष्टाचार विषयों पर विस्तृत रूप से प्रकाश डाला। मुख्य अतिथि को पुष्प-गुच्छ, मोमेन्टो एवं शाल भेंट कर अभिवादन किया

श्री मुकन्द सहाय सर्तकता जागरूकता सप्ताह का विवरण प्रस्तुत करते हुये

प्रतिभागी को पुरस्कार प्रदान करते हुये जनरल पी.आर. गंगाधरन

गया। सतर्कता जागरूकता सप्ताह-2013 के दौरान संस्थान में सतर्कता जागरूकता विषयों पर आयोजित वाद-विवाद प्रतियोगिता एवं निबन्ध प्रतियोगिताओं के विजयी प्रतियोगियों को क्रमशः प्रथम, द्वितीय, तृतीय एवं सान्त्वना पुरस्कार से सम्मानित किया गया। संस्थान के प्रशासनिक अधिकारी श्री मुकुन्द सहाय ने धन्यवाद ज्ञापन दिया।

CSIR-IITR Celebrated 47th Foundation Day

CSIR-Indian Institute of Toxicology Research (CSIR-IITR) celebrated its Foundation Day on November 4, 2012. Dr. Shashi Khandelwal, Scientist, IITR welcomed the guest Prof. M.M. Salunkhe, Vice-Chancellor, Central University of Rajasthan, Kishangarh and Dr. Girish Sahni, Director, CSIR- Institute of Microbial Technology, Chandigarh and dignitaries present on the occasion. The program commenced with lighting of lamp by dignitaries followed by recitation of IITR song. While welcoming the guests, Director, IITR presented the institute's achievements during the recent year in various research areas.

CSIR-IITR has continued to focus on the five broad areas: Systems Toxicology & Health Risk Assessment; Food, Drug & Chemical Toxicology; Environmental Toxicology; Nanomaterial Toxicology; Regulatory Toxicology. Selected findings of R & D carried out in the five areas are as follows:

Inauguration of CSIR-IITR Annual Day Function with lighting of lamp

1. Nanomaterial Toxicology.
   - The safe production and use of nanoparticles, in this era of nanotechnology, warrants improvement in understanding of environmental impact and possible ecotoxicity. Studies found that ZnO and TiO_2 nanoparticles induced oxidative stress and DNA damage leading to reduced viability of bacteria, *Escherichia coli*. Further, sub-acute oral exposure of mice to zinc oxide nanoparticles induced oxidative stress, DNA damage and apoptosis in liver. In addition, *in vitro* studies have shown that TiO_2 nanoparticles induced oxidative DNA damage and apoptosis in human HepG2 cells. These studies suggest the need for a complete risk assessment and careful monitoring of engineered nanoparticles.
   - Ameliorative effects of dimethylthiourea and N-acetylcysteine against titanium dioxide nanoparticles and multi-walled carbon nanotubes induced cyto-genotoxicity in human lung cancer cells were examined. The study also indicated the applicability of A549 cells as a pre-screening tool to identify target specific prophylactic and therapeutic potential of drug candidate molecules against nanoparticles induced cellular damages.

- In search of a universal transfection reagent which could cover a whole spectrum of cell lines, a series of polyethylenimine (PEI) based nano-composites were synthesized. These nano-composites had a blending of polyethylenimine with eitherpolyethyleneglycol, dextran, polyvinyl alcohol, glycidol or chitosan. These new transfection reagents were found to be either non-toxic in different cell lines or with negligible toxicity in Drosophila and mice models. The transfection efficiency was up to ~8 fold higher than the commercially available transfection reagents. Further, maximum *in vivo* gene expression was observed in spleen of Balb/c mice after 7 days of administration. These nano-composites can serve as efficient non-viral gene carriers for diverse biomedical and therapeutic applications, including *in vivo* gene delivery.

Recitation of CSIR-IITR song on the occasion of Annual Day Function

Dr K.C. Gupta welcoming Prof. M.M. Salunkhe

2. Environmental Toxicology

- An aptamer based quantitative polymerase chain probe was developed and used for tracking *Salmonella enterica*, sub species. S*almonella typhimurium* in sediments, water and aquatic flora collected from Gangetic riverine system. The assay in the form of serovar specific DNA aptamer based bio-capture of the bacterial cell was found to enhance the sensitivity of the probe in the presence of nonspecific DNA wherein one colony forming unit (cfu)/PCR could be detected. Further, information about the presence of environmental reservoirs of *Salmonella typhimurium* may pave the way for forecasting and management of non-typhoidal salmonellosis.

Release of Annual Report of the Institute standing on the podium (L-R) Dr. M.Das, Prof. M.M. Salunkhe, Dr. Girish Sahani and Dr K.C. Gupta

- Towards a clean and green environment, a bio-remediation study found that coupling of certain surfactants viz. rhamnolipid, sophorolipid and trehalose with *Sphingomonas sp*. results in significant enhancement in soil bound hexachlorocyclohexane (HCH) degradation with sophorolipid demonstrating the best efficiency among the three.
- In continuation of our thrust for alternate animal models for toxicological studies, a *Drosophila melanogaster* based alkaline comet assay for *in vivo* detection of oxidative DNA damage was developed and validated using three known oxidative stress generators viz. Hydrogen peroxide, cadmium chloride and copper sulphate and by employing lesion specific endonucleases such as formamidopyrimidine-DNA glycosylases (FPG) and endonuclease III. Another Drosophila based study has led to the identification of first protease cascade in insect seminal fluids, revealing the conservation of seminal protein function from insects to mammals, with potential implications to the fields of male infertility and reproductive toxicity.

3. Systems Toxicology & Health Risk Assessment
   - Resveratrol, an antioxidant found in the skin of red grapes, potentiates cytochrome P450 2d22-mediated neuroprotection in maneb- and paraquat-induced Parkinsonism in the mouse by influencing Cyp2d22 expression and paraquat accumulation. A strong association between polymorphisms of cytochrome P450 (CYP/Cyp) 2D6 gene and risk to Parkinson's disease (PD) is well-established.
   - The study on identifying the role of secondary mediators in caffeine-mediated neuroprotection in maneb- and paraquat-induced Parkinson's disease phenotype in mouse, demonstrated that caffeine down-regulates Nitric oxide production, neuro-inflammation and microglial activation, which possibly contributed to neuroprotection.
   - Curcumin was found to significantly modulate arsenic induced cholinergic dysfunctions in brain. The data suggested neuroprotective efficacy of curcumin.
   - Results demonstrate that Ser326Cys variant genotype of 8-oxoguanine DNA-glycosylase (OGG1) is associated with an increased risk of squamous cell carcinoma in head and neck (SCCHN) cancer patients in North India. Ser326Cys variant genotype was found to accumulate more of 8-hydroxydeoxyguanosine (8-OHdG), which may serve as a biomarker for early diagnosis of SCCHN. In another study, positive association of XPD Arg751Gln polymorphism was observed with an increased risk of SCCHN. Further, XRCC1 Arg280His variant though dormant individually, may also contribute to the development of cancer in combination with XPD Arg751Gln.
   - Epidemiological studies revealed adverse respiratory health effects in subjects residing in the vicinity of Special Economic Zone in National Capital Region (NCR). Data further showed that musculoskeletal pain is a significant burden of disease among the residents of NCR. Women and subjects doing heavy work load, like agriculture and dairy farming, constitute the chief demographic groups.
   - In an efforts to develop blood lymphocyte Cytochrome P450s (CYPs) as biomarkers of exposure, studies provided evidences for Cytochrome P450 2B1/2B2 isoenzymes in freshly prepared peripheral blood lymphocytes. In another study, similarities in ethanol induced induction of Cytochrome P450 2E1 and activation of mitogen activated protein kinases in peripheral blood lymphocytes and liver were observed.

4. Food, Drug and Chemical Toxicology
   - A simple method was developed for simultaneous determination of basic dyes encountered in food preparations by reverse phase HPLC. Usage pattern of synthetic food colours and exposure assessment was studied in different states of India through commodities preferentially consumed by children.
   - A new computational method was developed for allergenicity prediction of transgenic proteins expressed in genetically modified crops. In another study, Red kidney beans induced allergenic responses in BALB/c mice were found to be similar to that in human subjects.
   - *In vitro* studies on immunotoxic potential of orange II, a non-permitted azo dye, in splenocytes suggest that non-cytotoxic doses of Orange-II may have immunomodulatory

Dr. Girish Sahni honouring Dr. K.C. Gupta for his three best papers

Dr. Girish Sahni honouring Dr. Poonam Kakkar for most cited paper in the 70 year history of CSIR

effects. Studies suggest that argemone oil and butter yellow, the edible oil adulterants, are involved in the etiology of gallbladder cancer.

- Mechanistic study revealed that Resveratrol and black tea polyphenol combination synergistically suppress mouse skin tumour growth while tea polyphenols were found to induce apoptosis through mitochondrial pathway and by inhibiting nuclear factor-kappa B and Akt activation in human cervical cancer cells.
- The institute continued to provide toxicological information and antidote potential of medicinal plants and their constituents used in Ayurveda in the CSIR network project on Digitization of comprehensive information on medicinal plants.

5. Regulatory Toxicology

- A simple rapid quantitative method was developed and validated for the determination of Bisphenol A in milk and water samples using polydimethylsiloxane solid phase microextraction followed by analysis with gas chromatography-mass spectrometry. The method utilized ethyl chloroformate derivatization with a detection sensitivity of bisphenol A achievable to be 0.1 and 0.01 ug/L for milk and water samples respectively and limit of quantitation to be 0.38 and 0.052 ug/L respectively.
- In another study, a rapid method for the detection of cypermethrin in blood and tissue of rat was developed and validated using low density solvent dispersive liquid-liquid microextraction (LDS-DLLME) followed by gas chromatography-electron capture detector (GC-ECD) analysis with a sensitivity detection of cypermethrin between 0.043-0.314 ng/mg for tissue and 8.6ng/ml for blood respectively while limit of quantification was found to be within 0.143-1.03ng/mg and 28.3ng/ml for tissue and blood respectively.
- In the same line, a method developed for analyzing pesticide residues mainly organochlorines and organophosphates in drinking water samples using polydimethy-lsiloxane solid phase microextraction followed by gas chromatography-electron capture detector (GC-ECD) analysis. The method was found to be sensitive enough to detect both organochlorines and organophosphates in the limit of quantification ranging between 0.258-.0.829 ug/L and 0.143-0.294 ug/L respectively.
- Towards developing model for the prediction of urban air quality in big cities, linear and non-linear modelling was performed utilizing the meteorological and air quality monitoring data of five years (2005-2009) from Lucknow. Three different artificial neural network (ANN) models, viz. multilayer perceptron network (MLPN), radial-basis function network (RBFN) and generalized regression neural network (GRNN) were developed along with partial least squares regression (PLSR) and multivariate polynomial regression (MPR) approach based models to predict respirable suspended particulate matter, SO_2, NO_2 in the air. Among the tested models, ANN based models performed the best to predict the quality of air and may be useful tools in the air quality predictions.

S & T Achievements

The achievements of institutional R& D activities both nationally and internationally reflected in the form of recognition/awards/ fellowships etc. of a number of scientists. CSIR-IITR scientists published 126 research papers during the year, with an average impact factor to 3.188, an improvement over 3.121 last year with 103 publications. One paper appeared on the cover page of prestigious international journal. Under the stewardship of our Honourable Director General, Prof. Brahmachari, CSIR started the Academy of Scientific and Innovative Research (AcSIR), an autonomous body, with a mandate to create and train some of the best of tomorrow's science and technology leaders through a combination of innovative and novel curricula. The ACSIR-IITR Ph.D. programme is aimed at creating highest quality personnel with cross disciplinary knowledge in order to provide leaders in the field of toxicology and associated technology. As a part of Ph.D. programme both in biological and chemical sciences, CSIR-IITR, during the January and August sessions of 2011 and

CSIR-IITR staff and guests enjoying lunch after the function

2012, have enrolled 64 students with valid National fellowships to pursue their Ph.D. programme. Among the earlier batch of Ph.D. students registered with different reputed universities, this year, 21 research fellows were awarded PhD degree. Dr. Girish Sahni released the electronic and print version of the IITR Annual Report (2011-12). Prof. M.M. Salunkhe, Vice-chancellor, Central University of Rajasthan, Kishangarh released the Environmental status report (post-monsoon) for Lucknow city.

Prof. S.H. Zaidi oration

The Prof. S.H. Zaidi oration entitled "Harnessing societal value from smarter science through strategic planning" was delivered by Dr. Girish Sahni, Director CSIR-Indian Institute of Microbial Technology, Chandigarh. Dr. Girish Sahni while delivering the oration said that we all generally agree that the pursuit of science must be driven by curiosity and the satisfaction of the intellect, it should also lead to tangible value for society in one form or another. This could be a broad scientific concept, or service, or product, with even the most affluent societies increasingly conscious of the imperative of re-linking societal expectations from long-term to short-term benefits. For less affluent countries, this is a vital necessity, which must be actively pursued in parallel to, although not at the cost of fundamental research. The talk will focus on some reflections and experiences gained during 15 years of applications-oriented work at CSIR-IMTECH on the development of protein based drugs through studying their underlying mechanisms of action, especially in the area of Clot Dissolvers which are life-saving drugs with global ramifications. The efforts began with the need to develop thrombolytics' production technology for the first time in the country in the mid-nineteen. Till that time, all clot buster drugs were imported, and sold at comparatively high cost, varying between Rs 5000 for streptokinase, and Rs 50000 for TPA (tissue plasminogen activator, TPA). The need to develop an affordable alternative for the "gold standard" in thrombolytics was also felt acutely. Whilst the technology for an animal cell culture-based recombinant protein such as TPA was found fairly complex, the technological route, via fermentation of Streptococci, was successfully undertaken and led to transfer of know-how for the first clot buster in India (Streptokinase), produced by an Indian firm- M/s Cadila Pharmaceuticals Ltd., Ahmadabad. This product was launched in the year 2002, and is still selling well. The availability of a competitive, efficient process for streptokinase led to a strong product ("STPase") that rapidly gave rise to lowering of the price of this life saver drug across the board, thus greatly helping the economically sensitive consumer. STPase was followed by the launch of recombinant streptokinase by Shasun drugs, Chennai in 2009 from technology out-licensed by CSIR-IMTECH with a highly efficient process that further lowered the prices to a mere few hundred rupees. During the period of these developments, the fundamental science of streptokinase action was relentlessly pursued, leading to the understanding of a unique mechanism of action involving protein-protein interactions and the role of Exosites during the interplay of streptokinase with human plasminogen. These insights led to the design of novel clot busters with greatly advantageous properties and clinical potential. These include the much- coveted fibrin clot specificity, which causes localized action of the drug and overall decreased side effects (e.g. reduced risk of hemorrhage) that are often associated with clot buster therapy, as well as the capability to prevent the life-threatening re-occlusion often encountered during thrombolytic therapies. These technologies which have been licensed by CSIR to international pharma companies in multi-million dollar deals are currently at various levels of development, including Phase I human trials. Thus, the 'marriage' of pre-committed basic science with societal needs, on one hand, and innovative product and process

Dr. Girish Sahni delivering Prof. S.H. Zaidi oration

Dr. K.C. Gupta honouring Dr. Girish Sahni after delivering Prof. S.H. Zaidi oration

development on the other, led to four generations of Clot Busters with immediate benefits as well as great promise for the future. The challenges and opportunities involved, and the lessons learnt in this journey, will also be an intrinsic part of this narration. .

Prof. M.M. Salunkhe delivered the Foundation Day address. He congratulated IITR for its achievement in science relevant to society. He took the audience through the history of the CSIR and its evolution to modern CSIR under leadership of then Prime Minister Pandit Jawahar Lal Nehru, Dr. Shanti Swarup Bhatnagar to Dr. R.A. Mashelkar and Prof. Samir Brahmachari today.

The scientist with best 5 papers awarded with silver medals were Dr. R.K. Chaturvedi, Dr. Iqbal Ahmed and Dr. K.C. Gupta bagged the rest three for best papers. Certificate for best papers were also given to Dr. M.P. Singh, Dr. K.M. Ansari, Dr. Mukul Das, Dr. K.C. Gupta, Dr. Alok Dhawan . Dr. Poonam Kakkar was awarded silver medal for most cited paper among all CSIR system. Shri Putti Lal, Shri Lalit Kumar and Mrs. Sheela Kureel were awarded silver medal as the best employee of the year. Dr. Mukul Das, Chief Scientist and Chairman Foundation Day committee proposed the vote of thanks.

CONFERENCES/ WORKSHOPS

XXXII Annual Conference of Society of Toxicology

The XXXII Annual Conference of the Society of Toxicology (STOX), India and International Symposium on New Frontiers in Toxicology was inaugurated on December 5, 2012 at the Scientific Convection Centre, Lucknow. Dr. K.C. Gupta, Chairman, Organizing Committee and Director, CSIR-Indian Institute of Toxicology Research welcomed the guests, Padma Bhushan, Prof. R. Kumar, Emeritus Professor, Department of Chemical Engineering Indian Institute of Science, Bangalore, Prof. Y.K. Gupta, President, STOX (India), & Head, Department of Pharmacology All India Institute of Medical Sciences, New Delhi, Dr P.K Gupta, Patron, STOX and other dignitaries. In his opening remarks, Dr. P.K. Gupta, Founder Member and Patron STOX gave the genesis of establishment of the Society of Toxicology and what progress has it made till date. Dr. A.B. Pant, Scientist, IITR and Secretary General, Society of Toxicology said that the Society of Toxicology (India) is

Release of Sovenir and Abstract Book of the conference

Glipses of cultural programme organized in the evening

premier and versatile body of toxicologists and is an affiliate member of the International Union of Toxicology (IUTOX). The STOX was started with only a few members and in a span of 33 years it has increased its membership to over 900. On this occasion the Society of Toxicology presented awards to the following officials:

(1) Dr. David Vasantharaj Ballah of Chennai and Dr. S.J.S. Flora of DRDE, Gwalior was awarded Distinguished Scientist Lifetime Achievement Award in Toxicology.

(2) Dr. D. Parmar, Dr. Poonam Kakkar of CSIR-IITR and Dr. K. Krishnamurthi of CSIR-NEERI, Nagpur were awarded Fellow of Society of Toxicology.

(3) Dr. Kuntal Bhattacharyya of Medical College, Kolkata was awarded Ram Lal “Shad” Gold Medal Award for Best Paper Published in Toxicology International in last two years.

(4) Prof. Pradeep Bhatnagar and Dr. Priyanka Mathur were awarded Gold Medal for their contribution in organizing the XXXI STOX meeting at Jaipur

(5) Dr T.P Suresh Endowment award was bagged by Dr Krishnapa H. of Advinus Labs, Bangalore

Prof. R. Kumar released the Souvenir on the occasion. In his address, Prof. Y.K. Gupta discussed some of the issues related to toxicity of pesticides and metals and methods to mitigate them. He further said that the need is to develop a method which can mitigate pesticides and metals at an affordable cost-the method should be quick, reliable and cheap. Dr. Y. Shukla, Organizing Secretary and Chief Scientist, CSIR-IITR proposed the vote of thanks.

Lifetime achievement award

Fellow of Society of Toxicology

CSIR-IITR RESEARCH HIGHLIGHTS

Expression profiling of selected genes of toxication and detoxication pathways in peripheral blood lymphocytes as a biomarker for predicting toxicity of environmental chemicals.

[Sharma A, Saurabh K, Yadav S, Jain SK, Parmar D. Int J Hyg Environ Health. 2012 Dec 26. pii: S1438-4639(12)00135-6.]

To develop a rapid and sensitive tool for determining gene expression profiles of peripheral blood lymphocytes (PBL) as a surrogate for predicting toxicity associated with environmental exposures, studies were initiated using Taqman Low Density Array (TLDA), a medium throughput method for real time PCR (RT-PCR), for selected genes involved in toxication and detoxication processes. Total RNA was prepared from PBL and liver samples isolated from young rats treated with inducers of drug metabolizing enzymes, e.g. phenobarbital (PB, 80mg/kg i.p. X5 days) or methylcholanthrene (30mg/kg, i.p. X5 days) or ethanol (0.8ml/kg, i.p. X1 day). TLDA data showed that PBL expressed drug metabolizing enzymes (DMEs), though the level of expression was several folds lower when compared to liver. Treatment with different inducers of DMEs produced

a similar pattern of an increase in the expression of various phase I and phase II DMEs and their respective transcription factors in liver and PBL. While treatment with MC increased the expression of MC inducible cytochrome P450 (CYP) 1A1, 1A2, 1B1, 2A2 & 3A1 and their associated transcription factors in PBL, an increase in the expression of CYP2B1, 2B2, 2C11 & 3A1 and their transcription factor was observed in PBL after PB treatment. Similarly, treatment of ethanol increased the expression of CYP2E1 and 3A1 along with transcription factors in PBL. These inducers were found to increase the expression of various phase II enzymes such as glutathione S-transferases, GSTs (GSTM1, GSTA1, GSTP1 and GSTK1), NQO1, Ephx1 and Sod1, genes involved in inflammation and apoptosis (p53, BCl2, Apaf1 and Caspase9) in both PBL and liver. The data suggests that the low-density array of selected genes in PBL has the potential to be developed as a rapid and sensitive tool for monitoring of individuals exposed to environmental chemicals as well as in clinical studies.

Salsolinol induced apoptotic changes in neural stem cells: Amelioration by neurotrophin support.

[Shukla A, Mohapatra TM, Agrawal AK, Parmar D, Seth K. Neurotoxicology. 2012 Dec 21;35C:50-61.]

Salsolinol (SAL), a catechol isoquinoline has invited considerable attention due to its structural similarity with dopaminergic neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Its high endogenous presence in Parkinsonian brain implicated its possible association with the disease process. SAL is also present in alcohol beverages and certain food materials and can get access to brain especially in conditions of immature or impaired BBB. Besides this, the effect of SAL on neural stem cells (NSCs) which are potential candidates for adult neurogenesis and transplantation mediated rejuvenating attempts for Parkinson's disease (PD) brain has not been known so far. NSCs in both the cases have to overcome suppressive cues of diseased brain for their survival and function. In this study authors explored the toxicity of SAL toward NSCs focusing on apoptosis and status of PI3K survival signaling. NSCs cultured from embryonic day 11 rat fetal brain including those differentiated to TH(+ve) colonies, when challenged with SAL (1-100 µM), elicited a concentration and time dependent cell death/loss of mitochondrial viability. 10 µM SAL on which significant mitochondrial impairment initiated was further used to study mechanism of toxicity. Morphological impairment, enhanced TUNEL positivity, cleaved caspase-3 and decreased Bcl-2:Bax suggested apoptosis. Sal toxicity coincided with reduced pAkt level and its downstream effectors: pCREB, pGSK-3β, Bcl-2 and neurotrophins GDNF, BDNF suggesting repressed PI3K/Akt signaling. Multiple neurotrophic factor support in the form of Olfactory Ensheathing Cell's Conditioned Media (OEC CM) potentially protected NSCs against SAL through activating PI3K/Akt pathway. This was confirmed on adding LY294002 the PI3K inhibitor which abolished the protection. Authors inferred that SAL exerts substantial toxicity toward NSCs. These findings will lead to better understanding of endogenous threats that might affect the fate of transplanted NSCs and their probable antidotes.

Analysis of imidacloprid residues in fruits, vegetables, cereals, fruit juices, and baby foods and daily intake estimation in and around Lucknow, India.

[Kapoor U, Srivastava MK, Srivastava AK, Patel DK, Garg V, Srivastava LP. Environ Toxicol Chem. 2012 Dec 19. doi: 10.1002/etc.2104. (Epub ahead of print)]

A total of 250 samples-including fruits, fruit juices, and baby foods (50 samples each); vegetables (70 samples); and cereals (30 samples)-were collected from Lucknow, India, and analyzed for the presence of imidacloprid residues. The QuEChERS (quick, easy, cheap, effective, rugged, and safe) method of extraction coupled with high-performance liquid chromatographic analysis were carried out, and imidacloprid residues were qualitatively confirmed by liquid chromatography-mass spectrometry. Imidacloprid was not detected in samples of fruit juices and baby foods. It was, however, detected in 38 samples of fruits, vegetables, and cereals, which is about 15.20% of the total samples. Of samples of fruits, 22% showed the presence of imidacloprid, and 2% of samples showed residues above the maximal residue limit. Although imidacloprid was detected in 24% of vegetable samples, only 5.71% showed the presence of imidacloprid above the maximal residue limit. However, 33% of cereal samples showed the presence of imidacloprid, and about 3% of samples were above the maximal residue limit. The calculated estimated daily intake ranged between 0.004 and 0.131 µg/kg body weight, and the hazard indices ranged from 0.007 to 0.218 for these food commodities. It is therefore indicated that lifetime consumption of vegetables, fruits, fruit juices, baby foods, wheat, rice, and pulses may not pose a health hazard for the population of Lucknow because the hazard indices for imidacloprid residues were below 1.

A molecular insight of CTLA-4 in food allergy.

[Kumar S, Verma AK, Das M, Dwivedi PD. Immunol Lett. 2012 Dec 17;149(1-2):101-109.]

Food allergy is an immune provocation induced by certain

food in susceptible individuals. Most of the food allergic manifestations are evident in the individual having impaired oral tolerance. In spite of worldwide prevalence, there is no permanent cure of food allergy. Food allergic reactions are complex immunological events that comprises of several immune molecules like IgE, IL-4, IL-13 and T-cells, therefore, researchers are trying to pick the correct molecule to find out pivotal therapeutic solutions. Being a key regulatory molecule in suppressing T-cells functional activities, cytotoxic T-cell lymphocyte antigen-4 (CTLA-4) or cluster of differentiation-152 (CD-152) has contributed a novel and revolutionary dimension toward therapeutic research of several diseases. This review focuses on different immunological and mechanistic perspectives of CTLA-4 in correlation with food allergy.

Novel polyethylenimine-derived nanoparticles for *in vivo* gene delivery.

[Patnaik S, Gupta KC. Expert Opin Drug Deliv. 2013 Feb;10(2):215-28.] doi: 10.1517/17425247.2013.744964. (Epub 2012 Dec 19).]

Branched and linear polyethylenimines (PEIs) are cationic polymers that have been used to deliver nucleic acids both *in vitro* and *in vivo*. Owing to the high cationic charge, the branched polymers exhibit high transfection efficiency, and particularly PEI of molecular weight 25 kDa is considered as a gold standard in gene delivery. These polymers have been extensively studied and modified with different ligands so as to achieve the targeted delivery. The application of PEI *in vivo* promises to take the polymer-based vector to the next level wherein it can undergo clinical trials and subsequently could be used for delivery of therapeutics in humans. This review focuses on the various recent developments that have been made in the field of PEI-based delivery vectors for delivery of therapeutics *in vivo*. The efficacy of PEI-based delivery vectors *in vivo* is significantly high and animal studies demonstrate that such systems have a potential in humans. However, authors feel that though PEI is a promising vector, further studies involving PEI in animal models are needed so as to get a detailed toxicity profile of these vectors. Also, it is imperative that the vector reaches the specific organ causing little or no undesirable effects to other organs.

Determinants of oxidative stress and DNA damage (8-OhdG) in squamous cell carcinoma of head and neck.

[Kumar A, Pant MC, Singh HS, Khandelwal S. Indian J Cancer. 2012 Jul-Sep;49(3):309-15.]

Squamous cell carcinoma of head and neck (SCCHN) is a major concern of health risk in developing countries, such as India. Apart from genetic configuration, environmental and lifestyle factors, as well as poor oral hygiene, provide free radical-generating environment, which may contribute to the development of cancer through DNA damage. Here authors ascertained the various oxidative stress determinants in diagnosed SCCHN patients with health risk addictions. This study further evaluated the incremental effects inflicted by these lifestyle factors on redox status. The study included 100 consenting SCCHN patients and 90 matched healthy controls. Salivary total antioxidant capacity (TAC), glutathione (GSH), free radicals: such as reactive nitrogen species (RNS) and reactive oxygen species (ROS) along with oxidative DNA adduct (8-OHdG) were monitored. Findings indicated altered salivary oxidant-antioxidant status in SCCHN. A substantial rise in ROS (~2.0 folds) and RNS (~1.4 folds), together with significant lowering in TAC (~1.2 folds) and GSH (~1.7 folds) was observed. The 8-OHdG levels were also found to be considerably higher ($P < 0.001$) in salivary cell's DNA of these patients. Results demonstrate significant redox imbalance in cancer patients suggesting their paramount importance in the development of SCCHN.

Impact of thermal processing on legume allergens.

[Verma AK, Kumar S, Das M, Dwivedi PD. Plant Foods Hum Nutr. 2012 Dec;67(4):430-41.]

Food induced allergic manifestations are reported from several parts of the world. Food proteins exert their allergenic potential by absorption through the gastrointestinal tract and can even induce life threatening anaphylaxis reactions. Among all food allergens, legume allergens play an important role in induction of allergy because legumes are a major source of protein for vegetarians. Most of the legumes are cooked either by boiling, roasting or frying before consumption, which can be considered a form of thermal treatment. Thermal processing may also include autoclaving, microwave heating, blanching, pasteurization, canning, or steaming. Thermal processing of legumes may reduce, eliminate or enhance the allergenic potential of a respective legume. In most of the cases, minimization of allergenic potential on thermal treatment has generally been reported. Thus, thermal processing can be considered an important tool by indirectly prevent allergenicity in susceptible individuals, thereby reducing treatment costs and reducing industry/office/school absence in case of working population/school going children. The present review attempts to explore various possibilities of reducing or eliminating allergenicity of leguminous food using different methods of thermal processing. Further, this review summarizes different methods of food processing, major legumes and their

predominant allergenic proteins, thermal treatment and its relation with antigenicity, effect of thermal processing on legume allergens; also suggests a path that may be taken for future research to reduce the allergenicity using conventional/nonconventional methods.

Mitochondria targeted therapeutic approaches in Parkinson's and Huntington's diseases.

[Chaturvedi RK, Beal MF. Mol Cell Neurosci. 2012 Dec 5. pii: S1044-7431(12)00210-2.

Substantial evidence from both genetic and toxin induced animal and cellular models and postmortem human brain tissue indicates that mitochondrial dysfunction plays a central role in pathophysiology of the neurodegenerative disorders including Parkinson's disease (PD), and Huntington's disease (HD). This review discusses the emerging understanding of the role of mitochondrial dysfunction including bioenergetics defects, mitochondrial DNA mutations, familial nuclear DNA mutations, altered mitochondrial fusion/fission and morphology, mitochondrial transport/trafficking, altered transcription and increased interaction of pathogenic proteins with mitochondria in the pathogenesis of PD and HD. This review recapitulates some of the key therapeutic strategies applied to surmount mitochondrial dysfunction in these debilitating disorders. Authors discuss the therapeutic role of mitochondrial bioenergetic agents such as creatine, Coenzyme-Q10, mitochondrial targeted antioxidants and peptides, the SIRT1 activator resveratrol, and the pan-PPAR agonist bezafibrate in toxin and genetic cellular and animal models of PD and HD. Authors also summarize the phase II-III clinical trials conducted using some of these agents. Lastly, they discuss about PGC-1α, TORC and Sirtuins as potential therapeutic targets for mitochondrial dysfunction in neurodegenerative disorders.

Crystal structure of the hexachlorocyclohexane dehydrochlorinase (LinA-type2): mutational analysis, thermostability and enantioselectivity.

[Macwan AS, Kukshal V, Srivastava N, Javed S, Kumar A, Ramachandran R. PLoS One. 2012;7(11):e50373.

Hexachlorocyclohexane dehydrochlorinase (LinA) mediates dehydrochlorination of γ-HCH to 1, 3, 4, 6-tetrachloro-1,4-cyclohexadiene that constitutes first step of the aerobic degradation pathway. Authors reported the 3.5 Å crystal structure of a thermo stable LinA-type2 protein, obtained from a soil meta genome, in the hexagonal space group $P6_322$ with unit cell parameters a=b=162.5, c=186.3 Å, respectively. The structure was solved by molecular replacement using the co-ordinates of LinA-type1 that exhibits mesophile-like properties. Structural comparison of LinA-type2 and -type1 proteins suggests that thermo stability of LinA-type2 might partly arise due to presence of higher number of ionic interactions, along with 4% increase in the inter subunit buried surface area. Mutational analysis involving the differing residues between the -type1 and -type2 proteins, circular dichroism experiments and functional assays suggest that Q20 and G23 are determinants of stability for LinA-type2. It was earlier reported that LinA-type1 exhibits enantioselectivity for the (-) enantiomer of α-HCH. Contrastingly, authors identified that -type2 protein prefers the (+) enantiomer of α-HCH. Structural analysis and molecular docking experiments suggest that changed residues K20Q, L96C and A131G, vicinal to the active site are probably responsible for the altered enantioselectivity of LinA-type2. Overall the study has identified features responsible for the thermo stability and enantioselectivity of LinA-type2 that can be exploited for the design of variants for specific biotechnological applications.

Biosorption of arsenic in drinking water by submerged plant: *Hydrilla verticilata*.

[Nigam S, Gopal K, Vankar PS. Environ Sci Pollut Res Int. 2012 Dec 4. doi:10.1007/s11356-012-1342-x (Epub ahead of print)]

To evaluate the biosorption efficacy of submerged aquatic plant *Hydrilla verticilata* for arsenic uptake from drinking water. *H. verticillata*, a submerged aquatic plant was utilized successfully for arsenic uptake from aqueous solution. Batch studies with various parameters viz. pH, sorbent dose, contact time, initial metal ion concentration, and temperature were carried out. Data were utilized to plot Lagergren graph along with pseudo-second-order graphs for kinetic studies to estimate the removal efficacy and to determine the nature of reaction. Scanning electron microscopy (SEM) and Fourier transform infrared spectroscopy (FTIR) have been performed for characterization of metals on biomass. The study showed 96.35 % maximum absorption of arsenic by *H. verticilata* at initial concentration of 100 ppb with 0.5 g of biomass/ 100 ml for 5 h contact time at pH6.0 with 150 rpm agitation rate. Data followed Langmuir isotherm showing sorption to be monolayer on homogeneous surface of biosorbent. The negative values of $\Delta G°$ indicated spontaneous nature; whereas $\Delta H°$ indicates exothermic nature of system and negative value of $\Delta S°$ entropy change correspond to a decrease in the degree of freedom to the adsorbed species followed by pseudo-second-order adsorption kinetics. FTIR and SEM results showed apparent changes in functional group regions after metal chelation and the changes in surface morphology of biosorbent. This is a comparatively more effective, economic, easily available, and

environmentally safe source for arsenic uptake from solution due to its high biosorption efficacy than other biosorbents already used.

Epigenetic regulation of DNMT1 gene in mouse model of asthma disease.

[Verma M, Chattopadhyay BD, Paul BN. Mol Biol Rep. 2012 Nov 30. doi:10.1007/s11033-012-2317-1 (Epub 2012 Nov. 29)]

Asthma is a complex genetic disease, which arises from the interaction of multiple genes and environmental stimuli. These influences are important to asthma pathogenesis. These can be mechanically explained by the Epigenetic phenomenon, which consists of the chromatin and its modifications, as well as a covalent modification of cytosines residing at the dinucleotide sequence CG in DNA by methylation. This reaction is catalyzed by a family of DNA methyltransferase enzyme (DNMTs). DNMT1 is one of them which maintained the methylation status during replication and also critical for the development, differentiation and regulation of Th1 and Th2 cells. The authors studied the DNMT1 mRNA expression profiling as well as CpG methylation status in promoter region. For these studies they developed asthma mouse model, and used Flow cytometer, qRT(2)-PCR, Methylation specific PCR, bisulfate conversion and BiQ analyzer. Authors found that DNMT1 expression level was low in all the tissues (lung, trachea and BALF cells) of asthmatic in comparison to normal mice. This was due to the methylation of regulatory sites of DNMT1 promoter region at cytosine residue. As the incidence of asthma is increasing globally and in world, this study assumes greater significance in designing and developing therapeutic means.

Naringenin prevents high glucose-induced mitochondria-mediated apoptosis involving AIF, Endo-G and caspases.

[Kapoor R, Rizvi F, Kakkar P. Apoptosis. 2013 Jan;18(1):9-27. doi: 10.1007/s10495-012-0781-7(Epub 2012 Nov. 29)]

Oxidative stress is implicated in hyperglycemia-induced alterations in cell signaling pathways. Authors examined the toxicity of high glucose in primary rat hepatocytes and its amelioration by naringenin. Incubation of hepatocytes with 40 mM glucose for 1.5 h exhibited significant decrease in cell viability confirmed by MTT reduction and Alamar blue assay. At the same time primary rat hepatocytes exhibited significant decrease in mitochondrial membrane potential indicating organelle dysfunction. Enhanced translocation of Cyt-c from mitochondria to cytosol and AIF/Endo-G from mitochondria to nucleus, activation of caspase-9/3, DNA damage, and chromatin condensation were observed in glucose-stressed hepatocytes, indicating the involvement of mitochondrial pathway in high glucose-induced apoptosis. Transcript levels of antioxidant enzymes were significantly altered along with corresponding changes in their enzymatic activities. The level of intracellular antioxidant glutathione as well as superoxide dismutase, catalase, and glutathione peroxidase activities were observed to be significantly decreased in hepatocytes treated with high concentration of glucose. Naringenin, a flavanone, was effective in preventing loss of cell viability, reactive oxygen species generation, and decline in antioxidant defence. Translocation of AIF, Endo-G, and Cyt-c from mitochondria was also inhibited by naringenin in glucose-stressed cells. Messenger RNA expression of anti-apoptotic and apoptotic genes, externalization of phosphatidyl serine, DNA damage, chromatin condensation, and sub-diploid cell population were effectively altered by naringenin indicating its anti-apoptotic potential *in vitro*. Data suggests that naringenin can prevent apoptosis induced by high glucose through scavenging of reactive oxygen species and modulation of mitochondria-mediated apoptotic pathway.

Ochratoxin A-induced cell proliferation and tumor promotion in mouse skin by activating the expression of cyclin-D1 and cyclooxygenase-2 through nuclear factor-kappa B and activator protein-1.

[Kumar R, Alam S, Chaudhari BP, Dwivedi PD, Jain SK, Ansari KM, Das M. Carcinogenesis. 2012 Dec 9. doi:10.1093/carcin/bgs368 (Epub ahead of print)]

Authors' prior studies have indicated that ochratoxin A (OTA), a mycotoxin, has skin tumor initiating activity. In the present investigation, skin tumor promoting activity of OTA and the mechanism/(s) involved therein was undertaken. A single topical application of OTA (100 nmol/mouse) caused significant enhancement in short-term markers of skin tumor promotion such as ornithine decarboxylase activity, DNA synthesis, hyperplasia as well as expression of cyclin-D1 and COX-2 in mouse skin. In a two-stage mouse skin tumorigenesis protocol, twice-weekly exposure of OTA (50 nmol/mouse) to 7,12-dimethylbenz[α]anthracene (120 nmol/mouse) initiated mice skin for 24 weeks leads to tumor formation. Further, exposure of primary murine keratinocytes (PMKs) with non-cytotoxic dose of OTA (5.0 µM) caused (i) significant enhancement of DNA synthesis, (ii) +enhanced phosphorylation and subsequent activation of epidermal growth factor receptor (EGFR) and its downstream signaling pathways vizAkt, ERK1/2, p38 and JNK mitogen-activated protein kinases (MAPKs), (iii) overexpression of c-jun, c-

fos, cyclin-D1 and COX-2 and (iv) increased binding of nuclear factor-kappaB (NF-κB) and AP-1 transcription factors to the promoter region of cyclin-D1 and COX-2 genes. It was also observed that knocking down the messenger RNA expression of NF-κB, c-jun, c-fos, cyclin-D1 and COX-2 results in significant inhibition in OTA-induced PMKs proliferation. These results suggest that OTA has cell proliferative and tumor-promoting potential in mouse skin, which involves EGFR-mediated MAPKs and Akt pathways along with NF-κB and AP-1 transcription factors and that cyclin-D1 and COX-2 are the target genes responsible for tumor-promoting activity of OTA.

Biochemical and molecular mechanisms of N-acetyl cysteine and silymarin-mediated protection against maneb- and paraquat-induced hepatotoxicity in rats.

[Ahmad I, Shukla S, Kumar A, Singh BK, Kumar V, Chauhan AK, Singh D, Pandey HP, Singh C. Chem Biol Interact. 2012 Nov 16;201(1-3):9-18.]

Oxidative stress is one of the major players in the pathogenesis of maneb (MB) and paraquat (PQ)-induced disorders. N-acetyl cysteine (NAC), a glutathione (GSH) precursor and silymarin (SIL), a naturally occurring antioxidant, encounter oxidative stress-mediated cellular damage. The present study was aimed to investigate the effects of NAC and SIL against MB and/or PQ-induced hepatotoxicity in rats. The levels of hepatotoxicity markers - alanine aminotransaminase (ALT), aspartate aminotransaminase (AST) and total bilirubin, histological changes, oxidative stress indices, phase I and phase II xenobiotic metabolizing enzymes - cytochrome P450 (CYP) and glutathione S-transferase (GST) and pro-inflammatory molecules - inducible nitric oxide synthase (iNOS), tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) were measured in animals treated with MB and/or PQ in the presence or absence of NAC and SIL. MB and/or PQ augmented ALT, AST, total bilirubin, lipid peroxidation and nitrite contents and catalytic activities of superoxide dismutase and glutathione peroxidase however, the GSH content was attenuated. NAC and SIL restored the above-mentioned alterations towards basal levels but the restorations were more pronounced in SIL treated groups. Similarly, MB and/or PQ-mediated histopathological symptoms and changes in the catalytic activities/ expressions of CYP1A2, CYP2E1, iNOS, TNF-α, and IL-1β were alleviated by NAC and SIL. Conversely, MB and/or PQ-induced GSTA4-4 expression/activity was further increased by NAC/SIL and glutathione reductase activity was also increased. Results obtained thus suggest that NAC and SIL protect MB and/or PQ-induced hepatotoxicity by reducing oxidative stress, inflammation and by modulating xenobitic metabolizing machinery and SIL seems to be more effective.

Groundwater contaminated with hexavalent chromium [Cr (VI)]: a health survey and clinical examination of community inhabitants (Kanpur, India).

[Sharma P, Bihari V, Agarwal SK, Verma V, Kesavachandran CN, Pangtey BS, Mathur N, Singh KP, Srivastava M, Goel SK. PLoS One. 2012;7(10):e47877.]

Authors assessed the health effects of hexavalent chromium groundwater contamination (from tanneries and chrome sulfate manufacturing) in Kanpur, India. The health status of residents living in areas with high Cr (VI) groundwater contamination (N = 186) were compared to residents with similar social and demographic features living in communities having no elevated Cr (VI) levels (N = 230). Subjects were recruited at health camps in both the areas. Health status was evaluated with health questionnaires, spirometry and blood hematology measures. Cr (VI) was measured in groundwater samples by diphenylcarbazide reagent method. Residents from communities with known Cr (VI) contamination had more self-reports of digestive and dermatological disorders and hematological abnormalities. GI distress was reported in 39.2% vs. 17.2% males (AOR = 3.1) and 39.3% vs. 21% females (AOR = 2.44); skin abnormalities in 24.5% vs. 9.2% males (AOR = 3.48) and 25% vs. 4.9% females (AOR = 6.57). Residents from affected communities had greater RBCs (among 30.7% males and 46.1% females), lower MCVs (among 62.8% males) and less platelet (among 68% males and 72% females) than matched controls. There were no difference in leucocytes count and spirometry parameters. Living in communities with Cr (VI) groundwater is associated with gastrointestinal and dermatological complaints and abnormal hematological function. Limitations of this study include small sample size and the lack of long term follow-up.

Determination of t,t-muconic acid in urine samples using a molecular imprinted polymer combined with simultaneous ethyl chloroformate derivatization and pre-concentration by dispersive liquid-liquid microextraction.

[Mudiam MK, Chauhan A, Singh KP, Gupta SK, Jain R, Ratnshekhar CH, Murthy RC. Anal Bioanal Chem. 2013 Jan;405(1):341-9. doi: 10.1007/s00216-012-6474-9. (Epub 2012 Oct 19.)]

The present communication describes the preparation and evaluation of a molecularly imprinted polymer (MIP) as a

solid-phase extraction (SPE) sorbent and simultaneous ethyl chloroformate (ECF) derivatization and pre-concentration by dispersive liquid-liquid microextraction (DLLME) for the analysis of t,t-muconic acid (t,t-MA) in urine samples using gas chromatography-mass spectrometry. The imprinting polymer was prepared using methacrylic acid as a functional monomer, ethylene glycol dimethacrylate as a cross-linker, 2,2-azobisisobutyronitrile as the initiator and t,t-MA as a template molecule. The imprinted polymer was evaluated for its use as a SPE sorbent by comparing both imprinted and non-imprinted polymers in terms of the recovery of t,t-MA from urine samples. Molecular modelling studies were performed in order to estimate the binding energy and efficiency of the MIP complex formed between the monomer and the t,t-MA. Various factors that can affect the extraction efficiency of MIP, such as the loading, washing and eluting conditions, were optimized; other factors that can affect the derivatization and DLLME pre-concentration were also optimized. MIP in combination with ECF derivatization and DLLME pre-concentration for t,t-MA exhibits good linearity, ranging from 0.125 to 2 µg mL(-1) (R (2) = 0.9971), with limit of detection of 0.037 µg mL(-1) and limit of quantification of 0.109 µg mL(-1). Intra- and inter-day precision was found to be <6 %. The proposed method has been proven to be effective and sensitive for the selective pre-concentration and determination of t,t-MA in urine samples of cigarette smokers.

Pre-natal/juvenile chlorpyrifos exposure associated with immunotoxicity in adulthood in Swiss albino mice.

[Singh AK, Parashar A, Singh AK, Singh R. J Immunotoxicol. 2012 Oct 19. (Epub ahead of print)]

Chlorpyrifos (CPF) is a widely used agricultural organophosphorus insecticide (OP). Epidemiological studies have reported that children living in an OP contaminated environment, showed altered immune function. However, there is a paucity of experimental evidence for CPF-induced toxicity in the developmental phases of immune system. The current studies sought to ascertain the effect of CPF on the developing immune system of mice. Swiss albino dams were exposed orally with 0, 0.3, and 3.0 mg CPF/kg/day from GD12 to PND7, and then pups were directly dosed with CPF (by gavage) through PND42. One week after the final dose of CPF (i.e. on PND49), immunotoxicities in these offspring were assessed. These analyses revealed that there were increases in $Foxp3^{+}CD25^{+}CD4^{+}$ T-regulatory (T_{reg}) cell frequency in the spleens of 3.0 mg CPF/kg/day-exposed female mice, but not in males. In contrast, the anti-sheep red blood cells IgM response was reduced in both genders. Moreover, splenic lymphoproliferative response to phytohemagglutinin (PHA), concanavalin A (ConA), and lipopolysaccharide (LPS), as well as interferon (IFN)-γ, tumor necrosis factor (TNF)-α, and interleukin (IL)-6 production following LPS stimulation decreased in mice of both sexes at higher CPF doses. Together, these findings suggest that developmental CPF exposure might cause immunosuppression in mice. Some of these outcomes might arise, in part, through a suppression of pro-inflammatory cytokine production and/or changes in the responsivity (specifically to mitogens) of lymphocytes in these hosts.

Topical application of ochratoxin A causes DNA damage and tumor initiation in mouse skin.

[Kumar R, Ansari KM, Chaudhari BP, Dhawan A, Dwivedi PD, Jain SK, Das M. PLoS One. 2012;7(10):e47280.]

Skin cancer is one of the most common forms of cancer and 2-3 million new cases are being diagnosed globally each year. Along with UV rays, environmental pollutants/chemicals including mycotoxins, contaminants of various foods and feed stuffs, could be one of the aetiological factors of skin cancer. In the present study, authors evaluated the DNA damaging potential and dermal carcinogenicity of a mycotoxin, ochratoxin A (OTA), with the rationale that dermal exposure to OTA in workers may occur during their involvement in pre and post harvest stages of agriculture. A single topical application of OTA (20-80 µg/mouse) resulted in significant DNA damage along with elevated γ-H2AX level in skin. Alteration in oxidative stress markers such as lipid peroxidation, protein carbonyl, glutathione content and antioxidant enzymes was observed in a dose (20-80 µg/mouse) and time-dependent (12-72 h) manner. The oxidative stress was further emphasized by the suppression of Nrf2 translocation to nucleus following a single topical application of OTA (80 µg/mouse) after 24 h. OTA (80 µg/mouse) application for 12-72 h caused significant enhancement in- (a) reactive oxygen species generation, (b) activation of ERK1/2, p38 and JNK MAPKs, (c) cell cycle arrest at G0/G1 phase (37-67%), (d) induction of apoptosis (2.0-11.0 fold), (e) expression of p53, p21/waf1, (f) Bax/Bcl-2 ratio, (g) cytochrome c level, (h) activities of caspase 9 (1.2-1.8 fold) and 3 (1.7-2.2 fold) as well as poly ADP ribose polymerase cleavage. In a two-stage mouse skin tumorigenesis protocol, it was observed that a single topical application of OTA (80 µg/mouse) followed by twice weekly application of 12-O-tetradecanoylphorbol-13-acetate for 24 week leads to tumor formation. These results suggest that OTA has skin tumor initiating property which may be related to oxidative stress, MAPKs signaling and DNA damage.

Cellular internalization and stress response of ingested amorphous silica nanoparticles in the midgut of *Drosophila melanogaster*.

[Pandey A, Chandra S, Chauhan LK, Narayan G, Chowdhuri DK. Biochim Biophys Acta. 2013 Jan;1830(1):2256-66. doi: 10.1016/j.bbagen.2012.10.001. Epub 2012 Oct 6.]

Amorphous silica nanoparticles (aSNPs) are used for various applications including food industry. However, limited *in vivo* studies are available on absorption/ internalization of ingested aSNPs in the midgut cells of an organism. The study aims to examine cellular uptake of aSNPs (<30nm) in the midgut of *Drosophila melanogaster* (Oregon R(+)) owing to similarities between the midgut tissue of this organism and human and subsequently cellular stress response generated by these nanoparticles. Third instar larvae of *D. melanogaster* were exposed orally to 1-100 µg/mL of aSNPs for 12-36h and oxidative stress (OS), heat shock genes (hsgs), membrane destabilization (Acridine orange/Ethidium Bromide staining), cellular internalization (TEM) and apoptosis endpoints. A significant increase was observed in OS endpoints in the midgut cells of exposed Drosophila in a concentration- and time-dependent manner. Significantly increased expression of hsp70 and hsp22 along with caspases activation, membrane destabilization and mitochondrial membrane potential loss was also observed. TEM analysis showed aSNPs-uptake in the midgut cells of exposed Drosophila via endocytic vesicles and by direct membrane penetration. aSNPs after their internalization in the midgut cells of exposed Drosophila larvae show membrane destabilization along with increased cellular stress and cell death. Ingested aSNPs show adverse effects on the cells of GI tract of the exposed organism thus their industrial use as a food-additive may raise concern to human health.

Rapid and simultaneous determination of twenty amino acids in complex biological and food samples by solid-phase microextraction and gas chromatography-mass spectrometry with the aid of experimental design after ethyl chloroformate derivatization.

[Mudiam MK, Ratnasekhar CH, Jain R, Saxena PN, Chauhan A, Murthy RC. J Chromatogr B Analyt Technol Biomed Life Sci. 2012 Oct 15; 907:56-64.]

Amino acids play a vital role as intermediates in many important metabolic pathways such as the biosynthesis of nucleotides, vitamins and secondary metabolites. A sensitive and rapid analytical method has been proposed for the first time for the simultaneous determination of twenty amino acids using solid-phase microextraction (SPME). The protein samples were hydrolyzed by 6M HCl under microwave radiation for 120 min. Then the amino acids were derivatized by ethyl chloroformate (ECF) and the ethoxy carbonyl ethyl esters of amino acids formed were extracted using SPME by direct immersion. Finally the extracted analytes on the SPME fiber were desorbed at 260°C and analyzed by gas chromatography-mass spectrometer (GC-MS) in electron ionization mode. Factors which affect the SPME efficiency were screened by Plackett-Burmann design; most significant factors were optimized with response surface methodology. The optimum conditions for SPME are as follows: pH of 1.7, ionic strength of 733 mg, extraction time of 30 min and fiber of divinyl benzene/carboxen/polydimethylsiloxane (DVB/CAR/PDMS). The recovery of all the amino acids was found to be in the range of 89.17-100.98%. The limit of detection (LOD) of all derivatized amino acids in urine, hair and soybean was found to be in the range of 0.20-7.52 µg /L, 0.21-8.40 µg/ L and 0.18-5.62 µg/ L, respectively. Finally, the proposed technique was successfully applied for the determination of amino acids in complex biological (hair, urine) and food samples (soybean). The method can find wide applications in the routine analysis of amino acids in any biological as well as food samples.

Effects of C-Phycocyanin on the representative genes of tumor development in mouse skin exposed to 12-O-tetradecanoyl-phorbol-13-acetate.

[Gupta NK, Gupta KP. Environ Toxicol Pharmacol. 2012 Nov;34(3):941-8.]

C-Phycocyanin (C-PC), a biliprotein from the sea weed, has been shown to have the beneficial effects like antioxidant, anti-inflammatory, neuroprotective, and hepatoprotective properties and is used as food supplement. Authors are showing the effect of C-Phycocyanin on the early events altered by tumor promoter. TPA induced the expression of critical events of tumorigenesis like ornithine decarboxylase, cyclooxygenase-2, interleukin-6 and pSTAT3 in mouse skin after 5h of application, whereas expression of transglutaminase2 was decreased at this time point. This TPA-caused altered expression of genes was prevented in presence of C-Phycocyanin. This prevention by C-Phycocyanin appeared to be dependent on the dose of C-Phycocyanin used. The results are useful for the detailed study on the preventive effect of C-Phycocyanin on TPA induced tumor promotion.

Degradation of γ-HCH spiked soil using stabilized Pd/Fe0 bimetallic nanoparticles: pathways, kinetics and effect of reaction conditions.

[Singh R, Misra V, Mudiam MK, Chauhan LK, Singh RP. J Hazard Mater. 2012 Oct 30;237-238:355-64.]

This study investigates the degradation pathway of gamma-hexachlorocyclohexane (γ-HCH) in spiked soil using carboxymethyl cellulose stabilized Pd/Fe^0 bimetallic nanoparticles (CMC-Pd/nFe^0). GC–MS analysis of γ-HCH degradation products showed the formation of pentachlorocyclohexene, tri- and di-chlorobenzene as intermediate products while benzene was formed as the most stable end product. On the basis of identified intermediates and final products, degradation pathway of γ-HCH has been proposed. Batch studies showed complete γ-HCH degradation at a loading of 0.20 g/L CMC-Pd/nFe^0 within 6 h of incubation. The surface area normalized rate constant (k_{SA}) was found to be 7.6×10^{-2} L min^{-1} m^{-2}. CMC-Pd/nFe^0 displayed ~7-fold greater efficiency for γ-HCH degradation in comparison to Fe^0 nanoparticles (nFe^0), synthesized without CMC and Pd. Further studies showed that increase in CMC-Pd/nFe^0 loading and reaction temperature facilitates γ-HCH degradation, whereas a declining trend in degradation was noticed with the increase in pH, initial γ-HCH concentration and in the presence of cations. The data on activation energy (33.7 kJ/mol) suggests that γ-HCH degradation is a surface mediated reaction. The significance of the study with respect to remediation of γ-HCH contaminated soil using CMC-Pd/nFe^0 has been discussed.

Fatty acid composition including trans-fatty acids in edible oils and fats: probable intake in Indian population.

[Dixit S, Das M. J Food Sci. 2012 Oct;77(10):T188-99.]

The susceptibility of trans-fat to the human health risk prompted the Food and Agriculture Organization (FAO) and World Health Organization (WHO) to prepare regulations or compulsory claims for trans-fatty acids (TFA) in edible oils and fats. In this study, analysis of fatty acid composition and TFA content in edible oils and fats along with the possible intake of trans-fat in Indian population was carried out. The analysis was carried out as per the Assn. of Official Analytical Chemists (AOAC) methodology and the results were statistically analyzed. The average TFA content in non-refined mustard and refined soybean oils exceeded by 1.16- to 1.64-fold as compared to the Denmark limit of 2% TFA in fats and oils destined for human consumption. In branded/non-branded butter and butter oil samples, average TFA limit exceeded by 4.2- to 9.5-fold whereas hydrogenated vegetable oil (HVO) samples exceeded the limit by 9.8-fold, when compared to Denmark standards. The probable TFA intake per day through different oils in Indian population were found to be less than WHO recommendation. However Punjab having highest consumption of HVO (-15 g/d) showed 1.09-fold higher TFA intake than the WHO recommendation, which is alarming and may be one of the factors for high cardiovascular disease mortality rate that needs further elucidation. Thus there is a need to prescribe TFA limit for edible oil, butter, and butter oil in India and to reduce the already proposed TFA levels in HVO to safeguard the health of consumers. The study indicates that TFA intake through HVO consumption is higher in States like Punjab than the recommended daily intake prescribed by WHO. Hence, strategies should be adopted to either decrease the consumption of HVO or to modify the industrial processing method of HVO with less content of TFA to safeguard the health of consumers.

Cytochrome P450 2A isoenzymes in freshly prepared blood lymphocytes isolated from rats and validation as a biomarker for clinical studies in humans.

[Sharma A, Dinesh K, Yadav S, Jain SK, Pant MC, Parmar D. Xenobiotica. 2012 Aug 31. doi:10.3109/00498254.2012.717728. (Epub ahead of print)]

The present study aimed to identify the expression of carcinogen metabolizing cytochrome P4502A (CYP2A) isoenzymes in freshly prepared rat peripheral blood lymphocytes (PBL) isolated from adult rats and investigate similarities in the regulation of lymphocyte CYP2A-isoenzymes with the tissue enzyme. qRT-PCR studies demonstrated significant constitutive mRNA expression of CYP2A-isoenzymes in PBL isolated from male and female rats which further increases significantly after pretreatment with nicotine or 3-methylcholanthrene (MC) indicating responsiveness of CYP2A-isoenzymes in PBL. This increase in the CYP2A expression was associated with an increase in the protein expression and CYP2A3-dependent coumarin hydroxylase (COH) activity in PBL. Clinical studies further demonstrated significant increase in the expression of CYP2A6 and associated enzyme activity in PBL isolated from lung cancer patients. Data thus provided evidence for similarities in the regulation of carcinogen metabolizing CYP2A-isoenzymes in PBL with the tissue enzymes. Further, responsiveness of blood CYP2A6 in human blood lymphocytes isolated from lung cancer patients has led us to suggest that associating expression profiles of CYP2A6 and other polycyclic aromatic hydrocarbons (PAH)-responsive CYPs in PBL with the genotyping data could lead to the development of a

possible screen to monitor and predict environment-induced diseases and toxicity in humans.

Genetic predisposition for dermal problems in hexavalent chromium exposed population.

[Sharma P, Bihari V, Agarwal SK, Goel SK. J Nucleic Acids. 2012;2012:968641.]

Authors studied the effect of genetic susceptibility on hexavalent chromium induced dermal adversities. The health status of population was examined from the areas of Kanpur (India) having the elevated hexavalent chromium levels in groundwater. Blood samples were collected for DNA isolation to conduct polymorphic determination of genes, namely: NQO1 (C609T), hOGG1 (C1245G), GSTT1, and GSTM1 (deletion). Symptomatic exposed subjects (n = 38) were compared with asymptomatic exposed subjects (n = 108) along with asymptomatic controls (n = 148) from a non contaminated reference community. Exposed symptomatic group consisted of 36.8% subjects who were GSTM1 null genotyped as compared to asymptomatic where only 19.4% subjects were null. The exposed subjects with GSTM1 null genotype were more susceptible to dermal adversities in comparison with wild genotyped subjects (OR = 2.42; 95% CI = 1.071-5.451). Age, smoking, gender or duration of residence were not found to have any confounding effect towards this association. Association with other genes was not statistically significant, nonetheless, possible contribution by these genes cannot be ruled out. In conclusion, variation in the polymorphic status of GSTM1 gene may influence dermal outcomes among residents from Cr(VI) contaminated areas. Further studies are therefore, needed to examine these observations among different population groups.

Protective role of morin, a flavonoid, against high glucose induced oxidative stress mediated apoptosis in primary rat hepatocytes.

[Kapoor R, Kakkar P. PLoS One. 2012;7(8):e41663.]

Apoptosis is an early event of liver damage in diabetes and oxidative stress has been linked to accelerate the apoptosis in hepatocytes. Therefore, the compounds that can scavenge ROS may confer regulatory effects on high-glucose induced apoptosis. In the present study, primary rat hepatocytes were exposed to high concentration (40 mM) of glucose. At this concentration decreased cell viability and enhanced ROS generation was observed. Depleted antioxidant status of hepatocytes under high glucose stress was also observed as evident from transcriptional level and activities of antioxidant enzymes. Further, mitochondrial depolarisation was accompanied by the loss of mitochondrial integrity and altered expression of Bax and Bcl-2. Increased translocation of apoptotic proteins like AIF (Apoptosis inducing factor) & Endo-G (endonuclease-G) from its resident place mitochondria to nucleus was also observed. Cyt-c residing in the inter-membrane space of mitochondria also translocated to cytoplasm. These apoptotic proteins initiated caspase activation, DNA fragmentation, chromatin condensation, increased apoptotic DNA content in glucose treated hepatocytes, suggesting mitochondria mediated apoptotic mode of cell death. Morin, a dietary flavonoid from *Psidium guajava* was effective in increasing the cell viability and decreasing the ROS level. It maintained mitochondrial integrity, inhibited release of apoptotic proteins from mitochondria, prevented DNA fragmentation, chromatin condensation and hypodiploid DNA upon exposure to high glucose. This study confirms the capacity of dietary flavonoid Morin in regulating apoptosis induced by high glucose via mitochondrial mediated pathway through intervention of oxidative stress.

Pkb/Akt1 Mediates Wnt/GSK3β/β-Catenin Signaling-Induced Apoptosis in Human Cord Blood Stem Cells Exposed to Organophosphate Pesticide Monocrotophos.

[Kashyap MP, Singh AK, Kumar V, Yadav DK, Khan F, Jahan S, Khanna VK, Yadav S, Pant AB. Stem Cells Dev. 2013 Jan 15;22(2):224-38. doi: 10.1089/scd.2012.0220. (Epub 2012 Aug 16.)]

Inhibition mechanisms of protein kinase B (Pkb)/Akt and its consequences on related cell signaling were investigated in human umbilical cord blood stem cells (hUCBSCs) exposed to monocrotophos (MCP, an organophosphate pesticide). *In silico* data reveal that MCP interacts with kinase and c-terminal regulatory domains of Akt1, resulting into a total docking score of 5.2748 and also forms H-bond between its N-H and Thr-291 residue of Akt1, in addition to possessing several hydrophobic interactions. The main cause of Akt inhibition is considered to be the strong hydrogen bond between N-H and Thr-291, and hydrophobic interactions at Glu-234, and Asp-292 in the vicinity, which is usually occupied by the ribose of ATP, and interaction with residue Phe-161, thus leading to a significant conformational change in that particular portion of the protein. *In silico* data on Akt inhibition were confirmed by examining the downregulation of phosphorylated (Thr308/Ser493) Akt1 in MCP-exposed hUCBSCs. MCP-mediated altered levels of pAkt downstream targets viz., downregulated pGSK3β (Ser9), unchanged GSK3αβ, and upregulated levels of Bad, P(53), and caspase-9 further confirm the inhibition of pAkt. The cellular fate of such pAkt inhibition was confirmed by increased terminal deoxynucleotide transferase dUTP nick-end labeling

positive cells, reduced mitochondrial membrane potential, and the activation of various MAPKs, proapoptotic markers-Bax, and caspases-9/3. Data demonstrate that Akt1 plays a key role in MCP-induced apoptosis in hUCBSCs. Authors also identified that such cellular responses of human cord blood stem cells against MCP were due to strong binding and inhibition of kinase and AGC-Kinase-C terminal regulatory domains of Akt1.

Predicting adsorptive removal of chlorophenol from aqueous solution using artificial intelligence based modeling approaches.

[Singh KP, Gupta S, Ojha P, Rai P. Environ Sci Pollut Res Int. 2012 Aug 1. doi:10.1007/s11356-012-1102-y (Epub ahead of print)]

The research aims to develop artificial intelligence (AI)-based model to predict the adsorptive removal of 2-chlorophenol (CP) in aqueous solution by coconut shell carbon (CSC) using four operational variables (pH of solution, adsorbate concentration, temperature, and contact time), and to investigate their effects on the adsorption process. Accordingly, based on a factorial design, 640 batch experiments were conducted. Nonlinearities in experimental data were checked using Brock-Dechert-Scheimkman (BDS) statistics. Five nonlinear models were constructed to predict the adsorptive removal of CP in aqueous solution by CSC using four variables as input. Performances of the constructed models were evaluated and compared using statistical criteria. BDS statistics revealed strong nonlinearity in experimental data. Performance of all the models constructed here was satisfactory. Radial basis function network (RBFN) and multilayer perceptron network (MLPN) models performed better than generalized regression neural network, support vector machines, and gene expression programming models. Sensitivity analysis revealed that the contact time had highest effect on adsorption followed by the solution pH, temperature, and CP concentration. The study concluded that all the models constructed here were capable of capturing the nonlinearity in data. A better generalization and predictive performance of RBFN and MLPN models suggested that these can be used to predict the adsorption of CP in aqueous solution using CSC.

Involvement of STAT3, NF-κB and associated downstream molecules before and after the onset of urethane induced lung tumors in mouse.

[Pandey M, Gupta KP. Environ Toxicol Pharmacol. 2012 Sep;34(2):502-11.]

Here authors have shown the alteration of transcription factors STAT3, NF-κB and downstream associated molecules much before the appearance of lung tumor and their response to antitumor agent, inositol hexaphosphate. Histological examination revealed the pathophysiology of the lung tissues and the onset or progression of tumor from 4 or 9 to 24 weeks in terms of tumor volume and the number. Over expression of NF-κB (p50/Rel A), COX-2, STAT3, pSTAT3 (Tyr 705), IL-6 and cyclin D1 also progressed from the time of no tumor to the time of tumor appearance and was reduced in mice drinking 2% IP6. Authors suggest that the alterations of STAT3, NF-κB and downstream associated molecules are critical in the development of lung tumors and can be exploited as possible mechanisms after the exposure. Status of these altered genes before the tumor development suggests their possible use as targets for the tumor control in the predisposed conditions.

Nexrutine(R) inhibits tumorigenesis in mouse skin and induces apoptotic cell death in human squamous carcinoma A431 and human melanoma A375 cells.

[Kumar R, Das M, Ansari KM. Carcinogenesis. 2012 Oct;33(10):1909-18.]

Nexrutine(®) (NX), a herbal extract from *Phellodendron amurense*, has been shown to possess antitumor, antimicrobial, anti-inflammatory and other biological activities. In the present investigation, authors explored the mechanism of chemopreventive/chemotherapeutic efficacy of NX against skin cancer. Single application of NX (1.0mg/mouse) prior to 12-O-tetradecanoylphorbol 13-acetate (TPA) application significantly inhibited TPA-induced skin edema, hyperplasia, thymidine incorporation and ornithine decarboxylase (ODC) activity; expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS); phosphorylation of extracellular signal-regulated kinases (ERK) 1/2, p38 and c-jun N-terminal kinase (JNK) mitogen-activated protein kinases (MAPKs); and activation of I kappa B kinase (IKK), IκBα and nuclear factor-kappa B (NF-κB) in mouse skin. In a two-stage mouse skin tumorigenesis model, it was found that twice-weekly treatment of NX prior to TPA application in 7,12-dimethylbenz[α]anthracene (DMBA)-initiated animals showed reduced tumor incidence, lower tumor body burden and significant delay in latency period compared with DMBA-initiated and TPA-promoted animals. Furthermore, the therapeutic efficacy of NX was assessed against human squamous carcinoma (A431) and human melanoma (A375) cells. A431 and A375 cells treated with NX (2.5-10.0 µg/ml, 48h) showed a decrease in viability and enhanced cell cycle arrest at the G(0)/G(1) phase and apoptosis; however, NX had minimal cytotoxic effect on HaCaT cells and primary

murine keratinocytes, suggesting its high therapeutic index. In addition, NX treatment also modulates the levels of Bax and Bcl-2 proteins along with cytochrome c release, cleavage and enhanced expression of poly (adenosine diphosphate-ribose) polymerase as well as catalytic activities of caspases 3 and 9 in both A431 and A375 cells. Based on *in vivo* and *in vitro* studies, NX could be useful in the management (chemoprevention as well as chemotherapy) of skin cancer.

Association of CYP1A1, GSTM1, and GSTT1 gene polymorphism with risk of oral submucous fibrosis in a section of North Indian population.

[Ghosh T, Gupta S, Bajpai P, Agarwal D, Agarwal M, Gupta OP, Agrawal D. Mol Biol Rep. 2012 Oct;39(10):9383-9.]

Genetic alterations in the genes expressing drug metabolizing enzymes can make an individual susceptible to various cancers. This study detects the polymorphisms at CYP1A1, GSTM1, and GSTT1 genes in a section of North Indian population and determines the susceptibility to oral submucous fibrosis (OSF). In this case-control study one hundred and two OSF patients were genotyped to detect the GSTM1, GSTT1, CYP1A1 polymorphism. Two hundred healthy controls were also included. Genotypes were determined using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) approach. The frequency of GSTM1 and GSTT1 genotype was higher in OSF patients, as compared to controls. A trend risk analysis showed 7.6 fold increase in risk, when both the genes were absent. The frequency of CYP1A1 (m1) and CYP1A1 (m2) genotypes was higher in controls. No polymorphic alleles were detected in the m4 site. CYP1A1 (m1) wild genotype in the absence of GSTM1 null genotype, falls under the highest risk group (OR 3.74). Findings suggest that CYP1A1 (m1) genotype and (m2) genotype singly acts as a protective factor but in the absence of GSTM1 and/or GSTT1 gene significantly alters risk towards OSF.

Safety evaluation of genetically modified mustard (V4) seeds in terms of allergenicity: comparison with native crop.

[Misra A, Kumar S, Verma AK, Chanana NP, Das M, Dhawan V, Dwivedi PD. GM Crops Food. 2012 Oct-Dec;3(4):273-82.]

Genetically modified (GM) mustard line (V4) with increased carotenoid content was compared with native mustard to find the difference in allergenic potential, if any. Simulated gastric fluid (SGF) digestibility of crude protein extract from GM as well as its native counterpart mustard crop was envisaged to understand the intended or unintended changes in GM crop along with IgE immunoblotting. BALB/c mice were used as model for allergenicity studies for monitoring total and specific IgE, specific IgG1, histamine level, histopathology, and systemic anaphylaxis score. Allergenicity of mustard was checked in humans by clinical history, skin prick test and IgE levels. Similar results were evident by significant increase in total IgE, specific IgE, IgG1, histamine levels, in GM and native mustard in comparison to control group. Prominent anaphylactic symptoms (score 2: 60%; score 3: 20%; score 4: 20% in native mustard and score 2: 40%; score 3: 40%; score 4: 20% in GM mustard) and eruptive histopathological changes were observed in both GM and native mustard when compared with controls. One protein of approximately 16 kDa was found stable up to 1 h in both GM as well as non GM mustard. IgE immunoblotting detected three protein components of approximately 29, 24 and 16 kDa in both GM and non GM varieties. Collectively, data demonstrate substantially equivalent allergic responses against GM as well as its native counterpart. Therefore, the GM mustard may be as safe as its native counterpart with reference to allergenic responses.

Reduction of Chromium-VI by Chromium Resistant Lactobacilli: A Prospective Bacterium for Bioremediation.

[Mishra R, Sinha V, Kannan A, Upreti RK. Toxicol Int. 2012 Jan;19(1):25-30.]

Chromium is a toxic heavy metal, which primarily exists in two inorganic forms, Cr (VI) and Cr (III). Highly soluble hexavalent chromium is carcinogenic due to its oxidizing nature. It is well established that the intestinal bacteria including Lactobacilli have regulatory effect on intestinal homeostasis and a breakdown in the relationship between intestinal cells and bacteria results in the manifestation of gastrointestinal (GI) disorders. In this study Cr (VI) resistance was developed in Lactobacillus strains and the reduction of Cr (VI) was evaluated. All resistant strains showed similarities with their respective normal strains and did not acquire resistance to various antibiotics. A complete bacterial reduction of 32ppm Cr (VI) was observed within 6 to 8 hours. The presence of chromate reducing enzyme have also been established following the partial purification (2 to 5 fold) and characterization of chromate reductase in Lactobacillus strains. The chromate reductase of our strains showed optimum activity at pH 6.0 and 30°C. As per the knowledge; these strains are fast in Cr (VI) reduction than any other known bacteria. The results suggest that chromate- resistant Lactobacillus strains would be useful for chromium detoxification from GI-tract as well as for bioremediation of hexavalent chromium from contaminated environment.

Expression and inducibility of cytochrome P450s (CYP1A1, 2B6, 2E1, 3A4) in human cord blood CD34(+) stem cell-derived differentiating neuronal cells.

[Singh AK, Kashyap MP, Jahan S, Kumar V, Tripathi VK, Siddiqui MA, Yadav S, Khanna VK, Das V, Jain SK, Pant AB. Toxicol Sci. 2012 Oct;129(2):392-410.]

The status of xenobiotic metabolism in developing human brain cells is not known. The reason is nonavailability of developing human fetal brain. Authors investigated the applicability of the plasticity potential of human umbilical cord blood stem cells for the purpose. Characterized hematopoietic stem cells are converted into neuronal subtypes in eight days. The expression and substrate-specific catalytic activity of the cytochrome P450s (CYPs) CYP1A1 and 3A4 increased gradually till day 8 of differentiation, whereas CYP2B6 and CYP2E1 showed highest expression and activity at day 4. There was no significant increase in the expression of CYP regulators, namely, aryl hydrocarbon receptor (AHR), constitutive androstane receptor (CAR), pregnane X receptor (PXR), and glutathione-S-transferase (GSTP1-1) during differentiation. Differentiating cells showed significant induction in the expression of CYP1A1, 2B6, 2E1, 3A4, AHR, CAR, PXR, and GSTP1-1 when exposed to rifampin, a known universal inducer of CYPs. The xenobiotic-metabolizing capabilities of these differentiating cells were confirmed by exposing them to the organophosphate pesticide monocrotophos (MCP), a known developmental neurotoxicant, in the presence and absence of a universal inhibitor of CYPs-cimetidine. Early-differentiating cells (day 2) were found to be more vulnerable to xenobiotics than mature well-differentiated cells. For the first time, authors reported significant expression and catalytic activity of selected CYPs in human cord blood hematopoietic stem cell-derived neuronal cells at various stages of maturity. They also confirm significant induction in the expression and catalytic activity of selected CYPs in human cord blood stem cell-derived differentiating neuronal cells exposed to known CYP inducers and MCP.

Particulate matter concentration in ambient air and its effects on lung functions among residents in the National Capital Region, India.

[Kesavachandran C, Pangtey BS, Bihari V, Fareed M, Pathak MK, Srivastava AK, Mathur N. Environ Monit Assess. 2013 Feb;185(2):1265-72. doi: 10.1007/s10661-012-2630-0. (Epub 2012 Apr 22)]

The World Health Organization has estimated that air pollution is responsible for 1.4 % of all deaths and 0.8 % of disability-adjusted life years. NOIDA, located at the National Capital Region, India, was declared as one of the critically air-polluted areas by the Central Pollution Control Board of the Government of India. Studies on the relationship of reduction in lung functions of residents living in areas with higher concentrations of particulate matter (PM) in ambient air were inconclusive since the subjects of most of the studies are hospital admission cases. Very few studies, including one from India, have shown the relationship of PM concentration and its effects of lung functions in the same location. Hence, a cross-sectional study was undertaken to study the effect of particulate matter concentration in ambient air on the lung functions of residents living in a critically air-polluted area in India. PM concentrations in ambient air (PM(1,) PM(2.5)) were monitored at residential locations and identified locations with higher (NOIDA) and lower concentrations (Gurgaon). Lung function tests (FEV(1), PEFR) were conducted using a spirometer in 757 residents. Both air monitoring and lung function tests were conducted on the same day. Significant negative linear relationship exists between higher concentrations of PM(1) with reduced FEV(1) and increased concentrations of PM(2.5) with reduced PEFR and FEV(1). The study shows that reductions in lung functions (PEFR and FEV(1)) can be attributed to higher particulate matter concentrations in ambient air. Decline in airflow obstruction in subjects exposed to high PM concentrations can be attributed to the fibrogenic response and associated airway wall remodeling. The study suggests the intervention of policy makers and stake holders to take necessary steps to reduce the emissions of PM concentrations, especially PM(1,) PM(2.5), which can lead to serious respiratory health concerns in residents.

Allethrin-induced genotoxicity and oxidative stress in Swiss albino mice.

[Srivastava AK, Srivastava PK, Al-Khedhairy AA, Musarrat J, Shukla Y. Mutat Res. 2012 Aug 30;747(1):22-8.]

Allethrin ($C_{19}H_{26}O_3$) is non-cyano-containing pyrethroid insecticide that is used extensively for controlling flies and mosquitoes. Apart from its neurotoxic effects in non-target species, allethrin is reported to be mutagenic in bacterial systems. In this study, authors observed oxidative damage-mediated genotoxicity caused by allethrin in Swiss albino mice. The genotoxic potential of allethrin was evaluated using chromosome aberrations (CAs) and a micronuclei (MN) induction assay as genetic end-points. The oral intubation of allethrin (25 and 50mg/kg b.wt.) significantly induces CAs and MN in mouse bone marrow cells. The DNA-damaging potential of allethrin was estimated in mouse liver using the DNA alkaline unwinding assay

(DAUA) and by measuring the levels of 8-hydroxy-2'-deoxy-guanosine (8-OH-dG). Furthermore, a dose-dependent increase in reactive oxygen species (ROS) generation and lipid peroxidation (LPO), with a concurrent decrease in superoxide dismutase (SOD) and catalase, confirm its pro-oxidant potential. The DNA-damaging potential of allethrin was found to be mediated through the modulation of p53, p21, GADD45α and MDM-2. These results confirm the genotoxic and the pro-oxidant potential of allethrin in Swiss albino mice.

Similarities in diesel exhaust particles induced alterations in expression of cytochrome P-450 and glutathione S-transferases in rat lymphocytes and lungs.

[Srivastava A, Yadav S, Sharma A, Dwivedi UN, Flora SJ, Parmar D. Xenobiotica. 2012 Jul;42(7):624-32.]

Freshly prepared peripheral blood lymphocytes (PBL) are known to express cytochrome P450s (CYPs) and glutathione S-transferases (GSTs) involved in the bioactivation and detoxification of organic components of diesel exhaust particles (DEPs). To validate that blood lymphocyte expression profiles could be used as a biomarker to predict exposure to vehicular emissions, similarities in the alterations in the mRNA expression of CYPs and GSTs were studied in PBL and lungs of rats exposed to DEPs. Adult male Wistar rats were treated transtracheally with different doses of DEPs (3.75- or 7.5- or 15- or 30-mg/kg b.wt.). The animals were anaesthetized after 24h and blood was drawn and lungs were taken out and processed. DEP produced a similar pattern of increase in the mRNA expression of CYPs (CYP1A1, 1A2, 1B1, 2E1), associated arylhydrocarbon receptor (Ahr) and arylhydrocarbon nuclear translocator (Arnt) and GSTs (GSTPi, GSTM1 and GSTM2) at all the doses in lungs and PBL. The protein expression of CYP1A1/1A2 and 2E1 and catalytic activity of CYPs and GSTs also showed a similar pattern of increase in blood lymphocyte and in lungs isolated from DEP treated rats. Data indicating similarities in the alterations in the expression of carcinogen metabolizing CYPs and GSTs in PBL with the lung enzymes suggests the suitability of using expression profiles of blood lymphocyte CYPs and GSTs as a biomarker to predict exposure to vehicular emissions.

Achievement

Among the leading 70 research papers from CSIR in its 70 years history there are three papers from IITR. The most notable point is that a research paper by Dr Poonam Kakkar published in 1984 was **adjudged the highest cited research paper** (ranked first among top 70) in the history of CSIR (1942-2012) with total citations being **1362** at present as per SCOPUS data base.

She was felicitated for this achievement by **CSIR-NISCAIR** in a function held on 17th October 2012. Their findings declared that there are only **36 papers from India which have crossed 1000 citation mark** and her paper happens to be one of them.

The founder editor of Ind. J. Biochem. Biophys honouring Dr Poonam Kakkar

- **Kakkar P**, Das B and Viswanathan PN (1984). A modified spectrophotometric assay of superoxide dismutase. Ind. J. Biochem. Biophys., 21, 130-132.

Two more papers from Dr KP Singh's group of IITR also appeared in this list they are:

- Mohan D, Singh KP (2002). Single –and multi-component adsorption of cadmium and zinc using activated carbon derived from bagasse-an agriculture waste, Water Research, 36(9), 2002, 2304–2318
- Kunwar P. Singh, Amrita Malik, Dinesh Mohan, Sarita Sinha (2004). Multivariate statistical techniques for the evaluation of spatial and temporal variations in water quality of Gomti River (India)—a case study, Water Research, 38 (18), 2004, 3980–3992.

TOPIC OF INTEREST

Antioxidant and Redox Signaling : A Glimpse of the Indian Scenario

Polyphenols sensitization potentiates susceptibility of MCF-7 and MDA MB-231 cells to Centchroman.

[Singh N, Zaidi D, Shyam H, Sharma R, Balapure AK. PLoS One. 2012;7(6):e37736]

Polyphenols as "sensitizers" together with cytotoxic drugs as "inducers" cooperate to trigger apoptosis in various cancer cells. Hence, their combination having similar mode of mechanism may be a novel approach to enhance the efficacy of inducers. Additionally, this will also enable to achieve the physiological concentrations facilitating significant increase in the activity at concentrations which the compound can individually provide. Here authors propose that polyphenols (Resveratrol (RES) and Curcumin (CUR)) pre-treatment may sensitize MCF-7/MDA MB-231 (Human Breast Cancer Cells, HBCCs) to Centchroman (CC, antineoplastic agent). 6 h pre-treated cells with 10 µM RES/CUR and 100 µM RES/30 µM CUR doses, followed by 10 µM CC for 18 h were investigated for Ser-167 ER-phosphorylation, cell cycle arrest, redox homeostasis, stress activated protein kinase (SAPKs: JNK and p38 MAPK) pathways and downstream apoptosis effectors. Low dose RES/CUR enhances the CC action through ROS mediated JNK/p38 as well as mitochondrial pathway in MCF-7 cells. However, RES/CUR sensitization enhanced apoptosis in p53 mutant MDA MB-231 cells without/with involvement of ROS mediated JNK/p38 adjunct to Caspase-9. Contrarily, through high dose sensitization in CC treated cells, the parameters remained unaltered as in polyphenols alone. Authors conclude that differential sensitization of HBCCs with low dose polyphenol augments apoptotic efficacy of CC. This may offer a novel approach to achieve enhanced action of CC with concomitant reduction of side effects enabling improved management of hormone-dependent breast cancer.

Microarray analysis and biochemical correlations of oxidative stress responsive genes in retinoblastoma.

[Vandhana S, Lakshmi TS, Indra D, Deepa PR, Krishnakumar S. Curr Eye Res. 2012 Sep;37(9):830-41.]

Oxidative stress, which refers to the biological damage caused by free radicals produced in excess of innate antioxidant defences, is indicated in the ocular cancer retinoblastoma (RB). Here authors have analysed the differential expression of oxidative stress responsive genes in oxidant-induced RB cells, and in RB tumour tissues. The study included cultured RB cells, and four RB tumour tissues. The reactive oxygen species (ROS) levels in Y79 cells and the RB tumour induced by hydrogen peroxide were quantified by Dichlorofluorescein (DCF) fluorescence assay. Authors then analysed the gene expression profile of cultured RB cells induced with hydrogen peroxide (400 µM H_2O_2 for 8 h) by microarray analysis, and the expression of select genes were validated in Y79 cells and RB tumour tissues by real-time PCR analysis. The oxidant-induced RB tumours showed an average increase in ROS levels of 44-fold compared to induced non-neoplastic donor retina. H_2O_2-induced RB cell line showed a 3-fold increase in ROS levels. Microarray analysis on RB cell line induced with H_2O_2 showed differentially regulated genes involved in cellular processes such as: oxidative stress, angiogenesis, lipid metabolism, cell proliferation, and cell signaling pathways. Several up-regulated genes such as SOD, GPX, CAT, CDC25A, CREBBP, JUN, MMP-2, iNOS, CRYAA, RXRA, ACACB and HMGCR were validated by real-time PCR. These results corroborated with the gene expression analysis in RB tumour tissues. Relating the antioxidant gene expression with the clinico-pathologic features of the tumour tissues, authors found that the tumour with invasion of choroid, optic nerve and retinal pigment epithelium, had relatively higher ROS levels and minimal antioxidant gene expression, when compared with the tumour with only choroidal invasion. The study suggests active involvement of redox signaling pathways in the pathogenesis of RB. Consideration of oxidative stress components in the clinical management of RB patients is emphasized.

Role of glutathione in cancer pathophysiology and therapeutic interventions.

[Singh S, Khan AR, Gupta AK. J Exp Ther Oncol. 2012;9(4):303-16.]

Glutathione (GSH) is an important intracellular antioxidant that instills several vital roles within a cell including maintenance of the redox state, drug detoxification, and cellular protection from damage by free radicals, peroxides and toxins. Molecular alterations in the components of the

GSH system in various tumours can lead to increased survival and enhanced tumour drug resistance. Early identification of the importance of intracellular GSH to detoxification reactions has now led to investigating the potential importance that GSH chemistry has on signal transduction, molecular regulation of cellular physiology and regulation of apoptosis pathway. Several therapeutic agents that target this system have been developed and used experimentally and clinically in an attempt to improve cancer chemotherapy. This review highlights different roles played by GSH that finally regulate tumour growth and advances in the use of GSH-based drugs to specifically target this detoxifying system in cancer treatment as a means to increase therapeutic response and decrease chemotherapeutic drug resistance.

Dynamic action of carotenoids in cardioprotection and maintenance of cardiac health.

[Agarwal M, Parameswari RP, Vasanthi HR, Das DK. Molecules. 2012 Apr 23;17(4):4755-69.]

Oxidative stress has been considered universally and undeniably implicated in the pathogenesis of all major diseases, including those of the cardiovascular system. Oxidative stress activate transcriptional messengers, such as nuclear factor-κB, tangibly contributing to endothelial dysfunction, the initiation and progression of atherosclerosis, irreversible damage after ischemic reperfusion, and even arrhythmia, such as atrial fibrillation. Evidence is rapidly accumulating to support the role of reactive oxygen species (ROS) and reactive nitrogen species (RNS) as intracellular signaling molecules. Despite this connection between oxidative stress and cardiovascular disease (CVD), there are currently no recognized therapeutic interventions to address this important unmet need. Antioxidants that provide a broad, "upstream" approach via ROS/RNS quenching or free radical chain breaking seem an appropriate therapeutic option based on epidemiologic, dietary, and *in vivo* animal model data. Short-term dietary intervention trials suggest that diets rich in fruit and vegetable intake lead to improvements in coronary risk factors and reduce cardiovascular mortality. Carotenoids are such abundant, plant-derived, fat-soluble pigments that functions as antioxidants. They are stored in the liver or adipose tissue, and are lipid soluble by becoming incorporated into plasma lipoprotein particles during transport. For these reasons, carotenoids may represent one plausible mechanism by which fruits and vegetables reduce the risk of chronic diseases as cardiovascular disease (CVD). This review paper outlines the role of carotenoids in maintaining cardiac health and cardio-protection mediated by several mechanisms including redox signaling.

Diospyrin derivative, an anticancer quinonoid, regulates apoptosis at endoplasmic reticulum as well as mitochondria by modulating cytosolic calcium in human breast carcinoma cells.

[Kumar B, Kumar A, Ghosh S, Pandey BN, Mishra KP, Hazra B. Biochem Biophys Res Commun. 2012 Jan 13;417(2):903-9.]

Diospyrin diethylether (D7), a bisnaphthoquinonoid derivative, exhibited an oxidative stress-dependent apoptosis in several human cancer cells and tumour models. The present study was aimed at evaluation of the increase in cytosolic calcium [Ca^{2+}](c) leading to the apoptotic cell death triggered by D7 in MCF7 human breast carcinoma cells. A phosphotidylcholine-specific phospholipase C (PC-PLC) inhibitor, viz. U73122, and an antioxidant, viz. N-acetylcysteine, could significantly prevent the D7-induced rise in [Ca^{2+}](c) and PC-PLC activity. Using an endoplasmic reticulum (ER)-Ca^{2+} mobilizer (thapsigargin) and an ER-IP3R antagonist (heparin), results revealed ER as a major source of [Ca^{2+}](c) which led to the activation of calpain and caspase12, and cleavage of fodrin. These effects including apoptosis were significantly inhibited by the pretreatment of Bapta-AM (a cell permeable Ca^{2+}-specific chelator), or calpeptin (a calpain inhibitor). Furthermore, D7-induced [Ca^{2+}](c) was found to alter mitochondrial membrane potential and induce cytochrome c release, which was inhibited by either Bapta-AM or ruthenium red (an inhibitor of mitochondrial Ca^{2+} uniporter). Thus, these results provided a deeper insight into the D7-induced redox signaling which eventually integrated the calcium-dependent calpain/caspase12 activation and mitochondrial alterations to accentuate the induction of apoptotic cell death.

Probiotic *Enterococcus lactis* IITRHR1 protects against acetaminophen-induced hepatotoxicity.

[Sharma S, Chaturvedi J, Chaudhari BP, Singh RL, Kakkar P. Nutrition. 2012 Feb;28(2):173-81.]

Acetaminophen (APAP), an antipyretic/analgesic drug, is reported to cause toxicity on overdose. Dietary supplements are currently being explored to decrease toxicity. In the present study, the protective effect of probiotic *Enterococcus lactis* IITRHR1 was evaluated at different doses (10(7), 10(8), and 10(9) colony-forming units) against APAP-induced liver damage. Male Wistar rats were administered APAP (1 g/kg of body weight orally) for 14 d, and hepatotoxicity was assessed by marker enzymes in

serum and observation of histopathologic changes. Rats were pretreated with probiotic *E. lactis* IITRHR1 for 7 d and modulation of antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase), redox ratio, and ferric reducing antioxidant power was assessed. Oxidative damage by APAP to membrane lipids, proteins, and DNA was also observed. Involvement of Bax, Bcl2, cytochrome c (pro-/anti-apoptotic proteins), caspases, and their modulation was assessed by immunoblot analysis and reverse transcriptase polymerase chain reaction. The *E. lactis* IITRHR1 pretreatment lowered the level of biomarkers of hepatotoxicity in serum. A significant increase was observed in the level of antioxidant enzymes and redox ratio and decreased oxidative damage to membrane lipids and proteins. Probiotic *E. lactis* IITRHR1 also modulated key apoptotic/anti-apoptotic proteins such as cytochrome-c, Bcl2, Bax, expression of caspases, and resultant DNA damage. Probiotic strain *E. lactis* IITRHR1 was found to have antioxidant capacity and afforded protection against APAP-induced hepatotoxicity by modulating antioxidant status, pro-/anti-apoptotic proteins, caspases, and DNA damage.

Redox homeostasis in mycobacteria: the key to tuberculosis control?

[Kumar A, Farhana A, Guidry L, Saini V, Hondalus M, Steyn AJ. Expert Rev Mol Med. 2011 Dec 16;13:e39.]

Mycobacterium tuberculosis (Mtb) is a metabolically flexible pathogen that has the extraordinary ability to sense and adapt to the continuously changing host environment experienced during decades of persistent infection. Mtb is continually exposed to endogenous reactive oxygen species (ROS) as part of normal aerobic respiration, as well as exogenous ROS and reactive nitrogen species (RNS) generated by the host immune system in response to infection. The magnitude of tuberculosis (TB) disease is further amplified by exposure to xenobiotics from the environment such as cigarette smoke and air pollution, causing disruption of the intracellular prooxidant-antioxidant balance. Both oxidative and reductive stresses induce redox cascades that alter Mtb signal transduction, DNA and RNA synthesis, protein synthesis and anti-mycobacterial drug resistance. As reviewed in this article, Mtb has evolved specific mechanisms to protect itself against endogenously produced oxidants, as well as defend against host and environmental oxidants and reductants found specifically within the microenvironments of the lung. Maintaining an appropriate redox balance is critical to the clinical outcome because several antimycobacterial prodrugs are only effective upon bioreductive activation. Proper homeostasis of oxido-reductive systems is essential for Mtb survival, persistence and subsequent reactivation. The progress and remaining deficiencies in understanding Mtb redox homeostasis are also discussed.

Update on the chemopreventive effects of ginger and its phytochemicals.

[Baliga MS, Haniadka R, Pereira MM, D'Souza JJ, Pallaty PL, Bhat HP, Popuri S. Crit Rev Food Sci Nutr. 2011 Jul;51(6):499-523.]

The rhizomes of *Zingiber officinale* Roscoe (Zingiberaceae), commonly known as ginger, is one of the most widely used spice and condiment. It is also an integral part of many traditional medicines and has been extensively used in Chinese, Ayurvedic, Tibb-Unani, Srilankan, Arabic, and African traditional medicines, since antiquity, for many unrelated human ailments including common colds, fever, sore throats, vomiting, motion sickness, gastrointestinal complications, indigestion, constipation, arthritis, rheumatism, sprains, muscular aches, pains, cramps, hypertension, dementia, fever, infectious diseases, and helminthiasis. The putative active compounds are nonvolatile pungent principles, namely gingerols, shogaols, paradols, and zingerone. These compounds are some of the extensively studied phytochemicals and account for the antioxidant, anti-inflammatory, antiemetic, and gastroprotective activities. A number of preclinical investigations with a wide variety of assay systems and carcinogens have shown that ginger and its compounds possess chemopreventive and antineoplastic effects. A number of mechanisms have been observed to be involved in the chemopreventive effects of ginger. The cancer preventive activities of ginger are supposed to be mainly due to free radical scavenging, antioxidant pathways, alteration of gene expressions, and induction of apoptosis, all of which contribute towards decrease in tumour initiation, promotion, and progression. This review provides concise information from preclinical studies with both cell culture models and relevant animal studies by focusing on the mechanisms responsible for the chemopreventive action. The conclusion describes directions for future research to establish its activity and utility as a human cancer preventive and therapeutic drug. The above-mentioned mechanisms of ginger seem to be promising for cancer prevention; however, further clinical studies are warranted to assess the efficacy and safety of ginger.

Arsenic-induced oxidative stress and its reversibility.

[Flora SJ. Free Radic Biol Med. 2011 Jul 15;51(2):257-81.]

This review summarizes the literature describing the

molecular mechanisms of arsenic-induced oxidative stress, its relevant biomarkers, and its relation to various diseases, including preventive and therapeutic strategies. Arsenic alters multiple cellular pathways including expression of growth factors, suppression of cell cycle checkpoint proteins, promotion of and resistance to apoptosis, inhibition of DNA repair, alterations in DNA methylation, decreased immunosurveillance, and increased oxidative stress, by disturbing the pro/antioxidant balance. These alterations play prominent roles in disease manifestation, such as carcinogenicity, genotoxicity, diabetes, cardiovascular and nervous systems disorders. The exact molecular and cellular mechanisms involved in arsenic toxicity are rather unrevealed. Arsenic alters cellular glutathione levels either by utilizing this electron donor for the conversion of pentavalent to trivalent arsenicals or directly binding with it or by oxidizing glutathione via arsenic-induced free radical generation. Arsenic forms oxygen-based radicals ($OH^{\bullet}$, $O_2^{\bullet-}$) under physiological conditions by directly binding with critical thiols. As a carcinogen, it acts through epigenetic mechanisms rather than as a classical mutagen. The carcinogenic potential of arsenic may be attributed to activation of redox-sensitive transcription factors and other signaling pathways involving nuclear factor κB, activator protein-1, and p53. Modulation of cellular thiols for protection against reactive oxygen species has been used as a therapeutic strategy against arsenic. N-acetylcysteine, α-lipoic acid, vitamin E, quercetin, and a few herbal extracts show prophylactic activity against the majority of arsenic-mediated injuries in both *in vitro* and *in vivo* models. This review also updates the reader on recent advances in chelation therapy and newer therapeutic strategies suggested to treat arsenic-induced oxidative damage.

Soy isoflavone genistein induces cell death in breast cancer cells through mobilization of endogenous copper ions and generation of reactive oxygen species.

[Ullah MF, Ahmad A, Zubair H, Khan HY, Wang Z, Sarkar FH, Hadi SM. Mol Nutr Food Res. 2011 Apr;55(4):553-9.]

Worldwide geographical variation in cancer incidence indicates a correlation between dietary habits and cancer risk. Epidemiological studies have suggested that populations with high isoflavone intake through soy consumption have lower rates of breast, prostate, and colon cancer. Isoflavone genistein in soybean is considered a potent chemopreventive agent against cancer. Although several mechanisms have been proposed, a clear anticancer action mechanism of genistein is still not known. Here, authors show that the cytotoxic action of genistein against breast cancer cells involves mobilization of endogenous copper. Further, whereas the copper specific chelator neocuproine is able to inhibit the apoptotic potential of genistein, the molecules which specifically bind iron (desferroxamine mesylate) and zinc (histidine) are relatively ineffective in causing such inhibition. Also, genistein-induced apoptosis in these cells is inhibited by scavengers of reactive oxygen species (ROS) implicating ROS as effector elements leading to cell death. As copper levels are known to be considerably elevated in almost all types of cancers, in this proof-of-concept study authors show that genistein is able to target endogenous copper leading to prooxidant signaling and consequent cell death. Authors believe that such a mechanism explains the anticancer effect of genistein as also its preferential cytotoxicity towards cancer cells.

Matrix metalloproteinases in health and disease: regulation by melatonin.

[Swarnakar S, Paul S, Singh LP, Reiter RJ. J Pineal Res. 2011 Jan;50(1):8-20.]

Matrix metalloproteinases (MMPs) are part of a super family of metal-requiring proteases that play important roles in tissue remodeling by breaking down proteins in the extracellular matrix that provides structural support for cells. The intricate balance in protease/anti-protease stoichiometry is a contributing factor in a number of diseases. Melatonin possesses multifunctional bioactivities including antioxidative, anti-inflammatory, endocrinologic and behavioural effects. As melatonin affects the redox status of tissues, the association of reactive oxygen species (ROS) with tissue injury under different circumstances may be mitigated by melatonin. Redox signaling is expanding into all areas of basic and clinical sciences, and this timely review focuses on the topic of regulation of MMP activities by melatonin. This is a rapidly growing field. Accumulating evidence indicates that oxidative stress plays an important role in regulating the activities of MMPs that are involved in various cellular processes such as cellular proliferation, angiogenesis, apoptosis, invasion and metastasis. This review offers sections on MMPs, melatonin, major physiological and pathophysiological conditions in the context to MMPs, followed by redox signaling mechanisms that are known to influence the cellular processes. Finally, authors discuss the emerging molecular mechanisms relevant to regulatory actions of melatonin on the activities of MMPs. The possibility that melatonin might have therapeutic significance via regulation of MMPs may be a novel approach in the treatment of some diseases.

Quercetin regulates oxidized LDL induced inflammatory changes in human PBMCs by modulating the TLR-NF-κB signaling pathway.

[Bhaskar S, Shalini V, Helen A. Immunobiology. 2011 Mar;216(3):367-73.]

Toll-like receptors (TLRs) have been shown to play a pivotal role in both innate and adaptive immune responses. TLR family is the essential recognition and signaling component of mammalian host defence. Both genetic and biochemical data support a common signaling pathway that finally leads to the activation of NF-κB and induction of the cytokines and co-stimulatory molecules required for the activation of the adaptive immune response. The present study was designed to examine the involvement of TLR2 and TLR4 in the oxidized LDL induced inflammation in human PBMCs and the effect of flavonoid quercetin on TLR-NF-κB signaling mechanism. LDL was isolated from human plasma and oxidation of LDL was done by incubating with 10 μM $CuSO_4$ overnight at 37°C. The isolated human PBMCs in culture were used as the model system. 50 μg/ml ox-LDL treatments significantly up regulated TLR2 and TLR4 expression in isol human PBMCs after 24 h of culture and this was down regulated by quercetin at 25 μM concentration. ox-LDL caused a significant activation of NF-κB as evidenced by the detection of enhanced p65 subunit in nuclear extracts. Supplementation of quercetin significantly modulates the NF-κB p65 nuclear translocation. The cytokine IL-6 production was significantly increased in ox-LDL treated group and was decreased by quercetin treatment. Quercetin mediated reduction of TLR2 and TLR4 expression and the inhibition of nuclear translocation of NF-κB p65 in turn decreased the inflammatory enzymes like 5-LOX and COX and also decreased the mRNA expression of inducible enzymes like COX-2 and iNOS. Quercetin inhibited the ox-LDL induced TLR2 and TLR4 expression at mRNA level and modulated the TLR-NF-κB signaling pathway thereby inhibited the cytokine production and down regulated the activity of inflammatory enzymes thus have protective effect against the ox-LDL induced inflammation in PBMCs.

Alteration in mitochondrial thiol enhances calcium ion dependent membrane permeability transition and dysfunction in vitro: a cross-talk between mtThiol, Ca(2+), and ROS.

[Singh BK, Tripathi M, Pandey PK, Kakkar P. Mol Cell Biochem. 2011 Nov;357(1-2):373-85.]

Mitochondrial permeability transition (MPT) and dysfunctions play a pivotal role in many patho-physiological and toxicological conditions. The interplay of mitochondrial thiol (mtThiol), MPT, Ca(2+) homeostasis, and resulting dysfunctions still remains controversial despite studies by several research groups. Present study was undertaken to ascertain the correlation between Ca(2+) homeostasis, mtThiol alteration and reactive oxygen species (ROS) in causing MPT leading to mitochondrial dysfunction. mtThiol depletion significantly enhanced Ca(2+) dependent MPT (swelling) and depolarization of mitochondria resulting in release of pro-apoptotic proteins like Cyt c, AIF, and EndoG. mtThiol alteration and Ca(2+) overload caused reduced mitochondrial electron flow, oxidation of pyridine nucleotides (NAD(P)H) and significantly enhanced ROS generation (DHE and DCFH-DA fluorescence). Studies with MPT inhibitor (Cyclosporin A), Ca(2+) uniport blocker (ruthenium red) and Ca(2+) chelator (BAPTA) indicated that mitochondrial dysfunction was more pronounced under dual stress of altered mtThiol and Ca(2+) overload in comparison with single stress of excessive Ca(2+). Transmission electron microscopy confirmed the changes in mitochondrial integrity under stress. Findings suggest that the Ca(2+) overload itself is not solely responsible for structural and functional impairment of mitochondria. A multi-factorial cross-talk between mtThiol, Ca(2+) and ROS is responsible for mitochondrial dysfunction. Furthermore, minor depletion of mtThiol was found to be an important factor along with Ca(2+) overload in triggering MPT in isolated mitochondria, tilting the balance towards disturbed functionality.

Modulation of Bax/Bcl-2 and caspases by probiotics during acetaminophen induced apoptosis in primary hepatocytes.

[Sharma S, Singh RL, Kakkar P. Food Chem Toxicol. 2011 Apr;49(4):770-9.]

Oxidative stress is an important factor in drug induced hepatotoxicity and antioxidants from natural sources have potential to ameliorate it. The present study was aimed to investigate cyto-protective potential of probiotic *Enterococcus lactis* IITRHR1 (El(SN)) and Lactobacillus acidophilus MTCC447 (La(SN)) lysate against acetaminophen (APAP) induced hepatotoxicity. Cultured rat hepatocytes pretreated with El(SN)/La(SN) showed higher cell viability under APAP stress. Pre-treatment with El(SN,) restored glutathione level and reduced ROS generation significantly which are major biomarkers of oxidative stress. It also reduced NO

level, MDA formation and enhanced SOD activity. Pre-treatment with probiotic lysates significantly inhibited the translocation of pro-apoptotic protein (Bax), enhanced anti-apoptotic (Bcl-2) protein levels and prevented release of cyt c to cytosol; suggesting involvement of mitochondrial proteins in protection against APAP induced oxidative cellular damage. Loss in mitochondrial membrane potential due to APAP treatment was prevented in the presence of probiotic lysates. Protective action of El(SN)/La(SN) pretreatment was further supported by prevention of procaspase-3 activation, DNA fragmentation and chromatin condensation, in turn inhibiting APAP induced apoptotic cell death. The results indicate that probiotic preparations modulate crucial end points of oxidative stress induced apoptosis and may be used for management of drug induced liver injury.

Nrf2-ARE stress response mechanism: a control point in oxidative stress-mediated dysfunctions and chronic inflammatory diseases.

[Singh S, Vrishni S, Singh BK, Rahman I, Kakkar P. Free Radic Res. 2010 Nov;44(11):1267-88.]

Nrf2, a redox sensitive transcription factor, plays a pivotal role in redox homeostasis during oxidative stress. Nrf2 is sequestered in cytosol by an inhibitory protein Keap1 which causes its proteasomal degradation. In response to electrophilic and oxidative stress, Nrf2 is activated, translocates to nucleus, binds to antioxidant response element (ARE), thus upregulates a battery of antioxidant and detoxifying genes. This function of Nrf2 can be significant in the treatment of diseases, such as cancer, neurodegenerative, cardiovascular and pulmonary complications, where oxidative stress causes Nrf2 derangement. Nrf2 upregulating potential of phytochemicals has been explored, in facilitating cure for various ailments while, in cancer cells, Nrf2 upregulation causes chemoresistance. Therefore, Nrf2 emerges as a key regulator in oxidative stress-mediated diseases and Nrf2 silencing can open avenues in cancer treatment. This review summarizes Nrf2-ARE stress response mechanism and its role as a control point in oxidative stress-induced cellular dysfunctions including chronic inflammatory diseases.

DJ-1 loss by glutaredoxin but not glutathione depletion triggers Daxx translocation and cell death.

[Saeed U, Ray A, Valli RK, Kumar AM, Ravindranath V. Antioxid Redox Signal. 2010 Jul 15;13(2):127-44.]

Environmental and genetic causes are implicated in the etiopathogenesis of Parkinson's disease (PD), a neurodegenerative movement disorder. DJ-1, a putative gene recessively linked to early onset PD, functions as an antioxidant, transcriptional co-activator, and molecular chaperone. Authors examined DJ-1 status following global perturbation of protein thiol homeostasis by depleting cellular antioxidant glutathione or downregulating glutaredoxin 1, a thiol disulfide oxidoreductase, wherein both paradigms generate oxidative stress. While these perturbations did not affect expression of DJ-1 mRNA, down regulation of glutaredoxin 1 but not glutathione depletion caused loss of DJ-1 protein, translocation of Daxx (a death-associated protein) from nucleus, and cell death. Overexpression of wild-type DJ-1, but not the cysteine mutants, prevented Daxx translocation and cytotoxicity. Protease inhibitors prevented constitutive DJ-1 loss. Residual DJ-1 was present in reduced state, indicating that DJ-1 when oxidized was degraded through proteolysis. Thus, loss of DJ-1 occurring through its oxidative modification and subsequent proteolysis mediated through dysregulation of thiol disulfide oxidoreductase may contribute to pathogenesis of sporadic PD, thus providing a link between environmental challenges and constitutive levels of this vital protein.

Role of oxidation-triggered activation of JNK and p38 MAPK in black tea polyphenols induced apoptotic death of A375 cells.

[Bhattacharya U, Halder B, Mukhopadhyay S, Giri AK. Cancer Sci. 2009 Oct;100(10):1971-8.]

Theaflavins (TF) and thearubigins (TR) are the major polyphenols of black tea. Author's previous study revealed that TF- and TR-induced apoptosis of human malignant melanoma cells (A375) is executed via a mitochondria-mediated pathway. In present study authors observed the role of the three most important MAPK (ERK, JNK, and p38) in TF- and TR-induced apoptosis. TF and TR treatment of A375 cells led to sustained activation of JNK and p38 MAPK but not ERK, suggesting that JNK and p38 are the effector molecules in this polyphenol-induced cell death. This idea was further supported by subsequent studies in which JNK and p38 activation was inhibited by specific inhibitors. Significant inhibition was found in TF- and TR-treated A375 cell death pretreated with JNK- or p38-specific inhibitors only. Further, they have found that TF and TR treatment induces a time-dependent increase in intracellular reactive oxygen species generation in A375 cells. Interestingly, treatment with the antioxidant N-acetyl cystein inhibits TF- and TR-induced JNK and p38 activation as well as induction of cell death in A375 cells. Authors also provide

evidence demonstrating the critical role of apoptosis signal-regulating kinase 1 in TF- and TR-induced apoptosis in A375 cells. Taken together results strongly suggest that TF and TR induce apoptotic death of A375 cells through apoptosis signal-regulating kinase 1, MAPK kinase, and the JNK-p38 cascade, which is triggered by N-acetyl cystein intracellular oxidative stress.

Mitochondria: a hub of redox activities and cellular distress control.

[Kakkar P, Singh BK. Mol Cell Biochem. 2007 Nov;305(1-2):235-53.]

In their reductionist approach in unraveling phenomena inside the cell, scientists in recent times have focused attention to mitochondria. An organelle with peculiar evolutionary history and organization, it is turning out to be an important cell survival switch. Besides controlling bioenergetics of a cell it also has its own genetic machinery which codes 37 genes. It is a major source of generation of reactive oxygen species, acts as a safety device against toxic increases of cytosolic Ca^{2+} and its membrane permeability transition is a critical control point in cell death. Redox status of mitochondria is important in combating oxidative stress and maintaining membrane permeability. Importance of mitochondria in deciding the response of cell to multiplicity of physiological and genetic stresses, inter-organelle communication, and ultimate cell survival is constantly being unraveled and discussed in this review. Mitochondrial events involved in apoptosis and necrotic cell death, such as activation of Bcl-2 family proteins, formation of permeability transition pore, release of cytochrome c and apoptosis inducing factors, activation of caspase cascade, and ultimate cell death is the focus of attention not only for cell biologists, but also for toxicologists in unraveling stress responses. Mutations caused by ROS to mitochondrial DNA, its inability to repair it completely and creation of a vicious cycle of mutations along with role of Bcl-2 family genes and proteins has been implicated in many diseases where mitochondrial dysfunctions play a key role. New therapeutic approaches toward targeting low molecular weight compounds to mitochondria, including antioxidants is a step toward nipping the stress in the bud.

Regulation of ceruloplasmin in human hepatic cells by redox active copper: identification of a novel AP-1 site in the ceruloplasmin gene.

[Das D, Tapryal N, Goswami SK, Fox PL, Mukhopadhyay CK. Biochem J. 2007 Feb 15;402(1):135-41.]

Cp (ceruloplasmin), a copper containing plasma protein, mainly synthesized in the liver, is known to be functional between the interface of iron and copper metabolism. Authors have reported previously that Cp is regulated by cellular iron status, but the process of the regulation of Cp by copper still remains a subject for investigation. In the present paper, authors show that PDTC (pyrrolidine dithiocarbamate), a thiol compound widely known to increase intracellular redox copper, regulates Cp expression in hepatic cells by a copper-dependent transcriptional mechanism. To find out the mechanism of induction, chimeric constructs of the Cp 5'-flanking region driving luciferase were transfected into human hepatic cells. Deletion and mutational analyses showed the requirement of a novel APRE [AP-1 (activator protein-1) responsive element] present about 3.7 kb upstream of the translation initiation site. The role of AP-1 was confirmed by electrophoretic mobility-shift analysis. Western blot and overexpression studies detected the AP-1 as a heterodimer of c-jun and c-fos proteins. The activation of AP-1 was found to be copper-dependent as a specific extracellular chelator bathocuproine disulfonic acid blocked PDTC-mediated induction of AP-1-DNA binding and increased reporter gene activity. Whereas, in a copper-free medium, PDTC failed to activate either AP-1 or Cp synthesis, supplementation of copper could reverse AP-1 activation and Cp synthesis. Authors finding is not only the first demonstration of regulation of Cp by redox copper but may also explain previous findings of increased Cp expression in cancers like hepatocarcinoma, where the intracellular copper level is higher in a redox compromised environment.

Genomic effect of vitamin 'C' and statins within human mononuclear cells involved in atherogenic process.

[Kaul D, Baba MI. Eur J Clin Nutr. 2005 Aug;59(8):978-81.]

Deregulated crosstalk within nuclear receptor/transcription factor family, comprising of peroxisome proliferator-activated receptors (PPARs) and liver X receptor-alpha (LXR-alpha), can give rise to cooperativity between lipid peroxidation and inflammation leading to atherogenic process. The present study addressed to explore the effect of statins and vitamin 'C' on transcriptional expression of genes coding for this nuclear receptor/transcription factor family within mononuclear cells revealed for the first time that both mevastatin and vitamin 'C' have common action in that they significantly downregulate the expression of PPARs (alpha, gamma) genes and upregulate LXR-alpha gene expression as compared to the control. The similar phenomenon was observed in mononuclear cells obtained from coronary heart disease (CHD) patients who were receiving atorvastatin treatment (20 mg HS). Further, the observed upregulatory effect of LXR-alpha gene expression was in conformity with the downregulatory effect of LXR-

alpha on its effector gene matrix metalloproteinase-9. Based on these results, authors propose that LXR-alpha-dependent signaling pathway may be a crucial target for the therapeutic intervention in human CHD, and in addition to statins, vitamin 'C' deserves a close scrutiny for the treatment of CHD.

Apoptosis of lymphocytes induced by chromium(VI/V) is through ROS-mediated activation of Src-family kinases and caspase-3.

[Vasant C, Rajaram R, Ramasami T. Free Radic Biol Med. 2003 Nov 1;35(9):1082-100.]

Mechanistic insights into Cr(VI)-induced carcinogenicity and possible implication of Cr(V) species formed by the redox reactions of chromium-bearing species have attracted interest. Authors have previously demonstrated that when human peripheral blood lymphocytes are exposed to the Cr(V) complexes, viz., sodium bis(2-ethyl-2-hydroxybutyrato)oxochromate(V), Na[Cr(V)O(ehba)(2)] and sodium bis(2-hydroxy-2-methylbutyrato)oxochromate(V), Na[Cr(V)O(hmba)(2)], apoptosis and formation of reactive oxygen species (ROS) are observed. The molecular mechanisms involving cellular signaling pathways leading to apoptosis are addressed in the present study. Treatment of lymphocytes with Na[Cr(V)O(ehba)(2)] and $K_2Cr_2O_7$ leads to the activation of the Src-family protein tyrosine kinases namely, p56(lck), p59(fyn), and p56/53(lyn), which then activates caspase-3, both of which are under the partial influence of ROS. Inhibition of the Src-family tyrosine kinases activity by PP2 and of caspase-3 by Z-DEVD-FMK reverses apoptosis, thereby suggesting their importance. Antioxidants only partially reverse the apoptosis induced by Cr(VI/V), suggesting that pathways other than those induced by ROS cannot be ruled out. Although the complex, Na[Cr(V)O(ehba)(2)] is known to be relatively stable in aqueous solutions, previous studies have shown that the Cr(V) complex, Na[Cr(V)O(ehba)(2)] disproportionates to Cr(VI) and Cr(III) forms at pH 7.4 through complex mechanistic processes. Dynamics studies employing EPR data show that the Cr(V) state in Na[Cr(V)O(ehba)(2)] is relatively more stable in RPMI-1640 medium containing plasma. Formation of ROS during the reaction of redox partners with Na[Cr(V)O(ehba)(2)] is an early event and compares favourably in kinetic terms with the reported rate processes for disproportionation. This investigation presents evidence for the direct implication of Cr(V) in Cr(VI)-induced apoptosis of lymphocytes.

RESEARCH DIGEST

UV Radiation and Skin Cancer: The Science behind Age Restrictions for Tanning Beds

[Environ Health Perspect 120:a308-a313. http://dx.doi.org/10.1289/ehp.120-a308]

Every year, millions of people climb in various states of undress into warm, glowing tanning beds, where during a typical 2- to 15-minute session they will absorb a controlled dose of ultraviolet (UV) radiation at intensity up to two to three times stronger than the sunlight striking the equator at noon. The tanning industry has grown rapidly since the 1980s, rising to an estimated 28 million users in the United States. This rise has been accompanied by an increase in diagnoses of skin cancer.

The reasons behind the rising skin cancer diagnoses remain open to debate. Some experts attribute the rise to more frequent skin cancer screening, whereas others blame environmental and behavioural risk factors, particularly changes in UV exposure. In this latter context, UV-emitting tanning beds—classified as carcinogenic to humans by the International Agency for Research on Cancer (IARC)3—have come under growing scrutiny.

People tan to look healthy, but looks can be deceiving; UV radiation causes all three types of skin cancer. Melanoma, a tumour of the cells that produce the skin pigment melanin, is the rarest but deadliest type, accounting for 75% of skin cancer deaths worldwide. According to the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program, melanoma incidence among U.S. whites (who develop the disease more often than other races) rose

from 8.7 cases per 100,000 people in 1975 to 28 cases per 100,000 in 2009. Most of that increase occurred in older men, who rarely tan indoors. But a closer look at the age-stratified SEER data reveals that melanoma rates among white girls and women aged 15–39 rose by 3.6% per year between 1992 and 2006, compared with a 2% increase per year among boys and men of the same ages.6

Although they're not tracked by SEER, squamous cell carcinoma (SCC) and basal cell carcinoma (BCC)—the other two types of skin cancer—also appear to be on the rise, according to regional studies from the United States and Europe. A recent study by Anne Marie Skellett, a consulting dermatologist at Norfolk and Norwich University Hospital, reveals that BCC diagnoses among people under age 30 in the United Kingdom jumped 145% between 1981 and 2006. Statistics such as these have prompted 33 U.S. states and some municipalities to ban or restrict indoor tanning among children under age 18. California's ban, signed into law in October 2011, was the first, followed by other states have introduced legislation to limit indoor tanning among minors.

Reduced Bacterial Biodiversity is Associated with Increased Allergy

[Environ Health Perspect 120:a304-a304. http://dx.doi.org/10.1289/ehp.120-a304]

Early humans coevolved with an array of microbes and parasites that modern city dwellers no longer encounter. A growing body of evidence suggests that reduced contact with these ancient microbial partners may be helping to fuel an epidemic of inflammatory diseases such as asthma, allergies, multiple sclerosis, type 1 diabetes, and ulcerative colitis—all of which are on the rise in urban populations. Ecology and evolutionary biology professor Ilkka Hanski and his colleagues at the University of Helsinki have observed a link between the environments people inhabit, the diversity of microbes residing on their skin, and their susceptibility to allergic reactions. In a study of teenagers living in urban and rural environments in eastern Finland, Hanski's team used molecular analysis to show that allergic children hosted a less diverse array of bacteria on their skin compared with healthy counterparts. In addition, children living in homes with a greater diversity of native flowers in the yard had a more varied array of microbes on their skin and a lower risk of allergy. The expression of interleukin-10, a key anti-inflammatory cytokine, was positively correlated with abundance of one particular genus, *Acinetobacter*, on skin.

The diversity of plant and animal communities shapes the diversity of microbial communities—and a number of environmental microbes can interact with human immune systems in beneficial ways. "If people lose connection to environmental microbiota, there may be adverse consequences to immunologic tolerance," explains Hanski. The findings fit with the "old friends" hypothesis, which holds that organisms that coexisted with early hominids came to shape human immune responses. Examples include helminths, bacteria common in soils and in the human gut, and viruses such as hepatitis A. "These organisms had to be tolerated, because attacking them would lead to pointless tissue-damaging inflammation," says Graham Rook, emeritus professor of medical microbiology at the Centre for Clinical Microbiology at University College London. Some organisms that coexist with humans may produce molecules that activate regulatory T lymphocytes, which block inflammation. For instance, in experimental animal models, an array of chronic inflammatory diseases, including type 1 diabetes, colitis, arthritis, and asthma, can be blocked by infection with helminth parasites. A study of thousands of children living in Austria, South Germany, and Switzerland found that exposure to a greater diversity of bacteria and fungi was associated with less allergies and asthma in rural children. Rook notes that the observed relationship between abundant *Acinetobacter* and increased expression of interleukin-10 suggests that Hanski's team has documented a genuine case of immunoregulation by environmental bacteria.

Purifying Drinking Water with Sun, Salt, and Limes

[Environ Health Perspect 120:a305-a305. http://dx.doi.org/10.1289/ehp.120-a305]

Sun, salt, and lime juice may sound like ingredients for a vacation margarita, but recent research suggests they can also be used to help purify drinking water easily and cheaply—the type of solutions needed by millions of people in developing countries. Some 780 million people across the globe are still without reliable access to safe drinking water. Bringing safe water to these people will depend on making affordable, technically feasible solutions available. The solar disinfection of drinking water, or SODIS, method is one such solution now being used by more than 5 million people in 24 African, Asian, and Latin American countries. Water poured into clear or blue polyethylene terephthalate water bottles (glass bottles also can be used) is exposed to sunlight for at least 6 hours, or up to 48 hours in cloudy weather. The heat and ultraviolet radiation of the sunlight kill bacteria and protozoan parasites and inactivate assorted viruses. This method is reported to significantly reduce the number of children falling ill to diarrheal diseases (some studies suggesting by up to 70%) and cholera (by approximately 86%). Although questions have been raised about the leaching of plasticizers and other hormonally

active chemicals from heated plastic bottles, studies to date indicate the SODIS method does not impart an unusual burden of endocrine disruptors to drinking water. However, if the water placed in the bottles is very turbid, the method is rendered ineffective as soil particles in the water shield microorganisms from the disinfecting rays. Filtering the water before bottling it can solve this problem, but the additional equipment required may not be available. New work suggests, however, that adding a tiny amount of salt to turbid water causes the suspended clay particles to flocculate and sink to the bottom of the bottle, leaving clear water that can be decanted and subjected to the SODIS method. Using distilled water, researchers prepared 1-liter suspensions of bentonite, kaolinite, and illite (typical clays of tropical regions) with turbidities of 50, 100, and 200 nephelometric turbidity units (NTU). Then they added salt at a range of concentrations to determine how much was needed to reduce turbidity below 30 NTU, the threshold at which SODIS functions. Adding 1,250 mg salt (about a quarter teaspoon) per bottle brought all three 50-NTU suspensions to below this threshold within 1 hour. The more turbid solutions of bentonite, which flocculated more easily than the other clays, required less salt (1,000 mg/L) to achieve the same; the greater proximity of the clay particles to one another makes flocculation easier. The more turbid kaolinite and illite suspensions required the addition of a bentonite "jumpstarter" in order to be brought below the SODIS threshold. None of the treated samples in the study had salt concentrations below the taste threshold of 256 mg/L, but several had less residual salt than typical sports drink.

According to research leader Joshua Pearce, an associate professor in the Department of Materials Science and Engineering at Michigan Technological University, if you can read the headlines of a newspaper placed under a bottle of water, you have reduced the turbidity to below the 30-NTU SODIS threshold. "This provides an easy-to-understand sign for people outside of a laboratory that water has been sufficiently cleared for the SODIS treatment to work," he says. In other recent research, lime juice has been shown to speed up the disinfecting power of the SODIS method. Limes contain large quantities of psoralens. These molecules form covalent crosslinks between DNA strands in the presence of sunlight, a reaction that prevents DNA replication. This team prepared 2-liter plastic bottles of tap water spiked with 30 mL lime juice (about half a lime's worth) or 60 mL lime "slurry" produced by chopping, homogenizing, and centrifuging the entire fruit. They then added populations of either *Escherischia coli*, bacteriophage MS2 (a surrogate for many human viruses), or murine norovirus (MNV; a surrogate for human norovirus), and exposed the bottled waters to sunlight for up to 6 hours. Both lime slurry and plain lime juice, combined with SODIS, reduced *E. coli* by roughly 1 million times in just 30 minutes, whereas SODIS on its own was about one-quarter as effective. Reductions in MS2 were measured over a 2.5-hour solar exposure, with viable virus particles reduced by about 10,000 and 100 times with the lime slurry and lime juice, respectively, compared with a 25-times reduction by SODIS alone. The MNV virus was only modestly affected by any combination of methods. "Since limes are available in many places where SODIS is practiced, lime juice could be a useful way to speed up the process," says first author Alexander Harding, a medical student at the Johns Hopkins University School of Medicine. However, limes may not be available everywhere, and not all citrus fruits have such high psoralen concentrations, meaning limes might not be replaceable by other citrus fruits. "These research findings are useful, potentially improving the effectiveness of the SODIS approach," says Vincent Casey, technical support manager at the London offices of the nongovernmental organization WaterAid. But he points out there is no silver bullet solution that addresses all water quality challenges. Rather, a combination of approaches is required to ensure adequate water quality and disease prevention. For many communities, however, these new SODIS-associated techniques may be a step in the right direction.

Cigarette butts help urban birds ward off mites

[http://www.newscientist.com/article/dn22587-cigarette-butts-help-urban-birds-ward-off-mites.html]

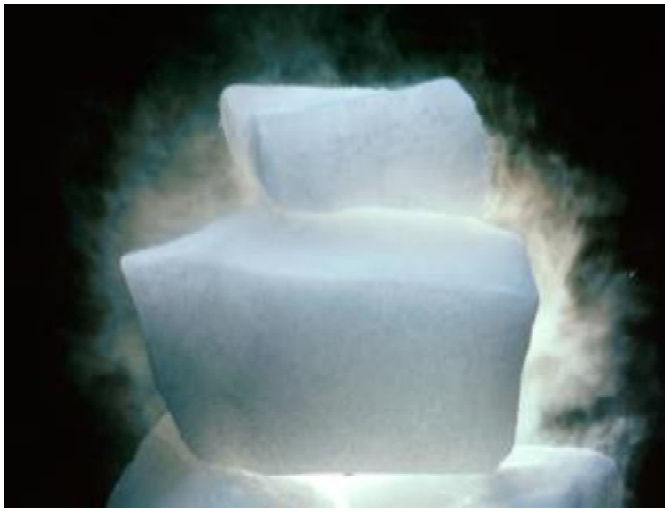
It's not just people that have a penchant for cigarettes. Birds living in urban environments often use cigarette butts to line their nests. Unlike in humans, the cigarettes seem to have a beneficial effect – they cut the number of parasites in the nests. Nicotine-based sprays are already used on some crops to repel insects. To see whether cigarette butts might have a similar effect in urban birds' nests, Constantino Macías Garcia from the National Autonomous University of Mexico in Mexico City and colleagues lured parasites

to these nests. The team set up thermal traps in the nests of 27 house finches and 28 house sparrows, species commonly found in cities. The traps had electrical resistors placed on either side of the nest to generate heat, attracting parasites – such as mites – which then got stuck to a strip of adhesive tape attached to the resistor. The team also placed cellulose fibres from smoked or unsmoked cigarettes on top of each resistor to see whether the mites had a preference for either. Once any chicks had left, the nests were collected for analysis. The team found that the more cigarette fibres the nest contained, the fewer parasites moved in. What's more, traps containing cellulose from used cigarettes butts attracted 60 per cent fewer mites, on average, than ones with unsmoked cigarettes. This suggests it is indeed the nicotine and other chemicals in a cigarette that repel mites, since these substances are only released once it has been smoked. Does that mean birds line their nests with cigarette butts to repel parasites? Not necessarily, says Macías Garcia. "One possibility is that the birds are using the cellulose from smoked cigarettes for its thermal properties, as a substitute for other materials such as feathers, down or fur," he says. "Much of the work on urban environments has focused on the negative impacts of human activities on birds and other animals," says Paige Warren of the University of Massachusetts, Amherst, who was not involved in the study. "But there are also many resources that humans provide for animals in the city." The team's next step is to determine whether birds that had a choice between spent butts and unsmoked cigarettes would prefer the former. Birds can distinguish between the two by their smell, and if they prefer to line their nests with spent butts, that would suggest they are aware of the butts' ability to deter parasites.

Could we geoengineer the climate with CO_2?

[http://www.newscientist.com/article/dn22244-could-we-geoengineer-the-climate-with-co2.html]

Schemes for artificially cooling the planet can often seem wild and woolly. The latest such geoengineering scheme is no different: it involves frozen carbon dioxide, Antarctica and a whole lot of freezers. While the proposal is not as daft as it sounds, the numbers may not stack up. Ernest Agee and colleagues of Purdue University in West Lafayette, Indiana, propose installing gigantic freezers in the heart of



Antarctica, where temperatures are already tens of degrees below zero. Once the air inside the freezers is cooled to -140 °C, the carbon dioxide within it will freeze out as "CO_2 snow". The solid CO_2 could then be stored underground. Agee's calculations suggest that it would be possible to remove 1 billion tonnes of CO_2 per year this way, using the energy provided by 16 wind farms, each generating 1200 megawatts of electricity. "There's a lot of wind energy in the Antarctic," Agee says.Authors annual greenhouse gas emissions reached 33 billion tonnes of CO_2 in 2010, and are likely to keep rising for years to come, so Agee's proposal would only go so far. The sheer scale of our emissions is a problem for similar concepts for sucking CO_2 out of the air, such as fertilising the ocean with iron. Their calculations are also rather optimistic, says Tim Kruger of the Oxford Geoengineering Programme at the University of Oxford. For instance, they assume that the power plants are 100 per cent efficient, which is impossible.

Furthermore, CO_2 makes up only slightly less than 400 parts per million of the atmosphere. This means for every volume of carbon dioxide that gets frozen, Agee would have to cool 2500 volumes of air – so a lot of the energy used would be wasted. It will also be difficult to store the CO_2 once it is frozen. Either it will have to be permanently cooled below its freezing point, which means running the freezers forever, or the CO_2 will have to be stored in sealed chambers that can withstand intense pressure once it warms up and expands."This is not really a credible solution," Kruger says.

हिंदी भाषा खंड

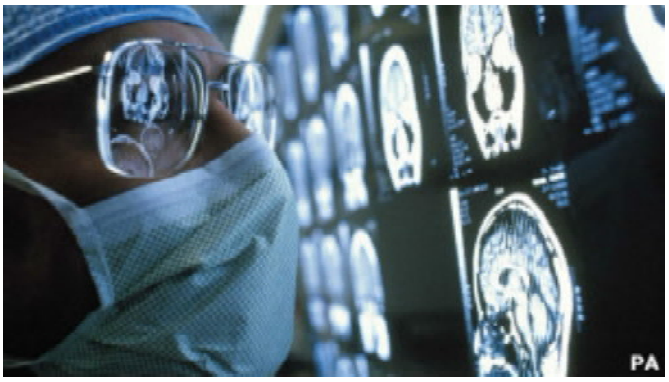
एक टेस्ट बता देगा सभी कैंसर का पता

[http://www.ncri.org.uk/ncriconference/2012abstracts/abstracts/B221.html]

कैंसर का पता लगाना आज भी डॉक्टरों के लिए चुनौती है, लेकिन कुछ वैज्ञानिकों ने दावा किया कि अब वो दिन दूर नहीं जब कैंसर का पता बहुत शुरूआती दौर में लग जाएगा। ब्रिटेन के ऑक्सफोर्ड विश्वविद्यालय के वैज्ञानिकों ने राष्ट्रीय कैंसर अध्ययन संस्थान में एक प्रेस कॉन्फ्रेंस कर इस क्षेत्र में मिली अभूतपूर्व सफलता पर रोशनी डाली। वैज्ञानिकों ने बताया कि उन्होंने एक चुहिया में स्तन कैंसर का पता तब लगा लिया था जब उसके भीतर कैंसर से होने वाली सूजन की शुरूआत हुई भी नहीं थी। वैज्ञानिकों के मुताबिक सिर्फ एक कैमिकल के कैंसर सेल में डालने से किसी भी तरह के कैंसर का पता उसके शुरूआती दौर में चल सकता है।

उनका कहना था इसी विधि को रेडियोथेरेपी के लिए भी आजमाया जा सकता है। ऑक्सफोर्ड विश्वविद्यालय के 'ग्रे इस्टीट्यूट फॉर रेडिएशन ऑन्कोलॉजी एंड बायोलॉजी' के वैज्ञानिक उस प्रोटीन की तलाश कर रहे थे जिसे 'गामा-एचटूएएक्स' कहा जाता है। ये प्रोटीन शरीर में डीएनए के क्षतिग्रस्त होने की अवस्था में निकलता है और यही कैंसर का प्राथमिक स्तर होता है। वैज्ञानिकों ने इसके लिए एंटीबॉडी का इस्तेमाल किया जो 'गामा-एचट्एएक्स' का सबसे बड़ा सहयोगी माना जाता है और इसे शरीर से पूरी तरह खत्म कर देता है।

वैज्ञानिकों का कहना है कि एंटीबॉडी के साथ कुछ रेडियोएक्टिव तत्वों का इस्तेमाल कर इसे किसी भी तरह के कैंसर टेस्ट किए जा सकते



हैं। ऐसे में अगर रेडिएशन एक जगह पर जमा होने लगे तो ये माना जाना चाहिए कि ये भविष्य में होने वाले ट्यूमर की तरफ इशारा कर रहा है। जबकि, एंटीबॉडी के साथ अधिक रेडियोएक्टिव ततवों का इस्तेमाल इसके इलाज के तौर पर भी काम आ सकता है। शोध करने वाले वैज्ञानिक प्रो. कैथरीन वैलीस ने अपनी टीम के साथ मिलकर एक चुहिया पर ये परीक्षण किया। उनका कहना है, हमने ट्यूमर के बारे में बहुत पहले पता लगा लिया, यहां तक कि उस वक्त तक ट्यूमर दिखना भी शुरू नहीं हुआ था। कैथरीन ने बीबीसी से कहा कि सभी तरह के कैंसर के लिए एक ही टेस्ट होये एक सपने की तरह ही है। हालांकि, ये शोध अभी बिल्कुल शुरूआती दौर में है और इस पर काफी लंबा शोध होना बाकी है। अगर शोध वृहत स्तर पर भी कामयाब रहा तो निश्चित तौर पर इससे कैंसर जैसी खतरनाक बिमारियों का पता बिल्कुल शुरूआती दौर में चल सकता है साथ ही एक टेस्ट से कई तरह के कैंसर का पता भी लगा पाना संभव हो जाएगा।

थाइरॉयड से बचना है तो कैल्शियम लें

[http://www.naturalnews.com/037999_calcium_ deficiency_bone_fractures_kidney_stones.html]

एक अध्ययन में पता चला है कि भोजन में कैल्शियम की कमी से महिलाओं में हॉरमोन की समस्या हो सकती है। इससे थाइरॉड से लेकर हड्डियों का कमजोर होना और किडनी में पत्थर होना शामिल है। अध्ययन के अनुसार आठ सो लोगों में से एक पीएचपीटी के शिकार हो सकते हैं और पोस्ट-मेनोपॉजॉल या रजोनिवृत्ति के बाद की महिलाओं में ये बीमारी सबसे आम है। ब्रिटिश मेडिकल पत्रिका में छपे एक लेख में शोधकर्ताओं ने कहा कि कैल्शियम की मात्रा बढ़ाने से इन बीमारियों के खतरे से बचा जा सकता है। वयस्कों को हर रोज़ 700 मिलीग्राम कैल्शियम लेने की सलाह दी गई है। लेकिन ज्यादा कैल्शियम लेने से पेट दर्द और हैजा हो सकता है। पीएचपीटी की बीमारी उस स्थिति में होती है जब पैराथाइरॉयल ग्लैंड ज्यादा मात्रा में पैराथाइरॉइल हॉरमोन छोड़ते हैं। हड्डी और किडनी के अलावा इससे हाई बल्ड प्रेशर और दिल की बीमारी होने का खतरा बना रहता है। अमरीका में नर्सेज हेल्थ स्टडी के तहत 58 हजार तीन सौ महिलाओं से बातचीत और उनकी जांच के नतीजों का

अध्ययन किया गया। अध्ययन में सामने आया है कि जिन महिलाओं के खाने में कैल्शियम की मात्रा सबसे ज्यादा थी, उनमें सबसे कम कैल्शियम लेने वाली बाकी महिलाओं के मुकाबले पीएचपीटी होने की आशंका 44 फीसदी कम हो जाती है। ब्रिटिश पत्रिका में शोध लिखने वाली टी की प्रमुख डॉक्टर जूली पाइक का कहला है, ''महिलाएं अगर अपने भोजन में सीधे कैल्शियम लेती रहें तो पीएचपीटी के खतरे को कम किया जा सकता है।'' फ्लोरिडा स्थित नॉर्मन पैराथाइरॉइड के जेम्स नॉर्मन का कहता है कि अगर रोजना कैल्शियम का डोज लिया जाए तो इसके खतरे कम और फायदे ज्यादा हैं। लेकिन ब्रिटेन में विशेषज्ञों का कहना है कि लोगों को पर्याप्त मात्रा में कैल्शियम अपने रोजना के भोजन से ही लेना चाहिए।

मानव अपशिष्ट से चलेगी कार

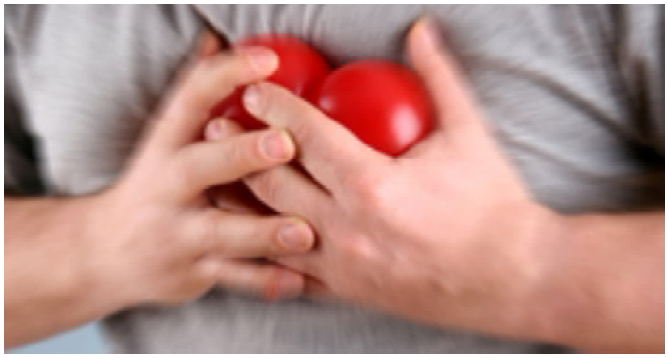
[http://www.sciencedaily.com/releases/2012/06/120626072942.htm]

अब पेट्रोल की जगह मानव अपशिष्ट से गाड़ी चलाने के लिये तैयार हो जाइये। एक रिपोर्ट के अनुसार अगले तीन सालों में एक ऐसी गाड़ी आने वाली है जिसमें पेट्रोल की जगह अपशिष्ट से तैयार सह उत्पाद को ईंधन की तरह इस्तेमाल किया जायेगा। जापान की एक कार निर्माता कंपनी ऐसे दल को प्रायोजित कर रही है जो अपशिष्ट को हाईड्रोजन में बदलने की प्रक्रिया पर शोध कर रहा है। इस दल की योजना है कि अपशिष्ट से हाईड्रोजन बनायी जाये और इस ही हाइड्रोजन को ईंधन की तरह प्रयोग किया जाये। जापान के 'निक्की' समाचार पत्र के अनुसार, फ्यूल सेल (हाइड्रोजन आधारित) वाहनों को बिजली से चलने वाले वाहनों से बेहतर माना जाता है क्योंकि वह ज्यादा लंबी दूरी तय कर सकते हैं और कोयले जेसे क्षय स्रोत से पैदा होने वाली बिजली पर आश्रित नहीं होते। इन वाहनों में हाइड्रोजन और ऑक्सीजन के बीच रसायनिक क्रिया होती है जिससे गाड़ी को चलाने के लिये बिजली पैदा होती है। इन वाहनों में से धुएं की जगह पानी बाहर आता है। हालांकि इन वाहनों के व्यापारिक इस्तेमाल में सबसे बड़ी बाधा हाइड्रोजन की निर्माण प्रक्रिया है। इसके निर्माण में शामिल क्रिया मंहगी और जटिल है। इसमें प्राकृतिक गैस या किसी जीवाश्म से बने ईंधन का इस्तेमाल करना होता है। वहीं शोध दल का कहना है कि अपशिष्ट से हाईड्रोजन पैदा करना सस्ता तो है ही साथ ही साथ यह पर्यावरण के लिये परंपरागत प्रक्रिया से ज्यादा हितकारी है। इस प्रक्रिया में अपशिष्ट के कीचड़ को सुखा कर उससे मीथेन गैस बनायी जाती है जिसे गर्म कर उसे हाइड्रोजन में तब्दील किया जाता है।

विटामिन डी की कमी से हृदय रोगों का खतरा

[http://news.ku.dk/all_news/2012/2012.9/vitamin-d-deficiency-increases-risk-of-heart-disease/]

यूनिवर्सिटी आफ कोपेनहेगन तथा कोपेनहेगन यूनिवर्सिटी होस्पिटल के सहयोग से किए गए अध्ययन से यह बात सामने आयी है। यूनिवर्सिटी के क्लिनिकल बायोकैमिकल डिपार्टमेंट के डा पीटर ब्रून्डम जैकोबसन ने कहा, ''अब हमने विटामिन डी की कमी और दिल की बीमारियों और उससे होने वाली मौतों के बीच संबंध का अध्ययन कर लिया है।'' उन्होंने एक बयान में कहा, ''हमने यह पाया कि शरीर में विटामिन डी की कमी के शिकार लोगों को दिल का दौरान पड़ने तथा अन्य संबंधित बीमारियां होने और दिल के दौर से मौत होने का खतरा बहुत अधिक रहता है।'' विटामिन डी की कमी का संबंध पारंपरिक रूप से कमजोर हड्डियों से होता है। अन्य अध्ययनों में भी पाया गया है कि विटामिन डी की कमी से रक्तचाप बढ़ सकता है और यह सर्वविदित है कि उच्च रक्तचाप दिल के दौरे का खतरा बढ़ा देता है।



सिरका बताएगा कैंसर है या नहीं

[www.theworld.org/2012/12/an-ounce-of-prevention/]

कुछ समय पहले तक अमरीका में जितनी भी महिलाओं की मौत कैंसर से होती थी, उनमें से सबसे ज्यादा मामले सर्वाइकल कैंसर के होते थे। लेकिन अब ऐसा नहीं है। अब अमरीका में सर्वाइकल कैंसर के जरिए होने वाली मोतों के बारे में लगभग न के बराबर सुना जाता है। ऐसा शायद इसलिए क्योंकि वहां लगभग एक दशक से 'पैप स्मियर' टेस्ट का प्रचलन काफी बढ़ गया है। यह टेस्ट एक तरह की मेडिकल जांच हे जिसमें महिलाओं के सर्वाइकल की कोशिकाओं पर जमी हुई गंदगी की जांच कर ये पता लगाया जाता है कि उनमें कैंसर पनपने की गुंजाइश तो नहीं है। इस जांच के जरित काफी पहले यह पता लग जाता है कि कहीं किसी महिला को सर्वाइकल कैंसर का

अंदेशा तो नहीं है। लेकिन स्मियर टेस्ट की प्रक्रिया काफी महंगी है। इन असामान्य कोशिकाओं की जांच के लिए एक खास तरह के प्रशिक्षण और मेडिकल किट की जरूरत होती है जो भारत जैसे विकासशील देश में संभव नहीं है।

भारत में अब भी हर साल हज़ारों महिलाओं की सर्वाइकल कैंसर की वजह से मौत होती है। इसलिए अब डॉक्टर इसका पता लगाने के लिए एक नए तरीके का इस्तेमाल कर रहे हैं जिसे 'सिरका-स्वाब' कहते हैं। मुंबई के टाटा मेमोरियल अस्पताल में कैंसर विशेषज्ञ डॉक्टर सुरेंद्र शास्त्री कहते हैं, ''हमारे लिए विदेशों की तरह बार-बार ये जांच करना मुमकिन नहीं है। पैप स्मियर टेस्ट करने के लिए ना सिर्फ हमें प्रशिक्षित कर्मचारियों की जरूरत है बल्कि अच्छी प्रयोगशाला की भी जरूरत पड़ती है जो भारत के कई हिस्सों में उपलब्ध नहीं है। लेकिन इसके अभाव में हम महिलाओं को मरने के लिए नहीं छोड़ सकते हैं'' इसके जवाब में जॉन हॉप्किन्स विश्वविद्यालय ने कुछ अन्य संस्थाओं की मदद से एक बेहद ही सरल और सस्ता विकल्प ढूंढ निकाला है। ये एक ऐसी चीज है जो हर रसोईघर में उपलब्ध है। भारत के महाराष्ट्र राज्य के छोटे से गांव डेरवान में कुछ डॉक्टरों ने एक अस्थाई क्लीनिक बनाया है। इस क्लीनिक में किसी भी तरह की आधुनिक सुविधा मौजूद नहीं है, यहां तक कि बिजली भी नहीं है। क्लीनिक चलाने वाली डॉक्टर अर्चना सौनके सिरके की मदद से सर्वाइकल की जांच करती हैं। डॉक्टर सौनके पूरी प्रक्रिया को समझाते हुए कहती हैं, '' योनि में सिरका लगाने के बाद हम तकरीबन एक मिनट तक रूकते हैं। अगर एक मिनट के बाद महिला के सर्वाइकल का सामान्य हल्की गुलाबी रंग सफेद या पीला पड़ने लगता है तो हम समझ जाते हैं कि वहां कैंसर कोशिकाएं मौजूद हैं।'' सर्वाइकल के रंग में किसी तरह का बदलाव नहीं होने पर महिला को अच्छी खबर के साथ वापिस भेज दिया जाता है। लेकिन अगर खबर बुरी है और किसी महिला के सर्वाइकल में असामान्य कोशिकाएं पाई जाती हैं तो उसेवहीं पर तरह नाइट्रोजनकी धार से साफ कर दिया जाता है। पीड़ित महिला को दोबारा डॉक्टर के पास आने की जरूरत भी नहीं पड़ती।

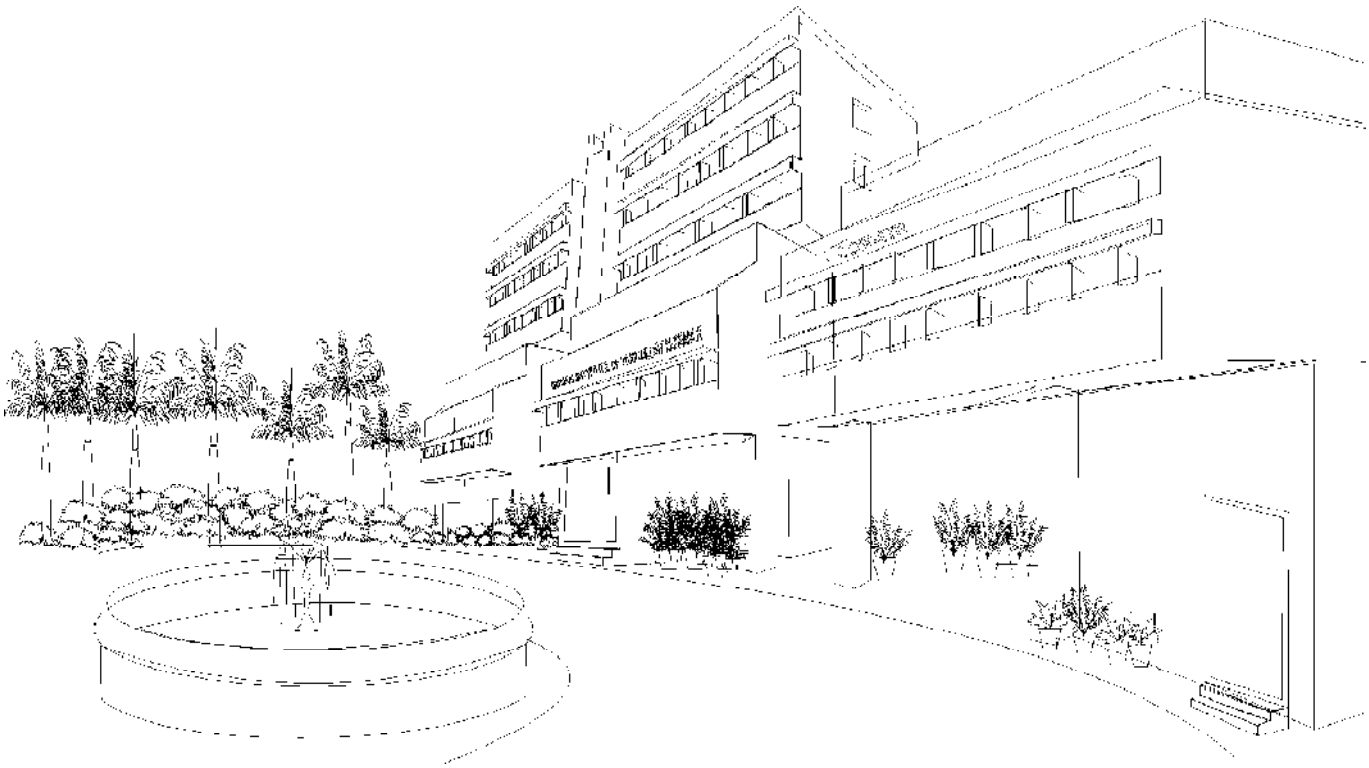
प्लास्टिक की खाली बोतलों से रौशन होगी देश की झुग्गियां

[http://www.lpu.in/FullNewsRelease.aspx?id=351and http://vijnanabharati.org/activities/e-i-i-f-energy-innovation-a-implementation-foundation.html]

देश भर में नयी-नयी खोजों को बढ़ावा देने वाले विज्ञान भारती ने एक ऐसी तकनीक विकसित की है जिससे खाली और बेकार पड़ी प्लास्टिक के बोतलों में पानी भर कर बिना किसी खर्च के देश के विभिन्न महानगरों की चौड़ी-चौड़ी सड़कों के किनारे बनी करोडों अंधेरी झुग्गियों को रौशन करने में सहायता मिलेगी। विज्ञान भारत ने राष्ट्रीय पर्यावरण एवं उर्जा विकास अभियान (एनईईडीएम) की सहायता से सूरज और सड़कों के किनोर खडे खंभों पर लगे हैलोजन के प्रकाश का इस्तेमाल कर झुग्गियों को बिल्कुल मुफ्त में रौशन करने के इंडोनेशियाई फार्मूले को विकसित किया है।

पानी भरी प्लास्टिक की बोतल को छत में छेद कर ऐसे लटकाया जिससे उसका आधा हिस्सा ऊपर की ओर और आधा हिस्सा अंदर की ओर हो। इस प्रक्रिया में बोतल में भरा पानी सूरज के प्रकाश को रिफलेक्ट कर कमरे को पूरी तरह रौशन करता है। डमी झुग्गी के अंदर इस प्रक्रिया से इतनी रौशनी है कि आप किताब भी पढ़ सकती हैं। रात में सड़कों के किनारे खंभों में लगे हैलोजन के प्रकाश को भी यह प्रतिबिंबित करता है और घर में काम करने के लिए जितनी रोशनी चाहिए उतनी इससे मिलती है। बोतल के पानी में अगर ब्लीचिंग पाउडर और नमक मिला दिया जाए तो पानी बदलने की जरूरत नहीं होगी। इससे रोशनी भी और तेज होगी। ब्लीचिंग पाडर पानी में काई और फफूंद बनने से रोकेगा। मध्य प्रदेश सरकार में भोपाल और अन्य शहर में झुग्गियों को रौशन करने के लिए ऐसा प्रयोग किया है। यह सफल रहा है। यह झुग्गियों में ही क्यों। अगर इस तकनीक को और विकसित किया गया तो इससे झुग्गियों के स्थान पर बनाये जाने वाले पक्के मकानों को भी रौशन करने में सहायता मिलेगी। विज्ञान भारती के महासचिव जय कुमार अप्पाकुट्टन ने कहा, प्रकृति ने हमें उपहार के तौर पर अनमोल चीजें दी हैं। जरूरत है उनकी पहचान और उनका दोहन कर उसे इस्तेमाल में

लाने की। उन्होंने कहा, संगठन का लक्ष्य वातावरण के अनुकूल और बिना किसी खर्च के इसे देश की बीस करोड़ झुग्गियों में लगा कर उन्हें रौशन करना है। यह दिन के वक्त तो प्रकाश का एक विकल्प है ही रात के दौरान भी हैलोजने लाइटों की रौशनी को एबजॉर्ब कर यह झुग्गियों को प्रकाशित करेगा।



SEVICES OFFERED BY IITR

A. Safety/toxicity evaluation of chemicals/ finished products

- Toxicity evaluation in mice, rat, guinea pig and rabbit
- Neurobehavioral Toxicity
- Neurotoxicity
- Teratogenicity
- Gastrointestinal Toxicity
- Immunotoxicity
- Dermal Toxicity
- Reproductive Toxicity
- Carcinogenicity and Genotoxicity (*In vivo*)
- Carcinogenicity and Genotoxicity (*In vitro*)
- Safety evaluation of plastics
- Cytotoxicity
- Phototoxicity of chemicals/cosmetics
- Food Contamination and Adulteration Monitoring

B. Analytical Services

- Metals in soil, air, water, food, biological samples and other matrices (24 metals)
- Pesticides in water, soil, food and biological samples
- PAHs in water, food and biological samples
- Scanning of spectra and kinetics on spectrophotometer and spectrofluorometer
- Measurement of beta counts on scintillation counter
- Analysis of total organic carbon (TOC) in water/effluents

C. Environmental Monitoring and Impact Assessment

D. Water Quality Assessment and Monitoring

- Drinking water (as per IS10500)
- Raw water (sewage/industrial effluents) as per Pollution Board

E. Epidemiological Studies

F. Environmental Monitoring and Impact Assessment

- Multi species tests for ecotoxicity evaluation
- Seed germination test Environmentally safe reuse of effluents for agriculture and aquaculture
- Safety evaluation and management of industrial solid wastes

Feedback on the publication are always welcome

For information and feedback please write to:

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