



# विष विज्ञान शोध पत्रिका Toxicology Research Bulletin

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विज्ञान परिक्रमा



**CSIR-Indian Institute of Toxicology Research**  
(Council of Scientific and Industrial Research)  
Lucknow, India

## CSIR-IITR: IN THE SERVICE OF THE NATION

CSIR-Indian Institute of Toxicology Research, Lucknow, a constituent laboratory of Council of Scientific & Industrial Research under Department of Scientific & Industrial Research, Government of India, was established in 1965. This multi disciplinary research institute with the motto "Safety to Environment & Health and Service to Industry" addresses problems critical to human health and environment.

CSIR-IITR is a unique, valuable and internationally competitive organisation meeting global challenges. Over four decades of expertise, manpower and knowledgebase in toxicology research empowers the institute to conduct research in niche areas of toxicology such as - Systems Toxicology & Health Risk Assessment; Food, Drug & Chemical Toxicology; Environmental Toxicology; Regulatory Toxicology; and Nanomaterial Therapeutics & Toxicology. CSIR-IITR scientists actively participate in national and international R&D programmes addressing - new paradigms in investigative toxicology, screening technologies for environmental contaminants, development and validation of alternate to animal models in toxicology as well as understanding the molecular mechanism(s) of toxicity of nanomaterials.

The institute has met national challenges and participated in societal mission programmes such as Drinking Water Mission, Technology Mission on Oil Seeds, Pulses & Maize, Ganga Action Plan, Bhopal Gas Tragedy, Monitoring of Gomti River. CSIR-IITR technologies were effectively utilized in providing potable water to the population of Orissa during the Super Cyclone. The institute plays an active role in human resource development as well as environmental awareness programmes for public and school children.

### Accreditation

Accredited since December 1, 2000 by NABL as biological and chemical testing laboratory for:

- ☆ Air quality
- ☆ Chemical and bacteriological quality of water and effluents
- ☆ Chemical and biological safety of plastics
- ☆ Environmental impact assessment
- ☆ Residue analysis for pesticides and metals
- ☆ Toxicity/safety evaluation of a vast variety of chemicals and products

### Recognition

- ☆ State Water Laboratory : U.P. Pollution Control Board, Lucknow (Gazette notification by U.P. Government, August 1986)
- ☆ State Air Laboratory: U.P. Pollution Control Board, Lucknow (Gazette notification by U.P. Government, March 1986)
- ☆ Laboratory for analysis of various types of environmental pollutants: Central Pollution Control Board, New Delhi (Gazette notification of India, July 1998)
- ☆ Safety evaluation of synthetic detergents: Bureau of Indian Standards (BIS), New Delhi, January 2001



## EVENTS

### हिंदी सप्ताह - 2013

सीएसआईआर-भारतीय विषविज्ञान अनुसंधान संस्थान (आई. आई.टी.आर.) लखनऊ के प्रेक्षागृह में दिनांक 16.09.2013 को प्रातः 11:00 बजे, हिंदी सप्ताह के उद्घाटन समारोह का आयोजन किया गया। इस अवसर पर डॉ. श्रीमती पूनम कक्कड़, मुख्य वैज्ञानिक, आई.आई.टी.आर. ने मुख्य अतिथि का औपचारिक परिचय दिया तथा समारोह में उपस्थित सभी लोगों का स्वागत किया। मुख्य अतिथि पद्मश्री प्रोफेसर मोहन चन्द्र पंत, निदेशक, राम मनोहर लोहिया इंस्टीट्यूट ऑफ मेडिकल साइंसेस, लखनऊ थे। उन्होंने कहा कि संस्थान के कर्मचारी हिंदी में काम करने के प्रति अत्यन्त जागरूक हैं। उन्होंने कैंसर रोग के बारे में जागरूकता लाने हेतु अत्यन्त सरल हिंदी में कैंसर से होने वाली हानियों,



डॉ. मुकुल दास प्रतिभागी को पुरस्कार प्रदान करते हुये



हिंदी सप्ताह का आयोजन

कारकों तथा इसके निदान के बारे में व्याख्यान दिया। उन्होंने आने वाले 12 वर्षों में होने वाले कैंसर के रोग के बारे में जानकारी दी। उन्होंने जानकारी दी कि कैंसर कितने प्रकार का होता है तथा यह भी बताया कि शरीर का कोई भी ऐसा अंग नहीं जो कैंसर ग्रस्त न हो सके। उन्होंने बताया कि कैंसर की प्रारम्भिक अवस्था में यदि उपचार हो जाए तो इससे निदान मिल सकता है। उन्होंने कहा मुझे मुख्य अतिथि के रूप में संस्थान में आमंत्रित किया गया इसके लिए दिल से आभारी हूँ तथा गौरव महसूस करता हूँ। अपने अध्यक्षीय संबोधन में संस्थान की ओर से डॉ. (श्रीमती) पूनम कक्कड़, मुख्य वैज्ञानिक ने मुख्य अतिथि पद्मश्री मोहन चन्द्र पंत को इस अवसर पर

स्मृति चिन्ह और शाल भेंट किया। डॉ. (श्रीमती) पूनम कक्कड़ ने हिंदी की प्रगति के बारे में जानकारी देते हुए कहा कि हिंदी की प्रगति कैसे बढ़ाई जा सकती है। हम हिंदी की उन्नति के लिए प्रयासरत रहें तथा आशा करती हूँ कि ज्यादा से ज्यादा लोग हिंदी सप्ताह के कार्यक्रमों में उत्साह से भाग लेंगे। उन्होंने हिंदी सप्ताह के दौरान आयोजित होने वाली विभिन्न प्रतियोगिताओं में सभी से प्रतिभागिता हेतु अनुरोध किया। दिनांक 23.9.2013 को पुरस्कार वितरण एवं समापन समारोह का आयोजन हुआ। इस अवसर पर अध्यक्षीय सम्बोधन में डॉ. मुकुल दास, मुख्य वैज्ञानिक, आईआईटीआर ने कहा कि हमें राजभाषा के विकास के लिए निष्ठा से कार्य करना चाहिए। हमें सहज और सरल हिंदी का प्रयोग करना चाहिए जो सभी को आसानी से समझ में आए। इस अवसर पर हिंदी 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। हिंदी डिक्टेशन पुरस्कार के अलावा हिंदी में कार्य करने की प्रोत्साहन योजना के अन्तर्गत विजयी प्रतिभागियों 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 संचालन श्री जगन्नाथ, प्रभारी राजभाषा ने किया।

## IITR CELEBRATED 71<sup>ST</sup> CSIR FOUNDATION DAY

The seventy first CSIR Foundation function was held in the auditorium of CSIR-Indian Institute of Toxicology Research, Lucknow on Sept. 26, 2013. Dr. K.C. Gupta, Director, CSIR-IITR while welcoming the chief guest, Prof. A.K. Bachhawat, Professor (Biology) & Dean (Faculty), Indian Institute of Science Education and Research (IISER), Mohali, Punjab and the guest of honour, Prof. Rakesh Shukla, Department of Neurology, King George's Medical University, Lucknow said that Dr. S.S. Bhatnagar was the first chief of CSIR who was instrumental in establishing a chain of CSIR laboratories. He further said that since the inception of CSIR, several pharmaceutical, chemical and engineering industries



Welcoming chief guest Dr. A.K. Bachhawat



Dr. Anand K. Bachhawat delivering foundation Day lecture

have benefited from technologies developed by various CSIR labs.

The Foundation Day lecture was delivered by Prof. Anand



Dr. K C Gupta honouring Prof. A K Bachhawat

K. Bachhawat on the topic "Re-searching Glutathione: The cells redox buffer". Prof. Bachhawat began his presentation with an introduction that touched upon the history of glutathione, its discovery in 1888 and the fact



Group photograph of retired staff members with dignitaries

that this year we are celebrating the 125<sup>th</sup> year of its discovery. He said that the cells in the human body counteract the harmful effects of reactive oxygen species (ROS) by two mechanisms – (a) by using natural antioxidant and (b) by reducing the oxygen atmosphere in the cell. Glutathione is mainly involved in the second mechanism and the same was demonstrated using the baker's yeast model to study glutathione homeostasis mechanism. He further said that out of the several attempts that were made to clone the gene for glutathione transporter, the reverse genetic approach appeared most useful. He then spoke about his experiences with glutathione research its synthesis and degradation



Winner of essay competition receiving prize

mechanisms, a novel pathway that is involved in glutathione degradation and depletion.

In his presidential address Prof. Rakesh Shukla said that

Lucknow is known as a city of culture and is now referred to as a scientific city because it has a chain of scientific institutions including four CSIR laboratories, four medical institutions and a few laboratories of ICAR. He further said that institutions like IITR should have a social responsibility – they must educate the public about environmental pollution, adulteration of foods and the risks involved and the methods for mitigation of such problems. A concerted effort in this direction is required to sensitize the general public and students.

On this occasion 13 members of staff who had superannuated during the last one year were felicitated by Dr. K.C.Gupta, Director, IITR. Earlier, an essay competition was organized for children. There were 3 winners in the junior group and 3 in the senior group. The winners were awarded prizes by Prof. Rakesh Shukla.

Dr. Mukul Das, Chief Scientist and Chairman, CSIR Foundation Day organizing committee proposed the vote of thanks.

## CSIR – INDIAN INSTITUTE OF TOXICOLOGY RESEARCH CELEBRATED ITS 48<sup>TH</sup> FOUNDATION DAY



Lighting of the lamp by Prof. Surolia (chief guest)  
at Foundation Day function

A premier institute of the Council of Scientific and Industrial Research, the Indian Institute of Toxicology Research celebrated its 48<sup>th</sup> Foundation day here on 08 Nov 2013. The programme began with the symbolic lighting of the lamp followed by rendition of the CSIR – IITR song by a choir group of IITR students. The Director, Dr. K. C. Gupta welcomed the guests – Prof. Indranil Manna, Director IIT Kanpur and Prof. Avadhesh Surolia from the Molecular Biophysics Unit, Indian Institute of Science Bengaluru. The Director then outlined the significant achievements of the institute for 2012 – 2013.

The emerging global trends in industrialization related to occupational and environmental issues, health care and food security make the scope of R & D more relevant and demanding on this institution. CSIR-IITR has continued to focus on the five broad areas: **Nanotherapeutics & Nanomaterial Toxicology; Environmental Toxicology; Systems Toxicology & Health Risk Assessment; Food, Drug & Chemical Toxicology; Regulatory Toxicology.**

One of the major thrust areas of research at IITR is **Nanotherapeutics and Nanomaterial Toxicology.** This group has carried out research and development addressing the issues on transfection agents and targeted gene delivery, method development for toxicity assessment as well as models for safety assessment. Oral administration of doxyrubicin loaded into self assembled, cell receptor targeted 6-O-(3-hexadecyloxy-2-hydroxypropyl)-hyaluronic acid nanoparticles along with a green tea polyphenol, Epigallocatechin-3-gallate showed significant inhibition on the growth of EAC cells with approximately 38-fold dose advantage compared to doxyrubicin alone. Similarly, PLGA-NPs loaded with polyphenolic constituents of black and green tea showed a superior ability to prevent DMBA-induced DNA damage at much lower concentrations, thus opening a new dimension in chemoprevention research. In a separate study, tea phenols in bulk and in nanoparticle form were found to modify *in vitro* DNA damage due to platinum



Dr. K.C. Gupta welcoming the guests and presenting Annual Report of the Institute

based chemotherapeutic drugs in human lymphocytes from colon cancer patients and healthy individuals.

The release of new chemical entities from unorganised sector, genetically modified organisms, and more recently smart materials make **Environmental Toxicology** one of the most important facets of toxicology research. In our endeavour to develop sensitive tool for the detection of viable water borne bacteria, the institute has developed a qPCR based assay for quantifying *Salmonellae* in source/potable waters. To develop alternate animal models for toxicological studies polices, *Caenorhabditis elegans* facility has been established at the institute.

In the area of **Systems Toxicology & Health Risk Assessment** certain noteworthy findings have been published and well received by the scientific community. A study was conducted to investigate the effect of Cypermethrin on global gene expression patterns which suggests that multiple pathways are involved in the neurodegeneration as well as in enhancing the vulnerability of neurons in cypermethrin exposed animals.

The area of **Food, Drug and Chemical Toxicology** finds immense importance due to paradigm shift in rapid urbanization and food security. Fungal contamination of cereals and cereal products is of common occurrence. To address the same, Wheat, Barley and Maize samples were collected from northern states of India and levels of Deoxynivalenol (DON) and Ochratoxin A (OTA), were measured using HPLC. Our studies showed that topical application of OTA causes DNA damage and tumour promotion in mouse skin indicating the risk of farmers during pre- & post – harvesting stages of cultivation of crops.

The institute has taken a proactive role in strengthening the **Regulatory Toxicology** discipline. CSIR-IITR has



A view of Audience

NABL accreditation for chemical and biological testing for the past 13 years. A step forward in this direction has been to initiate creation of a GLP certified toxicity testing facility. The scientists of Regulatory Toxicology group have addressed issues like developing sensitive methods of analytical importance and predictive tools.

**S & T Achievements** - The achievements of institutional R& D activities both nationally and internationally are reflected in the recognition of a number of scientists. Scientific publications provide a flavour of the quality of R&D being pursued in the institute. CSIR-IITR scientists published 121 research papers this year with an average



Release of CSIR-IITR Annual Report

impact factor of 3.248, an improvement over 2.011 five years ago. During this period, our scientists have published 16 papers with IF >5, 18 papers with IF >4.0 and 22 papers with IF >3. The institute contributed in New Indigo, Nanolinen and Nanovalid projects under the FP7



Dr. K.C. Gupta presenting memento to Prof. Avdhesha Surolia

programme of European Union, an Indo-Spanish project, several Grant-in-Aid and Sponsored projects and 15 CSIR Network Projects including two projects INDEPTH and NANOSHE where this institute serves as the nodal laboratory.

As a part of the foundation day celebrations, the 17<sup>th</sup> Prof. S. H. Zaidi Memorial Oration was delivered by Prof. Avdhesha Surolia on the topic titled, "Novel physical form of insulin for sustained treatment of diabetes". He delved on the current status of the disorder, its ramifications and the shortcomings in the treatment options currently available. A novel concept has been developed to address the issue of patient compliance using a Supramolecular



Dr. K.C. Gupta Welcoming Prof. Indranil Manna

Insulin Assembly (SIA-II). The folding reaction of Insulin is used to entice it to transform into a prodrug, administration of which allows a sustained treatment of diabetes. This is achieved without the use of any chemicals or pumps / patches. Other complications of diabetes such as damage

to kidneys and retina are also arrested. It is believed that this work could also be used for treating metabolic syndrome as well.

Following the S. H. Zaidi Oration, Prof. Avdhesha Surolia released the institute's report on the Assessment of Ambient Air Quality of Lucknow City during the Post-Monsoon period of 2013. The study conducted in October 2013 monitored selected air pollutants namely Respirable Particulate Matter (RSPM or  $PM_{10}$ ), Sulphur dioxide ( $SO_2$ ), Nitrogen dioxide ( $NO_2$ ) and noise level at 9 representative locations, categorized as residential (four), commercial (four) and industrial (one) areas in Lucknow city. The results revealed an average 24 hour concentration of  $PM_{10}$  of  $203.9 \mu g/m^3$ . The average values of  $PM_{10}$  irrespective of locations were found to be above the permissible limit



Refreshment after the celebration

( $PM_{10} = 100 \mu g/m^3$ ) prescribed by Ministry of Environment and Forests. Average 24 hours concentration of  $SO_2$  and  $NO_x$  were found to be  $15.9$  and  $54.8 \mu g/m^3$  respectively and all the values were below the permissible limits ( $80 \mu g/m^3$ ). Noise levels during day and night time were found in the range of  $62.2$  to  $74.5$  dB and  $54.2$  to  $71.5$  dB which was above the respective permissible limits except in industrial area which is  $68.9$  and  $65.5$  dB during day and night time respectively.

Prof. Indranil Manna delivered the Foundation Day address and stressed the need for a synergy between academia and industry for societal benefit and to ensure the transfer of technology from the lab to the land. He shared details on some technologies that have been developed by a CSIR laboratory. As is the tradition at the Institute, the scientists with outstanding publications during the past year were awarded with a certificate and silver coin. Dr. Mukul Das, Chairman Foundation Day Committee proposed the vote of thanks.

## CSIR-IITR RESEARCH HIGHLIGHTS

### **Genetic diversity of *Pinus roxburghii* sarg. Collected from different himalayan regions of India assessed by random amplified polymorphic DNA analysis.**

[Sinha D, Singh J, Tandon PK, Kakkar P. Toxicol Int. 2013 Sep;20(3):208-13.]

Present study was aimed at molecular genetic fingerprint profile of 15 genotypes of three populations of *Pinus roxburghii* Sarg. from Himalayan regions of India using random amplified polymorphic DNA (RAPD) based markers. Needles of *Pinus roxburghii* Sarg. were collected from Dharamshala, Himachal Pradesh (HP), Nainital, Uttarakhand (UK) and Darjeeling, West Bengal (WB) regions of India. The samples were subjected to DNA extraction and RAPD analysis using oligonucleotide purification cartridge (OPC) primers. Out of 15 primers tested, nine primers gave scorable bands. Altogether 48 bands were obtained, out of which 43 were found to be polymorphic. Number of amplified fragments with RAPD primers ranged from four to eight with the size of amplicon ranging from 500 to 7,000bp. Investigation of natural diversity at intraspecies level was performed with 15 genotypes. Forty-eight amplification products were scored by RAPD and showed 89.58% polymorphism with a mean intrapopulation genetic diversity (H<sub>pop</sub>) of 0.2754. A significant inter- and intrapopulation diversity was observed, with the percentage of polymorphic loci (P<sub>p</sub>) ranging from 50.09 to 70.83%, Shannon's information index (I) from 0.3262 to 0.4689 and Nei's gene diversity (h) from 0.2032 to 0.3335 with mean Nei's gene diversity 0.377 and the overall estimate of gene flow being (N<sub>m</sub>) 1.3555. Unweighted pair-group method with arithmetic average (UPGMA) analysis based Dendrogram showed single cluster. The variation amongst the samples of the three ecological regions can be attributed to varied climatic conditions and may help in conservation/future cultivation of these species.

### **Mechanism of uptake of ZnO nanoparticles and inflammatory responses in macrophages require PI3K mediated MAPKs signaling.**

[Roy R, Parashar V, Chauhan LK, Shanker R, Das M, Tripathi A, Dwivedi PD. Toxicol In Vitro. 2013 Dec 22. pii: S0887-2333(13)00321-4.]

The inflammatory responses after exposure to ZNPs are known, however, the molecular mechanisms and direct

consequences of particle uptake are still unclear. Dose and time-dependent increase in the uptake of ZNPs by macrophages has been observed by flow cytometry. Macrophages treated with ZNPs showed a significantly enhanced phagocytic activity. Inhibition of different internalization receptors caused a reduction in uptake of ZNPs in macrophages. The strongest inhibition in internalization was observed by blocking clathrin, caveolae and scavenger receptor mediated endocytic pathways. However, FcγR and complement receptor-mediated phagocytic pathways also contributed significantly to control. Further, exposure of primary macrophages to ZNPs (2.5μg/ml) caused (i) significant enhancement of Ras, PI3K, (ii) enhanced phosphorylation and subsequent activation of its downstream signaling pathways via ERK1/2, p38 and JNK MAPKs (iii) overexpression of c-Jun, c-Fos and NF-κB. Our results demonstrate that ZNPs induce the generation of reactive nitrogen species and overexpression of COX-2, iNOS, pro-inflammatory cytokines (IL-6, IFN-γ, TNF-α, IL-17 and regulatory cytokine IL-10) and MAPKs which were found to be inhibited after blocking internalization of ZNPs through caveolae receptor pathway. These results indicate that ZNPs are internalized through caveolae pathway and the inflammatory responses involve PI3K mediated MAPKs signaling cascade.

### **Selective blocking of primary amines in branched polyethylenimine with biocompatible ligand alleviates cytotoxicity and augments gene delivery efficacy in mammalian cells.**

[Tripathi SK, Gupta N, Mahato M, Gupta KC, Kumar P. Colloids Surf B Biointerfaces. 2013 Nov 21;115C:79-85.]

Recently, polyethylenimines (PEIs) have emerged as efficient vectors for nucleic acids delivery. However, inherent cytotoxicity has limited their *in vivo* applications. To address this concern as well as to incorporate hydrophobic domains for improving interactions with the lipid bilayers in the cell membranes, we have tethered varying amounts of amphiphilic pyridoxyl moieties onto bPEI to generate a small series of pyridoxyl-PEI (PyP) polymers. Spectroscopic characterization confirms the formation of PyP polymers, which subsequently form stable complexes with pDNA in nanometric range with

positive surface charge. The projected modification not only accounts for a decrease in the density of 1° amines but also allows formation of relatively loose complexes with pDNA (cf. bPEI). Alleviation of the cytotoxicity, efficient interaction with cell membranes and easy disassembly of the pDNA complexes have led to the remarkable enhancement in the transfection efficiency of PyP/pDNA complexes in mammalian cells with one of the formulations, PyP-3/pDNA complex, showing transfection in ~68% cells compared to ~16% cells by Lipofectamine/pDNA complex. Further, the efficacy of PyP-3 vector has been established by delivering GFP-specific siRNA resulting in ~88% suppression of the target gene expression. These results demonstrate the efficacy of the projected carriers that can be used in future gene therapy applications.

**Gas chromatography- mass spectrometry based metabolomic approach for optimization and toxicity evaluation of earthworm sub-lethal responses to carbofuran.**

[Mudiam MK, Ch R, Saxena PN. PLoS One. 2013 Dec 4;8(12):e81077.]

Despite recent advances in understanding mechanism of toxicity, the development of biomarkers (biochemicals that vary significantly with exposure to chemicals) for pesticides and environmental contaminants exposure is still a challenging task. Carbofuran is one of the most commonly used pesticides in agriculture and said to be most toxic carbamate pesticide. It is necessary to identify the biochemicals that can vary significantly after carbofuran exposure on earthworms which will help to assess the soil ecotoxicity. Initially, we have optimized the extraction conditions which are suitable for high-throughput gas chromatography mass spectrometry (GC-MS) based metabolomics for the tissue of earthworm, *Metaphire posthuma*. Upon evaluation of five different extraction solvent systems, 80% methanol was found to have good extraction efficiency based on the yields of metabolites, multivariate analysis, total number of peaks and reproducibility of metabolites. Later the toxicity evaluation was performed to characterize the tissue specific metabolomic perturbation of earthworm, *Metaphire posthuma* after exposure to carbofuran at three different concentration levels (0.15, 0.3 and 0.6 mg/kg of soil). Seventeen metabolites, contributing to the best classification performance of highest dose dependent carbofuran exposed earthworms from healthy controls were identified. This study suggests that GC-MS based metabolomic approach was precise and sensitive to measure the earthworm responses to carbofuran

exposure in soil, and can be used as a promising tool for environmental eco-toxicological studies.

**Comparative toxicity of carbaryl, carbofuran, cypermethrin and fenvalerate in *Metaphire posthuma* and *Eisenia fetida* -A possible mechanism.**

[Saxena PN, Gupta SK, Murthy RC. Ecotoxicol Environ Saf. 2014 Feb;100:218-25.]

To establish the use of *Metaphire posthuma* as a sensitive test model for ecotoxicological studies, acute toxicity testing of carbaryl, carbofuran, cypermethrin and fenvalerate on *Eisenia fetida* and *Metaphire posthuma* were carried out. Two different types of bioassays, contact filter paper toxicity and soil toxicity bioassays were used to determine LC50 values for these insecticides. Among the tested chemicals, carbofuran was the most toxic to both the earthworm species. In paper contact method, 72h-LC50 values of carbofuran in *M. posthuma* and *E. fetida* were found to be 0.08µg/cm(2) and 1.55µg/cm(2) respectively while in soil test, 14-d LC50 values were 0.49mg/kg and 21.15mg/kg respectively. On comparing the toxicity data of these chemicals for both the earthworm species, *M. posthuma* was found to be more sensitive than *E. fetida*. Based on the acute toxicity data, the order of toxicity of insecticides in both the test procedures was carbofuran>cypermethrin>carbaryl>fenvalerate for *M. posthuma* whereas for *E. fetida* it was carbofuran>carbaryl>fenvalerate>cypermethrin. Morphological changes also appeared in the organisms exposed to these chemicals which were more pronounced in *M. posthuma* at lower concentrations than *E. fetida* in both the test procedures. The results of the present study advocates the use of *M. posthuma* for ecotoxicity studies, being a more sensitive and reliable model than *E. fetida*. Based on the data on partial atomic charges, structural features and spectroscopic studies on carbaryl and carbofuran, a possible mechanism of toxicity of carbamate insecticides in earthworm was proposed.

**Molecularly imprinted polymer coupled with dispersive liquid-liquid microextraction and injector port silylation: A novel approach for the determination of 3-phenoxybenzoic acid in complex biological samples using gas chromatography-tandem mass spectrometry.**

[Mudiam MK, Chauhan A, Jain R, Dhuriya YK, Saxena PN, Khanna VK. J Chromatogr B Analyt Technol Biomed Life Sci. 2014 Jan 15;945-946:23-30.]

A novel analytical approach based on molecularly imprinted solid phase extraction (MISPE) coupled with dispersive liquid-liquid microextraction (DLLME), and

injector port silylation (IPS) has been developed for the selective preconcentration, derivatization and analysis of 3-phenoxybenzoic acid (3-PBA) using gas chromatography-tandem mass spectrometry (GC-MS/MS) in complex biological samples such as rat blood and liver. Factors affecting the synthesis of MIP were evaluated and the best monomer and cross-linker were selected based on binding affinity studies. Various parameters of MISPE, DLLME and IPS were optimized for the selective preconcentration and derivatization of 3-PBA. The developed method offers a good linearity over the calibration range of 0.02-2.5ngmg(-1) and 7.5-2000ngmL(-1) for liver and blood respectively. Under optimized conditions, the recovery of 3-PBA in liver and blood samples were found to be in the range of 83-91%. The detection limit was found to be 0.0045ngmg(-1) and 1.82ngmL(-1) in liver and blood respectively. SRM transition of 271→227 and 271→197 has been selected as quantifier and qualifier transition for 3-PBA derivative. Intra and inter-day precision for five replicates in a day and for five, successive days was found to be less than 8%. The method developed was successfully applied to real samples, i.e. rat blood and tissue for quantitative evaluation of 3-PBA. The analytical approach developed is rapid, economic, simple, eco-friendly and possess immense utility for the analysis of analytes with polar functional groups in complex biological samples by GC-MS/MS.

#### **Interactive threats of nanoparticles to the biological system.**

[Roy R, Kumar S, Tripathi A, Das M, Dwivedi PD. Immunol Lett. 2013 Dec 4;158(1-2):79-87.]

The use of nanoscale materials is growing exponentially, but concerns rise about the human hazards cannot be ignored. Nanotechnology has penetrated deep into our lives in diversified areas as engineering, information technology and diagnostics. Nonetheless owing to their peculiar properties these new materials also present new health risks upon interacting with biological systems. This is a typical case of technology preceding toxicity and therefore, various toxicological aspects for an array of nanomaterials are just beginning to be assessed. Several deleterious effects are being noticed, particularly *in vitro* situations as well as in mammalian system. Nanoparticles toxicity is compellingly related to oxidative stress, alteration of calcium homeostasis, gene expression, pro-inflammatory responses and cellular signalling events. It is therefore critical to understand the nature and origin of the toxicity imposed by nanomaterials. Keeping all these points in mind, the present review provides updated information on the various aspects such as sources of

production, effect of different physical properties, interaction with biological system and mechanisms of engineered nanoparticles induced toxicities.

#### **Enhanced efficiency of P-element mediated transgenesis in Drosophila: Microinjection of DNA complexed with nanomaterial.**

[Sonane M, Goyal R, Chowdhuri DK, Ram KR, Gupta KC. Sci Rep. 2013 Dec 3;3:3408.]

The efficiency of genetic transformation technology to generate stable transgenics depends upon the successful delivery of plasmid DNA in embryonic cells. The available gene vectors facilitate efficient plasmid DNA delivery to the cellular milieu but are exposed to nuclease degradation. Recent *in vitro* studies suggest encapsulation of plasmid DNA with nanomaterial(s) for better protection against nucleases. Therefore, in this study, we tested if complexing of free plasmid DNA with linear polyethylenimine (LPEI, 25 kDa) based nanoparticle (LPN) enhances the efficiency of transformation (transgenesis) by using Drosophila based germ-line transformation technology. Here, we show that the LPN-DNA complex not only enhances the efficiency of this transgenic technology at a DNA concentration of 0.04 µg/µl but also reduces the DNA quantity required to generate transgenics by ten folds. This approach has potential applications for other types of transgenesis and nucleic acid injection methods in Drosophila as well as other popular genetic model systems.

#### **Comparative toxicity of low dose tributyltin chloride on serum, liver, lung and kidney following subchronic exposure.**

[Mitra S, Gera R, Singh V, Khandelwal S. Food Chem Toxicol. 2014 Feb;64:335-43.]

Tributyltin (TBT) pollution is rampant worldwide and is a growing threat due to its bio-accumulative property. Isolated studies of TBT toxicity on different organs are available but consolidated information is greatly lacking. We planned this study to delineate the effect of subchronic (1month) exposure to low dose TBT-chloride (TBTC) (1 and 5mg/kg) in male Wistar rats. Total tin concentration was found to be significantly increased in liver, kidney and blood, and marginally in lungs. Organosomatic indices were seen to be altered with little effect on serum biochemical markers (liver and kidney function, and general parameters). Reactive oxygen species but not lipid peroxidation content was observed to be significantly elevated both in the tissues and serum. TBTC was found to act as a hyperlipidemic agent and it also affected heme biosynthetic pathway. Hematological analysis showed that TBTC exposure resulted in minor

alterations in RBC parameters. Histological studies demonstrated marked tissue damage in all the 3 organs. Calcium inhibitors (BAPTA-AM, EGTA) and antioxidants (NAC, C-PC) significantly restored TBTC induced loss in cell viability, under ex-vivo conditions. Antioxidants were evidently more efficient in comparison to the calcium inhibitors, implying major role of oxidative stress pathways in TBTC toxicity.

**Zinc oxide nanoparticles provide an adjuvant effect to ovalbumin via a Th2 response in Balb/c mice.**

[Roy R, Kumar S, Verma AK, Sharma A, Chaudhari BP, Tripathi A, Das M, Dwivedi PD. Int Immunol. 2013 Nov 13. doi:10.1093/intimm/dxt053 Epub ahead of print]

Zinc oxide nanoparticles (ZNPs) have been used in dietary supplements and may cause an immunomodulatory effect. The present study investigated the effect of ZNPs on antigen-specific immune responses in mice sensitized with the T-cell-dependent antigen ovalbumin (OVA). BALB/c mice were intraperitoneally administered ZNPs (0.25, 0.5, 1 and 3mg) once, in combination with OVA, and the serum antibodies, splenocyte reactivity and activation of antigen-presenting cells were examined. The serum levels of OVA-specific IgG1 and IgE were found significantly enhanced by treatment with ZNPs over control. An increased level of IL-2, IL-4, IL-6, IL-17 and decreased level of IL-10 and TNF- $\alpha$  in splenocytes administered with ZNPs were observed in comparison with control. The ZNPs and OVA-stimulated T lymphocytes showed enhanced proliferation compared with control. Macrophages and B cells showed high expression of MHC class II, whereas higher expression of CD11b in macrophages of the ZNPs and ZNPs/OVA treated groups was observed. The lungs and spleen had increased eosinophils and mast cell numbers. Also, myeloperoxidase activity in lungs was found to be increased by 2.5-fold in the case of ZNPs and 3.75-fold increase in ZNPs/OVA, whereas in intestine, there was significant increase in both the groups. Increased expression of the genes for GATA-3, SOCS-3, TLR-4, IL-13 and IL-5 in the intestine was observed. Collectively, these data indicate that systemic exposure to a single administration of ZNPs could enhance subsequent antigen-specific immune reactions, including the serum production of antigen-specific antibodies, and the functionality of T cells.

**Mathematically derived body volume and risk of musculoskeletal pain among housewives in North India.**

[Bihari V, Kesavachandran CN, Mathur N, Pangtey BS, Kamal R, Pathak MK, Srivastava AK. PLoS One. 2013 Nov 6;8(11):e80133.]

Global Burden of Disease Study 2010 demonstrates the

impact of musculoskeletal diseases as the second greatest cause of disability globally in all regions of the world. The study was conducted to determine the role of mathematically derived body volume (BV), body volume index (BVI), body mass index (BMI), body surface area (BSA) and body fat % (BF %) on musculoskeletal pain (MSP) among housewives in National Capital Region (NCR). A cross sectional study was undertaken among 495 housewives from Gurgaon and New Okhla Industrial Development Area (NOIDA) in National Capital Region (NCR), New Delhi, India. The study includes questionnaire survey, clinical examination and body composition monitoring among housewives. A significantly higher BMI, BVI, BV and BSA were observed in subjects with MSP as compared to those who had no MSP. This was also true for subjects with pain in knee for BMI category for overweight. Subjects with pain in limbs had significantly high BMI and BVI as compared to subjects with no MSP. A significant positive correlation of age with BMI, BVI, BV and BSA was observed among subjects having no MSP denoting a direct relationship of age and these body factors. The prevalence of MSP among housewives is associated with increasing age, BMI and BVI. This can possibly be used for formulating a strategy for prevention of MSP.

**Gene expression profiling of candidate genes in peripheral blood mononuclear cells for predicting toxicity of diesel exhaust particles.**

[Srivastava A, Sharma A, Yadav S, Flora SJ, Dwivedi UN, Parmar D. Free Radic Biol Med. 2013 Nov 9;67C:188-194.]

To validate gene expression profiling of peripheral blood mononuclear cells (PBMCs) as a surrogate for monitoring tissue expression, this study using RT-PCR-based TaqMan low-density array (TLDA) was initiated to investigate similarities in the mRNA expression of target genes altered by exposure to diesel exhaust particles (DEPs) in freshly prepared PBMCs and in lungs. Adult Wistar rats were treated transtracheally with a single dose of 7.5 or 15 or 30mg/kg DEPs and sacrificed 24h later. Blood and lungs were immediately taken out and processed for RT-PCR. DEP treatment induced similar patterns of increase in the expression of polycyclic aromatic hydrocarbon-responsive cytochrome P450s, the phase II enzymes, and their associated transcription factors in both lungs and PBMCs, at all doses. Similar to that seen in lungs, a dose-dependent increase was observed in the expression of genes involved in inflammation, such as cytokines, chemokines, and adhesion molecules, in PBMCs. The expression of various genes involved in DNA repair and apoptosis was

also increased in a dose-dependent manner in PBMCs and lungs. The present TLDA data indicating similarities in the responsiveness of candidate genes involved in the toxicity of DEPs between PBMCs and lungs after exposure to DEPs demonstrate that expression profiles of genes in PBMCs could be used as a surrogate for monitoring the acute toxicity of fine and ultrafine particulate matter present in vehicular emissions.

**Modulation of liver function, antioxidant responses, insulin resistance and glucose transport by *Oroxylum indicum* stem bark in STZ induced diabetic rats.**

[Singh J, Kakkar P. Food Chem Toxicol. 2013 Dec;62:722-31.]

A decoction of stem bark of *Oroxylum indicum* Vent. (OI) is taken (2-3 times/day) by the tribal people of Sikkim, India to treat diabetes but scientific validation of its overall potential is lacking. Present study was aimed to assess *in vitro* antihyperglycemic activity of standardized OI extract using inhibition of  $\alpha$ -glucosidase, BSA glycation and enhancement of insulin sensitivity. Antidiabetic and antioxidant modulatory effects of OI extract along with the blood biomarkers of toxic response were studied in streptozotocin (STZ) induced diabetic rats. *In vitro* analysis showed strong antioxidant capacity of OI -and potential to inhibit BSA glycation and  $\alpha$ -glucosidase activity which was comparable to standard counterparts. Extract also improved insulin sensitivity in mature 3T3-L1 adipocytes. *In vivo* effects of OI extract (oral 250 mg/kg b.wt.) on STZ induced type II diabetic rats normalized the antioxidant status ( $p \leq 0.01$ ). Analysis of blood biomarkers of toxic response indicated its safety. Lowering of total cholesterol and HDL levels ( $p \leq 0.05$ ) and restoration of glycated Hb ( $p \leq 0.01$ ) were also found in OI treated diabetic rats. HOMA-IR, QUICKI analysis along with area under the curve analysis showed the capacity of OI extract to enhance the insulin sensitivity significantly ( $p \leq 0.01$ ) which was confirmed by increased GLUT-4 translocation in skeletal muscles.

**Singlet oxygen mediated DNA damage induced phototoxicity by ketoprofen resulting in mitochondrial depolarization and lysosomal destabilization.**

[Ray RS, Mujtaba SF, Dwivedi A, Yadav N, Verma A, Kushwaha HN, Amar SK, Goel S, Chopra D. Toxicology. 2013 Dec 15;314(2-3):229-37]

Ketoprofen (KP) is a widely used nonsteroidal anti-inflammatory drug for the treatment of osteoarthritis and

various rheumatic diseases. Currently, KP is applied topically on skin as gel to treat symptoms of pain and inflammation. We have studied the photomodification of KP under natural environmental conditions. KP generates reactive oxygen species (ROS) like  $^1O_2$  through Type-II photodynamic reaction.  $^1O_2$  mediated 2'-dGuO photo-degradation, single and double strand breakage were significantly induced by photosensitized KP under sunlight/UV-R exposure. Significant intracellular ROS generation was measured through DCF-DA fluorescence. Linoleic acid photoperoxidation and role of  $^1O_2$  were substantiated by using specific quencher like sodium azide. KP induced cell cycle arrest in G2/M phase and cell death through MTT assay. We found apoptosis as the pattern of cell death which was confirmed through caspase-3 activation, cytochrome-c release from mitochondria, up-regulation of Bax protein and phosphatidylserine translocation. Our RT-PCR result strongly supports our view point of apoptotic cell death through up-regulation of p21 and pro-apoptotic Bax genes expression. Mitochondrial depolarization and lysosomal destabilization were also parallel to apoptotic process. Therefore, much attention should be paid to the topical application of KP and sunlight exposure in the light of skin related photosensitivity and cancers.

**Endosulfan induced cell death in Sertoli-germ cells of male Wistar rat follows intrinsic mode of cell death.**

[Rastogi D, Narayan R, Saxena DK, Chowdhuri DK. Chemosphere. 2014 Jan;94:104-15.]

Health of germ cells may affect production of quality gametes either due to endogenous or exogenous factors. Pesticides are among the exogenous factors that can enter the organisms through various routes of exposure and also can affect the reproductive system of an organism. Endosulfan is an organochlorine cyclodiene pesticide used widely for controlling agricultural pests. It has been shown to induce reproductive dysfunctions such as sperm abnormalities, reduced intracellular spermatid count in exposed organisms. Germ cells being the progenitor cells for male gametes and Sertoli cells as their nourishing cells, we examined whether endosulfan induces cell death in Sertoli-germ cells of male rats. Sertoli-germ cells, isolated from 28 d old male Wistar rats, were exposed to endosulfan (2.0, 20.0 and 40.0  $\mu$ g mL<sup>-1</sup>) for 24-72 h. Cytotoxicity, endosulfan concentration, reactive oxygen species (ROS) generation, oxidative stress parameters were measured in these cells in the absence or presence of endosulfan for the above mentioned exposure periods and subsequently, cell death endpoints were measured. We detected

endosulfan in the exposed cells and demonstrated increased cell death in exposed Sertoli-germ cells as evidenced by a significant increase in annexin-V staining, depolarization of mitochondrial membrane, caspase-9 and -3 activities and BAD and PARP cleavage activities and DNA ladder formation along with non-significant increase in autophagic cell death. The study suggests that endosulfan can cause cell death in exposed Sertoli-germ cells due to higher oxidative damage with the activation of intrinsic cell death pathway which may eventually affect the production of quality gametes.

### **Monocrotophos induced oxidative stress and alterations in brain dopamine and serotonin receptors in young rats.**

[Sankhwar ML, Yadav RS, Shukla RK, Singh D, Ansari RW, Pant AB, Parmar D, Khanna VK. Toxicol Ind Health. 2013 Oct 8. (Epub ahead of print)]

Human exposure to monocrotophos, an organophosphate pesticide, could occur due to its high use in agriculture to protect crops. Recently, we found that postlactational exposure to monocrotophos impaired cholinergic mechanisms in young rats and such changes persisted even after withdrawal of monocrotophos exposure. In continuation to this, the effect of monocrotophos on noncholinergic targets and role of oxidative stress in its neurotoxicity has been studied. Exposure of rats from postnatal day (PD) 22 to PD49 to monocrotophos (0.50 or 1.0 mg kg<sup>-1</sup> body weight, perorally) significantly impaired motor activity and motor coordination on PD50 as compared to controls. A significant decrease in the binding of 3H-spiperone to striatal membrane (26%,  $p < 0.01$ ; 30%,  $p < 0.05$ ) in rats exposed to monocrotophos at both the doses and increase in the binding of 3H-ketanserin to frontocortical membrane (14%,  $p > 0.05$ ; 37%,  $p < 0.05$ ) in those exposed at a higher dose, respectively, was observed on PD50 compared with the controls. Alterations in the binding persisted even after withdrawal of monocrotophos exposure on PD65. Increased oxidative stress in brain regions following exposure of rats to monocrotophos was also observed on PD50 that persisted 15 days after withdrawal of exposure on PD65. The results suggest that monocrotophos exerts its neurobehavioral toxicity by affecting noncholinergic functions involving dopaminergic and serotonergic systems associated with enhanced oxidative stress. The results also exhibit vulnerability of developing brain to monocrotophos as most of the changes persisted even after withdrawal of its exposure.

### **Emptying of intracellular calcium pool and oxidative stress imbalance are associated with the glyphosate-induced proliferation in human skin keratinocytes HaCaT cells.**

[George J, Shukla Y. ISRN Dermatol. 2013 Aug 29;2013:825180. doi: 10.1155/2013/825180. eCollection 2013.]

We demonstrated that glyphosate possesses tumor promoting potential in mouse skin carcinogenesis and SOD 1, calcyclin (S100A6), and calgranulin B (S100A9) have been associated with this potential, although the mechanism is unclear. We aimed to clarify whether imbalance in between  $[Ca^{2+}]_i$  levels and oxidative stress is associated with glyphosate-induced proliferation in human keratinocytes HaCaT cells. The  $[Ca^{2+}]_i$  levels, ROS generation, and expressions of G1/S cyclins, IP3R1, S100A6, S100A9, and SOD 1, and apoptosis-related proteins were investigated upon glyphosate exposure in HaCaT cells. Glyphosate (0.1mM) significantly induced proliferation, decreases  $[Ca^{2+}]_i$ , and increases ROS generation in HaCaT cells, whereas antioxidant N-acetyl-L-cysteine (NAC) pretreatment reverts these effects which directly indicated that glyphosate induced cell proliferation by lowering  $[Ca^{2+}]_i$  levels via ROS generation. Glyphosate also enhanced the expression of G1/S cyclins associated with a sharp decrease in G0/G1 and a corresponding increase in S-phases. Additionally, glyphosate also triggers S100A6/S100A9 expression and decreases IP3R1 and SOD 1 expressions in HaCaT cells. Notably,  $Ca^{2+}$  suppression also prevented apoptotic related events including Bax/Bcl-2 ratio and caspases activation. This study highlights that glyphosate promotes proliferation in HaCaT cells probably by disrupting the balance in between  $[Ca^{2+}]_i$  levels and oxidative stress which in turn facilitated the downregulation of mitochondrial apoptotic signaling pathways.

### **Tributyltin chloride induced testicular toxicity by JNK and p38 activation, redox imbalance and cell death in sertoli-germ cell co-culture.**

[Mitra S, Srivastava A, Khandelwal S. Toxicology. 2013 Dec 6;314(1):39-50.]

The widespread use of tributyltin (TBT) as biocides in antifouling paints and agricultural chemicals has led to environmental and marine pollution. Human exposure occurs mainly through TBT contaminated seafood and drinking water. It is a well known endocrine disruptor in mammals, but its molecular mechanism in testicular damage is largely unexplored. This study was therefore,

designed to ascertain effects of tributyltin chloride (TBTC) on sertoli-germ cell co-culture in *ex-vivo* and in the testicular tissue *in-vivo* conditions. An initial  $\text{Ca}(2+)$  rise followed by ROS generation and glutathione depletion resulted in oxidative damage and cell death. We observed p38 and JNK phosphorylation, stress proteins (Nrf2, MT and GST) induction and mitochondrial depolarization leading to caspase-3 activation. Prevention of TBTC reduced cell survival and cell death by  $\text{Ca}(2+)$  inhibitors and free radical scavengers specify definitive role of  $\text{Ca}(2+)$  and ROS. Sertoli cells were found to be more severely affected which in turn can hamper germ cells functionality. TBTC exposure *in-vivo* resulted in increased tin content in the testis with enhanced Evans blue leakage into the testicular tissue indicating blood-testis barrier disruption. Tesmin levels were significantly diminished and histopathological studies revealed marked tissue damage. Our data collectively indicates the toxic manifestations of TBTC on the male reproductive system and the mechanisms involved.

**Ultrasound assisted dispersive liquid-liquid microextraction followed by injector port silylation: a novel method for rapid determination of quinine in urine by GC-MS.**

[Jain R, Mudiam MK, Ch R, Chauhan A, Khan HA, Murthy R. Bioanalysis. 2013 Sep;5(18):2277-86.]

Silylation is a widely used derivatization method for the analysis of polar analytes by GC-MS. Ultrasound-assisted dispersive liquid-liquid microextraction (UA-DLLME) is an ecofriendly, rapid and simple microextraction method. For the first time, a novel approach has been developed and applied for the analysis of quinine in urine by combining UA-DLLME with injection port silylation. The LOD and LOQ were found to be 5.4 and 18 ng/ml. The intra- and inter-day precisions were less than 5 and 8%, respectively. Mean recoveries of quinine were found to be in the range of 87 to 96%. Ultrasound-assisted dispersive liquid-liquid microextraction is rapid, simple and consumes less reagent for the analysis of polar analytes such as quinine.

**SOCS3 dictates the transition of divergent time-phased events in granulocyte TNF- $\alpha$  signaling.**

[Chhabra JK, Chattopadhyay B, Paul BN. Cell Mol Immunol. 2014 Jan;11(1):105-6.]

Tumor-necrosis factor- $\alpha$  (TNF- $\alpha$ )-driven nuclear factor- $\kappa\text{B}$  (NF- $\kappa\text{B}$ ) activation and apoptosis are opposing pathways; the growing recognition of these conflicting roles of TNF- $\alpha$  is perplexing. Here, we show that

inflammation and apoptosis are time-phased events following TNF- $\alpha$  signaling and that emergence of suppressor of cytokine signaling 3 (SOCS3) expression limits the ongoing NF- $\kappa\text{B}$  activation and promotes apoptosis; further, we suggest an altered view of how inflammatory diseases are initiated and sustained. *In vitro*, TNF- $\alpha$  (50 ng/ml) induced granulocyte SOCS3 protein, inhibited nuclear accumulation of the p65NF- $\kappa\text{B}$  subunit and enhanced apoptosis, as shown by DNA laddering, annexin V positivity, and overexpression of caspase-3 and Bax in the late phase, whereas the early phase was marked by NF- $\kappa\text{B}$  activation. Conversely, SOCS3 knockdown by small interfering RNA (siRNA) inhibited granulocyte apoptosis and enhanced nuclear accumulation of p65 and 5' lipooxygenase expression in the late phase of TNF- $\alpha$  signaling. As apoptosis is associated with SOCS3 abundance, we suggest that these divergent TNF- $\alpha$ -driven events are time-phased, interconnected, opposing control mechanisms and one of the central features through which the immune system resolves pulmonary inflammation. Dysregulation may initiate mucosal inflammation, thus changing the landscape of asthma therapy.

**Recent advancements in the therapeutics of food allergy.**

[Kumar S, Gupta K, Das M, Dwivedi PD. Recent Pat Food Nutr Agric. 2013 Dec;5(3):188-200.]

Food allergy is a health complication induced by certain food in the susceptible individuals. Due to lack of permanent cure and the global prevalence, the preventive approach is highly required for food allergy. Recently published patents have shown significant improvements in the food allergy research. In this review, an attempt has been done to highlight the recently developed patents related to the detection of allergens in food mixture. Also, patents regarding treatment options like use of herbal therapy, antihistamines, pre-, pro and synbiotics, nanocarriers, hypoallergens and several immune molecules towards amelioration of food allergy have been reviewed in this article.

**Silymarin- and melatonin-mediated changes in the expression of selected genes in pesticides-induced Parkinsonism.**

[Singhal NK, Chauhan AK, Jain SK, Shanker R, Singh C, Singh MP. Mol Cell Biochem. 2013 Dec;384(1-2):47-58.]

Parkinson's disease (PD) is the second most unconcealed neurodegenerative disorder labelled with motor impairments. Two pesticides, manganese

ethylene-1,2-bisdithiocarbamate (maneb) and 1,1'-dimethyl-4,4'-bipyridinium dichloride (paraquat), together, are reported to increase the incidence of PD in humans and Parkinsonism in mice. Conversely, silymarin and melatonin, two naturally occurring antioxidants, rescue from maneb- and paraquat-induced Parkinsonism. The study examined silymarin- and melatonin-mediated changes in the expression of selected genes in maneb- and paraquat-induced Parkinsonism employing mouse discover chips microarrays. The mice were treated intraperitoneally (i.p.), daily, with silymarin (40 mg/kg) or melatonin (30 mg/kg) for 9 weeks along with vehicles. Subsets of animals were also treated with maneb (30 mg/kg; i.p.) and paraquat (10 mg/kg; i.p.), twice a week, for 9 weeks. Whilst the expression of genes in the striatum was determined by microarray, the expression of randomly selected transcripts was validated by quantitative real-time polymerase chain reaction (qRT-PCR). Combined maneb- and paraquat-treatment altered the expression of several genes associated with apoptosis, inflammation, cell cycle, cell-signalling, etc. pathways. Silymarin and melatonin significantly resisted the changes in the expression of a few genes related to apoptosis, inflammation, cell cycle, cell-signalling, etc. The expression patterns of seven randomly selected genes were analyzed by qRT-PCR, which were found to follow the similar trends, as observed with microarray. The results obtained from the study thus demonstrate that despite resemblances, silymarin and melatonin differentially offset maneb- and paraquat-induced changes in transcriptome.

**Adverse respiratory health and hematological alterations among agricultural workers occupationally exposed to organophosphate pesticides: a cross-sectional study in North India.**

[Fareed M, Pathak MK, Bihari V, Kamal R, Srivastava AK, Kesavachandran CN. PLoS One. 2013 Jul 25;8(7):e69755.]

Non-protective work practices followed by farm workers during spraying of pesticides lead to occupational exposure among them. This study is designed to explore the respiratory health and hematological profile of agricultural workers occupationally exposed to OP pesticides. A cross sectional study was undertaken among 166 pesticide sprayers working in mango orchards of Lucknow district in North India compared with 77 controls to assess the respiratory illness, lung functions, cholinesterase levels and hematological profile. A questionnaire based survey and clinical

examination for respiratory health were conducted among study subjects. Lung function test was conducted among study subjects by using spirometer. Cholinesterase level as biomarker of OP pesticides and hematological profile of study subjects were investigated in the laboratory by following the standard protocols. Overall respiratory morbidity observed among exposed subjects was 36.75%. Symptoms for respiratory illness like dry cough, productive cough, wheezing, irritation of throat and blood stained sputum were found to be significantly more ( $p < 0.05$ ) among pesticide sprayers than controls. Lung function parameters viz. PEFr, FEV1, %PEFr predicted, %FEV1 predicted and FEV1/FVC were found to be significantly decreased ( $p < 0.05$ ) among pesticide sprayers as compared to controls. Exposure wise distribution of respiratory illness and lung functions among pesticide sprayers show that the exposure duration significantly elevates ( $p < 0.05$ ) the respiratory problems and significantly decreases ( $p < 0.001$ ) lung functions among pesticide sprayers. Activities of acetylcholinesterase and butyrylcholinesterase were found to be significantly depleted ( $p < 0.001$ ) among pesticide sprayers as compared to controls which show the exposure of OP pesticides among them. The hematological profile viz. RBC, WBC, monocytes, neutrophils, MCV, MCH, MCHC and platelet count were significantly altered ( $p < 0.001$ ) in pesticide sprayers than controls. This study shows that the unsafe occupational exposure of OP pesticides causes respiratory illness, decreased lung functions and hematological alterations among pesticide sprayers.

**Nicotine-encapsulated poly(lactic-co-glycolic) acid nanoparticles improve neuroprotective efficacy against MPTP-induced parkinsonism.**

[Tiwari MN, Agarwal S, Bhatnagar P, Singhal NK, Tiwari SK, Kumar P, Chauhan LK, Patel DK, Chaturvedi RK, Singh MP, Gupta KC. Free Radic Biol Med. 2013 Dec;65:704-18.]

For some instances of Parkinson disease (PD), current evidence in the literature is consistent with reactive oxygen species being involved in the etiology of the disease. The management of PD is still challenging owing to its ambiguous etiology and lack of permanent cure. Because nicotine offers neuroprotection against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced parkinsonism, the neuroprotective efficacy of nicotine-encapsulated poly(lactic-co-glycolic) acid (PLGA) nanoparticles and the underlying mechanism of improved efficacy, if any, over bulk nicotine were assessed in this study. The selected indicators of oxidative stress, dopaminergic neurodegeneration and apoptosis, were

measured in both *in vitro* and rodent models of parkinsonism in the presence or absence of "nanotized" or bulk nicotine. The levels of dopamine and its metabolites were measured in the striatum, nicotine and its metabolite in the nigrostriatal tissues while the immunoreactivities of tyrosine hydroxylase (TH), metallothionein-III (MT-III), inducible nitric oxide synthase (iNOS) and microglial activation were checked in the substantia nigra of controls and treated mice. GSTA4-4, heme oxygenase (HO)-1, tumor suppressor protein 53 (p53), caspase-3, lipid peroxidation (LPO), and nitrite levels were measured in the nigrostriatal tissues. Nicotine-encapsulated PLGA nanoparticles improved the endurance of TH-immunoreactive neurons and the number of fiber outgrowths and increased the mRNA expression of TH, neuronal cell adhesion molecule, and growth-associated protein-43 over bulk against 1-methyl-4-phenyl pyridinium ion-induced degeneration in the *in vitro* model. MPTP reduced TH immunoreactivity and levels of dopamine and its metabolites and increased microglial activation, expression of GSTA4-4, iNOS, MT-III, HO-1, p53, and caspase-3, and levels of nitrite and LPO. Whereas both bulk nicotine and nicotine-encapsulated PLGA nanoparticles modulated the changes toward controls, the modulation was more pronounced in nicotine-encapsulated PLGA nanoparticle-treated parkinsonian mice. The levels of nicotine and cotinine were elevated in nicotine-encapsulated PLGA nanoparticle-treated PD mouse brain compared with bulk. The results obtained from this study demonstrate that nanotization of nicotine improves neuroprotective efficacy by enhancing its bioavailability and subsequent modulation in the indicators of oxidative stress and apoptosis.

#### **Similarities in lindane induced alteration in cytochrome P450s and associated signaling events in peripheral blood lymphocytes and brain.**

[Khan AJ, Sharma A, Dinesh K, Parmar D. Food Chem Toxicol. 2013 Oct;60:318-27.]

Studies were initiated to investigate the similarities in alterations in cytochrome P450s (CYPs) and associated signaling events in brain and peripheral blood lymphocytes (PBL) induced by lindane, an organochlorine pesticide. Adult male albino wistar rats were treated orally with different doses (2.5- or 5.0- or 10- or 15 mg/kg/body weight) of lindane daily for 4 days. In another experiment, the treatment of low dose (2.5mg/kg) of lindane was continued for 15- and 21 days. A dose- and time-dependent increase was observed in the activity of

CYP dependent enzymes in brain microsomes and PBL isolated from the treated rats. However, the magnitude of induction was several folds less in PBL. As observed in brain, RT-PCR and Western immunoblotting demonstrated that increase in CYP enzymes in PBL is due to the increase in the mRNA expression of specific CYP isoenzymes. Similarities were also observed in activation of ERK and JNK MAP kinases and c-jun in PBL or brain isolated from rats treated with lindane. Similarities in the induction of CYPs and activation of MAP kinases in PBL and brain suggest that CYP expression profiles in PBL could be used for monitoring the exposure and toxicity of environmental chemicals.

#### **Allergenicity potential of red kidney bean (*Phaseolus vulgaris* L.) proteins in orally treated BALB/c mice and passively sensitized RBL-2H3 cells.**

[Kumar S, Sharma A, Verma AK, Chaudhari BP, Das M, Jain SK, Dwivedi PD. Cell Immunol. 2013 Jul-Aug;284(1-2):37-44. doi: 10.1016/j.cellimm.2013.07.001.]

Red kidney bean (*Phaseolus vulgaris* L.) is one the most commonly consumed legumes that requires an in depth understanding of its allergenicity. Therefore, the aim of this study was to explore the allergenicity of red kidney bean proteins following oral exposure in BALB/c mice and elucidate the levels of Th1/Th2 transcription factors induced by red kidney bean proteins in rat basophilic leukemia cells (RBL-2H3 cells) passively sensitized with the sera of red kidney bean sensitized mice. Red kidney bean proteins showed enhanced levels of total and specific IgE, anaphylactic symptoms, thymic stromal lymphopoietin (TSLP) and peritoneal albumin over control. Enhanced release of  $\beta$ -hexosaminidase along with up regulated expressions of GATA-3, STAT-6, T-bet, c-MAF and NFAT were observed in the RBL-2H3 cells exposed with red kidney bean proteins when compared to that of the controls. Taken together, exposure of red kidney bean proteins may cause allergic symptoms in mice and the ambivalent effect on Th2/Th1 transcription factors in RBL-2H3 cells.

#### **Macrophages in food allergy: an enigma.**

[Kumar S, Dwivedi PD, Das M, Tripathi A. Mol Immunol. 2013 Dec;56(4):612-8.]

Macrophages, the characteristic cell type in inflammatory reactions, participate in a variety of immunological events in humans and other mammals. They act as regulatory switches for both innate and acquired arms of immune system and play a vital role in tissue repair. Recent studies have shown the possible role of macrophages in

food allergic reactions. Since, there is involvement of alveolar as well as peritoneal macrophages in the pathogenesis of several food allergies, the present review covers the relevance of macrophage related immunological response in food allergic reactions.

### **Does restraining nitric oxide biosynthesis rescue from toxins-induced parkinsonism and sporadic Parkinson's disease?**

[Gupta SP, Yadav S, Singhal NK, Tiwari MN, Mishra SK, Singh MP. Mol Neurobiol. 2013 Jul 31. (Epub ahead of print)]

Nitric oxide (NO) is an important inorganic molecule of the biological system owing to diverse physiological implications. NO is synthesised from a semi-essential amino acid L-arginine. NO biosynthesis is catalysed by a family of enzymes referred to as nitric oxide synthases (NOSs). NO is accused in many acute and chronic illnesses, which include central nervous system disorders, inflammatory diseases, reproductive impairments, cancer and cardiovascular anomalies. Owing to very unstable nature, NO gets converted into nitrite, peroxynitrite and other reactive nitrogen species that could lead to nitrosative stress in the nigrostriatal system. Nitrosative stress is widely implicated in Parkinson's disease (PD), and its beneficial and harmful effects are demonstrated in *in vitro*, rodent and primate models of toxins-induced parkinsonism and in the blood, cerebrospinal fluid and nigrostriatal tissues of sporadic PD patients. The current article updates the roles of NO and NOSs in sporadic PD and toxins-induced parkinsonism in rodents along with the scrutiny of how inhibitors of NOSs could open a new line of approach to moderately rescue from PD pathogenesis based on the existing literature. The article also provides a perspective concerning the lack of ample admiration to such an approach and how to minimise the underlying lacunae.

### **Skin tumorigenic potential of benzanthrone: prevention by ascorbic acid.**

[Dwivedi N, Kumar S, Ansari KM, Khanna SK, Das M. Food Chem Toxicol. 2013 Sep;59:687-95.]

Benzanthrone (BA) exposed occupational workers have been found to exhibit toxicological manifestations in the skin, thus it is quite likely that long term exposure may lead to skin tumorigenicity. Thus, attempts were made to elucidate the tumor initiating and promoting potentials of pure (PBA) and commercial benzanthrone (CBA). Additionally, the preventive role of ascorbic acid (AsA)

was also assessed. PBA showed tumor initiating activity while CBA demonstrated tumor initiating as well as promoting activities in two-stage mouse skin tumor protocol. Further, prior treatment of AsA to PBA and CBA followed by twice weekly application of 12-o-tetradecanoyl phorbol myristate acetate (TPA) resulted into delayed onset of tumor formation and similarly single application of 7,12-dimethylbenz [a] anthracene (DMBA) followed by twice weekly application of AsA and CBA showed an increase in the latency period. Thus, AsA showed a protective effect against CBA promoted skin tumor. Furthermore, the topical application of CBA significantly increased the levels of xenobiotic enzymes. The animals topically treated with AsA along with topical application of CBA, restored all the impairment observed in enzyme activities. Thus, this study suggested that AsA can be useful in preventing PBA and CBA induced skin tumorigenicity.

### **Predicting carcinogenicity of diverse chemicals using probabilistic neural network modeling approaches.**

[Singh KP, Gupta S, Rai P. Toxicol Appl Pharmacol. 2013 Oct 15;272(2):465-75.]

Robust global models capable of discriminating positive and non-positive carcinogens; and predicting carcinogenic potency of chemicals in rodents were developed. The dataset of 834 structurally diverse chemicals extracted from Carcinogenic Potency Database (CPDB) was used which contained 466 positive and 368 non-positive carcinogens. Twelve non-quantum mechanical molecular descriptors were derived. Structural diversity of the chemicals and nonlinearity in the data were evaluated using Tanimoto similarity index and Brock-Dechert-Scheinkman statistics. Probabilistic neural network (PNN) and generalized regression neural network (GRNN) models were constructed for classification and function optimization problems using the carcinogenicity end point in rat. Validation of the models was performed using the internal and external procedures employing a wide series of statistical checks. PNN constructed using five descriptors rendered classification accuracy of 92.09% in complete rat data. The PNN model rendered classification accuracies of 91.77%, 80.70% and 92.08% in mouse, hamster and pesticide data, respectively. The GRNN constructed with nine descriptors yielded correlation coefficient of 0.896 between the measured and predicted carcinogenic potency with mean squared error (MSE) of 0.44 in complete rat data. The rat carcinogenicity model (GRNN) applied to the mouse and hamster data yielded

correlation coefficient and MSE of 0.758, 0.71 and 0.760, 0.46, respectively. The results suggest for wide applicability of the inter-species models in predicting carcinogenic potency of chemicals. Both the PNN and GRNN (inter-species) models constructed here can be useful tools in predicting the carcinogenicity of new chemicals for regulatory purposes.

### **3-methylcholanthrene induces neurotoxicity in developing neurons derived from human CD34+Thy1+ stem cells by activation of aryl hydrocarbon receptor.**

[Singh AK, Kashyap MP, Kumar V, Tripathi VK, Yadav DK, Khan F, Jahan S, Khanna VK, Yadav S, Pant AB. Neuromolecular Med. 2013 Sep;15(3):570-92.]

Developing neurons, derived from the human umbilical cord blood stem cells (hUCBSCs), were investigated for their stage-specific responses against 3-methylcholanthrene (MC), a well-known polycyclic aromatic hydrocarbon. Three-dimensional (3D) molecular docking demonstrates the strong hydrogen bonding and hydrophobic interactions of MC with amino acids of aryl hydrocarbon receptor (AHR) and aryl hydrocarbon receptor nuclear translocator (ARNT) within 4 Å and subsequent inhibition of cAMP response element-binding protein (CREB),  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) and N-methyl-D-aspartate (NMDA) receptors. Protein-protein docking also confirms that induced levels of AHR inhibit the neurogenesis-related transcription factor (CREB) with maximum docking scores. In concurrence with *in silico* data, MC exposure significantly up regulates the expression and activity of AHR, CYP1A1 and glutathione S-transferase P1-1 (GSTP1-1) and down regulates the expression of CREB, AMPA and NMDA receptors in hUCBSC-derived neuronal cells at various maturity (0, 2, 4, 8 days of differentiation). MC-mediated significant down regulation in the expression of stage-specific neuronal markers (Nestin, neural cell adhesion molecule-NCAM, synaptophysin-SYP, CREB, AMPA and N-methyl-D-aspartate receptor subunit 2A-NR2A) was also noticed in cells all through the differentiation. Data identify the possible interference of MC in neuronal transmission and neurogenesis.

### **Micronucleus induction by oxidative metabolites of trichloroethylene in cultured human peripheral blood lymphocytes: a comparative genotoxicity study.**

[Varshney M, Chandra A, Chauhan LK, Goel SK. Environ Sci Pollut Res Int. 2013 Dec;20(12):8709-16.]

The genotoxic effects of oxidative metabolites of trichloroethylene (TCE), namely chloral hydrate, trichloroacetic acid (TCA), dichloroacetic acid (DCA), and trichloroethanol (TCEOH) were examined in human peripheral blood lymphocytes. In this context, lymphocytes were exposed *in vitro* to 25, 50, and 100  $\mu$ g/ml concentrations of these metabolites separately for a period of 48 h and examined for micronucleus (MN) induction through flow cytometer. At 50  $\mu$ g/ml TCE metabolites, TCA ( $6.33 \pm 0.56$  %), DCA ( $5.06 \pm 0.55$ ), and TCEOH ( $4.70 \pm 1.73$ ) induced highly significant ( $p < 0.001$ ) frequency of MN in comparison to control ( $1.03 \pm 0.40$ ) suggestive of their genotoxic potential. However, exposure of 100  $\mu$ g/ml of all the metabolites consistently declined the frequencies of MN which in some cases was equable to that of observed at 25  $\mu$ g/ml. Further, cytotoxicity and cell cycle disturbances were also measured to find out the association of these endpoints with the MN induction. DNA content analysis revealed 3-4-fold elevation of S-phase at all the concentrations tested. Particularly, at 100  $\mu$ g/ml, treatment elevation of S-phase was significantly ( $p < 0.0001$ ) higher as compared to the control. Present findings together with earlier reports indicate that TCE induces genotoxicity through its metabolites. Interaction of these metabolites with DNA, as evident by elevated S-phase, seems to be the major cause of MN induction. However, involvement of spindle disruption cannot be ruled out. This comparative study also suggests that after TCE exposure, the metabolic efficiency of human to generate oxidative metabolites determines the extent of genotoxicity.

### **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. 2013 Nov; 216(6):645-51.]

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.

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

[Chaturvedi RK, Beal MF. Mol Cell Neurosci. 2013 Jul;55:101-14.]

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. We 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. We also summarize the phase II-III clinical trials conducted using some of these agents. Lastly, we discuss PGC-1 $\alpha$ , TORC and Sirtuins as potential therapeutic targets for mitochondrial dysfunction in neurodegenerative disorders. This article is part of a Special Issue entitled 'Mitochondrial function and dysfunction in neurodegeneration'.

#### **A comprehensive review of legume allergy.**

[Verma AK, Kumar S, Das M, Dwivedi PD. Clin Rev Allergy Immunol. 2013 Aug;45(1):30-46.]

Legumes belonging to Fabaceae family of the order Fabales are a rich and important source of proteins and many essential elements. Due to its nutritious elements, these are preferably included in human diet in most part of the world. But, unfortunately, IgE binding proteins have been identified in majority of legumes, and allergenic response to these legumes may range from mild skin reactions to life-threatening anaphylactic reaction. Overall, allergenicity due to consumption of legumes in decreasing order may be peanut, soybean, lentil, chickpea, pea, mung bean, and red gram. So far, several allergens from different legumes have been identified and characterized. Most of identified allergens belong to storage proteins family, profilins, or the pathogenesis-related proteins. Legumes also have property of immunological cross-reactivity among themselves and from other sources that also increases the severity of allergenic response to a particular legume. This review summarizes the currently available knowledge on legume allergy and describes the allergenic problems associated with different legumes. It also tries to explore about the legume allergens identified so far by different scientific groups. The culmination of knowledge about identification and characterization of allergens from different legumes will be helpful in diagnosis and treatment of allergy, for development of novel therapeutic strategies, for strict avoidance of particular legume in diet by susceptible individual and also to produce hypoallergenic cultivars of leguminous crop through conventional breeding or genetic modification.

## RESEARCH DIGEST

### Uncertain inheritance: Transgenerational effects of environmental exposures

[Environ Health Perspect; DOI:10.1289/ehp.121-A298]



Andrea Cupp made a serendipitous discovery when she was a postdoctoral fellow at Washington State University: While investigating how chemicals affect sex determination in embryonic animals, she bred the offspring of pregnant rats that had been dosed with an insecticide called methoxychlor. When the males from that litter grew into adults, they had decreased sperm counts and higher rates of infertility. Cupp had seen these same abnormalities in the animals' fathers, which had been exposed to methoxychlor in the womb. But this latest generation hadn't been exposed that way, which suggested that methoxychlor's toxic effects had carried over generations. "At first I couldn't believe it," says Cupp's advisor, Michael Skinner, a biochemist and Washington State professor. "But then we repeated the breeding experiments and found that the results held up."

Skinner and Cupp, published their findings in 2005. Since that paper—which showed that reproductive effects not just from methoxychlor but also from the fungicide vinclozolin persisted for at least four generations—the number of published articles reporting similar transgenerational findings has increased steadily. "In the last year and half there's been an explosion in studies showing transgenerational effects from exposure to a wide array of environmental stressors," says Lisa Chadwick, a program administrator at the National Institute of Environmental Health Sciences (NIEHS). "This is a field that's really starting to take off." According to Chadwick, the new findings compel a reevaluation of how scientists perceive environmental health threats. "We have to think more long-term about the effects of chemicals that we're exposed to every day," she says. "This new research suggests they could have consequences not just for our own health and for that of our children, but also for the health of generations to come." The NIEHS recently issued requests for applications totaling \$3 million for research on transgenerational effects in mammals. Chadwick says funded studies will address two fundamental data needs, one pertaining to potential transgenerational mechanisms and another to the number of chemicals thought to exert these effects. These studies will extend to what's known as the  $F_3$  generation—the great-grandchildren of the originally exposed animal. That's because chemicals given to pregnant females (the  $F_0$  generation) interact not only with the fetal offspring (the  $F_1$  generation) but also the germ cells developing within those offspring, which mature into the sperm and eggs that give rise to the  $F_2$  generation. Thus, the  $F_3$  animals are the first generation to be totally unexposed to the original agent. Effects that extend to the  $F_2$  generation are known as "multigenerational," whereas those that extend to the  $F_3$  generation are known as "transgenerational." Transgenerational effects have now been reported for chemicals including permethrin, DEET, bisphenol A, certain phthalates, dioxin, jet fuel mixtures, nicotine, and tributyltin, among others. Most of these findings come from rodent studies. But preliminary evidence that chemical effects can carry over generations in humans is also emerging, although no  $F_3$  data have been published yet. Given the challenges of tracking effects over multiple human lifespans, the evidence is more difficult to interpret, particularly with respect to potential

mechanisms, says Tessa Roseboom, a professor of early development and health at the Academic Medical Center in Amsterdam, the Netherlands. Still, some reports have linked nutritional deficiencies from famine and exposure to diethylstilbestrol (DES)—a nonsteroidal estrogen used to protect against miscarriage from the 1940s to the 1970s—to effects that persist among the grandchildren of exposed women.

### **Burden of disease from toxic waste sites in india, indonesia, and the philippines in 2010**

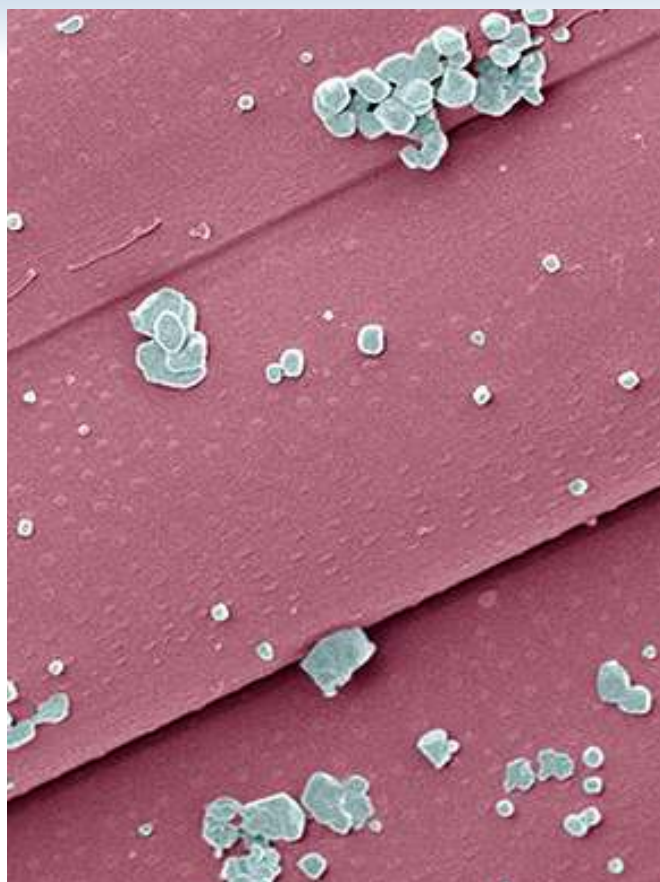
[Environ Health Perspect 121:791-796 (2013)]

Authors a disability-adjusted life year (DALY)-based estimate of the disease burden attributable to toxic waste sites. They focused on three low- and middle-income countries (LMICs): India, Indonesia, and the Philippines. Sites were identified through the Blacksmith Institute's Toxic Sites Identification Program, a global effort to identify waste sites in LMICs. At least one of eight toxic chemicals was sampled in environmental media at each site, and the population at risk estimated. By combining estimates of disease incidence from these exposures with population data, they calculated the DALYs attributable to exposures at each site. Authors estimated that in 2010, 8,629,750 persons were at risk of exposure to industrial pollutants at 373 toxic waste sites in the three countries, and that these exposures resulted in 828,722 DALYs, with a range of 814,934–1,557,121 DALYs, depending on the weighting factor used. This disease burden is comparable to estimated burdens for outdoor air pollution (1,448,612 DALYs) and malaria (725,000 DALYs) in these countries. Lead and hexavalent chromium collectively accounted for 99.2% of the total DALYs for the chemicals evaluated. Toxic waste sites are responsible for a significant burden of disease in LMICs. Although some factors, such as unidentified and unscreened sites, may cause our estimate to be an underestimate of the actual burden of disease, other factors, such as extrapolation of environmental sampling to the entire exposed population, may result in an overestimate of the burden of disease attributable to these sites. Toxic waste sites are a major, and heretofore underrecognized, global health problem.

### **Nanosilver: Weighing the risks and benefits**

[Environ Health Perspect 121:A220-A225 (2013)]

The use of silver as an antimicrobial is nothing new, but recent advances in the ability to manipulate nanosilver particles, plus evidence that silver can fight antibiotic-resistant bacteria, have led to a surge of new innovations.



But consensus remains elusive on subjects as essential as how nanosilver behaves in the body, how the influx of silver affects the environment, and the extent to which its use is apt to breed strains of resistant microbes.

### **Human cost of coal in the UK: 1600 lives a year**

[<http://www.newscientist.com/article/dn24694-human-cost-of-coal-in-the-uk-1600-lives-a-year.html#.UygoJM7-WVoJ>]

The days of pea-soupers may be long gone but Britons still suffer the effects of coal-burning power plants. In the UK, 1600 deaths per year and over 350,000 lost workdays can be attributed to air pollution from coal-burning, according to figures published by the Health and Environment Alliance (HEAL), a non-profit group in Brussels. It also found that breathing fumes from coal-fired power stations is to blame for more than a million cases of respiratory symptoms, for example, wheezing and shortness of breath, a year. The report coincides with a UK parliamentary debate on the future of coal-fired power stations and a vote on proposed targets for reducing greenhouse gas emissions, which may hasten the closure of many old coal plants. The findings add to mounting evidence of the effect of outdoor air pollution on

health. In October, the World Health Organization declared for the first time that outdoor air pollution was a direct cause of cancer, and a report commissioned by the WHO on the global burden of disease ranked such pollution as among the most important risk factors for chronic disease in Europe. Coal-fired power plants release pollutants such as sulphur dioxide, nitrogen oxides and fine particulates of soot in large quantities. These are known to contribute to cardiovascular diseases such as heart failure, and respiratory diseases such as emphysema. A Europe-wide report launched earlier this year, also by HEAL, estimated the total cost to healthcare as a result of coal fumes in the European Union at €43 billion per year. Fumes from coal-burning plants can travel thousands of kilometres, so they affect large swathes of the population, says Michal Krzyzanowski of King's College London. But even small changes in the amount of harmful particulates in the air could make a huge difference to health risks, he says. "At the moment coal is cheap, so countries are tempted to stay with it rather than invest in more expensive, cleaner fuel sources such as gas and renewables," Krzyzanowski says. "It's a political decision."

#### **Earth's poles are shifting because of climate change**

[<http://www.newscientist.com/article/dn24755-earths-poles-are-shifting-because-of-climate-change.html#.Uygnzs7-WVo>]

Climate change is causing the North Pole's location to drift, owing to subtle changes in Earth's rotation that result from the melting of glaciers and ice sheets. The finding suggests that monitoring the position of the pole could become a new tool for tracking global warming. Computer simulations had suggested that the melting of ice sheets and the consequent rise in sea level could affect the distribution of mass on the Earth's surface. This would in turn cause the Earth's axis to shift, an effect that has been confirmed by measurements of the positions of the poles. Now, Jianli Chen of the University of Texas at Austin and colleagues has shown that melting due to our greenhouse-gas emissions is making its own contribution to the shift. The wobble in Earth's axis of rotation is a combination of two major components, each with its own cause. One is called the Chandler wobble and is thought to arise because the Earth is not rigid. Another is the annual wobble, related to Earth's orbit around the sun. Remove these wobbles, and you are left with an additional signal. Since observations began in 1899, the North Pole has been drifting southwards 10 centimetres per year along longitude 70° west – a line running through eastern Canada. This drift is due to the changes in the distribution of Earth's mass as the crust slowly rebounds after the end

of the last ice age. But Chen's team found something surprising. In 2005, this southward drift changed abruptly. The pole began moving eastwards and continues to do so, a shift that has amounted to about 1.2 metres since 2005. To work out why the pole changed direction, Chen's team used data from NASA's GRACE satellite, which measures changes in Earth's gravity field over time. The data allowed them to calculate the redistribution of mass on Earth's surface due to the melting of the Greenland and Antarctic ice sheets and mountain glaciers, and the resulting rise in sea level. It correlated perfectly with the observed changes in the mean pole position (MPP).

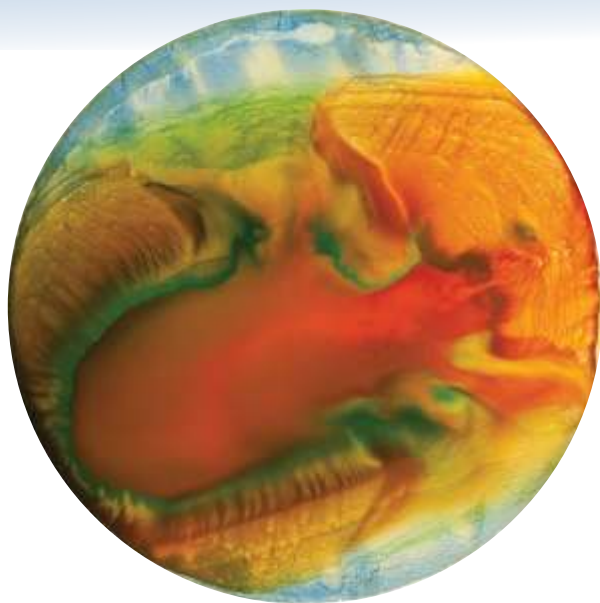
"Ice melting and sea level change can explain 90 per cent of the [eastward shift]," says Chen. "The driving force for the sudden change is climate change." Chen's team calculated that the biggest contribution is coming from the melting of the Greenland ice sheet, which is losing about 250 gigatonnes of ice each year. Another big factor is the melting of mountain glaciers, which contributes about 194 gigatonnes per year. The contribution from Antarctica adds up to 180 gigatonnes per year, but there is considerable uncertainty here because changes in the gravity field due to Earth's crust rebounding are less well understood over Antarctica than elsewhere. Since the MPP can be accurately measured using multiple independent techniques, its position and drift can be used to gauge the extent of ice sheet melting, especially in between the end of the ageing GRACE mission and the launch of the next generation of gravity-field-measuring satellites, says Chen. Jean Dickey of NASA's Jet Propulsion Laboratory in Pasadena, California, who was not associated with the study, agrees. "It's a way to monitor climate change by continuing to measure the deviation [of the MPP] from what we have seen in the past," she says. Chen presented his findings this week at the annual meeting of the American Geophysical Union in San Francisco.

#### **Toxic sludge from polluted rivers turned into art**

[<http://www.newscientist.com/article/mg21929300.100-toxic-sludge-from-polluted-rivers-turned-into-art.html#.Uygufs7-WVo>]

(Image source: John Sabraw/www.johnsabraw.com)

Not everything to do with pollution is ugly. This abstract art was created using paints made from the metallic run-off collected from polluted rivers in Ohio. The artwork is a collaboration between environmental engineer Guy Riefler and artist John Sabraw, both of Ohio University in Athens. When water from abandoned coal mines flows into local rivers, it can pollute them with iron, as well as making the water acidic. Once exposed to air at the surface, the iron oxidises to form a disgusting yet colourful



orange sludge that kills off much aquatic life. Riefler saw something beautiful in the muck. "I was coming back from

rivers with stained socks," says Riefler. "Most pigments are iron-based anyway, and we thought that we could use this water to create paints." Collecting underground water before it hits the air allows Riefler to control the rate of oxidation, generating different colours of iron sludge. When dried, these can be ground down and made into oil paints. "Iron is remarkably flexible," he says. "You can create a range of different colours: yellows, oranges, reds and blacks." Sabraw has been incorporating the paints into his artwork and advising Riefler on what makes a good pigment. "My job is to be the sensitive one," he says. "I play with the pigments and their mixing into paints, and discuss their viability with Guy." Despite their murky past, the pigments are safe to use and produce. Riefler hopes to be able to sell some of the paints commercially and then use the money generated to help restore the very rivers the pigments are derived from. "There aren't enough resources to clean up the rivers right now," Riefler says. "We could produce a tonne of pigment per day. If we can generate a strong pigment the paint companies like, we can fund our mission to restore the rivers."

## TOPIC OF INTEREST

### A Peep in to Indian Research: Mobile Phone Radiation

#### **Specific absorption rate variation in a brain phantom due to exposure by a 3G mobile phone: problems in dosimetry.**

[Behari J, Nirala JP. Indian J Exp Biol. 2013 Dec;51(12):1079-85.]

A specific absorption rate (SAR) measurements system has been developed for compliance testing of personal mobile phone in a brain phantom material contained in a Perspex box. The volume of the box has been chosen corresponding to the volume of a small rat and illuminated by a 3G mobile phone frequency (1718.5 MHz), and the emitted radiation directed toward brain phantom. The induced fields in the phantom material are measured. Set up to lift the plane carrying the mobile phone is run by a pulley whose motion is controlled by a stepper motor. The platform is made to move at a pre-determined rate of 2 degrees per min limited up to 20 degrees. The measured data for induced fields in various locations are used to compute corresponding SAR values and inter comparison obtained. These data are also compared with those when the mobile phone is placed horizontally with respect to the position of the animal. The SAR data is also

experimentally obtained by measuring a rise in temperature due to this mobile exposures and data compared with those obtained in the previous set. To seek a comparison with the safety criteria same set of measurements are performed in 10 g phantom material contained in a cubical box. These results are higher than those obtained with the knowledge of induced field measurements. It is concluded that SAR values are sensitive to the angular position of the moving platform and are well below the safety criteria prescribed for human exposure. The data are suggestive of having a fresh look to understand the mode of electromagnetic field -bio interaction.

#### **Effect of SAR on human head modeling inside cylindrical enclosures.**

[Mary TA, Ravichandran CS. Electromagn Biol Med. 2013 Sep;32(3):382-9.]

This study intends to discuss enclosed a realistic approach to determine and analyze the effects of radio frequency on human exposure inside a cylindrical enclosure. A scenario in which a mobile phone with

inverted-F antenna (IFA) operating in the Global System for Mobile Communication (GSM) band (900 MHz) is used inside a cylindrical enclosure. Metallic enclosures are known to have resonance and reflection effects, thereby increasing electric field strength and hence resulting in a change of the human exposure to electromagnetic absorptions. So, this study examines and compares the levels of absorption in terms of specific absorption rate (SAR) values under various conditions. In this study, a human phantom with dielectric properties is designed and its interaction is studied with IFA inside fully enclosed cylindrical enclosures. The results show that SAR values are increased inside cylindrical enclosures compared with those in free space. The method of computation uses method of moments. Simulations are done in FEKO software.

### **Biophysical evaluation of radiofrequency electromagnetic field effects on male reproductive pattern.**

[Kesari KK, Kumar S, Nirala J, Siddiqui MH, Behari J. Cell Biochem Biophys. 2013 Mar;65(2):85-96.]

There are possible hazardous health effects of exposure to radiofrequency electromagnetic radiations emitted from mobile phone on the human reproductive pattern. It is more effective while keeping mobile phones in pocket or near testicular organs. Present review examines the possible concern on radio frequency radiation interaction and biological effects such as enzyme induction, and toxicological effects, including genotoxicity and carcinogenicity, testicular cancer, and reproductive outcomes. Testicular infertility or testicular cancer due to mobile phone or microwave radiations suggests an increased level of reactive oxygen species (ROS). Though generation of ROS in testis has been responsible for possible toxic effects on physiology of reproduction, the reviews of last few decades have well established that these radiations are very harmful and cause mutagenic changes in reproductive pattern and leads to infertility. The debate will be focused on bio-interaction mechanism between mobile phone and testicular cancer due to ROS formation. This causes the biological damage and leads to several changes like decreased sperm count, enzymatic and hormonal changes, DNA damage, and apoptosis formation. In the present review, physics of mobile phone including future research on various aspects has been discussed.

### **SAR measurement due to mobile phone exposure in a simulated biological media.**

[Behari J, Nirala JP. Electromagn Biol Med. 2012 Sep;31(3):195-203.]

The specific absorption rate (SAR) measurements are

carried out for compliance testing of personal 3G Mobile phone. The accuracy of this experimental setup has been checked by comparing the SAR in 10 gm of simulated tissue and an arbitrary shaped box. This has been carried out using a 3G mobile Phone at 1718.5 MHz, in a medium simulating brain and muscle phantom. The SAR measurement system consists of a stepper motor to move a monopole E-field probe in two dimensions inside an arbitrary shaped box. The phantom is filled with appropriate frequency-specific fluids with measured electrical properties (dielectric constant and conductivity). That is close to the average for gray and white matters of the brain at the frequencies of interest (1718.5 MHz). Induced fields are measured using a specially designed monopole probe in its close vicinity. The probe is immersed in the phantom material. The measured data for induced fields are used to compute SAR values at various locations with respect to the mobile phone location. It is concluded that these SAR values are position dependent and well below the safety criteria prescribed for human exposure.

### **Effect of handheld mobile phone use on parotid gland salivary flow rate and volume.**

[Bhargava S, Motwani MB, Patni VM. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012 Aug;114(2):200-6.]

Handheld mobile phones emit nonionizing electromagnetic radiations and generate heat during use which can be absorbed by the adjacent tissues. This study observed functional and volumetric changes in the parotid glands associated with mobile phone use. Unstimulated parotid salivary flow rate was measured bilaterally in 142 individuals divided into 2 groups of heavy users and control subjects using a modified Schirmer test. Bilateral parotid ultrasonography was performed to evaluate gland volume. Variation and correlation tests were used to statistically analyze the results. A significant increase in salivary flow rate along with increased blood flow rate and volume of the parotid glands of the side where mobile phones are frequently placed was observed in the heavy user group. Heavy users of mobile phones demonstrated increased salivary flow rate, blood flow rate, and volume of parotid glands.

### **Biological responses of mobile phone frequency exposure.**

[Behari J. Indian J Exp Biol. 2010 Oct;48(10):959-81.]

Existence of low level electromagnetic fields in the environment has been known since antiquity and their biological implications are noted for several decades. As such dosimetry of such field parameters and their emissions from various sources of mass utilization has

been a subject of constant concern. Recent advancement in mobile communications has also drawn attention to their biological effects. Hand held children and adults alike generally use mobile sources as cordless phones in various positions with respect to the body. Further, an increasing number of mobile communication base stations have led to wide ranging concern about possible health effects of radiofrequency emissions. There are two distinct possibilities by which health could be affected as a result of radio frequency field exposure. These are thermal effects caused by holding mobile phones close to the body and extended conversations over a long period of time. Secondly, there could be possibly non thermal effects from both phones and base stations whereby the affects could also be cumulative. Some people may be adversely affected by the environmental impact of mobile phone base stations situated near their homes, schools or any other place. In addition to mobile phones, appliances like microwave oven etc are also in increasing use. Apart from the controversy over the possible health effects due to the non-thermal effect of electromagnetic fields the electromagnetic interaction of portable radio waves with human head needs to be quantitatively evaluated. Relating to this is the criteria of safe exposure to the population at large. While a lot of efforts have gone into resolving the issue, a clear picture has yet to emerge. Recent advances and the problems relating to the safety criteria are discussed.

#### **Audiologic disturbances in long-term mobile phone users.**

[Panda NK, Jain R, Bakshi J, Munjal S. J Otolaryngol Head Neck Surg. 2010 Feb;39(1):5-11.]

There is general concern regarding the possible hazardous health effects of exposure to radiofrequency electromagnetic radiation emitted from mobile phones. This study aimed to assess the effects of chronic exposure to electromagnetic waves emitted from Global System for Mobile Communication (GSM) mobile phones on auditory functions. A retrospective, cross-sectional, randomized, case control study was carried out in a tertiary care hospital. One hundred twelve subjects who were long-term mobile phone users (more than 1 year) and 50 controls who had never used a mobile phone underwent a battery of audiologic investigations including pure-tone audiometry (both speech and high frequency), tympanometry, distortion product otoacoustic emissions, auditory brain responses, and middle latency responses. Changes in the various parameters were studied in the mobile phone- and non-mobile phone-using ears of subjects and corresponding ears of the controls to ascertain the effects of electromagnetic exposure. There

was no significant difference between users and controls for any of the audiologic parameters. However, trends for audiologic abnormalities were seen within the users. High-frequency loss and absent distortion product otoacoustic emissions were observed with an increase in the duration of mobile phone use, excessive use of mobile phones, and age more than 30 years. Additionally, users with some complaints during mobile phone use demonstrated absent distortion product otoacoustic emissions and abnormalities in auditory brainstem response. Long-term and intensive mobile phone use may cause inner ear damage. A large sample size would be required to reach definitive conclusions.

#### **An epidemiological review of mobile telephones and cancer.**

[Hoskote SS, Kapdi M, Joshi SR. J Assoc Physicians India. 2008 Dec;56:980-4.]

Mobile telecommunication technology became commercially available about 20-25 years ago in different countries around the world. The industry has grown exponentially over the years and, currently, the number of mobile phone users is estimated to be over 3.8 billion, more than half the world's population. Thus, because of such a large population-at-risk, any health hazard from these devices promises to have a large epidemiological impact. Intense speculation and investigation into the relationship between mobile phone usage and cancer has led to the publication of numerous, often contradictory, reports on this subject. This review aims to provide a large body of reported evidence to help medical professionals disseminate evidence-based information to their patients.

#### **Health hazards of mobile phones: An Indian perspective.**

[Kapdi M, Hoskote SS, Joshi SR. J Assoc Physicians India. 2008 Nov;56:893-7.]

The mobile phone industry has been one of the fastest growing industries in modern history. Today, India has million mobile phone users, and mobile phones account for 88% of all telecommunication users. The rural sector accounts for more than 25% of all wireless phone users and this proportion is bound to grow as affordability of mobile phones continues to increase. In the years ahead, an ever-increasing number exposed for long periods of time to radiation from mobile phones. In 2008, the Telecom Commission (the policy-making body of the Department of Telecommunications, Government of India) adopted the emission guidelines prescribed by the International Commission on Non-Protection (ICNIRP). Studies have demonstrated that usage behaviours, such as duration of usage and predominant, one-sided use of

mobile phones are some of the chief risks that increase likelihood of hazards resulting from mobile phone use. This article attempts to present the basic biophysics of these devices and explain the health hazards of electromagnetic radiation exposure in terms of thermal and non-thermal effects. We also present some preventive measures that can reduce the risk of these hazards.

**Combinative exposure effect of radio frequency signals from CDMA mobile phones and aphidicolin on DNA integrity.**

[Tiwari R, Lakshmi NK, Surender V, Rajesh AD, Bhargava SC, Ahuja YR. Electromagn Biol Med. 2008;27(4):418-25.]

The aim of present study is to assess DNA integrity on the effect of exposure to a radio frequency (RF) signal from Code Division Multiple Access (CDMA) mobile phones. Whole blood samples from six healthy male individuals were exposed for RF signals from a CDMA mobile phone for 1 h. Alkaline comet assay was performed to assess the DNA damage. The combinative exposure effect of the RF signals and APC at two concentrations on DNA integrity was studied. DNA repair efficiency of the samples was also studied after 2 h of exposure. The RF signals and APC (0.2 microg/ml) alone or in synergism did not have any significant DNA damage as compared to sham exposed. However, univariate analysis showed that DNA damage was significantly different among combinative exposure of RF signals and APC at 0.2 microg/ml ( $p < 0.05$ ) and at 2 microg/ml ( $p < 0.02$ ). APC at 2 microg/ml concentration also showed significant damage levels ( $p < 0.05$ ) when compared to sham exposed. DNA repair efficiency also varied in a significant way in combinative exposure sets ( $p < 0.05$ ). From these results, it appears that the repair inhibitor APC enhances DNA breaks at 2 microg/ml concentration and that the damage is possibly repairable. Thus, it can be inferred that the *in vitro* exposure to RF signals induces reversible DNA damage in synergism with APC.

**Effect of mobile phone radiation on heart rate variability.**

[Ahamed V, Karthick NG, Joseph PK. Comput Biol Med. 2008 Jun;38(6):709-12.]

The rapid increase in the use of mobile phones (MPs) in recent years has raised the problem of health risk connected with high-frequency electromagnetic fields. There are reports of headache, dizziness, numbness in the thigh, and heaviness in the chest among MP users.

This paper deals with the neurological effect of electromagnetic fields radiated from MPs, by studies on heart rate variability (HRV) of 14 male volunteers. As heart rate is modulated by the autonomic nervous system, study of HRV can be used for assessing the neurological effect. The parameters used in this study for quantifying the effect on HRV are scaling exponent and sample entropy. The result indicates an increase in both the parameters when MP is kept close to the chest and a decrease when kept close to the head. MP has caused changes in HRV indices and the change varied with its position, but the changes cannot be considered significant as the *p* values are high.

**Increased frequency of micronucleated exfoliated cells among humans exposed *in vivo* to mobile telephone radiations.**

[Yadav AS, Sharma MK. Mutat Res. 2008 Feb 29;650(2):175-80.]

The health concerns have been raised following the enormous increase in the use of wireless mobile telephones throughout the world. This investigation had been taken, with the motive to find out whether mobile phone radiations cause any *in vivo* effects on the frequency of micronucleated exfoliated cells in the exposed subjects. A total of 109 subjects including 85 regular mobile phone users (exposed) and 24 non-users (controls) had participated in this study. Exfoliated cells were obtained by swabbing the buccal-mucosa from exposed as well as sex-age-matched controls. One thousand exfoliated cells were screened from each individual for nuclear anomalies including micronuclei (MN), karyolysis (KL), karyorrhexis (KH), broken egg (BE) and binucleated (BN) cells. The average daily duration of exposure to mobile phone radiations is 61.26 min with an overall average duration of exposure in term of years is 2.35 years in exposed subjects along with the  $9.84 \pm 0.745$  micronucleated cells (MNCs) and  $10.72 \pm 0.889$  total micronuclei (TMN) as compared to zero duration of exposure along with average  $3.75 \pm 0.774$  MNC and  $4.00 \pm 0.808$  TMN in controls. The means are significantly different in case of MNC and TMN at 0.01% level of significance. The mean of KL in controls is  $13.17 \pm 2.750$  and in exposed subjects is  $13.06 \pm 1.793$ . The value of means of KH in exposed subjects ( $1.84 \pm 0.432$ ) is slightly higher than in controls ( $1.42 \pm 0.737$ ). Mean frequency of broken egg is found to be more in exposed subjects ( $0.65 \pm 0.276$ ) as compared to controls ( $0.50 \pm 0.217$ ). Frequency of presence of more than one nucleus

in a cell (binucleated) is also higher in exposed ( $2.72 \pm 0.374$ ) in comparison to controls ( $0.67 \pm 0.231$ ). Although there is a slight increase in mean frequency of KH, BE and BN in exposed subjects but the difference is not found statistically significant. Correlation between 0-1, 1-2, 2-3 and 3-4 years of exposure and the frequency of MNC and TMN has been calculated and found to be positively correlated.

#### Use of mobile phones in ICU--why not ban?

[Yeolekar ME, Sharma A. J Assoc Physicians India. 2004 Apr;52:311-3.]

Due to the rapid growth of mobile telecommunications it is predicted that by 2005 there will be 1.6 billion mobile phone users worldwide. The usage of cellphones in Intensive Care Units carries with it a high incidence of interference with a number of medical devices like implantable defibrillators, cardioverters, pacemakers, monitors and other important devices like ventilators. It is in this context that this article will throw a light on complications of cellphones use in the Intensive Care Units and various strategies that can be taken to restrict their use in the Intensive Care Units.

#### Cellular phones and their hazards: The current evidence.

[Munshi A, Jalali R. Natl Med J India. 2002 Sep-Oct;15(5):275-7.]

The past decade has seen an exponential increase globally in the use of cellular phones (popularly known as mobile or cell phones). These phones are convenient and trendy. Discarding the wire means that the communication is through electromagnetic waves, which could have potential hazards. Alarmist reports in the lay press and high profile lawsuits, particularly in the West, have attracted attention to the possible harmful effects of cellular phones. Adverse effects investigated by various clinical trials include the possible link to increased risk of vehicular accidents, leukaemias, sleep disturbances and the more serious brain tumours. Available level II evidence suggests that the only proven side-effect is an increased risk of vehicular accidents. So far, all studies have consistently negated any association between cellular phones and brain tumours. Yet, the final word remains to be said.

## विज्ञान परिक्रमा

### बोस ने रखा था नोबेल पुरस्कार दिलाने वाली खोज का आधार

हाल ही में जिस हिग्स बोसोन कण की खोज करने वाले वैज्ञानिकों को नोबेल पुरस्कार देने की घोषणा की गई है, उस कण की खोज करने में भारतीय वैज्ञानिक सत्येंद्रनाथ बोस के सबसे योगदान है, और उन्हीं के नाम पर इसका नामकरण भी किया गया है। सत्येंद्रनाथ बोस के सबसे बड़े बेटे रतिंद्रनाथ बोस ने बुधवार को इस बात पर खुशी जाहिर की कि उनके पिता के काम ने दूसरों को प्रेरित किया और नोबेल पुरस्कार पाने में सहायक हुआ। हिग्स बोसोन की खोज के लिए इंग्लैंड के पीटर हिग्स और बेल्जियम के फ्रांसवा एंग्लर्ट को इस वर्ष का भौतिकी का नोबेल पुरस्कार दिए जाने की घोषणा की गई। हिग्स बोसोन में बोसोन नाम सत्येंद्रनाथ बोस के नाम के आधार पर रखा गया। बोसोन मूल कणों को कहते हैं। बोसोन कणों का सिद्धांत देने वाले प्रख्यात वैज्ञानिक एल्बर्ट आइंस्टीन के साथ एस.एन. बोस ने इस पर अनुसंधान किया था। बोस को तो हालांकि

प्रतिष्ठित नोबेल पुरस्कार प्रदान नहीं किया गया, लेकिन उनके काम ने 'गॉड पार्टिकल' के नाम से लोकप्रिय इन कणों की खोज के लिए वैज्ञानिकों की कई पीढ़ियों को आकर्षित किया। इस कण के खोज की पुष्टि इसी वर्ष स्विट्जरलैंड में अनुसंधान के लिए यूरोपियाई संगठन (सर्न) ने की। बोस के बेटे रतिंद्रनाथ ने कहा कि उनके कार्य को किसी अवार्ड के तराजू में नहीं तौला जा सकता। हमने देखा कि उनका काम कितना महत्वपूर्ण था... इतना महत्वपूर्ण कि उनके महान अनुसंधान पर आधारित अन्य वैज्ञानिकों के कार्य को नोबेल से नवाजा गया।

(<http://zeenews.india.com/hindi/news/sci-tech/bose-had-laid-the-base-of-discovery-in-winning-nobel-prize/192247>)

### 2030 तक जलसंकट से गुजर सकती है आधी दुनिया

संयुक्त राष्ट्र महासचिव बान की-मून ने चेतावनी दी है कि यदि समुचित कदम नहीं उठाए गए तो वर्ष 2030 तक पृथ्वी पर आधी आबादी के सामने पानी का संकट पैदा हो सकता है। जलसंकट का मतलब प्रति व्यक्ति प्रति वर्ष 1,700 घन मीटर से कम पानी की

उपलब्धता। समाचार एजेंसी सिन्हुआ की रपट के मुताबिक, मंगलवार को हंगरी के राष्ट्रपति जेनोस एडर के साथ बुडापेस्ट जल शिखर सम्मेलन को संबोधित करते हुए बान ने कहा कि पानी किसी भी सरकार की प्राथमिकता है, लेकिन कोई भी सरकार इस पर अकेले काम नहीं कर सकती। उन्होंने कहा कि हमें सभी घटकों, समुदायों और समाजों को पूरी तरह इससे जोड़ने की जरूरत है। बान ने घोषणा की कि अगले सितम्बर में संयुक्त राष्ट्र महासभा के दौरान जलवायु परिवर्तन पर विशेष रूप से एक सम्मेलन आयोजित किया जाएगा। उन्होंने इस सम्मेलन में उच्च स्तर पर भागीदारी करने का देशों का आह्वान किया।

(<http://zeenews.india.com/hindi/news/sci-tech/half-the-world-will-suffer-from-water-shortage-by-2030/192202>)

### शहरी क्षेत्रों में घातक बनती मधुमेह और उच्च रक्तचाप की समस्या

महानगरों में रहने वाली और 30 साल से अधिक उम्र की भारत की 20 प्रतिशत जनसंख्या मधुमेह तथा उच्च रक्तचाप के खतरे से पीड़ित है। यह खुलासा हाल ही में व्यापक स्तर पर हुए एक सरकारी अध्ययन में किया गया है। सरकार के कैंसर, मधुमेह, हृदय संबंधी बीमारियों और आघात रोकथाम व नियंत्रण कार्यक्रम (एनपीसीडीसीएस) के तहत देश के लगभग 4 करोड़ लोगों को शामिल किया गया। इसमें पाया गया कि 6.34 प्रतिशत आबादी मधुमेह से पीड़ित है और 6 प्रतिशत से ज्यादा लोग उच्च रक्तचाप से पीड़ित हैं। एस्कॉर्ट्स हार्ट इंस्टिट्यूट एंड फोर्टिस अस्पताल के कार्यकारी निदेशक और कार्डियोलॉजी के डीन डॉक्टर उपेंद्र कौल ने कहा, 'जब तक हम कड़े उपाय नहीं करते, तब तक उच्च रक्तचाप और मधुमेह का खतरा ज्यादा से ज्यादा लोगों को अपनी चपेट में लेता रहेगा। इनकी वजह से हृदयाघात, मानसिक आघात, गुर्दा संबंधी बीमारी और जल्दी अंधापन हो सकता है। शुरूआती जीवन में ही सुरक्षात्मक उपाय अपनाकर इन्हें रोका जा सकता है।' दिल्ली, बेंगलूर, अहमदाबाद, चेन्नई और कामरूप (असम) सहित देश के नगरीय क्षेत्रों में किए गए अध्ययन में पाया गया कि लगभग 11 प्रतिशत लोगों को मधुमेह से पीड़ित होने और 13 प्रतिशत लोगों के उच्च रक्तचाप से पीड़ित होने का संदेह है। मध्य प्रदेश में मधुमेह के सबसे कम (2.61 प्रतिशत) मामले पाए गए जबकि सिक्किम में मधुमेह पीड़ितों का प्रतिशत सबसे ज्यादा (13.67) था। सिक्किम

में उच्च रक्तचाप का प्रतिशत भी सबसे ज्यादा (18.16) था। मधुमेह के मामलों में गुजरात दूसरे नंबर (9.57 प्रतिशत) पर है। इसके बाद कर्नाटक (9.41 प्रतिशत) और फिर पंजाब (9.38 प्रतिशत) रहे। डॉक्टर कौल का कहना है कि उच्च रक्तचाप को 'मौन हत्यारा' कहा जाता है क्योंकि इसके कोई लक्षण दिखाई नहीं देते। इसलिए इसकी नियमित निगरानी जरूरी है। उच्च रक्तचाप के मामलों में सिक्किम के बाद दिल्ली (13.38 प्रतिशत) है। इसके बाद असम (10.49 प्रतिशत), तमिलनाडु (9.73 प्रतिशत) और पंजाब (9.26 प्रतिशत) हैं।

(<http://zeenews.india.com/hindi/news/sci-tech/in-urban-areas-diabetes-and-high-blood-pressure-problem-becomes-deadly/192111>)

### गर्म वातावरण से निचली सतह से खत्म हो रहे हैं पौधे

तेजी से गर्म हो रहे वातावरण और उसमें आ रही शुष्कता के कारण पौधों की वे प्रजातियां अब दक्षिणी परिजोना पर्वत पर ऊँचाइयों की ओर पाई जाने लगी हैं जो पहले इससे काफी नीचे के इलाकों में मिलती थीं। परिजोना विश्वविद्यालय के नेतृत्व में किए गए शोध में आज से 50 साल पहले किए गए सर्वेक्षण से आज के पौधों की प्रजातियों की तुलना करते हुए पहली बार इस बात के सबूत पाए गए कि दक्षिणी पश्चिमी पौधे जलवायु परिवर्तन के कारण अब अधिक ऊँचाई वाली जगहों में पाए जा रहे हैं। शोध के परिणाम पहले समय में दी गई उन अवधारणाओं की पुष्टि करते हैं, जिनमें कहा गया था कि दक्षिण पश्चिम के पर्वतों पर तेजी से गर्म होते और शुष्क होते वातावरण का तेज प्रभाव पड़ेगा। इस इलाके की वनस्पति में भारी परिवर्तन देखा जा रहा है।

प्रमुख शोधकर्ता रिचर्डसी ब्रूस्का ने कहा, हमारा अध्ययन इस बात का पहला जमीनी स्तर पर हासिल किया गया सबूत देता है कि जलवायु में गर्माहट के कारण दक्षिणी परिजोना में पौधों को ऊँचाई की ओर प्रतिस्थापित होने के लिए बाध्य होना पड़ रहा है। ब्रूस्का ने कहा, अगर जलवायु में गर्माहट बढ़ना जारी रहता है तो ऊँचाई पर पाए जाने वाले पौधे, शंकु वन और उन पर निर्भर जानवर शीर्ष से विस्थापित होकर विलुप्त हो सकते हैं। शोधकर्ताओं का मानना है कि इस अध्ययन से मुख्य बिंदु यह सामने आया है कि पर्वतों पर 50 साल पहले जो वनस्पति समुदाय था वह आज की प्रजातियों से भिन्न था

क्योंकि जरूरी नहीं कि पौध ऊँचाई की ओर एक समुदाय के ही रूप में बढ़ें। यह अध्ययन इकोलॉजी एंड एवोल्यूशन नामक पत्रिका में प्रकाशित हुआ था।

(<http://zeenews.india.com/....गर्म-वातावरण-से-निचली-सतह-से-खत्म-हो-रहे-हैं-पौधे/177357>)

### टमाटर और सेब के छिलके से दूर होगा पानी का प्रदूषण

भारतीय मूल के एक वैज्ञानिक ने पानी का प्रदूषण दूर करने वाली दुनिया की पहले ऐसे तकनीक का विकास किया है जो प्रदूषण फैलाने वाले तत्वों को दूर करने के लिए टमाटर और सेब के छिलकों का उपयोग करेगा। नेशनल यूनिवर्सिटी ऑफ सिंगापुर (एनयूएस) में पीएचडी के छात्र रामकृष्ण मल्लमपति ने कम मूल्य पर स्वच्छ जल उपलब्ध कराने की कोशिश के तहत आसपास मौजूद वस्तुओं का उपयोग पानी को शुद्ध करने के लिए किया। एनयूएस के फ़ैकल्टी ऑफ साइंस के रसायन विभाग के एसोसिएट प्रोफेसर सुरेश वालियावीत्तिल की देखरेख में यह प्रयोग किया गया है। शोध दल के टमाटर के छिलकों का प्रयोग कर पानी में मिले हुए धातु कण सहित अन्य ऑर्गेनिक प्रदूषकों को भी निकालने में सफलता पायी। इन छिलकों की मदद से पानी में पीएच की स्थिति में भी सुधार हुआ है। इसके अलावा वह कीटनाशकों आदि को भी पानी से अलग कर देता है। इस शोध के परिणाम रॉय सोसायटी ऑफ केमिस्ट्री के जर्नल परएससी एडवांसेज में प्रकाशित हुए हैं।

(<http://zeenews.india.com/....टमाटर-और-सेब-के-छिलके-से-दूर-होगा-पानी-का-प्रदूषण/1753050>)

### 300 अरब टन प्रति वर्ष की दर से पिघल रहे हैं ग्लेशियर

एक उपग्रह से पता चला है कि पिछले एक दशक में अंटार्कटिका और ग्रीनलैंड ग्लेशियर की बर्फ करीब 300 अरब टन की दर से पिघल रही है। शोधकर्ताओं ने बताया कि ग्रीनलैंड एवं अंटार्कटिका की विशाल बर्फ की चादरों में बदलाव की वजह से पृथ्वी के गुरुत्व में होने वाले परिवर्तन का पता लगाने वाले एक उपग्रह ने इस गलन का पता लगाया। इससे दुनिया भर में समुद्र के स्तरों पर नाटकीय प्रभाव पड़ सकता है। अंतरिक्ष में परिक्रमा कर रहे उपग्रह ग्रेविटी रिकवरी एंड क्लाइमेट एक्सपेरिमेंट (ग्रेस) ने 2002 के बाद से बर्फ के इतनी तेजी से पिघलने के बारे में पता लगाया। वैज्ञानिकों ने चेतावनी दी कि इन जानकारीयों से आने वाले दशक में कितनी बर्फ पिघलेगी और समुद्र स्तरों में कितनी तेजी से बढ़ोतरी होगी, इसका सही आकलन करना मुश्किल है क्योंकि यह एक अल्पकालीन

अध्ययन के दौरान यह स्पष्ट हुआ कि बर्फ की चादरें बहुत अधिक मात्रा में बर्फ खो रही हैं। इसकी दर 300 अरब टन प्रतिवर्ष है। ग्लेशियर के पिघलने की दर बेहद तेज हो रही है। नेचर जियोसाइंस पत्रिका में प्रकाशित हुए इस शोध के मुख्य अध्ययनकर्ता वोडटर्स ने कहा कि ग्रेस मिशन के शुरू होने के बाद के पहले कुछ वर्षों की तुलना में हाल के साल में बर्फ की चादरों के पिघलने से समुद्र स्तर में होने वाली वृद्धि पर लगभग दोगुना असर पड़ रहा है।

(<http://zeenews.india.com/....300-अरब-टन-प्रति-वर्ष-की-दर-से-पिघल-रहे-हैं-ग्लेशियर/174578>)

### हर साल 20 लाख लोगों को लील जाता है वायु प्रदूषण

मानवीय कारणों से फैलने वाले वायु प्रदूषण के कारण हर साल दुनिया में 20 लाख से अधिक लोगों की जान चली जाती है, जिनमें सबसे अधिक संख्या एशिया तथा पूर्वी एशिया के लोगों की है। यह दावा 'एनवायरमेंटल रिसर्च लेटर्स' नामक पत्रिका में एक शोध के आधार पर किया गया है। इसके अनुसार, मानवीय कारणों से ओजोन में छिद्र बढ़ता जा रहा है, जिसके कारण दुनियाभर में हर साल करीब चार लाख 70 हजार लोगों की मौत हो जाती है। इसका यह भी कहना है कि मानवीय कारणों से 'फाइन पार्टिकुलेट मैटर' में भी वृद्धि होती है, जिससे सालाना करीब 21 लाख लोगों की मौत हो जाती है। 'पार्टिकुलेट मैटर' मोटर गाड़ियों, बिजली उत्पादन, औद्योगिक प्रतिष्ठानों, लकड़ी के चूल्हों, कृषि उत्पादों को जलाने से वातावरण में होने वाली रासायनिक अभिक्रियाओं से बनते हैं। ये हवा में घुल जाते हैं और सांस के माध्यम से हमारे फेफड़ों में पहुंच जाते हैं, जिससे कैंसर तथा श्वसन संबंधी अन्य समस्याएं हो सकती हैं। शोध के सह लेखक उत्तरी कैरोलिना विश्वविद्यालय के जैसन वेस्ट ने एक बयान में कहा, "स्वास्थ्य पर पड़ने वाले पर्यावरणीय प्रभावों में वायु प्रदूषण सबसे अधिक महत्वपूर्ण है। इसके कारण सबसे अधिक पूर्वी एशिया तथा दक्षिणी एशिया में लोगों की मौत होती है।" शोधकर्ताओं ने वर्ष 1850 में औद्योगीकरण शुरू होने से वर्ष 2000 तक ओजोन पर भी ध्यान केंद्रित किया। शोधकर्ताओं ने हालांकि पाया कि ओजोन में इस दौरान मामूली बदलाव आए। बयान के अनुसार, जलवायु परिवर्तन कई तरीके से हवा की गुणवत्ता को प्रभावित करता है। इससे स्थानीय स्तर पर वायु प्रदूषण में वृद्धि या कमी हो सकती है। उदाहरण के लिए, तापमान एवं आद्रता से रासायनिक अभिक्रिया में

पविर्तन आ सकता है, जिससे प्रदूषण फैलाने वाले कारकों का निर्माण होता है। इसी तरह बारिश से यह तय हो सकता है कि प्रदूषण फैलाने वाले कारक कब संघटित होंगे।

(<http://zeenews.india.com/.../हर-साल-20-लाख-लोगों-को-लील-जाता-है-वायु-प्रदूषण/174487>)

### धूम्रपान से हर साल होती है 60 लाख मौतें : WHO

जन स्वास्थ्य अभियानों के जोर पकड़ने के बावजूद धूम्रपान की वजह से दुनिया भर में होने वाले मौतों की संख्या बढ़ रही है। विश्व स्वास्थ्य संगठन यानी डब्ल्यूएचओ के अनुसार धूम्रपान की वजह से हर साल लगभग 60 लाख लोग मारे जा रहे हैं और इनमें से अधिकतर मौतें कम तथा मध्यम आय वाले देशों में हो रही हैं। डब्ल्यूएचओ ने कल पनामा में एक सम्मेलन के दौरान अपनी रिपोर्ट जारी करते हुए कहा कि अगर ऐसा ही रहा तो वर्ष 2030 में हर साल धूम्रपान की वजह से मारे जाने लोगों की संख्या बढ़कर 80 लाख हो जाएगी। रिपोर्ट के अनुसार, वर्ष 2030 में तंबाकू की वजह से होने वाली अनुमानित मौतों में से लगभग 80 प्रतिशत मौतें कम और मध्यम आय वाले देशों में होंगी। डब्ल्यूएचओ की महानिदेशक डॉक्टर मार्ग्रेट चान ने कहा कि अगर हम तंबाकू के विज्ञापन, प्रचार और प्रायोजन पर रोक नहीं लगाते तो पहले की तुलना में अधिक लुभावने तरीके से प्रचार करने वाला तंबाकू उद्योग, तंबाकू सेवन के प्रति किशोरों और युवाओं को आकर्षित करता रहेगा। चान ने कहा

कि हर देश की जिम्मेदारी है कि वह अपने लोगों की तंबाकू जनित बीमारियों, विकारों और मौतों से बचाव करे। डब्ल्यूएचओ के अनुसार, इस साल धूम्रपान की वजह से मरने वाले लोगों में से 50 लाख लोग तंबाकू का सेवन कर रहे थे या पूर्व में किया करते थे जबकि 6,00,000 से अधिक लोगों ने परोक्ष धूम्रपान की वजह से जान गंवाई। माना जाता है कि तंबाकू सेवन की वजह से 20वीं सदी में 10 करोड़ लोगों की मौत हुई थी। डब्ल्यूएचओ ने आगाह किया है कि किसी नाटकीय बदलाव को छोड़ दें तो इस सदी में तंबाकू सेवन की वजह से मारे जाने वाले लोगों की संख्या बढ़कर 1 अरब हो सकती है। विश्व स्वास्थ्य संगठन के 'प्रीवेन्शन ऑफ नॉनकम्युनिकेबल डिजीज' विभाग के निदेशक डॉ. डगलर बेचर ने पनामा में संपन्न बैठक में कहा 'हम जानते हैं कि तंबाकू के विज्ञापन, प्रचार और प्रायोजन पर पूरी तरह प्रतिबंध ही कारगर हो सकता है।' उन्होंने कहा 'तंबाकू नियंत्रण उपायों के साथ साथ इस पर पूर्ण प्रतिबंध लगाने वाले देश कुछ वर्ष के अंदर ही तंबाकू के उपयोग में कमी लाने में सफल रहे हैं।' इस रिपोर्ट में कहा गया है कि 92 देशों के 2.3 अरब लोगों को धूम्रपान पर किसी न किसी तरह लगाए गए प्रतिबंधों से लाभ हुआ है। यह संख्या पांच साल पहले के आंकड़े की तुलना में दोगुनी लेकिन विश्व आबादी की मात्र एक तिहाई ही है।

(<http://zeenews.india.com/.../धूम्रपान-से-हर-साल-होती-है-60-लाख-मौतें-who/174169>)



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