ISSN : 0970-437X

Toxicology Research Bulletin

Vol 31, Number 2, 2011

Inside

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

EVENTS

CSIR Foundation Day Celebrated

The sixty ninth CSIR Foundation Day function was held in the auditorium of Indian Institute of Toxicology Research, Lucknow on September 26, 2011. Dr. K.C. Gupta, Director, IITR while welcoming, the guests and members of IITR family said that CSIR with its 37 laboratories spread all over the country is one of the largest public funded organization in the world. He further said that recently CSIR has formed AcSIR (Academy of Scientific & Industrial Research), the bill of which has been cleared by Lok Sabha and has to be passed by the Rajya Sabha. 36 students of IITR have been registered with AcSIR. Dr. Ashok Kumar, Department of Biological Sciences & Bioengineering, Indian Institute of Technology, Kanpur was the chief guest on the occasion. Dr. Mukul Das, Chairman, CSIR Foundation Day organizing committee introduced Dr. Ashok Kumar to the audience. Dr. Ashok Kumar, spoke on **"Tissue engineering – towards new era of regenerative medicine".** The talk gave an introduction to the new type of cryogel biomaterial, their unique properties and an overview of the applications where it had shown the potential. Tissue engineering is an interdisciplinary area that applies the concepts of biology and engineering for the development of tissue substitutes for replacing the damaged or diseased tissue or organ. Tissue engineering plays a significant role in the area of regenerative medicine by improving the health and quality of life of millions of people worldwide by restoring, maintaining or enhancing the tissue or organ function. Tissue engineering depends upon three core components like cells, biomolecules/growth factors and biomaterials. Out of this, biomaterial presents a vital component as it mimics the extracellular matrix of the native tissue. It can be fabricated in the form of a three dimensional support called scaffold for the growth and proliferation of cells. Dr Ashok Kumar told that his research group is fabricating the scaffolds from different biomaterials by a novel technology called *cryogelation*. These cryogel materials have been characterized by number of different techniques which show their macroporous and interconnected pore structure, high porosity, *in vivo* and *in vitro* biocompatibility and biodegradability. Scaffolds have exhibited good mechanical properties which can be modulated by altering the concentrations of either polymer or cross linker. They have revealed the application of different cryogel scaffolds on a number of technologically challenging processes like, cell separations, tissue engineering, bioreactors for therapeutic protein production and extracorporeal devices in various tissue engineering application and bioseparations. The specific cells bound on the chromatographic column can be effectively released by mechanically squeezing the cryogel matrix. The other interesting application of the macroporous matrices have been the cultivation of the mammalian cells on the gelatin modified cryogels. The cells grow, proliferate and secrete the protein therapeutic continuously in the circulating medium when allowed to culture on the cryogel matrices. This application has also been extended to design a bioartificial lever support as an extracorporal device by allowing the hepatocytes to grow on the cryogel bioreactor. They have explored the role of cryogels as scaffolds for tissue engineering and stem cell proliferation and differentiation. They have focused in the direction of designing a bilayer model system for skin tissue engineering, where the bottom layer of gelatin was used for the regeneration of the skin and the top layer sheet of polyvinylpyrolidone-Iodine complex served as a protective barrier for infection. The cryogel scaffolds generated from agarose-gelatin provided a gradient pore size and mechanical strength mimicking the cartilage and thus was used for designing cartilage tissue engineering scaffold. In this direction they have been able to design a neo-cartilage that mimics the native cartilage in biochemical and mechanical properties and have also been able to integrate well with the native tissue. They have also designed conducting cryogels for neural and cardiac tissue engineering applications. The combination of inorganic-organic materials designed as porous scaffolds have shown promise for bone tissue engineering. Further, they have also modified the surfaces of these cryogel materials by plasma polymerization to improve its cell-material interaction properties. In conclusion the cryogel polymeric biomaterials have shown diverse applications in biomedical science and regenerative medicine.

On this occasion fourteen members of staff who had superannuated during the last one year were felicitated by Director. They were Dr. D.K. Agarwal, Sri Neeraj Mathur, Dr. R.K. Upreti, Dr. R.K. Hans, Sri M.C. Tiwari, Dr. C.S. Ojha, Dr. G.S.D. Gupta, Dr. Kewal Lal, Sri M.D. Rana, Sri Mohd. Ashquin, Sri Ram Chandra, Sri Dan Bahadur, Sri M.L. Kanojia, Sri Rajesh Mishra. Director also presented mementos to four members of IITR who had completed 25 years of service. They were Dr. D.C. Purohit, Smt. Mumtaz Jahan, Ms. Mona Hemrajani, Mr. Vinod Kumar. A cash prize was given to Master Debarchan Kar Chowdhuri Son of Dr. D. Kar Chowdhuri for securing above 90% marks in three science subjects. Earlier an essay competition was organized for the wards of CSIR staff. The winners were awarded certificates. Dr. Poonam Kakkar, Convener, CSIR Foundation Day programme proposed the vote of thanks.

EVENTS

Group photograph with retired staff of IITR

Director honoring the staff completing 25 years of service

IITR Foundation Day Celebrated

Indian Institute of Toxicology Research (IITR) celebrated its Foundation Day on November 4, 2011. While welcoming the guests, Prof. D.K. Gupta Vice Chancellor, CSM Medical University, Lucknow and Dr. Rajesh S. Gokhale, Director, CSIR- Institute of Genomics' & Integrative Biology, New Delhi, Dr K. C. Gupta, Director, IITR highlighted the activities of the Institute carried out in the last one year. IITR continued to focus on the five broad areas: Systems Toxicology & Health Risk Assessment; Food, Drug & Chemical Toxicology; Environmental Toxicology; Nanomaterial Toxicology and Regulatory Toxicology. Some of the findings of R&D carried out in four of the areas are:

Nanomaterial Toxicology

In search of a universal transfection reagent which could cover a whole spectrum of cell lines, a series of polyethylenimine (PEI) based nano-composites were synthesised. These nano-composites had a blending of polyethylenimine with either 1, 4-Butanediol diglycidyl ether or gellan gum or y-polyglutamic acid or alginic acid. These nano-composites can serve as efficient non-viral gene carriers for diverse biomedical applications. Nanoparticle-mediated delivery of phytochernicals could serve as a basis for enhancing bioavailability and limiting the unwanted toxicity of chemotherapeutic agents. The encapsulated tea polyphenols alone or in combination with cisplatin were found to be more effective in inhibiting cell proliferation, metastasis. angiogenesis and apoptosis biomarkers. These polyphenols retained biological effectiveness with over 20-fold dose advantage than bulk tea polyphenols in exerting anti-cancer effects.

Systems Toxicology & Health Risk Assessment

Alcoholic liver cirrhosis is an irreversible change that occurs on chronic alcohol consumption. To predict alcohol induced toxicity induction of blood lymphocyte cytochrome P450 2E1 (CYP2E1) expression was estimated. Study findings suggest significant increase in the CYP2E1 mRNA and protein expression in the blood lymphocytes, isolated from early stage alcoholic liver cirrhotic patients.

Food, Drug & Chemical Toxicology

In a study related to edible oil adulterant, argemone oil, patients of dropsy showed generation of reactive oxygen and nitrogen species. This led to enhancement of secretion of inflammatory mediators leading to DNA damage followed by apoptosis and histopathological changes in target organs of dropsy patients. Combinations of chemopreventive agents in cancer treatment are gaining popularity due to failure of single agent intervention in clinical trials. Studies evaluated the chemopreventive effects of: (1) resveratrol and black tea polyphenol or (2) pomegranate fruit extract and diallyl sulfide in suppressing two- stage mouse skin carcinogenesis. The combinations were found to impart better suppressive activity than either of these agents alone and the studies accentuated that development of novel combination therapies/ chemoprevention using dietary agents will be more beneficial against cancer.

Environmental Toxicology

A Flow cytometry based method was developed to characterize and culture stem cells from neonate mouse

epidermis after transplacental bromo-deoxyuridine administration that may be useful for studying transplacental carcinogenesis. Molecular beacon probe developed was used for tracking environmental reservoirs for enterotoxigenic *Eschefichia coli (*ETEC) in a sewage-impacted Gangetic riverine system. The probe detected ETEC in eight species of aquatic flora and four leafy vegetables grown along the banks.An oligonucleotide microarray was developed and validated for assessing biodegradative potential and composition of environmentally useful bacteria in hazardous waste sites and polluted ecosystems. The array named as Biodeg-Phylo-Chip was based on 60-mer oligonucleotide probes. The array comprises 14327 unique probes derived from 1057 biodegradative genes involved in the transformation of 133 chemical pollutants as well as 880 probes representing 110 phylogenetic genes from diverse bacterial communities.

Societal Activities

In a study on usage pattern and exposure assessment of food colors in different age group of consumers in the State of Uttar Pradesh, a total 478 eatables was analyzed. The study showed a marked improvement in the trend of use of permitted colors over previous surveys, with 90% foods now resorting to approved food colors. However, 59% of foods employing permitted colors exceeded the maximum allowable limit, with average quantities crossing the threshold of 100 mg kg^{-1} in most food commodities. It was observed that children and adolescents are more vulnerable to higher intake of food colors compared to adult population. Hence, a technological need based levels of individual colors are desired to be prescribed.

S & T Achievements

A number of scientists brought laurels to the institute by being conferred honours. Some were elected to various academies and also served on the committees of different government departments.

CSIR-IITR scientists published 103 research papers this year, with an average impact factor of 3.121, an improvement over the previous year when it was 2.297. Two papers appeared on the cover page of prestigious international journals.

The Prof. S.H Zaidi oration entitled **"Black and White Facts of Vitiligo and Skin Pigmentation"** was delivered by Dr. Rajesh S. Gokhale. While delivering the oration Dr Gokhale said that epidermal skin pigmentation is an intricate process that involves a complex interplay between melanocytes and keratinocytes. The melanin pigment is a hetero-polymer generated by the enzymatic oxidation of tyrosine. Melanocytes produce at least two distinct kinds of melanin the brown — black eumelanin and red — yellow pheomelanin. The synthesis of melanin is spatially restricted to lysosome — related organelles (LROs) called melanosomes and proceeds in distinctly characterized stages inside melanocytes. The mature melanosomes are then transferred to keratinocytes providing the visually apparent colour of human skin. Mechanistic insights into melanin synthesis have revealed the crucial role of the transcription factor microphthalmia — associated transcription factor (MITF) as the central positive regulator that governs melanogenesis, development and proliferation of melanocytes. The targets of MITE includes tyrosinase (TYR), tyrosinase related protein-1 (TYR P1) and dopachrome tautomerase (DCT), the key enzymes that catalyse melanin synthesis. Mutation in all these three proteins are known to affect the quantity and quality of melanin synthesized. The depigmenting disorder of skin, vitiligo, is characterized by the loss of cutaneous pigmentation with the concomitant loss of melanocytes. Several theories including autoimmune disorder that targets melanocytes at the basal layer of epidermis are believed to be the cause of this depigmentation. Dr. Gokhale and his team have hypothesised that a breakdown of melanocyte — keratinocytes network could precipitate vitiligo in different forms. They are investigating the underlying molecular and cellular mechanisms of depigmentation leading to vitiligo. On this occasion Dr. Gokhale released the document entitled "Assessment of ambient air quality of Lucknow city (post- Monsoon) findings of a random survey" Ambient air quality study was carried out during the month on October 2011 at ten locations of Lucknow city. The study revealed that the concentration of respirable particulate matter (RSPM) and fine particles (PM2.4) were found to be higher than the respective permissible limits. The concentration of gaseous pollutants, SO_2 and NO_x were found within limits but higher than the last year. The noise level at all the locations was higher than the permissible limit except in one industrial area.

Prof. D.K. Gupta, Vice Chancellor CSMMU and guest of honour on the occasion said that the Foundation Day is a special day which gives us an opportunity to take stock of our achievements and lacunae and plan for the future. He complimented Director IITR and his team of scientists in pursuing R&D in the exceptionally important area of nanotoxicology.

Prof. D.K. Gupta released the electronic and print version

of the IITR annual report (2010-11).

On this occasion three staff members namely, Mr. Dharmraj Section Officer Finance & Accounts, Mr. Anuj Deep, Assistant Finance and Accounts and Mr. Mohd. Javed, Staff car driver were presented with a cash prize and a silver medal for their outstanding contributions. Dr Mukul Das, Chief Scientist and Chairman Foundation Day committee proposed the vote of thanks.

Inauguration of CSIR-IITR foundation day with lighting of the lamp

Going Green: release of electronic version of IITR Annual Report

A view of the audience

Dr. Rajesh S. Gokhale delivering Prof. S.H Zaidi oration

Director CSIR-IITR presenting memento to Prof. D.K. Gupta, Vice Chancellor CSMMU

Lighter moments during foundation day function

EVENTS

सतर्कता जागरूकता सप्ताह

संस्थान में सतकता जागरूकता सप्ताह-2011 के अवसर पर सप्ताह के दौरान विभिन्न कार्यक्रम आयोजित किये गये। कार्यक्रमों का आरम्भ संस्थान में कार्यरत वैज्ञानिकों एवं कर्मचारियों को दिनांक 31 अक्टूबर, 2011 प्रातः 11:00 बजे निदेशक द्वारा प्रतिज्ञा (Pledge) दिला कर किया गया। सतर्कता जागरूकता सप्ताह-2011 के दौरान संस्थान में कार्यरत कर्मचारियों हेतु सतर्कता जागरूकता विषयों पर वाद-विवाद (Debate) प्रतियोगिता एवं निबन्ध (Essay) प्रतियोगिता दिनांक 2.11.2011 को क्रमशः प्रातः 11.30 बजे एवं अपरान्ह 3.30 बजे आई.आई.टी.आर. के गोष्ठीकक्ष में आयोजित की गयी। साथ ही दिनांक 5.11.2011 को अपरान्ह 3.30 बजे विभिन्न स्कूल/कालेज के छात्र/छात्राओं एवं आई.आई.टी.आर. के कर्मचारियों के बच्चों हेतु जूनियर ग्रुप कक्षा 5 से 8 तक एवं सीनियर ग्रुप कक्षा 9 से 12 तक के लिये निबन्ध प्रतियोगिता का आयोजन किया गया जिसमें 50 बच्चे सम्मिलित हुए।

अतिथि व्याख्यान एवं पुरस्कार वितरण समारोह का शुभारम्भ करते हुए संस्थान के प्रशासनिक अधिकारी श्री मुकुन्द सहाय ने सतर्कता जागरूकता सप्ताह 2011 पर संक्षिप्त विवरण प्रस्तुत किया। संस्थान के निदेशक डा.के.सी. गुप्ता ने अपने अध्यक्षीय भाषण में सतर्कता विषयों पर प्रकाश डाला। डा. मुकुल दास, वरिष्ठ वैज्ञानिक ने मुख्य अतिथि का संक्षिप्त परिचय दिया। सतर्कता जागरूकता सप्ताह-2011 के अन्तर्गत संस्थान में दिनांक 8 नवम्बर, 2011 को अपरान्ह 4:00 बजे आई.आई.टी.आर. के प्रेक्षागृह में एक अतिथि व्याख्यान का आयोजन किया गया। यह व्याख्यान जस्टिक सुधीर चन्द्र वर्मा, पूर्व लोक आयुक्त, उत्तर प्रदेश ने दिया। जस्टिस वर्मा ने अपने व्याख्यान में सतर्कता एवं भ्रष्टाचार विषयों पर विस्तृत रूप से प्रकाश डाला। मुख्य अतिथि को पुष्प-गुच्छ, मोमेन्टो एवं शाल भेंट कर अभिवादन किया गया। सतर्कता जागरूकता सप्ताह-2011 के दौरान संस्थान में सतर्कता जागरूकता विषयों पर आयोजित वाद-विवाद प्रतियोगिता एवं निबन्ध प्रतियोगिता जो कि क्रमशः दिनांक 2.11.2011 को प्रातः 11.30 बजे एवं अपरान्ह 3.30 बजे आई. आई.टी.आर. के गोष्ठीकक्ष में सम्पन्न हुई, के विजयी प्रतियोगियों को क्रमशः प्रथम, द्वितीय, तृतीय एवं सान्त्वना पुरस्कार से सम्मानित किया गया। संस्थान के प्रशासनिक अधिकारी श्री मुकुन्द सहाय ने धन्यवाद ज्ञापन दिया।

संस्थान सतर्कता जागरूकता सप्ताह का आयोजन : मंच पर बाये से दाये डॉ मुकुल दास, डॉ. के.सी. गुप्ता, जस्टिस सुधीर चन्द्र वर्मा एवं श्री मुकुंद सहाय

डॉ. के.सी. गुप्ता जस्टिस सुधीर चन्द्र वर्मा का स्वागत करते हुए

CSIR-IITR Research Highlights

In vitro development of resistance to arsenite and chromium-VI in Lactobacilli strains as perspective attenuation of gastrointestinal disorder.

[Upreti RK, Sinha V, Mishra R, Kannan A. J Environ Biol. 2011 May;32(3):325-32.]

Inadvertent intake of inorganic arsenic and chromium through drinking water and food causing their toxic insults is a major health problem. Intestinal bacteria including Lactobacilli play important regulatory roles on intestinal homeostasis, and their loss is known to cause gastrointestinal (GI) disorders. Probiotic Lactobacilli resistance to arsenite and chromium-VI could be an important factor for the perspective attenuation of GI-disorders caused by these toxic metals/metalloid. In the present study resistance of arsenite (up to 32 ppm), Cr-VI (up to 64 ppm), and arsenite plus Cr-VI (32 ppm each) were developed under *in vitro* condition following chronological chronic exposures in Lactobacilli strains. Comparative study of biochemical parameters such as membrane transport enzymes and structural constituents; dehydrogenase and esterase activity tests, which are respective indicators for respiratory and energy producing processes, and the general heterotrophic activity of cells, of resistant strains showed similarities with their respective normal parent strains. The resistant strains were also found to be sensitive to antibiotics. Findings indicate that these resistant probiotic Lactobacilli would be useful in the prophylactic interventions of arsenic and chromium GI-toxicity.

Pesticides and cancer: insights into toxicoproteomic-based findings.

[George J, Shukla Y. J Proteomics. 2011 Nov 18;74(12):2713-22.]

Humans are often exposed to a variety of pollutants that contribute to an individual's risk for diseases including cancer. Animal, cell cultures and epidemiological lines of evidence demonstrate that exposure to various environmental pollutants including pesticides are associated with increasing frequency of cancers. Organophosphates, organochlorines, carbamates, pyrethroids, the major groups of pesticides, have been reported to be carcinogenic in various models. However, the results of these studies are still controversial, nevertheless, their mechanism of action is clear. Therefore, new strategies in toxicological research are needed for efficient screening for adverse effects of pesticides on complex living systems. Biomarkers can be employed to identify causal associations and to make better quantitative and qualitative estimates of those associations at relevant levels of exposure. This will enable authors to deepen understanding of mechanism behind their carcinogenic potential. Deciphering the associations between pesticide exposure and cancer, following toxicoproteomics application, will be useful in the development of potential predictive biomarkers of pesticide induced carcinogenicity. Therefore, the thrust of this article was to review the risk of cancer due to pesticide exposure and significant toxicoproteomic-based studies conducted so far, to identify the novel molecules as possible biomarkers for cancer following pesticide exposure.

Evidence for cytochrome P450 2B1/2B2 isoenzymes in freshly prepared peripheral blood lymphocytes.

[Saurabh K, Parmar D. Biomarkers. 2011 Dec;16(8):649-56.]

Cytochrome P450 2B1 and 2B2, the major hepatic drug metabolizing enzymes belonging to CYP2 family and associated constitutive androstane receptor (CAR) were found to be expressed in peripheral blood lymphocytes (PBL) isolated from rats. As observed in liver, pretreatment of phenobarbital (PB) or phenytoin were found to increase the expression of CYP2B1, CYP2B2 and associated enzyme activity in PBL. Like in liver, blood lymphocyte CYP2B1/2B2 catalyzed the activity of 7-pentoxyresorufin O-dealkylase (PROD). The present data, demonstrating similarities in the regulation of blood lymphocyte CYP2B-isoenzymes with the liver enzymes, suggests that blood lymphocyte CYP2B-isoenzymes could be used as a biomarker to monitor tissue levels.

Role of OGG1 Ser326Cys polymorphism and 8-oxoguanine DNA damage in risk assessment of squamous cell carcinoma of head and neck in North Indian population.

[Kumar A, Pant MC, Singh HS, Khandelwal S. Mutat Res. 2011 Dec 24;726(2):227-33.]

Squamous cell carcinoma of head and neck (SCCHN), one of the leading cancers worldwide, is most prevalent in Indian sub-continent. The major risk factors involved are smoking and consumption of alcohol, since they provide high free radical generating environment. Authors studied 8-oxoguanine DNA-glycosylase (OGG1) Ser326Cys polymorphism in 278 SCCHN cases and 278 matched controls by PCR-RFLP and observed that the variant genotype Ser/Cys exhibited an enhanced risk of 1.7 folds (OR=1.71, 95% CI=1.20-2.93) and Cys/Cys 2.5 folds (OR=2.55, 95% CI=1.29-5.00). Furthermore, authors found a significant increase in salivary cell 8-OHdG with respect to Ser/Cys and Cys/Cys genotypes of OGG1 in SCCHN cases, when compared to Ser/Ser and Ser/Cys genotypes of the control population. The results demonstrate that Ser326Cys variant genotype is

associated with an increased risk of SCCHN in north India. Ser326Cys variant genotype was found to accumulate more of 8-OHdG, which may serve as a biomarker for early diagnosis of SCCHN.

Ameliorative effects of dimetylthiourea and N-acetylcysteine on nanoparticles induced cyto-genotoxicity in human lung cancer cells-A549.

[Srivastava RK, Rahman Q, Kashyap MP, Lohani M, Pant AB. PLoS One. 2011;6(9):e25767.]

Authors study the ameliorative potential of dimetylthiourea (DMTU), an OH radical trapper and N-acetylcysteine (NAC), a glutathione precursor/H_2O_2 scavenger against titanium dioxide nanoparticles (TiO_2-NPs) and multi-walled carbon nanotubes (MWCNTs) induced cyto-genotoxicity in cultured human lung cancer cells-A549. Cytogenotoxicity was induced by exposing the cells to selected concentrations (10 and 50 µg/ml) of either of TiO_2-NPs or MWCNTs for 24 h. Anti-cytogenotoxicity effects of DMTU and NAC were studied in two groups, i.e., treatment of 30 minutes prior to toxic insult (short term exposure), while the other group received DMTU and NAC treatment during nanoparticles exposure, i.e., 24 h (long term exposure). Investigations were carried out for cell viability, generation of reactive oxygen species (ROS), micronuclei (MN), and expression of markers of oxidative stress (HSP27, CYP2E1), genotoxicity (P^{53}) and CYP2E1 dependent n-nitrosodimethylamine-demethylase (NDMA-d) activity. In general, the treatment of both DMTU and NAC was found to be effective significantly against TiO_2-NPs and MWCNTs induced cytogenotoxicity in A549 cells. Long-term treatment of DMTU and NAC during toxic insults has shown better prevention than short-term pretreatment. Although, cells responded significantly to both DMTU and NAC, but responses were chemical specific. In part, TiO_2-NPs induced toxic responses were mediated through OH radicals generation and reduction in the antioxidant defense system. While in the case of MWCNTs, adverse effects were primarily due to altering/hampering the enzymatic antioxidant system. Data indicate the applicability of human lung cancer cells-A549 as a pre-screening tool to identify the target specific prophylactic and therapeutic potential of drugs candidate molecules against nanoparticles induced cellular damages.

Phytoremediation of Cd, Cr, Cu, Mn, Fe, Ni, Pb and Zn from aqueous solution using *Phragmites cummunis, Typha angustifolia* and *Cyperus esculentus.*

[Chandra R, Yadav S. Int J Phytoremediation. 2011 Jul;13(6):580-91.]

A comparative bioaccumulation pattern and ultra structural changes were studied in *Phragmites cummunis, Typha angustifolia* and *Cyperus esculentus* in mixed metals solution of cadmium (Cd), chromium (Cr), copper (Cu), iron (Fe), manganese (Mn), nickel (Ni), lead (Pb) and zinc (Zn). *P. cummunis* was observed to be a shoot accumulator for Cr, Fe, Mn, Ni, Pb, and Zn. However, *T. angustifolia* was found to be a root accumulator for Cd, Cr, Cu, Fe, Ni and Pb. In addition, *C. esculentus* also accumulated most of the tested heavy metals in the roots, while Mn and Fe were translocated up to leaves. Further, the long term metal treatment showed maximum accumulation of all heavy metals in *P. cummunis* followed by *T. angustifolia* and *C. esculentus*. Among heavy metals, Fe was accumulated maximum, i.e., >1000 microg $g^{(-1)}$ by all three plants. Simultaneously, the adverse effects on biochemical parameters were noted earlier in *C. esculentus* than *T.* angustifolia and *P. cummunis*. Ultra structural observation showed the cellular changes in wetland plants after longer exposure. Results revealed that *P. cummunis* and *T. angustifolia* had more potential for tested metals than *C. esculentus*. This study established that these wetland plants could be used for heavy metals phytoremediation from metal containing industrial wastewater.

Role of mitogen activated protein kinases in skin tumorigenicity of patulin.

[Saxena N, Ansari KM, Kumar R, Chaudhari BP, Dwivedi PD, Das M. Toxicol Appl Pharmacol. 2011 Dec 1;257(2):264-71.]

WHO has highlighted the need to evaluate dermal toxicity of mycotoxins including Patulin (PAT), detected in several fruits. In this study the skin carcinogenic potential of topically applied PAT was investigated. Single topical application of PAT (400 nmol) showed enhanced cell proliferation (~2 fold), along with increased generation of ROS and activation of ERK, p38 and JNK MAPKs, in mouse skin. PAT exposure also showed activation of downstream target proteins, c-fos, c-Jun and NF-κB transcription factors. Further, single topical application of PAT (400 nmol) followed by twice weekly application of TPA resulted in tumor formation after 14 weeks, indicating the tumor initiating activity of PAT. However no tumors were observed when PAT was used either as a complete carcinogen (80 nmol) or as a tumor promoter (20 nmol and 40 nmol) for 25 weeks. Histopathological findings of tumors found in PAT/TPA treated mice showed that these tumors were of squamous cell carcinoma type and similar to those found in the positive control group (DMBA/TPA) along with significant increase of lipid peroxidation and decrease in free sulfydryls, catalase, superoxide dismutase and glutathione reductase activities. The

results suggest the possible role of free radicals in PAT mediated dermal tumorigenicity involving MAPKs.

Polymorphism in glutathione S-transferases: susceptibility and treatment outcome for head and neck cancer.

[Ruwali M, Singh M, Pant MC, Parmar D. Xenobiotica. 2011 Dec;41(12):1122-30.]

The study investigates the association of polymorphism in glutathione S-transferases (GSTs) with susceptibility for head and neck squamous cell carcinoma (HNSCC) and its sites as well as treatment response in cases receiving chemotherapy (CT) and combination of CT-radiotherapy (CT-RT). The case-control study included 500 male cases and an equal number of healthy male controls. Odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated for the association between genotypes and cancer risk. An increase in the risk for HNSCC and cancers of oral cavity, larynx or pharynx was observed in cases with null genotypes of GSTM1 or GSTT1. The interaction of alcohol or tobacco with variant genotypes of GSTM1 or GSTT1 also resulted in a significant increase in the risk for HNSCC. Further, HNSCC cases carrying the null genotypes of GSTM1 and GSTT1 or variant genotypes of GSTP1 showed a significant and superior treatment response. The present data thus provides evidence for the association of polymorphisms in GSTs with risk for HNSCC and its treatment response.

Toxicological impact of technical imidacloprid on ovarian morphology, hormones and antioxidant enzymes in female rats.

[Kapoor U, Srivastava MK, Srivastava LP. Food Chem Toxicol. 2011 Dec;49(12):3086-9.]

Technical imidacloprid was evaluated for its effect on ovarian morphology, hormones and antioxidant enzymes in female rats after 90 days oral exposure. Luteinizing hormone (LH), follicle stimulating hormone (FSH) and progesterone levels were estimated in serum of rats and activity of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and level of reduced glutathione (GSH) and lipid peroxidation (LPO) were estimated in ovary after oral administration of imidacloprid (5, 10, and 20mg/kg/day) for 90 days. Decreased ovarian weight together with significant patho-morphological changes in follicles, antral follicles and atretic follicles were observed at 20mg/kg/day. Imidacloprid at 5 and 10mg/kg/day has not produced any significant changes in ovarian morphology, hormones and antioxidant status of ovary. However 20mg/kg/day dose has produced significant alterations in the levels of LH, FSH and progesterone. Similarly significant changes in SOD, CAT, GPx, GSH, and LPO were observed at 20mg/kg/day dose level. Therefore, it is concluded that imidacloprid at 20mg/kg/day dose level has produced significant toxicological impact on ovary of female rats as evident by pathomorphological changes, hormonal imbalance and generating oxidative stress and can be considered primarily as Lowest Observed Effect Level (LOEL) for chronic study.

Engineered ZnO and TiO_2 nanoparticles induce oxidative stress and DNA damage leading to reduced viability of *Escherichia coli*.

[Kumar A, Pandey AK, Singh SS, Shanker R, Dhawan A. Free Radic Biol Med. 2011 Nov 15;51(10):1872-81.]

Extensive use of engineered nanoparticle (ENP)-based consumer products and their release into the environment have raised a global concern pertaining to their adverse effects on human and environmental health. The safe production and use of ENPs requires improvement in authors understanding of environmental impact and possible ecotoxicity. This study explores the toxicity mechanism of ZnO and TiO_2 ENPs in a gram-negative bacterium, *Escherichia coli*. Internalization and uniform distribution of characterized bare ENPs in the nano range without agglomeration was observed in *E. coli* by electron microscopy and flow cytometry. Authors data showed a statistically significant concentration-dependent decrease in *E. coli* cell viability by both conventional plate count method and flow cytometric live-dead discrimination assay. Significant ($p<0.05$) DNA damage in *E. coli* cells was also observed after ENP treatment. Glutathione depletion with a concomitant increase in hydroperoxide ions, malondialdehyde levels, reactive oxygen species, and lactate dehydrogenase activity demonstrates that ZnO and TiO_2 ENPs induce oxidative stress leading to genotoxicity and cytotoxicity in *E. coli*. Authors study substantiates the need for reassessment of the safety/toxicity of metal oxide ENPs.

Cypermethrin exposure leads to regulation of proteins expression involved in neoplastic transformation in mouse skin.

[George J, Srivastava AK, Singh R, Shukla Y. Proteomics. 2011 Nov;11(22):4411-21.]

Cypermethrin, a synthetic pyrethroid insecticide is shown to exert carcinogenic effects in rodents; however, its underlying mechanism remains elusive. Here, authors showed the effect of cypermethrin on protein expression involved in neoplastic transformation in mouse skin. Comparative protein expression profiles between untreated control and cypermethrin-treated mouse skin were explored using 2-DE. A total of 27 spots that were statistically significant ($p<0.05$) and differentially expressed in response to cypermethrin exposure were

identified by MALDI-TOF/TOF and LC-MS/MS. Among them, six up-regulated proteins (carbonic anhydrase 3 (Ca 3), Hsp-27, S100A6, galectin-7, S100A9, S100A11) and one down-regulated protein (superoxide dismutase [Cu-Zn] (Sod 1)) are associated with cancer-related key processes. These selected dysregulated proteins were further validated in 2-DE gels of mouse skin treated with known tumorigens (benzo-[a]-pyrene, 12-O-tetradecanoyl-phorbol-13-acetate and mezerein), respectively. Comparative studies showed that Ca 3, S100A6, S100A9, S100A11 and Sod 1 are specific for stages of development and progression of tumors whereas Hsp-27 and galectin-7 are specific for tumor promotion stage by cypermethrin in mouse skin. Furthermore, these chosen proteins confirmed by Western blotting and immunofluorescence staining were consistent with changes in 2-DE check. This proteomic investigation for the first time provides key proteins that will contribute in understanding the mechanism behind cypermethrin-induced neoplastic transformation.

Support vector machines in water quality management.

[Singh KP, Basant N, Gupta S. Anal Chim Acta. 2011 Oct 10;703(2):152-62.]

Support vector classification (SVC) and regression (SVR) models were constructed and applied to the surface water quality data to optimize the monitoring program. The data set comprised of 1500 water samples representing 10 different sites monitored for 15 years. The objectives of the study were to classify the sampling sites (spatial) and months (temporal) to group the similar ones in terms of water quality with a view to reduce their number; and to develop a suitable SVR model for predicting the biochemical oxygen demand (BOD) of water using a set of variables. The spatial and temporal SVC models rendered grouping of 10 monitoring sites and 12 sampling months into the clusters of 3 each with misclassification rates of 12.39% and 17.61% in training, 17.70% and 26.38% in validation, and 14.86% and 31.41% in test sets, respectively. The SVR model predicted water BOD values in training, validation, and test sets with reasonably high correlation (0.952, 0.909, and 0.907) with the measured values, and low root mean squared errors of 1.53, 1.44, and 1.32, respectively. The values of the performance criteria parameters suggested for the adequacy of the constructed models and their good predictive capabilities. The SVC model achieved a data reduction of 92.5% for redesigning the future monitoring program and the SVR model provided a tool for the prediction of the water BOD using set of a few measurable variables. The performance of the nonlinear models (SVM, KDA, KPLS) was comparable and these performed relatively better than the corresponding linear methods (DA, PLS) of classification and regression modeling.

Studies on oxidative stress induced nerve conduction deficits in cigarette smokers.

[Singh VK, Pathak MK, Bihari V, Jyoti, Patel DK, Mathur N, Kesavachandran CN, Siddiqui MK. J Environ Biol. 2011 Jan;32(1):39-42.]

An important role of oxidative stress for the development of vascular and neurological complications has encouraged us to undertake a study to assess the oxidative stress induced nerve conduction deficits among cigarette smokers. Eighteen regular male cigarette smokers and twenty nine male non-smokers were diagnosed for clinical neuro-physiological tests viz., motor and sensory nerve conduction velocity (MNCV and SNCV) and redox status. Significant depletion of reduced glutathione (GSH) level ($p < 0.05$) and significant increase in malondialdehyde (MDA) level ($p < 0.01$) was found in smokers compared to non-smokers. Motor and sensory nerve conduction velocity showed no significant difference among smokers compared to non-smokers. The present study shows that smoking can induce oxidative stress among smokers but could not exacerbate to nerve conduction deficits.

MiR-497 and miR-302b regulate ethanol-induced neuronal cell death through BCL2 protein and cyclin D2.

[Yadav S, Pandey A, Shukla A, Talwelkar SS, Kumar A, Pant AB, Parmar D. J Biol Chem. 2011 Oct 28;286(43):37347-57.]

In chronic alcoholism, brain shrinkage and cognitive defects because of neuronal death are well established, although the sequence of molecular events has not been fully explored yet. Authors explored the role of microRNAs (miRNAs) in ethanol-induced apoptosis of neuronal cells. Ethanol-sensitive miRNAs in SH-SY5Y, a human neuroblastoma cell line, were identified using real-time PCR-based TaqMan low-density arrays. Long-term exposure to ethanol (0.5% v/v for 72 h) produced a maximum increase in expression of miR-497 (474-fold) and miR-302b (322-fold). Similar to SH-SY5Y, long-term exposure to ethanol induced miR-497 and miR-302b in IMR-32, another human neuroblastoma cell line. Using *in silico* approaches, BCL2 and cyclin D2 (CCND2) were identified as probable target genes of these miRNAs. Cotransfection studies with 3'-UTR of these genes and miRNA mimics have demonstrated that BCL2 is a direct target of miR-497 and that CCND2 is regulated negatively by either miR-302b or miR-497. Overexpression of either miR-497 or miR-302b reduced expression of their

identified target genes and increased caspase 3-mediated apoptosis of SH-SY5Y cells. However, overexpression of only miR-497 increased reactive oxygen species formation, disrupted mitochondrial membrane potential, and induced cytochrome c release (mitochondria-related events of apoptosis). Moreover, ethanol induced changes in miRNAs, and their target genes were substantially prevented by pre-exposure to GSK-3B inhibitors. In conclusion, authors have shown that ethanol-induced neuronal apoptosis follows both the mitochondria-mediated (miR-497- and BCL2-mediated) and non-mitochondria-mediated (miR-302b- and CCND2-mediated) pathway.

Bt Brinjal in India: A long way to go.

[Kumar S, Misra A, Verma AK, Roy R, Tripathi A, Ansari KM, Das M, Dwivedi PD. GM Crops. 2011 Apr 1;2(2).]

Brinjal occupies the major proportion amongst all vegetable crops in India and is vulnerable to many diseases caused by insect-pests, fungus, bacteria and virus. Brinjal production is extensively affected by the insect brinjal fruit and shoot borer. Use of conventional chemical pesticides not only damage environment including the biotic and abiotic components but, also affect human health. Bt Brinjal was developed to combat brinjal fruit and shoot borer that has an advantage minimizing use of chemical pesticides. Extensive biosafety investigations, nutritional studies, substantial equivalence studies, relative toxicity and allergenicity assessment using animal models like Sprague Dawley rats, Brown Norway rats, rabbit, fish, chicken, goats, etc. revealed no significant differences between genetically modified brinjal and its native counterpart. Bt brinjal could effectively control the target pest and was found to be safe for environment and human health. In spite of all the scientific studies, release of Bt Brinjal has been put under moratorium. Indian government has constituted an expert committee to address this issue. In this review authors have tried to explore the facts related to Bt Brinjal including its production, use of Bt toxin, use of chemical pesticides in controlling the FSB in native brinjal, along with perspective of public opinion and government initiatives.

Contamination of potable water by enterotoxigenic *Escherichia coli*: qPCR based culture-free detection and quantification.

[Patel CB, Vajpayee P, Singh G, Upadhyay RS, Shanker R. Ecotoxicol Environ Saf. 2011 Nov;74(8):2292-8.]

Tourists visiting to endemic zones may acquire Enterotoxigenic *Escherichia coli* (ETEC) infection resulting into diarrhea due to consumption of contaminated potable waters. In this study, a qPCR assay (SYBR Green), targeting LT1 and ST1 genes was designed to quantify ETEC in potable waters derived from civic water supply. The assay could detect lowest 1CFU/PCR targeting LT1/ST1 gene from ten-fold diluted culture of the reference strain (*E. coli* MTCC 723) and is ten-fold more sensitive than the conventional PCR. The quantification of the ETEC in potable waters collected from civic supply of a major city of the northern India exhibiting high flow of tourists reveals that all the sites that ran along sewage line were contaminated by the ETEC. Contamination was due to percolation of sewage. The assay could be used for the regular monitoring of potable water in places exhibiting heavy flow of tourists to prevent ETEC induced diarrhea.

Neuroprotective efficacy of curcumin in arsenic induced cholinergic dysfunctions in rats.

[Yadav RS, Chandravanshi LP, Shukla RK, Sankhwar ML, Ansari RW, Shukla PK, Pant AB, Khanna VK. Neurotoxicology. 2011 Dec;32(6):760-8.]

Authors recent studies have shown that curcumin protects arsenic induced neurotoxicity by modulating oxidative stress, neurotransmitter levels and dopaminergic system in rats. As chronic exposure to arsenic has been associated with cognitive deficits in humans, the present study has been carried out to implore the neuroprotective potential of curcumin in arsenic induced cholinergic dysfunctions in rats. Rats treated with arsenic (sodium arsenite, 20mg/kg body weight, p.o., 28 days) exhibited a significant decrease in the learning activity, assessed by passive avoidance response associated with decreased binding of (3)H-QNB, known to label muscarinic-cholinergic receptors in hippocampus (54%) and frontal cortex (27%) as compared to controls. Decrease in the activity of acetylcholinesterase in hippocampus (46%) and frontal cortex (33%), staining of Nissl body, immunoreactivity of choline acetyltransferase (ChAT) and expression of ChAT protein in hippocampal region was also observed in arsenic treated rats as compared to controls. Simultaneous treatment with arsenic and curcumin (100mg/kg body weight, p.o., 28 days) increased learning and memory performance associated with increased binding of (3)H-QNB in hippocampus (54%), frontal cortex (25%) and activity of acetylcholinesterase in hippocampus (41%) and frontal cortex (29%) as compared to arsenic treated rats. Increase in the expression of ChAT protein, immunoreactivity of ChAT and staining of Nissl body in hippocampal region was also observed in rats simultaneously treated with arsenic and curcumin as compared to those treated with arsenic alone. The results of the present study suggest that curcumin significantly

modulates arsenic induced cholinergic dysfunctions in brain and also exhibits neuroprotective efficacy of curcumin.

Glutathione-S-transferase M1 and T1 genes and gastric cancer: a case control study in North Indian population.

[Yadav D, Chandra R, Saxena R, Agarwal D, Agarwal M, Ghosh T, Agrawal D. Gene. 2011 Nov 10;487(2):166-9.]

Difference in the capacity of xenobiotic metabolising enzymes might be an important factor in genetic susceptibility to cancer. A case control study involving forty one gastric cancer patients and one hundred and thirty controls was carried out to determine the frequency of GSTM1 and GSTT1 null genotypes. The frequency of GSTM1 and GSTT1 null genotype was observed by carrying out multiplex PCR. There was no difference in the frequencies of the GSTM1 and GSTT1 null and the combined GSTM1 and GSTT1 null genotype between patients and control. The data suggest that GSTM1 and GSTT1 status may not influence the risk of developing gastric cancer.

Tiny non-coding RNAs in Parkinson's disease: Implications, expectations and hypes.

[Srivastava G, Dixit A, Prakash O, Singh MP. Neurochem Int. 2011 Nov;59(6):759-69.]

Parkinson's disease (PD) is the second most prevalent, progressive and aging related neurodegenerative disorder, characterized by the irreversible and selective degeneration of the nigrostriatal dopaminergic neurons. The early diagnosis, molecular explanation and permanent cure of this devastating and baffling disease have not yet been completely deciphered. Tiny non-coding RNAs, which consist of small or short interfering RNA (siRNA) and micro RNA (miRNA), intervene with and silence the expression of the specific genes through the evolutionary conserved process of RNA interference and act as post-transcriptional regulators. The differential expression patterns of miRNAs operate as key watchdogs and facilitate the identification of the potential therapeutic targets; however, miRNA modifiers aid in designing the strategies to encounter PD. Similarly, siRNA-mediated gene silencing paves the way to understand the function of the specific genes in PD pathogenesis by knocking down their expression. Applications of siRNAs and contributions of the potential miRNAs in investigating the etiology and molecular mechanisms of PD as well as in therapeutic interventions have been discussed in this article. The review also highlights the achievements, expectations and hypes associated with these tiny non-coding RNAs in PD.

Combinatorial strategies employing nutraceuticals for cancer development.

[Shukla Y, George J. Ann N Y Acad Sci. 2011 Jul;1229:162-75.]

Cancer is the second leading cause of death worldwide. Therefore, the fight against cancer is one of the most important areas of research in medicine, and one that possibly contributes to the increased interest in chemoprevention as an alternative approach to the control of cancer. Cancer prevention by nutraceuticals present in fruits and vegetables has received considerable attention because of their low cost and wide safety margin. A substantial amount of evidence from human, animal, and cell culture studies has shown cancer chemopreventive effects from these natural products. However, single-agent intervention has failed to produce the expected outcome in clinical trials; therefore, combinations of nutraceuticals are gaining increasing popularity. Thus, combinations of nutraceuticals that mimic real-life situations and are competent in targeting multiple targets with very little or virtually no toxicity are needed. In this review, authors summarize the results of those studies that report combinatorial cancer chemopreventive action of various nutraceuticals and their combinations with anticancer drugs.

Oxidative stress in zinc-induced dopaminergic neurodegeneration: implications of superoxide dismutase and heme oxygenase-1.

[Singh BK, Kumar A, Ahmad I, Kumar V, Patel DK, Jain SK, Singh C. Free Radic Res. 2011 Oct;45(10):1207-22.]

The study was undertaken to investigate the effect of zinc (Zn) on glutathione S-transferase (GST) and superoxide dismutases (SOD) activities and on the expressions of cytosolic Cu, Zn-SOD (SOD1), mitochondrial Mn-SOD (SOD2), γ-glutamyl cysteine synthetase (γ-GCS) and heme oxygenase-1 (HO-1) in the nigrostriatal tissue of rats. Additionally, Zn-induced alterations in the neurobehavioral parameters, lipid peroxidation (LPO), striatal dopamine and its metabolites and tyrosine hydroxylase (TH) protein expression were measured to assess their correlations with the oxidative stress. Zn exposure reduced the locomotor activity, rotarod performance, striatal dopamine and its metabolites and TH protein expression. LPO, total SOD, SOD1 and SOD2 activities were increased while GST and catalase were reduced in a dose and time dependent manner. Expressions of SOD1 and HO-1 were increased while no change was observed in SOD2 and γ-GCS expressions. The results obtained suggest that Zn-induced augmentation of total SOD, SOD1, SOD2 and HO-1 was associated with increased oxidative stress and

neurodegenerative indexes indicating the involvement of both cytosolic and mitochondrial machinery in Zn-induced oxidative stress leading to dopaminergic neurodegeneration.

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

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

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

Application of ethyl chloroformate derivatization for solid-phase microextraction-gas chromatography-mass spectrometric determination of bisphenol-A in water and milk samples.

[Mudiam MK, Jain R, Dua VK, Singh AK, Sharma VP, Murthy RC. Anal Bioanal Chem. 2011 Sep;401(5):1695-701.]

A simple and rapid analytical method based on in-matrix ethyl chloroformate (ECF) derivatization has been developed for the quantitative determination of bisphenol-A (BPA) in milk and water samples. The samples containing BPA were derivatised with ECF in the presence of pyridine for 20 s at room temperature, and the non-polar derivative thus formed was extracted using polydimethylsiloxane solid-phase microextraction (SPME) fibres with thicknesses of 100 µm followed by analysis using gas chromatography-mass spectrometry. Three alkyl chloroformates (methyl, ethyl and isobutyl chloroformate) were tested for optimum derivatisation yields, and ECF has been found to be optimum for the derivatisation of BPA. Several parameters such as amount of ECF, pyridine and reaction time as well as SPME parameters were studied and optimised in the present work. The limit of detection for BPA in milk and water samples was found to be 0.1 and 0.01 µg $L^{(-1)}$, respectively, with a signal-to-noise ratio of 3:1. The limit of quantitation for BPA in milk and water was found to be 0.38 and 0.052 µg $L^{(-1)}$, respectively, with a signal-to-noise ratio of 10:1. In conclusion, the method developed was found to be rapid, reliable and cost-effective in comparison to silylation and highly suitable for the routine analysis of BPA by various food and environmental laboratories.

Interplay of early biochemical manifestations by cadmium insult in sertoli-germ coculture: an *in vitro* study.

[Khanna S, Lakhera PC, Khandelwal S. Toxicology. 2011 Sep 5;287(1-3):46-53.]

Cadmium is a common environmental and occupational hazard and its adverse effect on reproductive organ has been well documented. The present study is planned to delineate the mechanism of Cd toxicity in rat testes. The study shows that Cd causes apoptosis in sertoli-germ cells which is governed by oxidative stress. Authors assayed ROS, GSH and MMP to ensure the role of oxidative stress further confirmed it by thiol modulators. The initial biochemical response shown in sertoli-germ cells was a significant rise in intracellular calcium followed by a drastic fall in MMP and then ROS generation. The downstream events included cytochrome c release leading to caspase-3 activation and culminating in cell death via apoptosis. Furthermore Cd disrupted the spermatogenic pathway as evident by suppression in tesmin and LDH-X levels.

Computational allergenicity prediction of transgenic proteins expressed in genetically modified crops.

[Verma AK, Misra A, Subash S, Das M, Dwivedi PD. Immunopharmacol Immunotoxicol. 2011 Sep;33(3):410-22.]

Development of genetically modified (GM) crops is on increase to improve food quality, increase harvest yields, and reduce the dependency on chemical pesticides.

IITR RESEARCH HIGHLIGHTS

Before their release in marketplace, they should be scrutinized for their safety. Several guidelines of different regulatory agencies like ILSI, WHO Codex, OECD, and so on for allergenicity evaluation of transgenic are available and sequence homology analysis is the first test to determine the allergenic potential of inserted proteins. Therefore, to test and validate, 312 allergenic, 100 non-allergenic, and 48 inserted proteins were assessed for sequence similarity using 8-mer, 80-mer, and full FASTA search. On performing sequence homology studies, ~94% the allergenic proteins gave exact matches for 8-mer and 80-mer homology. However, 20 allergenic proteins showed non-allergenic behavior. Out of 100 non-allergenic proteins, seven qualified as allergens. None of the inserted proteins demonstrated allergenic behavior. In order to improve the predictability, proteins showing anomalous behavior were tested by Algpred and ADFS separately. Use of Algpred and ADFS softwares reduced the tendency of false prediction to a great extent (74-78%). In conclusion, routine sequence homology needs to be coupled with some other bioinformatic method like ADFS/Algpred to reduce false allergenicity prediction of novel proteins.

TOPIC OF INTEREST

Nanotoxicology The Emerging Science and its Impact on Human Life: Indian Studies

Ahmad, I. (2011). "Nanotoxicity of natural minerals: an emerging area of nanotoxicology." J Biomed Nanotechnol 7(1): 32-33.

Nanotoxicity of two natural minerals, talc and silica were evaluated *in vitro* studying their effects on cell viability, LDH leakage, LPO induction, ROS production, GSH depletion, modulation of GR and GPx activities. Both mineral particles mediated their toxicity through oxidative stress. Differently, silica nanoparticles showed insignificant effect on GSH depletion. Talc nanoparticles significantly enhanced transcription and translation of TNF-alpha which was mediated by both ERK1/2 and P38. This aspect of study on silica nanoparticles is in progress.

Akhtar, M. J., M. Ahamed, et al. (2010). "Nanotoxicity of pure silica mediated through oxidant generation rather than glutathione depletion in human lung epithelial cells." Toxicology 276(2): 95-102.

Though, oxidative stress has been implicated in silica nanoparticles induced toxicity both *in vitro* and in vivo, but no similarities exist regarding dose-response relationship. This discrepancy may, partly, be due to associated impurities of trace metals that may present in varying amounts. Here, cytotoxicity and oxidative stress parameters of two sizes (10 nm and 80 nm) of pure silica nanoparticles was determined in human lung epithelial cells (A549 cells). Both sizes of silica nanoparticles induced dose-dependent cytotoxicity as measured by MTT [3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyl tetrazolium bromide] and lactate dehydrogenase (LDH) assays. Silica nanoparticles were also found to induce oxidative stress in dose-dependent manner indicated by induction of reactive oxygen species (ROS) generation, and membrane lipid peroxidation (LPO). However, both sizes of silica nanoparticles had little effect on intracellular glutathione (GSH) level and the activities of glutathione metabolizing enzymes; glutathione reductase (GR) and glutathione peroxidase (GPx). Buthionine-[S,R]-sulfoximine (BSO) plus silica nanoparticles did not result in significant GSH depletion than that caused by BSO alone nor N-acetyl cysteine (NAC) afforded significant protection from ROS and LPO induced by silica nanoparticles. The rather unaltered level of GSH is also supported by finding no appreciable alteration in the level of GR and GPx. Data suggest that the silica nanoparticles exert toxicity in A549 cells through the oxidant generation (ROS and LPO) rather than the depletion of GSH.

Akhtar, M. J., S. Kumar, et al. (2010). "The primary role of iron-mediated lipid peroxidation in the differential cytotoxicity caused by two varieties of talc nanoparticles on A549 cells and lipid peroxidation inhibitory effect exerted by ascorbic acid." Toxicol *In vitro* 24(4): 1139-1147.

Talc particles, the basic ingredient in different kinds of talc-based cosmetic and pharmaceutical products, pose a health risk to pulmonary and ovarian systems due to domestic and occupational exposures. Two types of talc nanoparticles depending on the source of geographical origin - indigenous- and commercial talc nanoparticles were assessed for their potential *in vitro* toxicity on A(549) cells; along with indigenous conventionally used microtalc particles. Cell viability, determined through live/dead staining and 3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay, decreased as a function of concentration, origin and size of particles. Both varieties of talc nanoparticles differentially induce lipid peroxidation (LPO), which was correlated with the pattern of lactate dehydrogenase (LDH) leakage, reactive oxygen species (ROS) generation, and glutathione (GSH)

depletion. Relatively higher cytotoxicity of indigenous nanotalc could be attributed to its higher content of iron as compared to commercial nanotalc. The known scavenger of ROS, l-ascorbic acid significantly inhibited LPO induction due to talc particles. Data suggest that nanotalc toxicity on A(549) cells was mediated through oxidative stress, wherein role of iron-mediated LPO was much pronounced in differential cytotoxicity.

Baweja, L., D. Gurbani, et al. (2011). "C60-fullerene binds with the ATP binding domain of human DNA topoiosmerase II alpha." J Biomed Nanotechnol 7(1): 177-178.

C60-fullerene has promising biological applications, such as drug delivery, biosensors, diagnosis and theraupetics. Despite of these applications, several *in vitro* studies have also reported the DNA damaging potential of this nanomaterial. Though, very little is known about the mechanism involved behind the fullerene mediated DNA damage. Authors study was aimed at identifying the binding site of fullerene in the ATP binding domain of human topoisomerase II alpha, a major enzyme involved in maintaining DNA topology. *In silico* studies of fullerene with the enzyme demonstrated that it can interact with the active site residues of this enzyme through hydrophobic, pi-stacking and van der Waals interactions and could inhibit the activity of this enzyme.

Bendre, V., M. Gautam, et al. (2011). "Characterisation of nanoparticle size and concentration for toxicological studies." J Biomed Nanotechnol 7(1): 195-196.

The assessment of the complete distribution of nanoparticle sizes within a suspension is notoriously difficult to carry out. Authors demonstrate the Nanoparticle Tracking Analysis (NTA) technique that sizes nanoparticles in suspension, based on their Brownian motion. This technique has found significant use in the field of nano- and eco-toxicology, in several research groups showing of the technique to assess a range of engineered nanoparticles including gold, SiO_2, TiO_2 and polystyrene. This capability shares many features in common with conventional flow cytometry but is unique in this deeply sub-micron size range. NTA is a direct and fast technique by which nanoparticles in their natural solvated state in a liquid can be rapidly detected, sized and counted. The technique can be used to complement existing techniques for the sizing of nanoparticles (e.g., DLS, PCS) allowing data obtained from these methods to be validated by direct microscopical observation of the sample.

Dandekar, P., R. Dhumal, et al. (2010). "Toxicological evaluation of pH-sensitive nanoparticles of curcumin: acute, sub-acute and genotoxicity studies." Food Chem Toxicol 48(8-9): 2073-2089.

Research in nanotoxicology is still in nascent stages. This hampers the design of appropriate regulatory policies for these beneficial nano-drug delivery systems thus affecting their routine employment as therapeutics. Establishing the entire toxicological profile is thus indispensable for proving the human safety of nanocarriers, which was the primary objective of the current investigation. The developed curcumin loaded polymeric nanoparticles of Eudragit S100 were subjected to various toxicological evaluations which included acute-toxicity study, sub-acute-toxicity study (28 days) and various genotoxicity studies like *in vivo* Micronucleus assay, *in vivo* Chromosomal Aberration assay and *in vivo* Comet assay. The formulation was found to be non-toxic at the dose equivalent to 2000 mg/kg of body weight of curcumin in the acute-toxicity study. Sub-acute-toxicity study proved the safety of the formulation for prolonged administration at the commonly used therapeutic dose of 100mg/kg of body weight of curcumin and at twice the therapeutic dose. Genotoxicity studies proved the cellular safety of the developed formulation at the therapeutic dose, and even at doses equivalent to thrice the therapeutic dose. Thus the developed curcumin loaded polymeric nanoparticles of Eudragit S100 were found to be safe for oral administration for a short as well as a prolonged duration.

Das, M., K. M. Ansari, et al. (2011). "Need for safety of nanoparticles used in food industry." J Biomed Nanotechnol 7(1): 13-14.

Nanotechnology derived products are now used in various spheres of life including food industry. Indeed nanotechnology may transform entire food industry in terms of production, processing and packaging and consumption. Due to their small size, nanoparticles find application as a carrier of antimicrobial polypeptides required against microbial deterioration of food quality. Detection of food pathogens, fungus producing mycotoxins, viruses and bacteria through nanosensors, which are quick, sensitive and less labour intensive procedures, is another area having potential application. The use of nanosensors in plastic packaging to detect gases released due to food spoilage is of consumer's relevance. Majority of nanoparticles for food use are organic moieties, hence it is of utmost importance to investigate their physico-chemical characteristics followed by toxicological implications to intestinal cells. It remains to be seen that nanostructured ingredients and nutrient delivery system may also carry other foreign substances to blood. Nano sized particles for food usage,

TOPIC OF INTEREST

having new chemical and physical properties may vary from normal macro particles that may also influence the interaction with living systems. Hence *in vitro* and *in vivo* studies are required for nanoparticles to be used in foods prior to their commercialization.

Dhawan, A., A. Pandey, et al. (2011). "Toxicity assessment of engineered nanomaterials: resolving the challenges." J Biomed Nanotechnol 7(1): 6-7.

The concern over the adverse effects of nanomaterials on humans has lead to an extensive research on the fate of nanoparticles in biological systems. However, unique properties of engineered nanomaterials yield many technical challenges which impede nanotoxicity studies. Some of these challenges are: interference of nanoparticles with *in vitro* toxicity assays, dissolution, studying cellular uptake and visualization, proper characterization, agglomeration etc. In the present study, zinc oxide (ZnO) nanoparticles were characterized for their size by dynamic light scattering which revealed their monodisperse nature. The cellular uptake of ZnO nanoparticles was analysed by flow cytometry. A significant increase in the percentage intensity of side scattering of cells treated with nanoparticles was observed as compared to the granularity of control cells. Further, the role of dissolution was evaluated by exposing cells to $ZnCl_2$ at an equimolar dose of released zinc. No decrease in the cell viability was observed suggesting minimal role of dissolution in ZnO nanoparticle induced toxicity.

Dhawan, A., R. Shanker, et al. (2011). "Guidance for safe handling of nanomaterials." J Biomed Nanotechnol 7(1): 218-224.

The materials at the nanoscale can have different properties compared with same materials at the larger scale. This change in behaviour can be attributed to increased relative surface area and dominance of quantum effects. It has been shown that the nanomaterials can cause adverse effects to human and environmental health. Therefore there is need for developing guidelines for safe use of nanomaterials in the laboratory to minimise exposure to researchers and environment. The purpose of this document is to provide the guidance on proper handling and disposal of nanomaterials (NMs) for personnel involved in activities that entail handling of NMs, in order to minimize risks from exposure to NMs in a laboratory.

Dhawan, A., R. Shanker, et al. (2011). "NanoLINEN: nanotoxicology link between India and European Nations." J Biomed Nanotechnol 7(1): 203-204.

Nanotoxicology link between India and European Nations (NanoLINEN) is a consortium of 7 European laboratories and Indian Institute of Toxicology Research (CSIR Laboratory) from India to strengthen the research ties in the area of Nanomaterial Toxicology. The goal of this project is to develop robust risk assessment methodologies that will be useful for the community manufacturing and using nano-products.

Dhawan, A. and V. Sharma (2010). "Toxicity assessment of nanomaterials: methods and challenges." Anal Bioanal Chem 398(2): 589-605.

The increasing use of nanomaterials in consumer and industrial products has aroused global concern regarding their fate in biological systems, resulting in a demand for parallel risk assessment. A number of studies on the effects of nanoparticles in *in vitro* and *in vivo* systems have been published. However, there is still a need for further studies that conclusively establish their safety/toxicity, due to the many experimental challenges and issues encountered when assessing the toxicity of nanomaterials. Most of the methods used for toxicity assessment were designed and standardized with chemical toxicology in mind. However, nanoparticles display several unique physicochemical properties that can interfere with or pose challenges to classical toxicity assays. Recently, some new methods and modified versions of pre-existing methods have been developed for assessing the toxicity of nanomaterials. This review is an attempt to highlight some important methods employed in nanomaterial toxicology and to provide a critical analysis of the major issues/challenges faced in this emerging field.

Dwivedi, P. D., A. Tripathi, et al. (2011). "Impact of nanoparticles on the immune system." J Biomed Nanotechnol 7(1): 193-194.

Nanotechnology is a fast growing field and its increasing exposure to humans and environment has generated the need to study the impact of nano-materials on host's immune system. Though, the effect of different particles on the various physiological functions will largely depend on their chemical composition and expectations of fundamentally large deviations in the particle activity or their mode of action at nanoscale size should not be over stretched. Nonetheless, owing to their small size, nanoparticles can penetrate and accumulate much deeper breaching the cellular and even sub-cellular boundaries which can cause many undesirable and un-characterized effects. Nanoparticles may escape the phagocytic activity of macrophages, bind to serum proteins and act as haptens; activate complement cascades; disturb the Th1/Th2 balance; cause hemolysis or thrombogenecity and may perturb the adaptive or innate immunity leading to a hyper-activated immune

state or even a suppressed immunophenotype. Since none of the cellular or even subcellular barriers are impervious to nanoparticles, author's earlier studies thoroughly characterizing the activity of diverse compounds or formulations at macro size level may not hold relevance at nano-dimensions. Moreover, authors understanding of the properties of matter when it squeezes to nano dimensions is still in very preliminary phase, therefore it becomes extremely critical to thoroughly evaluate the nanoparticles before adopting them for widespread usage in environment and direct or indirect human exposure.

Gupta, S. K., L. Baweja, et al. (2011). "Interaction of C60 fullerene with the proteins involved in DNA mismatch repair pathway." J Biomed Nanotechnol 7(1): 179-180.

Fullerenes are fascinating symmetric carbon nanostructures with a potential to bind DNA and proteins. Computational studies were performed to investigate the interaction of fullerenes with the proteins involved in DNA mismatch repair (MMR) pathway. Significant interactions of fullerene with PMS2, RFC3 and PCNA proteins were observed. These findings suggested that fullerene interferes in the human MMR process hence the subsequent disturbance may confer a large increase in spontaneous mutability and a strong predisposition to tumour development.

Gupta, S. K., A. Dhawan, et al. (2011). "*In silico* approaches: prediction of biological targets for fullerene derivatives." J Biomed Nanotechnol 7(1): 91-92.

Fullerene and their derivatives have many potential new applications. However, there is increasing concern regarding toxicity as very little information is available about fullerene derivatives--protein interactions. In the present work, to identify proteins interacting with chiral fullerene derivatives, Potential Drug Target Database was searched using reverse docking approach. Hypoxanthine phosphoribosyltransferase and Beta-secretase-1 were found to be the most favorable protein targets for fullerene derivatives.

Gurbani, D., R. K. Shukla, et al. (2011). "Stable metal oxide nanoparticle formulation for toxicity studies." J Biomed Nanotechnol 7(1): 104-105.

Metal oxide nanoparticles such as TiO_2 (< 100 nm) are used in lotions and sunscreens. Toxicity studies so far have reported the use of TiO_2 NPs with size > 100 nm as determined by dynamic light scattering (DLS) technique. Authors used non-reactive chemical agents such as propylene glycol (PG), glycerol (G), ethylene glycol (EG) to prevent aggregation and maintain NPs in monodispersed state closer to the reported TEM size. The lowest concentration of PG (0.1%) along with complete culture media (RPMI 1640) showed mean hydrodynamic diameter of TiO_2 NPs as 33.71 nm measured by DLS. The present study demonstrates a method to prepare stable TiO_2 NPs in culture media for toxicity assessment. This is a significant contribution as the biological properties of NPs vary considerably with decrease in size.

Jyoti, A., P. Pandey, et al. (2010). "Colorimetric detection of nucleic acid signature of shiga toxin producing *Escherichia coli* using gold nanoparticles." J Nanosci Nanotechnol 10(7): 4154-4158.

Enterohemorrhagic *E. coli* (EHEC) serotype O157:H7 is one of the major pathogens, responsible for the severe disease outbreaks. EHEC causes diseases in humans through production of shiga-like toxin leading to bloody diarrhea. The toxin is encoded by stx2 gene in *E. coli*. The current methodology for detection of EHEC relies on fluorogenic-substrate based culture media or nucleic acid amplification based Real-Time Polymerase Chain Reaction assays that are either time consuming or need expensive instrumentation. In this study, the optical properties of gold nanoparticles (GNPs) have been exploited for detection of nucleic acid of *Escherichia coli* O157:H7. The stx2 gene representing EHEC signature has been targeted using the gold nanoparticle probes. Gold nanoparticles (GNPs) of 20 +/- 0.2 nm were synthesised by citrate reduction method and characterised by spectroscopy and transmission electron microscopy. The GNPs were functionalised with 19 and 22 bp of thiolated single stranded DNA complementary to target highly conserved 149 bp region of stx2 gene. Transmission Electron Microscopy revealed the hybridization, aggregation and reduction in the interparticle distances of the GNP probes in the presence of target DNA. The aggregation and the spectral shift in the plasmon band observed with 10(6) copies of target DNA indicates feasibility of a simple and quick colorimetric 'spot and read' test in contrast to amplification based detection methods.

Jyoti, A., S. P. Singh, et al. (2011). "Rapid detection of enterotoxigenic *Escherichia coli* gene using bio-conjugated gold nano-particles." J Biomed Nanotechnol 7(1): 170-171.

In this study, a simple gold nanoparticle based colorimetric detection system for onsite diagnostics of Enterotoxigenic *Escherichia coli* (ETEC) has been developed. The developed assay could detect LT1 gene as evident from UV-visible spectra, the broadening of peak on hybridization of GNP probes with different copy

numbers of the target gene. The present study suggests that hybridization induced changes in optical properties of GNPs can be translated into a rapid and simple colorometric" spot and read test detection method for ETEC.

Khan, A. H., A. Mishra, et al. (2011). "Measurement techniques and instruments for airborne nanoparticles." J Biomed Nanotechnol 7(1): 165.

PM10 and PM2.5 are being monitored for asssessment of human health exposure. Laser aerosol spectrometry (25-300 nm), Aerasense Nano Monitors (10-300 nm), Aerasense Nano Tracer (10-300 nm) could be used for qualitative and quantitative detection. There is a need to develop instrumentation and methods for a wide range of engineered nanomaterials that are smaller in size and in very low concentrations in aerial, terrestrial and aquatic environment.

Khan, M. I., A. A. Sahasrabuddhe, et al. (2011). "Nano-talc stabilizes TNF-alpha m-RNA in human macrophages." J Biomed Nanotechnol 7(1): 112-113.

Particle size reduction of talc from micro- to nanoscale gradually enhanced its cytotoxicity however its inflammatory potential is still not explored. In the current study authors observed increased TNF-alpha, IL-1beta and IL-6 mRNA levels in macrophages exposed to Nano-Talc (NT). Further, NT particles also showed constituent phosphorylation of both p38 and ERK1/2 pathway however JNK phosphorylation was transient. Pre-treatment of macrophages with p38 and ERK1/2 inhibitors either alone or in combination showed significant reduction in TNF-alpha mRNA stability, clearly suggesting their role in TNF-alpha mRNA stabilization and expression. Authors observations clearly demonstrated the inflammatory potential of NT particles which might be at least partial and potential mechanism in talc mediated pathogenecity in the exposed population.

Mittal, S., V. Sharma, et al. (2011). "Toxicity evaluation of carbon nanotubes in normal human bronchial epithelial cells." J Biomed Nanotechnol 7(1): 108-109.

Carbon nanotubes (CNTs) are well known for their exceptional thermal, mechanical and electrical properties. For many CNT applications it is of the foremost importance to know their health hazards related to their exposure. Normal human bronchial epithelial cells (BEAS-2B) has been used for assessment the cytotoxicity of SWCNT (Diameter--1.2-1.5 nm) and DWCNT (Diameter--1.3-5 nm). Clear interference of CNTs with conventional *in vitro* cytotoxicity assays (MTT, NRU and LDH) dye was found which was confirmed by a cellular system. However morphological changes and flow cytometry showed the characteristics of cytotoxicity. Thus the study showed that there is a need of appropriate method for the assessment of cytotoxicity of CNT.

Patil, G., M. I. Khan, et al. (2011). "Nanotoxicity of dolomite mineral of commercial importance in India." J Biomed Nanotechnol 7(1): 114-115.

The risk of occupational exposure to dolomite, an important mineral exists both in organized as well as unorganized sectors. Toxicological profiles of bulk dolomite are meagerly known in general and its nanotoxicity in particular. Effects of micro- and nano particles on cell viability, LDH leakage and markers of oxidative stress were observed. The study indicated that cytotoxicity of dolomite nanoparticles is significantly higher than the microparticles. The study thus suggests for the prescription of exposure limit for nanodolomite in the best interest of health of workers at risk of exposure under mining, milling and industrial environment.

Rama Narsimha Reddy, A., Y. Narsimha Reddy, et al. (2011). "Induction of oxidative stress and cytotoxicity by carbon nanomaterials is dependent on physical properties." Toxicol Ind Health 27(1): 3-10.

In this study, authors investigated the mechanisms involved in multi-wall carbon particles/nanomaterials (MWCNM) induced cytotoxicity using human embryonic kidney (HEK293) cells and to assess the effect of physicochemical properties on the cytotoxicity and oxidative stress induced by the carbon nanomaterials (CNM). To elucidate the possible mechanisms of CNM-induced cytotoxicity, cell viability (3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide [MTT assay]), cell membrane damage (lactate dehydrogenase enzyme [LDH] assay), reduced glutathione (GSH), interleukin-8 (IL-8) and lipid peroxidation levels were quantitatively assessed under carbon nanomaterials exposed (48 h) conditions. Exposure of different sizes of four CNM at dosage levels between 3 and 300 µg/mL decreased cell viability in a concentration- and size-dependent manner. Exposure of CNM (10-100 µg/mL) to HEK cells resulted in size-, surface area- and concentration-dependent cell membrane damage, increased production of IL-8, increased thiobarbituric acid reactive substances (TBARS) and decreased intracellular glutathione levels. In summary, the physical properties of carbon nanoparticles may alter the CNM-induced concentration-dependent cytotoxicity and oxidative stress.

Reddy, A. R., Y. N. Reddy, et al. (2010). "Multi wall carbon nanotubes induce oxidative stress and cytotoxicity in human embryonic kidney (HEK293) cells." Toxicology 272(1-3): 11-16.

The present study was aimed at evaluating the potential toxicity and the general mechanism involved in multi wall

carbon nanotubes (MWCNT)-induced cytotoxicity using human embryonic kidney cell line (HEK293) cells. Two multi wall carbon nanotubes (coded as MWCNT1, size: 90-150nm and MWCNT2, size: 60-80nm) used in this study are MWCNT1 (produced by the electric arc method and size of the nanotubes was 90-150nm) and MWCNT2 (produced by the chemical vapor deposition method with size of 60-80nm). To elucidate the possible mechanisms of MWCNT induced cytotoxicity, cell viability, mitochondrial function (MTT assay), cell membrane damage (LDH assay), reduced glutathione (GSH), interleukin-8 (IL-8) and lipid peroxidation levels were quantitatively assessed under carbon nanotubes exposed (48h) conditions. Exposure of different sizes of two carbon nanotubes at dosage levels between 3 and 300µg/ml decreased cell viability in a concentration dependent manner. The IC(50) values (concentration of nanoparticles to induce 50% cell mortality) of two (MWCNT1, MWCNT2) nanoparticles were found as 42.10 and 36.95µg/ml. Exposure of MWCNT (10-100µg/ml) to HEK cells resulted in concentration dependent cell membrane damage (as indicated by the increased levels of LDH), increased production of IL-8, increased TBARS and decreased intracellular glutathione levels. The cytotoxicity and oxidative stress was significantly more in MWCNT2 exposed cells than MWCNT1. In summary, exposure of carbon nanotubes resulted in a concentration dependent cytotoxicity in cultured HEK293 cells that was associated with increased oxidative stress.

Sarkar, A., J. Das, et al. (2011). "Nano-copper induces oxidative stress and apoptosis in kidney via both extrinsic and intrinsic pathways." Toxicology 290(2-3): 208-217.

In the modern medicine nano particle has been used as a power tool but recently it has been established that nano particle pathophysiologically affects different organs. Recently, researchers have investigated the role of copper nano particle in liver dysfunction. In the literature, practically little is known about the nano-copper induced renal dysfunction. Authors, therefore, conducted the present study as a continuation of our earlier one to investigate the molecular mechanism in nano-copper induced kidney dysfunction. Nano-copper exposure increased the production of reactive oxygen species (ROS), reactive nitrogen species (RNS) and altered the levels of oxidative stress related biomarkers in kidney tissue. Signal transduction mechanism studies showed that nano copper exposure reciprocally regulated Bcl-2 family protein expression, disturbed mitochondrial membrane potential and subsequently helped releasing cytochrome c from mitochondria to cytosol. Apoptotic nature of cell death is confirmed by activation of caspases 3 which is also supported by histological study. In addition, authors also observed the activation of Fas, caspase 8 and tBid in kidney tissue in this pathophysiology, suggesting the involvement of extrinsic pathways. Combining all, results suggest that nano copper can trigger both intrinsic and extrinsic apoptotic pathways in oxidative stress mediated kidney dysfunction.

Sharma, M. (2010). "Understanding the mechanism of toxicity of carbon nanoparticles in humans in the new millennium: A systemic review." Indian J Occup Environ Med 14(1): 3-5.

Manmade nanoparticles range from the well-established multi-ton production of carbon black and fumed silica for applications in plastic fillers and car tyres to microgram quantities of fluorescent quantum dots used as markers in biological imaging. While benefits of nanotechnology are widely publicized, the discussion of the potential effects of their widespread use in the consumer and industrial products are just beginning to emerge. Acceptance of nanoparticle toxicity led to wide acceptance of the fact that nanotoxicology, as a scientific discipline shall be quite different from occupational hygiene in approach and context. Understanding the toxicity of nanomaterials and nano-enabled products is important for human and environmental health and safety as well as public acceptance. Assessing the state of knowledge about nanotoxicology is an important step in promoting comprehensive understanding of the health and environmental implications of these new materials. Very limited data exist for health effects secondary to inhalation of very fine respirable particles in the occupational environment. Nanomaterials may have effects on health due to their size, surface, shape, charge, or other factors, which are not directly predictable from mass concentration measurements. Numerous epidemiological studies have associated exposure to small particles such as combustion-generated fine particles with lung cancer, heart disease, asthma and/or increased mortality. The omnipresence of nanoparticles shifts focus of research toward efforts to mitigate the health effects of nanoparticles. Newer health assessment methods and newer techniques need to be developed for diagnosing sub-optimal health in populations exposed to carbon nanoparticles.

Sharma, V., D. Anderson, et al. (2011). "Zinc oxide nanoparticles induce oxidative stress and genotoxicity in human liver cells (HepG2)." J Biomed Nanotechnol 7(1): 98-99.

Zinc oxide (ZnO) is being used worldwide in consumer products and industrial applications. As humans are being directly exposed to ZnO nanoparticles (NPs) through

different routes, it is likely that the NPs would gain access to the liver. Therefore, the present study investigated the cytotoxic and genotoxic potential of ZnO nanoparticles in human liver cells (HepG2). The MTT and neutral red uptake assay showed a significant ($p < 0.05$) concentration and time dependent toxicity after 12 and 24 h at 14 and 20 µg/ml. A ($p < 0.05$) significant increase in DNA damage was observed in cells exposed to ZnO NPs for 6 h as evident with an increase in the Olive tail moment (OTM) and % tail DNA in the Comet assay. The generation of intracellular reactive oxygen species further suggest the role of oxidative stress in ZnO nanoparticle mediated DNA damage and cytotoxicity in HepG2 cells.

Sharma, V., R. K. Shukla, et al. (2009). "DNA damaging potential of zinc oxide nanoparticles in human epidermal cells." Toxicol Lett 185(3): 211-218.

At present, more than 20 countries worldwide are manufacturing and marketing different varieties of nanotech-based consumer products of which cosmetics form the largest category. Due to the extremely small size of the nanoparticles (NPs) being used, there is a concern that they may interact directly with macromolecules such as DNA. The present study was aimed to assess the genotoxicity of zinc oxide (ZnO) NPs, one of the widely used ingredients of cosmetics, and other dermatological preparations in human epidermal cell line (A431). A reduction in cell viability as a function of both NP concentration as well as exposure time was observed. ZnO NPs demonstrated a DNA damaging potential as evident from an increased Olive tail moment (OTM) of 2.13 +/- 0.12 (0.8 g/ml) compared to control 1.37 +/- 0.12 in the Comet assay after an exposure of 6 h. ZnO NPs were also found to induce oxidative stress in cells indicated by depletion of glutathione (59% and 51%); catalase (64% and 55%) and superoxide dismutase (72% and 75%) at 0.8 and 0.08 g/ml respectively. Data demonstrates that ZnO NPs even at low concentrations possess a genotoxic potential in human epidermal cells which may be mediated through lipid peroxidation and oxidative stress. Hence, caution should be taken in their use in dermatological preparations as well as while handling.

Sharma, V., S. K. Singh, et al. (2011). "Zinc oxide nanoparticle induced genotoxicity in primary human epidermal keratinocytes." J Nanosci Nanotechnol 11(5): 3782-3788.

Zinc oxide (ZnO) nanoparticles are widely used in cosmetics and sunscreens. Human epidermal keratinocytes may serve as the first portal of entry for these nanoparticles either directly through topically applied cosmetics or indirectly through any breaches in the skin integrity. Therefore, the objective of the present study was to assess the biological interactions of ZnO nanoparticles in primary human epidermal keratinocytes (HEK) as they are the most abundant cell type in the human epidermis. Cellular uptake of nanoparticles was investigated by scanning electron microscopy using back scattered electrons imaging as well as transmission electron microscopy. The electron microscopy revealed the internalization of ZnO nanoparticles in primary HEK after 6 h exposure at 14 µg/ml concentration. ZnO nanoparticles exhibited a time (6-24 h) as well as concentration (8-20 µg/ml) dependent inhibition of mitochondrial activity as evident by the MTT assay. A significant ($p < 0.05$) induction in DNA damage was observed in cells exposed to ZnO nanoparticles for 6 h at 8 and 14 µg/ml concentrations compared to control as evident in the Comet assay. This is the first study providing information on biological interactions of ZnO nanoparticles with primary human epidermal keratinocytes. Findings demonstrate that ZnO nanoparticles are internalized by the human epidermal keratinocytes and elicit a cytotoxic and genotoxic response. Therefore, caution should be taken while using consumer products containing nanoparticles as any perturbation in the skin barrier could expose the underlying cells to nanoparticles.

Shukla, R. K., A. Kumar, et al. (2011). "Titanium dioxide nanoparticles induce oxidative stress-mediated apoptosis in human keratinocyte cells." J Biomed Nanotechnol 7(1): 100-101.

Titanium dioxide nanoparticles (TiO_2 NPs) are the most commonly used metal oxide NPs in various industrial and commercial products. The present study has demonstrated a significant cellular uptake of TiO_2 NPs in the human keratinocyte cells (HaCaT) using transmission electron microscopy and flow cytometry. The data exhibited a significant ($p < 0.05$) concentration dependent decrease in cell viability and glutathione with concomitant increase in lipid peroxidation and reactive oxygen species. The increased oxidative stress further leads to apoptosis after 48 h of exposure. Present study demonstrates oxidative stress mediated apoptosis in human keratinocyte cells exposed to TiO_2 NPs.

Shukla, R. K., V. Sharma, et al. (2011). "ROS-mediated genotoxicity induced by titanium dioxide nanoparticles in human epidermal cells." Toxicol *In vitro* 25(1): 231-241.

Titanium dioxide nanoparticles (TiO_2 NPs) are among the top five NPs used in consumer products, paints and pharmaceutical preparations. Since, exposure to such nanoparticles is mainly through the skin and inhalation,

the present study was conducted in the human epidermal cells (A431). A mild cytotoxic response of TiO_2 NPs was observed as evident by the MTT and NR uptake assays after 48 h of exposure. However, a statistically significant ($p<0.05$) induction in the DNA damage was observed by the Fpg-modified Comet assay in cells exposed to 0.8 µg/ml TiO_2 NPs (2.20+/-0.26 vs. control 1.24+/-0.04) and higher concentrations for 6 h. A significant ($p<0.05$) induction in micronucleus formation was also observed at the above concentration (14.67+/-1.20 vs. control 9.33+/-1.00). TiO_2 NPs elicited a significant ($p<0.05$) reduction in glutathione (15.76%) with a concomitant increase in lipid hydroperoxide (60.51%; $p<0.05$) and reactive oxygen species (ROS) generation (49.2%; $p<0.05$) after 6h exposure. Data demonstrate that TiO_2 NPs have a mild cytotoxic potential. However, they induce ROS and oxidative stress leading to oxidative DNA damage and micronucleus formation, a probable mechanism of genotoxicity. This is perhaps the first study on human skin cells demonstrating the cytotoxic and genotoxic potential of TiO_2 NPs.

Singh, M., P. Bhatnagar, et al. (2011). "Enhancement of cancer chemosensitization potential of cisplatin by tea polyphenols poly(lactide-co-glycolide) nanoparticles." J Biomed Nanotechnol 7(1): 202.

Anti-cancer potential of polymer based nanoparticle of EGCG and TF alone and in combination with anti-cancer drug cisplatin have been studied in human cancer lines: A549 (lung carcinoma), HeLa (cervical carcinoma) and THP-1 (acute monocytic leukemia) using cell proliferation assay and cell cycle analysis. Encapsulated polyphenols retained biological effectiveness with over 20-fold dose advantage than EGCG/TF in exerting anti-cancer effects and also enhanced the potential of a widely used anti-cancer drug cisplatin. Subsequently, encapsulated polyphenols alone or in combination with cisplatin were more effective in inhibiting cell proliferation, metastasis, angiogenesis and apoptosis biomarkers. Collectively, the observations reveal that nanoparticle-mediated delivery of phytochemicals could serve as a basis for enhancing bioavailability and limiting the unwanted toxicity of chemotherapeutic agents.

Singh, R., A. Singh, et al. (2011). "Degradation of lindane contaminated soil using zero-valent iron nanoparticles." J Biomed Nanotechnol 7(1): 175-176.

Lindane, has been classified by the United States Environment Protection Agency as a potent carcinogen and teratogen. Zero-valent iron nanoparticles (nZVI) have been shown to effectively transform chlorinated hydrocarbons, organochlorine pesticides. An attempt has been made to explore the potential of nZVI for the remediation of Lindane contaminated soil. nZVI was synthesized by reducing $FeCl_3$ with $NaBH_4$. Lindane (10 µg/g) completely disappeared from spiked soil within 24 hours at nZVI concentration of 1.6 g/L, indicating its possible use in environmental cleanup. Reductive dehalogenation is the predominant mechanism for the removal of Lindane from spiked soil by nZVI. Dechlorination was further confirmed by the chloride ion release.

Srivastava, R. K., A. B. Pant, et al. (2011). "Multi-walled carbon nanotubes induce oxidative stress and apoptosis in human lung cancer cell line-A549." Nanotoxicology 5(2): 195-207.

Multi-walled carbon-nanotubes (MWCNTs)-induced apoptotic changes were studied in human lung epithelium cell line-A549. Non-cytotoxic doses of MWCNTs were identified using tetrazolium bromide salt (MTT) and lactate dehydrogenase (LDH) release assays. Cells were exposed to MWCNTs (0.5-100 µg/ml) for 6-72 h. Internalization and characterization of CNTs was performed by electron microscopy. Apoptotic changes were estimated by nuclear condensation, DNA laddering, and confirmed by expression of associated markers: p(53), p(21WAF1/CIP1), Bax, Bcl(2) and activated caspase-3. MWCNTs induced the production of reactive oxygen species and malondialdehyde along with significant decrease in the activity of catalase and glutathione. MWCNTs-induced ROS generation was found not to be associated with the mitochondrial activity. In general, the changes were significant at 10 and 50 µg/ml only. Results indicate the involvement of oxidative stress and apoptosis in A549 cells exposed to MWCNTs. These studies provide insights of the mechanisms involved in MWCNTs-induced apoptosis at cellular level.

Srivastava, R. K., Q. Rahman, et al. (2011). "Ameliorative effects of dimetylthiourea and N-acetylcysteine on nanoparticles induced cyto-genotoxicity in human lung cancer cells-A549." PLoS One 6(9): e25767.

Authors study the ameliorative potential of dimetylthiourea (DMTU), an OH* radical trapper and N-acetylcysteine (NAC), a glutathione precursor/HO scavenger against titanium dioxide nanoparticles (TiO_2-NPs) and multi-walled carbon nanotubes (MWCNTs) induced cyto-genotoxicity in cultured human lung cancer cells-A549. Cytogenotoxicity was induced by exposing the cells to selected concentrations (10 and 50 µg/ml) of either of TiO_2-NPs or MWCNTs for 24 h. Anti-cytogenotoxicity effects of DMTU and NAC were studied in two groups, i.e., treatment of 30 minutes prior to toxic insult (short term exposure), while the other group

TOPIC OF INTEREST

received DMTU and NAC treatment during nanoparticles exposure, i.e., 24 h (long term exposure). Investigations were carried out for cell viability, generation of reactive oxygen species (ROS), micronuclei (MN), and expression of markers of oxidative stress (HSP27, CYP2E1), genotoxicity (P(3)) and CYP2E1 dependent n-nitrosodimethylamine-demethylase (NDMA-d) activity. In general, the treatment of both DMTU and NAC was found to be effective significantly against TiO_2-NPs and MWCNTs induced cytogenotoxicity in A549 cells. Long-term treatment of DMTU and NAC during toxic insults has shown better prevention than short-term pretreatment. Although, cells responded significantly to both DMTU and NAC, but responses were chemical specific. In part, TiO_2-NPs induced toxic responses were mediated through OH* radicals generation and reduction in the antioxidant defense system. While in the case of MWCNTs, adverse effects were primarily due to altering/hampering the enzymatic antioxidant system. Data indicate the applicability of human lung cancer cells-A549 as a pre-screening tool to identify the target specific prophylactic and therapeutic potential of drugs candidate molecules against nanoparticles induced cellular damages.

Vallabani, N. V., S. Mittal, et al. (2011). "Toxicity of graphene in normal human lung cells (BEAS-2B)." J Biomed Nanotechnol 7(1): 106-107.

Graphite nanomaterials such as thermally exfoliated graphite oxide (GO) are versatile in many applications. However, little is known about its effects on biological systems. In this study authors characrerized the GO using dynamic light scattering (DLS) along with the toxicological aspects related to cytotoxicity and apoptosis in normal human lung cells (BEAS-2B). A significant concentration and time dependent decrease in cell viability was observed at different concentrations (10-100 µg/ml) by the MTT assay after 24 and 48 h of exposure and significant increase of early and late apoptotic cells was observed as compared to control cells. Present study demonstrates that GO induces cytotoxicity and apoptosis in human lung cells.

RESEARCH DIGEST

How to design a safer chemical

Nature 29 July 2011

When chemists design new detergents, shampoos, paints and lubricants, they don't immediately consider whether their molecules will have toxic side effects. That task has traditionally been left to toxicologists further down the production line. But synthetic chemists can and should take earlier responsibility for the safety of their molecules, urges a group led by Julie Zimmerman at Yale University in New Haven, Connecticut. In a paper published in *Green Chemistry*, the researchers show how obeying two key rules of thumb greatly reduces the chances of a molecule being acutely toxic to fish and other aquatic organisms. They plan to follow this up with similar design guidelines to avoid other types of damage, such as toxicity to birds. That such design guidelines are possible would hardly surprise toxicologists. But the research demonstrates to synthetic chemists how our growing understanding of toxicity puts the onus on them to deliberately avoid making molecules that fall in the danger zone, argues co-author Paul Anastas, science adviser to the US Environmental Protection Agency (EPA). Decades of safety tests have generated enough data for researchers to learn how chemicals produce toxic effects, and computer models are picking out the molecular properties that underlie this activity. "Rather than measuring how bad something is after it's made, and then going back to the drawing board, you can start to design molecules in what is likely to be a safer chemical space," says Anastas.

Avoid the danger zone

Zimmerman's team analysed data on hundreds of chemicals that have already been tested by the EPA and the Japanese environment ministry for their acute toxicity. Following established toxicology research, the team was not surprised to find that the most toxic chemicals tended to be quite soluble in fat relative to water, because this makes it easier for a molecule to pass through a cell's

membrane — the first hurdle for a chemical to overcome in order to have a biological effect. The group also found, as expected, that the toxic chemicals are adept at ripping electrons from other molecules, a property that makes it more likely they will cause damage once inside a cell. Combining the data on all species, the team quantified a range of values for variables relating to these two properties, within which fell 77% of the "desirable" chemicals; those with low or no toxicity. When they applied these rules to chemicals that had been tested on the green alga *Pseudokirchneriella subcapitata*, they found that 23 out of 29 desirable compounds fell inside the range. Staying within the safer range increases the chances of designing a compound with very low acute aquatic toxicity by two- to fivefold, the authors found.

Toxicology for beginners

Thomas Hartung, a toxicology expert at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland points out, computational models that correlate biological activity and toxicity with chemical structure — known as quantitative structure–activity relationships (QSARs) — already indicate the key variables leading to acute aquatic toxicity. "This is just an illustrative example, in an area where toxicity prediction is working and we already know the descriptors," Hartung says. But Hartung agrees with the Yale team's contention that this message needs to be absorbed by synthetic chemists, who tend not to be educated in toxicology. To chemists, QSARs seem like after-the-fact mathematical algorithms that don't give any indication of how to change a structure to avoid toxicity, says Adelina Voutchkova, another member of the Yale team. "We need QSARs, but we also need chemists to have a better chance of designing a molecule that passes the QSAR stage and *in vivo* tests," she says. The design of inherently safer molecules is a goal that Anastas has been working towards for years. He is well known as one of the co-founders of the 'green chemistry' movement, which aims to cut down on toxic chemicals and processes. He admits that there are many aspects of toxicity (such as reproductive toxicity) that are currently not sufficiently well understood for design 'rules' to be created that would steer past them. This point is also emphasized by Mark Thompson, director of chemical company DuPont's Haskell Global Centers for Health and Environmental Sciences in Newark, Delaware. He says that, in general, DuPont agrees with the Yale team's approach, but adds that "there's still a long way to go in our capability to predict toxicity". But that is just a matter of more research, Anastas thinks. "The key is to reduce the complexity to a small number of molecular properties which can be manipulated. That is a level very accessible to the molecular designers, the synthetic chemists," he says. Hartung notes. "Most chemical companies — with the exception of the really big ones that are forward-thinking — have no toxicology departments".

Geochemistry: Air pollutants make a comeback

Nature,28 July 2011

Climate warming is remobilizing toxic pollutants deposited in Arctic ice and sea water. Long-lived or 'persistent' organic pollutants (POPs), which include chlorinated pesticides and industrial chemicals, travel in the atmosphere to the high north, where they accumulate. They have been regulated for several decades, but sea-ice retreat and rising temperatures seem to be returning some of the more volatile compounds stored in Arctic reservoirs to the atmosphere. Jianmin Ma and Hayley Hung of Environment Canada in Toronto and their team analysed the concentrations of POPs measured since 1993 at two Arctic stations. When the effect of regulation was removed, several of the compounds showed increasing atmospheric levels, corresponding with rising Arctic temperatures and decreasing sea-ice cover. A simulation of the impact of climate change on the chemicals' atmospheric abundance confirmed this finding.

Bleak Prospects for Avoiding Dangerous Global Warming

ScienceNOW , 23 October 2011

The bad news just got worse: A new study finds that reining in greenhouse gas emissions in time to avert serious changes to Earth's climate will be at best extremely difficult. Current goals for reducing emissions fall far short of what would be needed to keep warming below dangerous levels, the study suggests. To succeed, we would most likely have to reverse the rise in emissions immediately and follow through with steep reductions through the century. Starting later would be far more expensive and require unproven technology. Published online in *Nature Climate Change*, the new study merges model estimates of how much greenhouse gas society might put into the atmosphere by the end of the century

RESEARCH DIGEST

with calculations of how climate might respond to those human emissions. Climate scientist Joeri Rogelj of ETH Zurich and his colleagues combed the published literature for model simulations that keep global warming below 2°C at the lowest cost. They found 193 examples. Modelers running such optimal-cost simulations tried to include every factor that might influence the amount of greenhouse gases society will produce —including the rate of technological progress in burning fuels efficiently, the amount of fossil fuels available, and the development of renewable fuels. The researchers then fed the full range of emissions from the scenarios into a simple climate model to estimate the odds of avoiding a dangerous warming. The results suggest challenging times ahead for decision makers hoping to curb the greenhouse. Strategies that are both plausible and likely to succeed call for emissions to peak this decade and start dropping right away. They should be well into decline by 2020 and far less than half of current emissions by 2050. Only three of the 193 scenarios examined would be *very* likely to keep the warming below the danger level, and all of those require heavy use of energy systems that actually remove greenhouse gases from the atmosphere. That would require, for example, both creating biofuels and storing the carbon dioxide from their combustion in the ground. "The alarming thing is very few scenarios give the kind of future we want," says climate scientist Neil Edwards of The Open University in Milton Keynes, U.K. Both he and Rogelj emphasize the uncertainties inherent in the modeling, especially on the social and technological side, but the message seems clear to Edwards: "What we need is at the cutting edge. We need to be as innovative as we can be in every way." And even then, success is far from guaranteed.

Pollutants' role in birth defects becomes clearer

Nature 18 July 2011

Babies who were exposed to certain organic pollutants in the womb are at a highly increased risk of neural tube defects leading to conditions such as spina bifida, according to researchers in China. Neural tube defects, in which the spinal cord, the brain or their coverings fail to develop completely, arise very early in pregnancy and affect more than 320,000 infants worldwide every year. They can lead not just to spina bifida, in which the spinal covering does not close completely, but also to severe cranial abnormalities such as anencephaly, which often leads to stillbirth, and other conditions. Previous studies have linked certain pollutants, in particular polycyclic aromatic hydrocarbons (PAHs), from sources such as indoor coal stoves, smoking and vehicle exhausts, to neural tube defects. But most of the evidence has been anecdotal, based on mothers saying they had been exposed to certain pollutants, or has relied on tests of the mother's blood alone. Now an interdisciplinary team of researchers in China has shown the risk of a newborn or foetus having a neural tube defect is much higher when certain organic pollutants are found in the placenta, which shows what is actually reaching the foetus, rather than just what is circulating in the mother's blood stream. "We only see the high levels of pollutants in the placenta, but we don't know if it's a true causal relationship," cautions reproductive health scientist Aiguo Ren of the Institute of Reproductive and Child Health at Peking University in

Beijing, one of the authors of the new study. Still, these defects happen in the first few weeks of pregnancy and the more information there is available on their causes, the more chance there is of reducing their occurrence. The new study also discovered one indication of a true link, the so-called 'dose-response relationship'.

Working on the relationship

With Ren, environmental scientist Tong Zhu, also at Peking University, investigated levels of PAHs and other pollutants in the placentas associated with 80 fetuses or newborns with neural tube defects between 2005 and 2007. They matched these fetuses to healthy newborns

from the same area, giving a control group of 50 healthy placenta samples. In all those studied, the risk of a defect was 4.5 times greater where the levels of PAHs were above the average of 597 nano-grams per gram of lipid. As the amount of PAHs in the placenta rises, those risk rises also, to over 11 times the risk of a defect in the cases with the highest levels of PAHs. This 'dose-response relationship' is important as it is one indication that the link is real, and not merely an artifact of the data. "It's not that we didn't know that this could be a problem," says Judith Rankin, a maternal and prenatal epidemiologist at Newcastle University, UK, who was not involved in the study. She notes, however, that in this study the researchers are using actual biomarkers in the blood rather than asking the mothers what they have been exposed to. To ensure that the link between PAHs and neural tube defects is clear, the team also took account of other factors that affect the incidence of the defects, such as folic acid supplementation, which decreases risk, and smoking, which increases it.

Climate change will hit genetic diversity

Nature 21 August 2011

Climate change represents a threat not only to the existence of individual species, but also to the genetic diversity hidden within them, researchers say. The finding promises to complicate assessments of how climate change will affect biodiversity, as well as conservationists' task in preserving it. DNA studies have revealed that traditional species, as defined by taxonomists, contain a vast amount of 'cryptic' diversity — such as different lineages, or even species within species. Carsten Nowak, a conservation biologist at the Senckenberg Research Institutes and Natural History Museum in Gelnhausen, Germany, and his colleagues have made a first attempt to understand how global warming might affect this form of diversity. Their findings are published in *Nature Climate Change*. The team looked at aquatic insects living in the mountain streams of central Europe — seven species of caddishly, a mayfly and a stonefly. The insects were chosen because they are likely to be especially vulnerable to rising temperatures — they need cold water, and have limited ability to travel large distances. To measure genetic diversity, Nowak's team sequenced genes in the animals' mitochondria — energy-generating cellular organelles that have their own small genome. This allowed the authors to divide each species into a number of evolutionary significant units (ESUs) — the technical term for a population within a species that is genetically distinct from the rest of its kind. On the basis of where in Europe each ESU is found, the researchers then analyzed whether the associated insect would be able to tolerate higher temperatures or move to somewhere cooler, using two models developed by the Intergovernmental Panel on Climate Change (IPCC).

Lost potential

Under the IPCC's business-as-usual climate scenario, 79% of ESUs included in the study are projected to become extinct by 2080; for a reduced-emissions scenario this fell to 59%. ESUs suffered a much greater rate of extinctions than species. This lost evolutionary potential could hinder species' ability to adapt to change. "This genetic diversity is the most fundamental form of biodiversity — essentially, it's the substrate for evolution," says Nowak. The study "shows how global climate change may lead to the loss of significant amounts of hidden diversity, even if some of the traditionally defined species will persist," says Michael Balke, an entomologist at the Bavarian State Collection of Zoology in Munich, Germany.

Diversity danger zone

"For Europe, it turns out that the most genetically diverse regions are also the most endangered," says Nowak. The study predicts that loss of genetic diversity in the study insects will be greatest in the Mediterranean region, where all but two populations are projected to become extinct. This is also the region with the greatest genetic diversity. This combination of genetic diversity and vulnerability has been found for other Mediterranean species, such as the seaweed, *Chondrus crispus*, which has already shifted northward during the past 40 years. Many European species retreated to the Mediterranean during past ice ages, meaning that their southerly populations are especially ancient and diverse. The loss of these populations might compromise species' ability to adapt to future warming. Combining genetics and ecology should aid conservation efforts. "This study highlights the huge potential of DNA-sequencing initiatives to reveal high levels of cryptic diversity, of utmost importance to informed conservation decision making," says Balke.

Genetic diversity is gaining increased attention in conservation circles. "Through our work to determine climate-adaptation strategies, we realize that genetics is one way to get an overall better view of how species are affected by climate change," says Ahmed Djoghlaf, executive secretary of the Convention on Biological Diversity, the United Nations, treaty that commits signatories to develop national strategies to sustainably use and conserve biodiversity.

Air pollution is stunting India's monsoon

New Scientist 30 September 2011

India has been drying out for half a century, and air pollution thousands of kilometres away is partly to blame. The monsoon has been weakening since the 1950s. Indian air pollution has been blamed, but now it seems that emissions further afield are also a factor. "The summer monsoon provides up to 80 per cent of total annual rainfall in south Asia, and supports 20 per cent of the world's population," says Yi Ming of Princeton University in New Jersey. With his colleagues, Ming used climate models to assess how different factors changed the monsoon. The monsoon is brought by large-scale wind patterns that transport heat between the northern and southern hemispheres. For half the year the northern hemisphere experiences more solar heating and so is warmer than the southern hemisphere; the situation is reversed during the other six months. As the winds head north over the Indian Ocean during the northern hemisphere's summer they pick up moisture, which falls as rain over south Asia. Air pollution in the form of aerosols can weaken these long-distance wind patterns, however. That's because it reflects sunlight back into space, cooling the polluted area. Thick aerosol pollution over Europe in summer ensures that the northern hemisphere isn't much warmer than the southern hemisphere, so there is nothing to drive the winds – and nothing to trigger the monsoon.

Lurching rains

Ming says his modelling suggests that the effect of European aerosol pollution accounts for about half the drop in the volume of monsoon rainfall – the other half is down to pollution over south Asia. In as-yet-unpublished experiments, he confirmed the important role that the European pollution plays in weakening the monsoon. He ran his models again, this time assuming no aerosol pollution over south Asia. Even so, India had a significantly weaker monsoon. The study supports existing evidence that air pollution is weakening the monsoon, says Veerabhadran Ramanathan of the University of California, San Diego. Another form of pollution – greenhouse gas emissions – is pushing the monsoon in the other direction, towards greater rainfall, says Ramanathan. The competing forces of the greenhouse effect and air pollution may lead to a much more variable monsoon, with drought one year followed by floods the next. He says this erratic behaviour is "more worrisome" than the overall decrease in rainfall.

Hookahs: Hot and Hazardous

Environ Health Perspect 01 August 2011

Hookah cafes are an increasingly popular venue for socializing. In addition to beverages, appetizers, and desserts, habitués can order different flavors of tobacco that they smoke through waterpipes. Many patrons of hookah cafes believe smoking a waterpipe is safer than smoking cigarettes—an unsubstantiated belief “as old as the waterpipe itself,” according to the World Health Organization. A new field trial shows that carbon monoxide (CO) levels were 3 times higher in people visiting hookah cafes than in people who visited traditional bars. Tracey Barnett, a social and behavioral scientist at the University of Florida, Gainesville, and colleagues measured CO levels of 173 patrons leaving three local hookah cafes and 198 patrons leaving five traditional bars that allow smoking. Hookah cafe patrons had an average CO level of 30.8 ppm compared with 8.9 ppm for traditional bar patrons. Even hookah cafe patrons who did not smoke from the waterpipe had average elevated CO levels of 11.5 ppm, similar to cigarette smokers The Occupational Safety and Health Administration established a cutoff of 50 ppm for CO exposure over an 8-hour period; 18% of hookah cafe patrons had CO levels exceeding this level, and 5% tested above 90 ppm. Symptoms of CO poisoning such as lightheadedness and nausea start at about 70 ppm. Some hookah smokers claim they experience a “high,” but “they're probably in the early stages of CO poisoning,” Barnett says. Emergency rooms have reported visits for CO poisoning after hookah smoking. Hookah smoke contains toxicants not only from burning tobacco but also from the charcoal used to heat the tobacco in the pipe's bowl, including CO, heavy metals, and polycyclic aromatic hydrocarbons. Shared hookahs also can raise the risk for communicable diseases. The water in a waterpipe does absorb some nicotine, so hookah smokers may inhale more smoke seeking a satisfying amount of the drug. A hookah session typically lasts 20–80 minutes, and the number and depth of puffs taken means a patron may inhale the smoke equivalent of 100 or more cigarettes. Hookah cafes are popular in university towns and large cities. By one 2005 estimate, up to 20% of some U.S. populations of young adults engage in hookah smoking. Norman Edelman, chief medical officer at the American Lung Association, says his organization is working with states to pass laws to ban hookah smoking. “People realize more and more that this is a dangerous practice,” Edelman says.

कुछ जानकारियाँ

अक्ल के लिए घातक है धूम्रपान

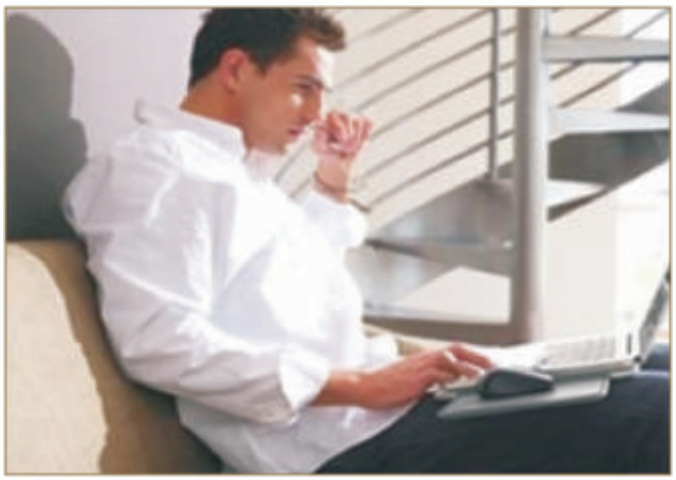
अगर आप चाहे हैं कि आपकी बुद्धि बरकरार रहे तो धूम्रपान करना बंद कर दें, धूम्रपान से इंसान की बुद्धिमंद हो जाती है।

धूम्रपान छोड़ने के लिए एक कारण और है। वह यह कि इसका सेवन बुद्धि हर लेता है। जर्नल आर्काइब्स आफ जनरल फिजिक्स के आनलाइन संस्करण में प्रकाशित एक नया अध्ययन बताता है कि अक्ल के लिए धूम्रपान घातक है। खासकर इसका सेवन करने वाले पुरूषों के लिए। अध्ययन की खास बात यह है कि धूम्रपान करने वाली महिलाओं में बुद्धि का इस तरह क्षरण नहीं होता। प्रमुख लेखक यूनिवर्सिटी कालेज लंदन के सेवराइन साबिया के अनुसार हम इस बात से वाकिफ थे कि धम्रपान फेफड़े की बीमारी कैंसर तथा दिल की बीमारी के लिए जोखिम है लेकिन यह अध्ययन दर्शाता है कि इसका असर दिमाग पर भी पड़ता है और इसका असर अक्सर 45 साल की उम्र में सामने आने लगता है। मीडिया ने साबिया के हवाले से बताया कि लगातार धम्रपान करने वाले ही नहीं बल्कि कभी कभार इसका सेवन करने वालों पर भी प्रभाव बराबर पड़ता है। यह इस बात की महत्ता दर्शाता है कि धूम्रपान से तौबा कर लेनी चाहिये। अपने अध्ययन के लिए अनुसंधानकर्ताओं ने करीब 6000 पुरूषों और 2100 महिलाओं के 25 साल की अवधि में धम्रपान की आदत का विश्लेषण किया। इसमें धम्रपान की मौजूदा स्थिति तथा अतीत का लत का विश्लेषण कर उनकी याददाश्त शब्द ज्ञान तथा तार्किक ज्ञान को परखा गया। अध्ययन में पाया गया कि धम्रपान करने वालों में तेजी से बौद्धिक हास अधेड़ उम्र में होता है।

खतरनाक है लैपटाप पर वाईफाई का प्रयोग

वाईफाई के प्रयोग वाले लैपटाप से पुरूष की पितृत्व क्षमता पर असर पड़ता है।

लैपटाप पर वायरलैस तकनीक की मदद से इंटरनेट का प्रयोग करने वाले पुरूषों के लिए यह खबर सचेत करने वाली है। एक नए अध्ययन में खुलासा हुआ है कि ऐसा करने से शुक्राणुओं को नुकसान पहुंच सकता है। एक अंतराष्ट्रीय दल ने पता लगाया है कि वाईफाई के प्रयोग वाला लैपटाप किसी पुरूष के जननांगों के पास रखने से पुरूष के शुक्राणु की गुणवत्ता में कमी आती है और उसके पितृत्प क्षमता पर भी असर पड़ता है। अर्जेंटीना के कोरडोबा में नासेंटिस सेंटर फार रिप्रोडक्टिव मेडिसिन और ईस्टर्न वर्जीनिया मेडिकल स्कूल

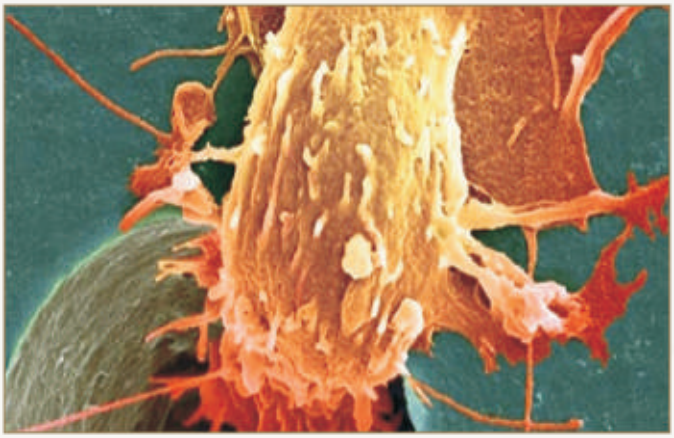


के नेतृत्व में हुए अध्ययन में पाया गया कि लैपटाप के पास मौजूदा शुक्राणु कुछ घंटों में भी मर जाते हैं। इस अध्ययन में यह भी पता चला कि इससे डीएनए को नुकसान पहुंचता है। इसके अलावा वाईफाई से नहीं जुड़े कम्प्यूटर के पास शुक्राणुओं से ज्यादा क्षति नहीं पहुंची। इस अध्ययन का नेतृत्व

डाक्टर कानराडो एवेंडानों ने किया।

चार नये कैंसर रोधी यौगिकों की पहचान हुई

वैज्ञानिकों ने चार नए कैंसर रोधी यौगिकों का पता लगाया है जिसके बारे में उनका कहना है कि यह ट्यूमर को बढ़ने से रोकने में कामयाब पाए गए हैं।



वैज्ञानिकों का कहना है कि इससे इस रोग से निपटने के लिए दवाओं की एक नयी श्रेणी का इजाद किया जा सकता है। ऑस्ट्रेलिया के मैक्वॉयर विश्वविद्यालय के एक दल ने कैंसर रोधी तत्वों की पहचान के लिए विशेष तौर पर तैयार किये गये रसायनों के साथ एन्जाइम इन्डोलएमीन 2, 3-डाईऑक्सीजिनेस के मौजूदा ज्ञान का मिश्रण किया। सटीक निशाना साधने वाली दवा के तौर पर इस एन्जाइम की भूमिका को लेकर विशेषज्ञ खासे उत्साहित हैं। खासतौर पर कैंसर जैसे रोगों के मामले में।

आईआईपी के वैज्ञानिकों ने प्लास्टिक से बनाया पेट्रोल

आईआईपी में वैज्ञानिकों की एक टीम ने प्लास्टिक से पेट्रोलियम बनाने की एक नई प्रौद्योगिकी विकसित की है।

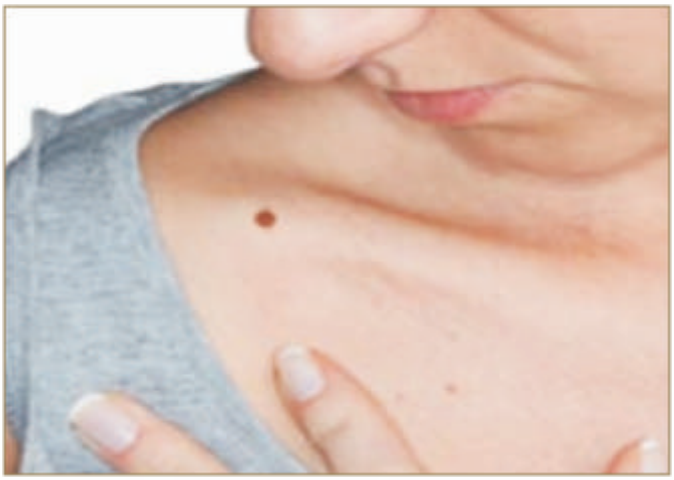
भारतीय पेट्रोलियम संस्थान (आईआईपी) में वैज्ञानिकों की एक टीम ने पर्यावरण के लिए खतरनाक माने जाने वाले

प्लास्टिक से पेट्रोलियम बनाने की एक नई प्रौद्योगिकी विकसित की है करीब एक दशक के लंबे प्रयोग के बाद आईआईपी के छह वैज्ञानिकों की टीम अपने निदेशक मधुकर ओंकारनाथ गर्ग के नेतृत्व में यह कामयाबी हासिल की है। उन्होंने 'उत्पेरकों का एक संयोजन' विकसित किया, जो प्लास्टिक को गैसोलीन या डीजल या 'एरोमेटिक' के साथ-साथ एलपीजी (रसोई गैस) के रूप में एक गौण उत्पाद में तब्दील कर सकता है। वैज्ञानिकों ने बताया कि इस परियोजना का प्रयोजक गेल भी बड़े पैमाने पर पेट्रोलियम उत्पाद तैयार करने के लिए परियोजना की आर्थिक व्यवहरिकता को तलाश रही है। शोध दल के सदस्य सनत कुमार ने बताया। 'इस प्रौद्योगिकी की खास विशेषता यह है कि तरल ईंधन-गैसोलीन एवं डीजल-ईंधन के यूरो-3 मानकों का पूरा करना है और उत्प्रेरकों एवं संचालन मापदंड में बदलाव के जरिए इसी कच्चे पदार्थ से विभिन्न उत्पाद प्राप्त किए जा सकते हैं। 'उन्होंने कहा कि इसके अलावा यह प्रक्रिया पूरी तरह से पर्यावरण हितैषी भी है। क्योंकि इससे कोई जहरीला पदार्थ उत्सर्जित नहीं होता है। उन्होंने बताया कि 100 फीसदी रूपांतरण प्राप्त किया गया है। अवशेष बचना कच्चे माल की गुणवत्ता पर निर्भर है। जो स्वच्छ कच्चा माल की स्थिति में आधा प्रतिशत से भी कम हो सकता है। इस परियोजना में शामिल एक अन्य वैज्ञानिक श्रीकांत ननोती ने बताया कि यह प्रक्रिया छोटे एवं बड़े उद्योग, दोनों के अनुकूल है। गौरतलब है कि 'वेस्ट प्लास्टिक्स टू फ्यूल एंड

पेट्रोकेमिकल्स' नाम से इस परियोजना की व्यवहार्यता पर 2002 में कार्य शुरू किया गया था और इस तथ्य तक पहुँचने में चार साल का वक्त लगा कि बेकार हो चुके प्लास्टिक को ईंधन में तब्दील करना संभव है। एक अनुमान के मुताबिक दुनिया भर में 300 टन से अधिक प्लास्टिक का इस्तेमाल किया जाता है और इसमें सालाना 10 से 12 फीसदी की बढ़ोतरी हो रही है। पेट्रोल तैयार करने के लिए पॉलीथीलीन जैसे पॉलीओलेफीनीक प्लास्टिक मुख्य कच्चा माल है।

शरीर पर अधिक तिल से त्वचा कैंसर का खतरा

शरीर पर अधिक तिल हो तो सावधान हो जाइए, वैसे यह वंशानुगत माना जाता है।



आस्ट्रेलियाई शोधकर्ताओं ने एक उत्परिवर्ती जीन खोज निकालने का दावा किया है जो एक तरह के त्वचा कैंसर (मेलानोमा) के खतरे को बढ़ाता है। एबीसी की रिपोर्ट के मुताबिक वेस्टमीड मिलेनियम इंस्टीट्यूट फॉर मेडिकल रिसर्च के ग्रहम मान ने बताया कि इस उत्परिवर्ती जीन को एमआईटीएफ के नाम से जाना जाता है जो आमतौर पर उन लोगों में पाया जाता है जिनके शरीर पर कई तिल होते हैं और जिनके पूर्वज 'मेलानोमा' से ग्रसित रहे होते हैं। उन्होंने बताया कि कई नमूनों के अध्ययन में पाया गया कि करीब दो लाख आस्ट्रेलियाई नागरिकों में यह जीन मौजूदा है। यह शोध विज्ञान जर्नल 'नेचर' के अंक में प्रकाशित किया गया है। मान ने कहा कि यह शोध लोगों के बेहतर उपचार के लिए उम्मीद की एक किरण की तरह है। उन्होंने कहा कि हम ऐसी उम्मीद करते हैं क्योंकि हम इस बात को समझते हैं कि प्रणाली कैसे काम करती है। इसे सुरक्षित दवा के माध्यम से रोका जा सकता है।

पृथ्वी के तापमान में एक डिग्री सेल्सियस की बढ़ोतरी

एक नए शोध का कहना है कि 1950 के दशक से अभी तक पृथ्वी के औसत तापमान में एक डिग्री सेल्सियस का इजाफा हुआ है।

अपने शोध के लिए शोधकर्ताओं ने 1800 से वर्ष 2009 तक के आंकड़ों का अध्ययन किया है। यह शोध बेरकेली यूनिवर्सिटी ऑफ कैलिफोर्निया के 'बेरकेली अर्थ सरफेस टेम्परेचर्स प्रोजेस्ट' (बीईएसटी) के विवादित भौतिक शास्त्री प्रोफेसर रिचर्ड मुल्लर के नेतृत्व में किया गया। बीईएसटी का डाटा दुनिया भर के 15 स्रोतों से 19वीं सदी के शुरू से रिकार्ड तापमान के 1.6 अरब आंकड़ों पर निर्भर है। उनके धरती के औसत तापमान में एक डिग्री सेल्सियस की बढ़ोत्तरी इस मामले में आधिकारिक रिकार्ड रखने वाले दुनिया के सभी संस्थानों से मेल खाती है। इन संस्थानों में यूनिवर्सिटी ऑफ ईस्ट एंग्लिया, नासा का न्यूयॉर्क स्थित गोडार्ड इंस्टिट्यूट फॉर स्पेस स्टडीज और अमेरिकी नेशनल ओसेनिक एण्ड एटमोसफियरिक एडमिनिस्ट्रेशन का मौसम विभाग शामिल है।

स्वच्छ पानी के लिए अल्ट्रा सोनिक नली

ब्रिटिश वैज्ञानिकों का कहना है कि उन्होंने नलों के लिए एक अल्ट्रा सोनिक उपकरण इजाद किया है जो पानी को बढ़े पैमाने पर शुद्ध करेगा।

साउथम्पटन विश्वविद्यालय के एक दल के एक उपकरण बनाया है जो ठंडे पानी और कम संयोजकों के साथ उतनी ही बिजली में काम करता है जितनी की एक बल्ब के लिए जरूरी होती है। बल्कि यह उपकरण पानी और बिजली की खपत की

तकनीक के लिहाज से मौजूदा तकनीकों से ज्यादा व्यापक है। दल के अगुवा प्रोफेसर टिम लिग्टन ने कहा कि समाज इसकी शुद्धिकरण की क्षमता पर चलता है। अप्रभावी सफाई भोजन ही विषाक्तता का कारण बनती है। उन्होंने कहा, ''अस्पतालों से होने वाले संक्रमण, सही तरीके से साफ नहीं हुए उपकरणों का स्वास्थ्य पर गंभीर असर पड़ता है। एक ऐसे उपकरण की बहुत जरूरत है जो हमारी शुद्धता की क्षमता को बढ़ाए साथ ही हमारे महत्वपूर्ण संसाधनों, पानी और बिजली को भी बचाए।'' अब दल को ऐसे उत्पादों के निर्माण की

उम्मीद है जो अल्ट्रा सोनिक नलियों पर आधारित होंगे, जिन्हें नल या पाइप के सिरे पर लगाया जा सके। इस उपकरण का एक अन्य फायदा यह है कि यह एसरोसोल (जल के छोटे वायुमंडलीय कण जो हवा में अशुद्धिया ले जा सकते हैं और अन्य सतहों को भी प्रदूषित करते हैं) आदि कम उत्पन्न करते हैं। शोधकर्ताओं का कहना है कि चूंकि इसमें ठंडे पानी का इस्तेमाल किया जाता है इसलिए पानी को गर्म करने में इस्तेमाल ऊर्जा की बचत होती है।

रोजाना एस्प्रिन ले सकती है आंखों की रोशनी

हृदय रोग में फायदा पहुंचाने वाली दवा एस्प्रिन आंखों के लिए बेहद नुकसान दायक भी साबित हो सकती हैं।

एक ताजा अध्ययन के अनुसार इसके लगातार सेवन से आंखों की रोशनी तक जा सकती है। यूरोप में हुए एक ताजा अध्ययन के मुताबिक एस्प्रिन लेने वाले लोगों में बढ़ती हुई उम्र में मांसपेशियों के शिथिल होने का खतरा इसे नहीं लेने वालो की तुलना में दोगुना तक बढ़ जाता है साथ ही आंखों की रोशनी जाने का भी खतरा काफी अधिक होता है। नीदरलैंड के इंस्टीटयूट फार न्यूरोसाइंस के शोधकर्ता पाल्स डि जॉग की अगुवाई में हुए इस शोध में नार्वे, एस्टोनिया, ब्रिटेन, फ्रांस, इटली और स्पेन के करीब 4700 लोगों को शामिल किया गया। शोध में शामिल लोगों की उम्र 65 वर्ष से अधिक थी। अध्ययन के मुताबिक एस्प्रिन लेने वाले 839 लोगों में से 36 लोगों को आंखों से संबंधित बीमारी, वेट मस्कुलर डिजनरेशन से पीड़ित पाया गया। आंखों की रक्त नलिकाओं में रिसाव होने से होती है। इसके कारण आंखों की रोशनी धीरे-धीरे कम होने लगती है। बीमारी का यह स्तर घातक होता है। अमेरिकी में 60 वर्ष से ऊपर के लाखों लोग मस्कुलर डिजेनरेशन से प्रभावित हैं। डि जोंग ने बताया कि हृदय रोगों और आंखों की बीमारी के बीच संबंध काफी विवादित है। उन्होंने कहा कि हृदय संबंधी रोगों के लिए एस्प्रिन लेने वाले लोगों में आंखों की रोशनी जाने अथवा आंख संबंधी रोग होने का खतरा काफी अधिक पाया गया है। हालांकि उन्होंने यह भी कहा कि यदि शरीर में हृदय ही ठीक से काम न करें तो स्वस्थ आंखों का भी क्या फायदा। बोस्टन के ब्रिगहेम एंड विमेंस अस्पताल के डाक्टर विलियम क्रिस्टीन ने कहा, बढ़ती उम्र में जब आंखे

कमजोर होने लगती हैं तब भी मैं लोगों को यही सलाह दूंगा कि वे एस्प्रिन नहीं ले।

वैज्ञानिकों का दावा है कि अंटार्कटिक पर ओजोन में हुए छिद्र का आकार उत्तरी अमेरिका जितना बड़ा हो गया है।

उन्होंने कहा कि दक्षिण ध्रुव पर हुए ओजोन में इस छिद्र का आकार 2.5 करोड़ वर्ग किलोमीटर हो गया। 14 सितम्बर को इसका वार्षिक क्षेत्रफल सबसे अधिक दर्ज किया गया। सालाना आकार के मुताबिक यह रिकार्ड में पांचवा सबसे बड़ा छिद्र बन गया। लाइवसाइंस की रिपोर्ट के अनुसार, नासा के अर्थ-ऑबजर्विंग और सेटेलाइट द्वारा ली गई माप के अनुसार वर्ष 2006 में अंटार्कटिक पर ओजोन में सबसे बड़ा छिद्र हुआ था जिसका आकार 2.75 करोड़ वर्ग किलोमीटर था। अंटार्कटिक पर ओजोन में छिद्र का पता पहली बार 1970 के दशक में लगा था। इसे 'नेशनल ओसिएनिक एण्ड एटमोसफियरिक एडमिनिस्ट्रेशन (नोआ) द्वारा ओजोन मापने के लिए संचालित अंतरिक्षयान ने मापा था। यह छिद्र 1980 और 90 की दशक में लगातार बढ़ता रहा। सिर्फ 21वीं सदी के आरंभ में इसके आकार में थोड़ी स्थिरता नज़र आयी। विज्ञान पत्रिका 'नेचर' में वैज्ञानिकों की रिपोर्ट के अनुसार, पिछले साल सर्दियों में आर्कटिक क्षेत्र में कड़ाके की ठंड ने ओजोन को नष्ट करने वाले रसायनों की सक्रिय कर दिया जिससे छिद्र बड़ा होने लगा। धरती की सतह पर ओजोन एक प्रदूषक है मगर समताप मंडल में यह सूर्य से आने वाली खतरनाक पराबैगनी किरणों से बचाव के लिए सुरक्षा कवच का निर्माण करती है। यह पराबैंगनी किरणों से वापस अंतरिक्ष में परावर्तित कर देती है। ओजोन को नुकसान पहुंचाने वाले रसायनों जैसे क्लोरोफ्लोरो कार्बन पर अंतराष्ट्रीय रोक के बाद ओजोन को नुकसान पहुँचना काफी कम हो गया है। इसके बावजूद ये रसायन अभी भी समताप मंडल में मौजूद हैं।

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Any feedback on this publication is welcome
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