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Inside

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

CSIR-IITR, Lucknow is the only multidisciplinary research institute in the field of toxicology in South East Asia with the motto:

"Safety to environment & health and service to industry".

R&D Areas

- ✓ Nanotherapeutics & Nanomaterial Toxicology
- ✓ Environmental Toxicology
- ✓ Food, Drug & Chemical Toxicology
- ✓ Regulatory Toxicology
- ✓ Systems Toxicology & Health Risk Assessment

Recognitions

- ➢ Scientific & Industrial Research Organizations (SIROs)
- ➢ UP Pollution Control Board (Water & Air)
- ➢ Indian Factories Act (Drinking Water)
- ➢ Bureau of Indian Standards (Synthetic Detergents)
- ➢ Food Safety & Standards Authority of India (FSSAI)

Services Offered

- ➢ GLP certified for pre-clinical toxicity studies
- ➢ Safety / toxicity evaluation of NCEs
- ➢ Water quality assessment and monitoring
- ➢ Analytical services
- ➢ Environmental monitoring and impact assessment
- ➢ Epidemiological studies
- ➢ Information on chemicals / products

Technologies Developed/ Available

- ❑ Water Analysis Kit
- ❑ Mobile Laboratory Van for on spot water quality analysis
- ❑ Argemone Detection Kit for rapid screening of Argemone in mustard oil
- ❑ CD-Strip for detection of butter yellow, an adulterant in edible oils
- ❑ Arsenic Detection Kit

Certifications

GLP certificate for toxicity studies

NABL accredited since 2000

CSIR-Indian Institute of Toxicology Research

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ANNUAL EVENTS

सीएसआईआर-भारतीय विषविज्ञान अनुसंधान संस्थान, में हिंदी सप्ताह मनाया गया

सीएसआईआर-भारतीय विषविज्ञान अनुसंधान संस्थान, लखनऊ में दिनांक 15.09.2014 को प्रातः 10:00 बजे प्रेक्षागृह में हिंदी सप्ताह-2014 के उद्घाटन समारोह का आयोजन किया गया। डा. सी.एस. नौटियाल, निदेशक, सीएसआईआर-आई.आई.टी.आर. ने इस अवसर पर मुख्य अतिथि श्री महेन्द्र मोदी, आई.पी.एस., अपर पुलिस महानिदेशक/विशेष निदेशक, उत्तर प्रदेश सतर्कता अधिष्ठान, लखनऊ का पुष्प और स्मृति चिन्ह देकर स्वागत किया। मुख्य अतिथि ने "जल प्रबन्धन से आर्थिक समृद्धि एवं जन सहभागिता" विषय पर व्याख्यान दिया। आरम्भ में उन्होने कहा कि मेरे विचार से हिंदी दिवस को भारतीय भाषा दिवस के रूप में मनाया जाना चाहिए। मेरे दिल में वैज्ञानिकों के लिए बहुत जगह है, यह वैज्ञानिकों की उपलब्धि है कि आज हम मंगल ग्रह पर पहुँच चुके हैं। जल प्रबन्धन पर अपना व्याख्यान देते हुए उन्होने कहा कि बरसने वाले पानी का 20 प्रतिशत रिचार्ज कर लें, तब भी 80 प्रतिशत पानी नदियों में जाने के लिए स्वतंत्र है। इसलिए मैं कहता हूँ कि छोटे-छोटे प्रयास में हम लोग कुछ भी कर सकते हैं। पानी की कमी होने पर जल संचय से हम कृषि कार्य इत्यादि कर सकते हैं। इससे हम बिजली भी बचा सकते हैं। छोटे-छोटे प्रयास और जनशक्ति से हम इसे व्यापक स्तर पर कर सकते हैं। डा. सी.एस. नौटियाल, निदेशक, सीएसआईआर-भारतीय विषविज्ञान अनुसंधान संस्थान, लखनऊ ने कार्यक्रम की अध्यक्षता करते हुए कहा कि संस्थान में राजभाषा कार्यान्वयन की स्थिति अच्छी है। इसका सम्मान किया जाना चाहिए। उन्होंने कहा कि मुख्य अतिथि के व्याख्यान से नया दृष्टिकोण मिला है। हमें यह भी ज्ञात हुआ है कि जल संचय से बिजली का क्या संबंध है और इससे बिजली भी बचा सकते हैं। यह पर्यावरण के मुद्दे से भी जुड़ा है। कार्यक्रम का संचालन श्री चन्द्र मोहन तिवारी, हिन्दी अधिकारी ने किया। श्री सी.पी. अरूणन, प्रशासन नियंत्रक ने धन्यवाद प्रस्ताव दिया। हिंदी सप्ताह के दौरान 15.09.2014 को क्विज एवं वाद-विवाद,16.09.2014 को आशुभाषण, हिंदीतर भाषी का हिंदी ज्ञान और अनुवाद तथा 17.09.2014 को लेख, टिप्पण व मसौदा लेखन एवं हिंदी टंकण प्रतियोगिताएं आयोजित की गई। दिनांक 19.9.2014 को अपराह्न 3:00 बजे हिंदी सप्ताह 14 से 20 सितंबर, 2014 के पुरस्कार वितरण एवं समापन समारोह का आयोजन किया गया। इस अवसर पर संस्थान के मुख्य वैज्ञानिक, डा. मुकुल दास ने समारोह की अध्यक्षता करते हुए प्रतियोगिताओं में भाग लेने वाले सभी प्रतिभागियों और पुरस्कार विजेताओं को बधाई दी । उन्होंने कहा कि यदि

डा. सी.एस.नौटियाल, निदेशक, मुख्य अतिथि श्री महेन्द्र मोदी का स्वागत करते हुए।

वैज्ञानिक चर्चाएं सरल हिंदी में की जाए तो कोई कठिनाई नहीं होगी। हिंदी हर विषय को अपने में समाए हुए है। उन्होंने कहा कि प्रत्येक वर्ष हिंदी सप्ताह के दौरान ज्यादा से ज्यादा कर्मियों को प्रत्येक प्रतियोगिता में बढ़-चढ़ कर भाग लेना चाहिए। सप्ताह के दौरान आयोजित वाद-विवाद, आशुभाषण, लेख, टिप्पण व मसौदा लेखन, हिंदीतर भाषी का हिंदी ज्ञान, हिंदी टंकण, अनुवाद एवं क्विज प्रतियोगिताओं में विजयी प्रतिभागियों को प्रथम, द्वितीय व तृतीय पुरस्कार एवं प्रमाणपत्र प्रदान किया। इसके अलावा वर्ष में हिंदी में कार्य करने की प्रोत्साहन योजना के अन्तर्गत विजयी प्रतियोगियों को दो प्रथम, तीन द्वितीय और पांच तृतीय और सबसे अधिक हिंदी में डिक्टेशन का एक पुरस्कार और प्रमाण पत्र भी प्रदान किए गए। श्री सी.पी. अरूणन, प्रशासन नियंत्रक ने धन्यवाद प्रस्ताव दिया। कार्यक्रम का संचालन श्री चन्द्र मोहन तिवारी, हिंदी अधिकारी ने किया ।

हिन्दी में कार्य करने की प्रोत्साहन योजना के अन्तर्गत विजयी प्रतिभागी

CSIR Foundation Day Celebrated

The 72nd CSIR Foundation Day function was organised in the auditorium of CSIR-Indian Institute of Toxicology Research, Lucknow on September 29, 2014. Dr C.S. Nautiyal, Director, CSIR-IITR while welcoming the chief guest, Prof. Ravi Kant, Vice Chancellor, King George's Medical University, Lucknow, said that this day is open for students who visit the institute to have a glimpse of the R&D activities being pursued. This helps the institute in attracting talent who could take-up science as a career in future.

Dr Devendra Parmar, Chief Scientist, CSIR-IITR introduced Prof. Ravi Kant to the audience. While delivering the foundation day lecture, Prof Ravi Kant informed about a new medicine system POEM to the audience. POEM- Patient Oriented Evidence based Medicine is the way forward in tackling and treating diseases. He stressed upon the need for a continuous and comprehensive co-ordination between physical, chemical and biological sciences in order to ensure success in treating gastric cancers. He opined that early diagnosis of gastric cancers ensures a better survival rate in gastric cancer patients. Japan has introduced an extensive screening mechanism to catch early cases of gastric cancer which has resulted in a 30% survival rate in such patients, compared to a global average of 12-15%. Improved diagnostic techniques like fluorescence endoscopy, photodynamic therapy and endoscopic ultrasonography aid in early gastric cancer detection. He encouraged the students to follow Dr APJ Abdul Kalam's advice to dream big and with eyes open to scale new heights. On this occasion the following members of staff who had

Sitting on podium Dr Devendra Parmar, Dr C.S. Nautiyal, Prof. Ravi Kant and Dr Poonam Kakkar

Dr C.S. Nautiyal, welcoming Prof. Ravi Kant

A view of audience

A group shoot with all the felicitated superannuated employees

superannuated during the last one year were felicitated by Director, CSIR-IITR. They were Dr K.C. Gupta, Dr (Smt.) Shashi Khandelwal, Dr L.P. Srivastava, Smt. Leela S. Pillai, Smt. C.K. Takru, Smt. A.T. Burrows, Sri Hira Lal, Sri Mata Prasad, Sri Munni Lal. Prof. Ravi Kant also presented mementoes to members of IITR family who had completed 25 years of service. They were Dr Ram Chandra, Dr Vipin Bihari, Sri Mukund Sahai, Sri B.K. Mishra, Sri Ram Narayan, Sri A.K. Pathak, Sri Bal Kishan, Sri Kaleemuddin, Sri Tajuddin Ahmad, Sri Dheer Kumar, Sri Hari Ram. On the occasion of Foundation Day function earlier an essay competition was organized for the wards of CSIR employees on the following topics:

(1) Contribution of science in meeting food demands and security.

(2) Natural disaster management: Past and present

The winners were awarded certificates. The winners from junior group (Class V to Class VIII) were: First prize - Anushka Singh, Second prize - Ms. Deeparati Datta, Third prize - Mr. Aprameya H. Iyengar. The winners from senior group (Class X to XII) were: First prize - Ms. Shweta Yadav, Second prize - Ms. Sakshi Yadav, Third prize - Ms. Shreya Shukla. Dr Poonam Kakkar, Chief Scientist, IITR proposed the vote thanks.

CSIR-IITR Foundation Day Celebrated

The 49th Foundation Day of CSIR - Indian Institute of Toxicology Research was celebrated with enthusiasm and gaiety at the institute on 07 November 2014. The programme began with the traditional lighting of the lamp and rendition of the IITR Song by the IITR Choir Group. Dr C.S. Nautiyal, Director, CSIR-IITR welcomed the guests and presented the annual report for the year 2013-2014. The institute has made several notable contributions in thrust areas viz Food, Drug and Chemical Toxicology; Environmental Toxicology; Regulatory Toxicology; Nanotherapeutics and Nanomaterial Toxicology and Systems Toxicology and Health Risk Assessment. The area of Food, Drug and Chemical Toxicology is of immense importance given the paradigm shift in rapid urbanization and food security. Studies conducted at the institute demonstrated the anti-diabetic and anti oxidative effects of stem bark of *Oroxylum indicum* in animal models and the allergenicity of red kidney bean, a commonly consumed legume. In the area of Environmental Toxicology, towards a clean and green environment, studies were conducted on air quality in relation to the risks associated with human health. Six groups of fungi of environmental origin have been found to be associated with respirable particulate matter in the Lucknow environment along with traffic linked ultra fine particle fraction in the atmosphere. The institute has taken a proactive role in strengthening Regulatory Toxicology by being the first CSIR laboratory to be accredited by the National GLP Compliance Monitoring Authority as a GLP Certified Laboratory for the conduct of acute toxicity, sub acute toxicity, micronucleus assay and chromosomal aberration assays. The scientists of this group have developed sensitive methods of analytical importance and predictive tools. In the area of Nanotherapeutics and Nanomaterial Toxicology, the institute has carried out research addressing the issues on transfection agents and

Commencement of function with lighting of lamp

Sitting on the podium (L-R) Dr Mukul Das, Dr K.C. Gupta, Prof. S.B. Nimse, Dr C.S. Nautiyal and Dr Poonam Kakkar

Coir reciting on CSIR-IITR theme song

Release of CSIR-IITR Annual Report

targeted gene delivery, method development for toxicity assessment as well as models for safety assessment. Creditable achievements in the area of Systems Toxicology and Health Risk Assessment include development of differentiating neuronal cells from human umbilical cord blood stem cells as an *in vitro* tool for the assessment of developmental neurotoxicity; standardization of a protocol for quick isolation of primary microglia from mice brain and studies to investigate the protective effects of curcumin in arsenic induced cholinergic alterations. Several scientists of the institute have received recognition at the national and international level for their scientific achievements, are serving on the editorial boards of various international journals and various committees of government departments like DBT, DST, MoEF, ICMR, CPCB, FSSAI etc. CSIR - IITR scientists have published 148 research papers this year with an average impact factor of 3.372. The Academy of Scientific and Innovative Research (AcSIR), an autonomous body with a mandate to create and train S & T leaders of the future, continues to do so through a combination of novel and innovative curricula. During the period Aug 2013 to Jan 2014, 15 students with national fellowships have been enrolled under the programme. Delivering the 18th Prof Sibte Hasan Zaidi Memorial Oration, Dr K. C. Gupta, former Director, CSIR - IITR, stressed upon the role of gene therapy in ensuring targeted cancer therapy as against the traditional methods of cancer treatment. One of the major challenges in gene therapy is to identify safe and efficient vectors to transfer and deliver therapeutic genetic material to specific tissues. Among the several candidate carriers evaluated, chitosans, a natural polysaccharide emerged a promising gene carrier given its biodegradable nature and non toxic properties. Extensive *in-vivo* studies conducted have demonstrated that tumour specific natural polysaccharide based nanocomposites could epitomize a viable alternative for targeted gene therapy. Following the oration Dr K. C. Gupta released the report on Assessment of Ambient Air Quality of Lucknow City in the Post Monsoon season. The study was carried out in October 2014 by monitoring levels of a few selected air pollutants viz., Respirable particulate Matter (RSPM), Sulphur dioxide (SO_2). Oxide of Nitrogen (NOx) and noise levels at 9 representative locations categorized as residential (4), commercial (4) and industrial (1). Results revealed 24 hour concentrations of RSPM between 123.5 and 342.7 µg/m^3, well above the permissible limit of 100 µg/m^3 as prescribed by the Ministry of Environment and Forests. 24 hour concentrations of SO_2 and NOx were in the range of 8.4 to 25.5 and 39.9 to 108.3 µg/m^3 with an average concentration of 17.3 and 61.2 µg/m^3 respectively, both being below the permissible limit of 80 µg/m^3. Noise levels during the day and night were in the range of 66.1 to 78.8 dB(A) and 54.6 to 72.5 dB(A), both above the respective permissible limits for different areas. The report also recommends strengthening the public mass transport system and minimizing the use of personal vehicles with better traffic management and an effective ban on the use of pressure horns from vehicles. In his Foundation Day Address, Prof. S. B. Nimse, Vice Chancellor, Lucknow University commended the work carried out by the institute towards human health and environmental safety. He opined that, Lucknow, with its abundance of scientific / academic and R & D institutes / organizations / universities has a tremendous potential to ensure that the benefits of science reach all citizens of this country. He stressed

the need for a greater co-ordination between all the institutions to bring them all on a single platform towards achieving this goal. The function concluded with the singing of the National Anthem followed by a splendid lunch for all guests, invitees and staff of the institute.

Swach Bharat Abhiyan at CSIR-IITR

As a part of the Swach Bharat Abhiyaan undertaken by the Institute, volunteers from the GLP Team of CSIR- IITR offered shramdaan in Oct 2014. Incessant rains, an effect of the cyclone Hudhud, did not dampen the spirits of the volunteers who turned up in good numbers at the Gheru Campus of CSIR-IITR. Two tasks were planned for the day -

1. Clearing and plantation of the area adjacent to the Animal Facility (erstwhile SWIM Park)
2. Cleaning and painting of all pots at the campus.

The senior management of the GLP team lead from the front with the Dy TFM and QAU head along with other senior staff members from both the campuses. Several research scholars, project assistants also participated in cleaning and painting of pots. Pots were cleaned and painted. In addition, activities like outer cleaning and painting of the water cooler, cleaning of the notice board were also carried out. A few photographs from the shramdaan are below:

CLEANING AND POT PAINTING

GLP Facility Inauguration at CSIR - Indian Institute of Toxicology Research

25 Jul 2014 shall always remain etched as an important milestone in the history of CSIR - Indian Institute of Toxicology Research. Having received the GLP Certification from the National GLP Compliance Monitoring Authority on 05 Jun 2014, each member of the GLP team was eagerly looking forward to a formal inauguration of the facility. Prof. Ram Rajasekharan, Director CSIR - Central Food Technology Research Institute, Mysore kindly consented to be the chief guest for the function. Underlining the fact that this was indeed a momentous occasion in the history of CSIR- IITR, the three sister institutes in Lucknow were represented by their respective directors, Dr C. S. Nautiyal (CSIR- NBRI), Dr S. K. Puri (CSIR- CDRI) and Dr A. K. Tripathi (CSIR-CIMAP). Vice Chancellor of King George Medical University, Dr D. K. Gupta also graced the occasion. Keeping with the pro - environment mandate of the institute plantation of saplings by the guests was also organized on the day. The programme culminated with a sumptuous spread of snacks for all present on the occasion.

Uncovering of stone & dedication of GLP Test Facility to the nation by Prof. Ram Rajasekharan

Dedication of GLP Test Facility to the nation sitting on dais (L-R)
Dr Poonam Kakkar, Prof. Ram Rajasekharan, Dr K. C. Gupta and Dr Mukul Das

Dr K. C. Gupta welcoming the guests

Honourable spectators

Planting of tree by Prof. Ram Rajasekharan

CSIR-IITR RESEARCH HIGHLIGHTS

Superoxide mediated photomodification and DNA damage induced apoptosis by benz(a)anthracene via mitochondrial mediated pathway.

[Mujtaba SF, Dwivedi A, Yadav N, Ch R, Kushwaha HN, Mudiam MK, Singh G, Ray RS. J Photochem Photobiol B. 2014 Dec 2;142C:92-102.]

Benz(a)anthracene (BA) is an ubiquitous environmental pollutant of polycyclic aromatic hydrocarbon's (PAHs) family. Authors showed superoxide (O_2^-) catalyzed BA photo modification and apoptosis in HaCaT keratinocytes under sunlight exposure. O_2^- generation was confirmed by quenching through superoxide dismutase (SOD). BA induced photocytotoxicity were investigated through MTT and NRU assay. Authors proposed DNA insults such as single and double strand breakage and CPDs formation which results in cell cycle arrest and apoptosis by photosensitized BA. BA induced apoptosis was caspase dependent and occurred through a mitochondrial pathway. Reduction of mitochondrial membrane potential, translocation of Bax to mitochondria and cytochrome C release favors involvement of mitochondria in BA phototoxicity. AO/EB double staining and TEM analysis also support apoptotic cell death. Authors propose a p21 regulated apoptosis via expression of Bax, and cleaved PARP under sunlight exposure. Thus, authors conclude that it is imperative to avoid solar radiation during peak hr (between 11A.M. and 3P.M.) when the amount of solar radiation is high, in the light of DNA damage which may lead to mutation or skin cancer through photosensitized BA under sunlight exposure. Concomitantly, investigation is urgently required for the photosafety of BA photoproducts reaching in the environment through photomodification.

Exposure to endosulfan influences sperm competition in *Drosophila melanogaster*.

[Misra S, Kumar A, Ratnasekhar Ch, Sharma V, Mudiam MK, Ram KR. Sci Rep. 2014 Dec 11;4:7433.]

Dwindling male fertility due to xenobiotics is of global concern. Accordingly, male reproductive toxicity assessment of xenobiotics through semen quality analysis in exposed males, and examining progeny production of their mates is critical. These assays, in part, are biased towards monogamy. Females soliciting multiple male partners (polyandry) is the norm in many species. Polyandry incites sperm competition and allows females to bias sperm use. However, consequences of xenobiotic exposure to the sperm in the light of sperm competition remain to be understood. Therefore, authors exposed *Drosophila melanogaster* males to endosulfan, and evaluated their progeny production as well as the ability of their sperm to counter rival control sperm in the storage organs of females sequentially mated to control/exposed males. Endosulfan (2 µg/ml) had no significant effect on progeny production and on the expression of certain genes associated with reproduction. However, exposed males performed worse in sperm competition, both as 1(st) and 2(nd) male competitors. These findings indicate that simple non-competitive measures of reproductive ability may fail to demonstrate the harmful effects of low-level exposure to xenobiotics on reproduction and advocate consideration of sperm competition, as a parameter, in the reproductive toxicity assessment of xenobiotics to mimic situations prevailing in the nature.

Combinatorial chemopreventive effect of butyric acid, nicotinamide and calcium glucarate against the 7,12-dimethylbenz(a)anthracene induced mouse skin tumorigenesis attained by enhancing the induction of intrinsic apoptotic events.

[Tiwari P, Sahay S, Pandey M, Qadri SS, Gupta KP. Chem Biol Interact. 2014 Dec 3;226C:1-11.]

Authors explored the basis of the combinatorial chemopreventive effect of butyric acid (BA), nicotinamide (NA) and calcium glucarate (CAG) on mouse skin exposed to 7,12-dimethylbenz (a)anthracene (DMBA). Authors studied the effects of topical application of DMBA in the presence or absence of BA, NA and CAG on the regulators of apoptosis. DMBA treatment suppressed Bax, Bax/Bcl-2 ratio, release of cyt c, Apaf1, caspase-9, -3 mediated apoptosis. Downregulation of p21 and upregulation of Bcl-2, mut p53 were also observed in only DMBA treated mice. Simultaneous application of BA, NA and CAG induced a mitochondria-mediated apoptosis, characterized by a rise in the Bax, Bax/Bcl-2 ratio, release of cyt c, upregulation of Apaf1 with down-stream activation of caspase-9, -3. Furthermore treatment with BA, NA and CAG demonstrated an upregulation of p21 and

downregulation of Bcl-2, mut p53. But this effect was enhanced in the presence of all the three compounds together in combination. Chemoprevention by a combination of BA, NA and CAG by inducing the apoptosis, the natural cell death, suggest the importance of the potential combinational strategies capable of preventing skin tumor development.

miRNA profiling provides insights on adverse effects of Cr(VI) in the midgut tissues of *Drosophila melanogaster*.

[Chandra S, Pandey A, Chowdhuri DK. J Hazard Mater. 2015 Feb 11;283:558-67.]

Cr(VI), a well-known environmental chemical, is reported to cause various adverse effects on exposed organisms including genomic instability and carcinogenesis. Despite available information on the underlying mechanism of Cr(VI) induced toxicity, studies regarding toxicity modulation by epigenetic mechanisms are limited. It was therefore, hypothesized that the global miRNA profiling in Cr(VI) exposed Drosophila, a genetically tractable model organism, will provide information about mis-regulated miRNAs along with their targeted genes and relevant processes. Third instar larvae of *Drosophila melanogaster* (Oregon R(+)) were exposed to 5.0-20.0µg/ml of Cr(VI) for 24 and 48h. Following miRNA profile analysis on an Agilent platform, 28 of the 36 differentially expressed miRNAs were found to be significantly mis-regulated targeting major biological processes viz., DNA damage repair, oxidation-reduction processes, development and differentiation. Down-regulation of mus309 and mus312 under DNA repair, acon to oxidation-reduction and pyd to stress activated MAPK cascade respectively belonging to these gene ontology classes concurrent with up-regulation of dme-miR-314-3p, dme-miR-79-3p and dme-miR-12-5p confirm their functional involvement against Cr(VI) exposure. These findings assume significance since majority of the target genes in Drosophila have functional homologues in humans. The study further recommends Drosophila as a model to explore the role of miRNAs in xenobiotic induced toxicity.

QSTR modeling for predicting aquatic toxicity of pharmacological active compounds in multiple test species for regulatory purpose.

[Singh KP, Gupta S, Basant N. Chemosphere. 2015 Feb;120:680-9.]

High concentrations of pharmacological active compounds (PACs) detected in global drinking water resources and their toxicological implications in aquatic life has become a matter of concern compelling for the development of reliable QSTRs (qualitative/quantitative structure-toxicity relationships) for their risk assessment. Robust QSTRs, such as decision tree boost (DTB) and decision tree forest (DTF) models implementing stochastic gradient boosting and bagging algorithms were established by experimental toxicity data of structurally diverse PACs in daphnia using molecular descriptors for predicting toxicity of new untested compounds in multiple test species. Developed models were rigorously validated using OECD recommended internal and external validation procedures and predictive power tested with external data of different trophic level test species (algae and fish). Classification QSTRs (DTB, DTF) rendered accuracy of 98.73% and 97.47%, respectively in daphnia and 84.38%, 85.94% (algae), 78.46% and 79.23% (fish). On the other hand, the regression QSTRs (DTB, DTF) yielded squared correlation coefficient values of 0.831, 0.852 (daphnia), 0.534, 0.556 (algae) and 0.620, 0.637 (fish). QSTRs developed in this study passed the OECD validation criteria and performed better than reported earlier for predicting toxicity of PACs, and can be used for screening the new untested compounds for regulatory purpose.

Benzanthrone induced immunotoxicity via oxidative stress and inflammatory mediators in Balb/c mice.

[Tewari P, Roy R, Mishra S, Mandal P, Yadav A, Chaudhari BP, Chaturvedi RK, Dwivedi PD, Tripathi A, Das M. Immunobiology. 2014 Oct 18. pii: S0171-2985(14)00202-2.]

Benzanthrone (BA) is an important dye intermediate which is used in the manufacturing of several polycyclic vat and disperse dyes in textile industries. Several studies have indicated that the general population is also exposed to BA owing to its release from furnace effluents and automobile exhausts in the environment. In several clinical studies, it has been shown that workers exposed to BA developed itching, burning sensation, erythema and hyperpigmentation of the skin, which could be an outcome of the dysregulated immune response. In this study, authors have used female Balb/c mice as a model to study the immuno-inflammatory changes after systemic administration of BA (7.5mg/kgb.w. and 15mg/kgb.w.) for one week. BA exposed

animals exhibited the signs of intense systemic inflammation as evident by enhanced DTH response, MPO activity, hyperplastic and dysplastic histopathological organization of spleen and lung tissue. Splenic evaluation revealed enhanced oxidative stress, upregulation of prominent inflammatory markers like iNOS and COX-2 and DNA damage. In coherence with the observed immuno-inflammatory alterations, the levels of several inflammatory and regulatory cytokines (IL-17, TNF-α, IFN-γ, IL-1, IL-10, IL-4) were significantly enhanced in serum as well as the spleen. In addition, BA administration significantly induced the activation of ERK1/2, p38, JNK MAPKs and their downstream transcription factors AP-1 (c-fos, c-jun), NF-κB and Nrf2 which comprise important mechanistic pathways involved in inflammatory manifestations. These results suggest the immunotoxic nature of the BA and have implications for the risk assessment and management of occupational workers, and even common masses considering its presence as an environmental contaminant.

Oroxylin A, a constituent of *Oroxylum indicum* inhibits adipogenesis and induces apoptosis in 3T3-L1 cells.

[Singh J, Kakkar P. Phytomedicine. 2014 Oct 15;21(12):1733-41.]

Oroxylin A (OA) is a flavonoid found in *Oroxylum indicum*, a medicinal plant with multiple biological activities. This study was taken up to investigate the effect of OA, on adipogenesis, lipolysis and apoptosis in 3T3 L1 cells. Pre-adipocytes were treated with 10-40 µM OA on various days of adipogenesis treatment schedule. Mature adipocytes were treated with OA for lipolysis and apoptosis studies. In maturing pre-adipocytes, 10 µM OA suppressed intracellular lipid accumulation by 42.19% which was confirmed by lipidTox imaging of cells. In addition, OA decreased the nuclear translocation of PPARγ and mRNA expression of its downstream genes (FAS and LPL) along with adiponectin secretion. In mature adipocytes, 40 µM of OA decreased cell viability by 30% of control. Annexin V/PI staining showed induction of apoptosis which was further confirmed by enhanced levels of pro-apoptotic proteins Bax, cyt c, AIF and chromatin condensation. OA enhanced TNF-α secretion, lipolysis and decreased Akt phosphorylation in mature adipocytes. Findings suggest that OA possibly exerts its anti-obesity effect by affecting adipocyte life cycle at critical points of differentiation and maturity. When authors compared the potency of OA with non-methoxylated flavonoids morin, naringenin and kaempferol on adipocyte life cycle OA was far more potent. Thus, study clearly indicates a new role for oroxylin A as regulator of adipocyte life cycle. In addition, study also suggested a specific role of methoxylated group in exerting lipolysis and cytotoxic effects in mature adipocytes.

Metabolomic analysis provides insights on paraquat-induced Parkinson-like symptoms in *Drosophila melanogaster*.

[Shukla AK, Ratnasekhar C, Pragya P, Chaouhan HS, Patel DK, Chowdhuri DK, Mudiam MK. Mol Neurobiol. 2014 Nov 27. doi: http://dx.doi.org/10.1007/s12035-014-9003-3.]

Paraquat (PQ) exposure causes degeneration of the dopaminergic neurons in an exposed organism while altered metabolism has a role in various neurodegenerative disorders. Therefore, the study presented here was conceived to depict the role of altered metabolism in PQ-induced Parkinson-like symptoms and to explore Drosophila as a potential model organism for such studies. Metabolic profile was generated in control and in flies that were fed PQ (5, 10, and 20 mM) in the diet for 12 and 24 h concurrent with assessment of indices of oxidative stress, dopaminergic neurodegeneration, and behavioral alteration. PQ was found to significantly alter 24 metabolites belonging to different biological pathways along with significant alterations in the above indices. In addition, PQ attenuated brain dopamine content in the exposed organism. The study demonstrates that PQ-induced alteration in the metabolites leads to oxidative stress and neurodegeneration in the exposed organism along with movement disorder, a phenotype typical of Parkinson-like symptoms. The study is relevant in the context of Drosophila and humans because similar alteration in the metabolic pathways has been observed in both PQ-exposed Drosophila and in postmortem samples of patients with Parkinsonism. Furthermore, this study provides advocacy towards the applicability of Drosophila as an alternate model organism for pre-screening of environmental chemicals for their neurodegenerative potential with altered metabolism.

Gene-environment interactions in determining differences in genetic susceptibility to cancer in subsites of the head and neck.

[Maurya SS, Katiyar T, Dhawan A, Singh S, Jain SK, Pant MC, Parmar D. Environ Mol Mutagen. 2014

Nov 14. doi: 10.1002/em.21920.]

Genetic differences in susceptibility to cancer in subsites of the head and neck were investigated in a case-control study involving 750 cases of cancers of the oral cavity, larynx, or pharynx, and an equal number of healthy controls. The prevalence of variant genotypes of cytochrome P450 (CYP) 1A1, 1B1, 2E1, or glutathione-S-transferase M1 (null) in cases suggests that polymorphisms in drug metabolizing enzymes (DMEs) modify cancer risk within subsites of the head and neck. Tobacco or alcohol use was found to increase the risk in cases of laryngeal, pharyngeal, or oral cavity cancers. Interaction between genetic variation in DMEs and tobacco smoke (or smoking) exposures conferred significant risk for laryngeal cancer. Likewise, strong associations of the polymorphic genotypes of DMEs with cases of pharyngeal and oral cavity cancer who were tobacco chewers or alcohol users demonstrate that gene-environment interactions may explain differences in genetic susceptibility for cancers of the oral cavity, larynx, and pharynx

Inhibitory effects of bisphenol-a on neural stem cells proliferation and differentiation in the rat brain are dependent on wnt/β-catenin pathway.

[Tiwari SK, Agarwal S, Seth B, Yadav A, Ray RS, Mishra VN, Chaturvedi RK. Mol Neurobiol. 2014 Nov 9. doi: http://dx.doi.org/10.1007/s12035-014-8940-1.]

Neurogenesis, a process of generation of new neurons, occurs throughout the life in the hippocampus and sub-ventricular zone (SVZ). Bisphenol-A (BPA), an endocrine disrupter used as surface coating for packaged food cans, injures the developing and adult brain. However, the effects of BPA on neurogenesis and underlying cellular and molecular mechanism(s) are still unknown. Herein, authors studied the effect(s) of prenatal and early postnatal exposure of low dose BPA on Wnt/β-catenin signaling pathway that controls different steps of neurogenesis such as neural stem cell (NSC) proliferation and neuronal differentiation. Pregnant rats were treated with 4, 40, and 400 µg BPA/kg body weight orally daily from gestational day 6 to postnatal day 21. Both *in vivo* and *in vitro* studies showed that BPA alters NSC proliferation and differentiation. BPA impaired NSC proliferation (5'-bromo-2'-deoxyuridine (BrdU+) and nestin+ cells) and neuronal differentiation (BrdU/doublecortin+ and BrdU/neuronal nuclei (NeuN+) cells) in the hippocampus and SVZ as compared to control. It significantly altered expression/protein levels of neurogenic genes and the Wnt pathway genes in the hippocampus. BPA reduced cellular β-catenin and p-GSK-3β levels and decreased β-catenin nuclear translocation, and cyclin-D1 and TCF/LEF promoter luciferase activity. Specific activation and blockage of the Wnt pathway suggested involvement of this pathway in BPA-mediated inhibition of neurogenesis. Further, blockage of GSK-3β activity by SB415286 and GSK-3β small interfering RNA (siRNA) attenuated BPA-induced downregulation of neurogenesis. Overall, these results suggest significant inhibitory effects of BPA on NSC proliferation and differentiation in the rat via the Wnt/β-catenin signaling pathway.

Simultaneous determination of acetaminophen and synthetic color(s) by derivative spectroscopy in syrup formulations and validation by HPLC: Exposure risk of colors to children.

[Rastogi SD, Dixit S, Tripathi A, Das M. AAPS PharmSciTech. 2014 Nov 6. doi: http://dx.doi.org/10.1208/s12249-014-0228-2.]

Colour additives are used in paediatric syrup formulations as an excipient; though not pre-requisite, but paediatric syrup formulations are normally coloured. An attempt has been made to measure simultaneously the single drug, acetaminophen (AT), along with the colours, carmoisine (CA), erythrosine (ET), and sunset yellow FCF (SSY) added in it by three derivative spectroscopy methods namely, 1st order, ratio, and differential derivative methods. Moreover, evaluation has been made for the exposure assessment of the colours added as excipient because some colours have been reported to cause allergic reactions and hypersensitivity in children. The present methods provide simple, accurate, and reproducible quantitative determination of the drug, AT, along with the colour in synthetic mixtures and commercial drug formulations without any interference. The limit of detection varied from 0.0001-0.31 µg/ml while limit of quantification ranged from 0.002-1.04 µg/ml in all the three methods. The calibration curve of all the three derivative methods exhibited good linear relationship with excellent regression coefficients (0.9986-1.000). Both intra-day and inter-day precisions showed %RSD value less than 2% while the percentage recovery was found between 96.8-103.8%. The sensitivity of the proposed methods is almost comparable to HPLC and thus, can be used for determination of drug AT, and colour simultaneously in pharmaceutical formulation on

routine basis. The present methods also showed that colours like SSY and ET are saturating more than 50% of acceptable daily intake (ADI) value which is alarming and needs to be considered for modification by regulatory authorities to safeguard the health of children.

Cyclosporine A and MnTMPyP alleviate α-synuclein expression and aggregation in cypermethrin-induced Parkinsonism.

[Agrawal S, Dixit A, Singh A, Tripathi P, Singh D, Patel DK, Singh MP. Mol Neurobiol. 2014 Nov 5. doi: http://dx.doi.org/10.1007/s12035-014-8954-8.]

Cypermethrin induces the mitochondrial dysfunction and oxidative damage to the nigrostriatal dopaminergic neurons leading to Parkinsonism in rats. Despite α-synuclein aggregation is reported to be critical in Parkinson's disease, its role and alliance with the mitochondrial dysfunction and oxidative damage leading to cypermethrin-induced Parkinsonism have not yet been deciphered. The present study aimed to examine the effect of cypermethrin on the expression and aggregation of α-synuclein and its subsequent connection with oxidative damage and mitochondrial dysfunction leading to the nigrostriatal dopaminergic neurodegeneration in the presence or absence of a mitochondrial membrane transition pore opening inhibitor, cyclosporine A and a superoxide dismutase/catalase mimetic, manganese (III) tetrakis (1-methyl-4-pyridyl) porphyrin pentachloride (MnTMPyP). The expression of α-synuclein, 3-nitrotyrosine (3-NT), 4-hydroxynonenal (4-HNE)-modified proteins, mitochondrial dysfunction-dependent apoptotic proteins, nitrite content, lipid peroxidation (LPO) and number of tyrosine hydroxylase (TH)-positive neurons were estimated in the substantia nigra and dopamine content in the striatum of control and treated rats employing standard procedures. Cypermethrin augmented the expression of α-synuclein, 3-NT, 4-HNE-modified proteins, caspase-3, mitochondrial Bax and cytosolic cytochrome-c along with nitrite and LPO and reduced the expression of cytosolic Bax, mitochondrial cytochrome-c, dopamine and number of TH-positive neurons. Cyclosporine A or MnTMPyP alleviated the expression and aggregation of α-synuclein along with indicators of the mitochondrial dysfunction, oxidative damage and dopaminergic neurodegeneration. The results demonstrate that cypermethrin induces α-synuclein expression and aggregation while cyclosporine A or MnTMPyP rescues from α-synuclein over-expression and aggregation along with the mitochondrial dysfunction and oxidative damage leading to Parkinsonism in rats.

Lead intoxication synergies of the ethanol-induced toxic responses in neuronal cells-PC12.

[Kumar V, Tripathi VK, Jahan S, Agrawal M, Pandey A, Khanna VK, Pant AB. Mol Neurobiol. 2014 Nov 4.doi.: http://dx.doi.org/10.1007/s12035-014-8928-x.]

Lead (Pb)-induced neurodegeneration and its link with widespread neurobehavioral changes are well documented. Experimental evidences suggest that ethanol could enhance the absorption of metals in the body, and alcohol consumption may increase the susceptibility to metal intoxication in the brain. However, the underlying mechanism of ethanol action in affecting metal toxicity in brain cells is poorly understood. Thus, an attempt was made to investigate the modulatory effect of ethanol on Pb intoxication in PC12 cells, a rat pheochromocytoma. Cells were co-exposed to biological safe doses of Pb (10 μM) and ethanol (200 mM), and data were compared to the response of cells which received independent exposure to these chemicals at similar doses. Ethanol (200 mM) exposure significantly aggravated the Pb-induced alterations in the end points associated with oxidative stress and apoptosis. The finding confirms the involvement of reactive oxygen species (ROS)-mediated oxidative stress, and impairment of mitochondrial membrane potential, which subsequently facilitate the translocation of triggering proteins between cytoplasm and mitochondria. authors further confirmed the apoptotic changes due to induction of mitochondria-mediated caspase cascade. These cellular changes were found to recover significantly, if the cells are exposed to N-acetyl cysteine (NAC), a known antioxidant. Data suggest that ethanol may potentiate Pb-induced cellular damage in brain cells, but such damaging effects could be recovered by inhibition of ROS generation. These results open up further possibilities for the design of new therapeutics based on antioxidants to prevent neurodegeneration and associated health problems.

***In silico* assay development for screening of tetracyclic triterpenoids as anticancer agents against human breast cancer cell line MCF7.**

[Prakash O, Ahmad A, Tripathi VK, Tandon S, Pant AB, Khan F. PLoS One. 2014 Nov 3;9(11):e111049.]

Experimental activity of a compound on cancer cell

line/target is mostly analyzed in the form of percentage inhibition at different concentration gradient and time of incubation. In this study a statistical model has been developed referred as *in silico* assay using support vector regression model, which can act with change in concentration gradient and time of incubation. This model is a function of concentration gradient, treatment hour and independent components; which calculate the percentage inhibition in combination of above three components. This model is designed to screen tetracyclic triterpenoids active against human breast cancer cell line MCF7. The model has been statistically validated, checked for applicability domain and predicted results were reconfirmed by MTT assay, for example Oenotheranstrol derivatives, Oen A & B. Computational SAR, target and docking studies were performed to understand the cytotoxic mechanism of action of Oenotheranstrol compounds. The proposed *in silico* assay model will work for specific chemical family for which it will be optimized. This model can be used to analyze growth kinetics pattern on different human cancer cell lines for designed compounds.

Understanding the mechanism of atovaquone drug resistance in *Plasmodium falciparum* cytochrome b mutation Y268S using computational methods.

[Akhoon BA, Singh KP, Varshney M, Gupta SK, Shukla Y, Gupta SK. PLoS One. 2014 Oct 15;9(10):e110041.]

The rapid appearance of resistant malarial parasites after introduction of atovaquone (ATQ) drug has prompted the search for new drugs as even single point mutations in the active site of Cytochrome b protein can rapidly render ATQ ineffective. The presence of Y268 mutations in the Cytochrome b (Cyt b) protein is previously suggested to be responsible for the ATQ resistance in *Plasmodium falciparum* (*P. falciparum)*. In this study, authors examined the resistance mechanism against ATQ in *P. falciparum* through computational methods. Here, authors reported a reliable protein model of Cyt bc1 complex containing Cyt b and the Iron-Sulphur Protein (ISP) of *P. falciparum* using composite modelling method by combining threading, *ab initio* modelling and atomic-level structure refinement approaches. The molecular dynamics simulations suggest that Y268S mutation causes ATQ resistance by reducing hydrophobic interactions between Cyt bc1 protein complex and ATQ. Moreover, the important histidine contact of ATQ with the ISP chain is also lost due to Y268S mutation. Authors noticed the induced mutation alters the arrangement of active site residues in a fashion that enforces ATQ to find its new stable binding site far away from the wild-type binding pocket. The MM-PBSA calculations also shows that the binding affinity of ATQ with Cyt bc1 complex is enough to hold it at this new site that ultimately leads to the ATQ resistance.

Exposure to As-, Cd-, and Pb-mixture induces Aβ, amyloidogenic APP processing and cognitive impairments via oxidative stress-dependent neuroinflammation in young rats.

[Ashok A, Rai NK, Tripathi S, Bandyopadhyay S. Toxicol Sci. 2015 Jan;143(1):64-80.]

Environmental pollutants act as risk factors for Alzheimer's disease (AD), mainly affecting the aging population. authors investigated early manifestations of AD-like pathology by a mixture of arsenic (As), cadmium (Cd), and lead (Pb), reported to impair neurodevelopment. Authors treated rats with As+Cd+Pb at their concentrations detected in groundwater of India, ie, 0.38, 0.098, and 0.22 ppm or 10 times of each, respectively, from gestation-05 to postnatal day-180. Authors identified dose-dependent increase in amyloid-beta (Aβ) in frontal cortex and hippocampus as early as post-weaning. The effect was strongly significant during early-adulthood, reaching levels comparable to an Aβ-infused AD-like rat model. The metals activated the proamyloidogenic pathway, mediated by increase in amyloid precursor protein (APP), and subsequent beta secretase (BACE) and presenilin (PS)-mediated APP-processing. Investigating the mechanism of Aβ-induction revealed an augmentation in oxidative stress-dependent neuroinflammation that stimulated APP expression through interleukin-responsive-APP-mRNA 5'-untranslated region. Authors then examined the effects of individual metals and binary mixtures in comparison with the tertiary. Among individual metals, Pb triggered maximum induction of Aβ, whereas individual As or Cd had a relatively non-significant effect on Aβ despite enhanced APP, owing to reduced induction of BACE and PS. Interestingly, when combined the metals demonstrated synergism, with a major contribution by As. The synergistic effect was significant and consistent in tertiary mixture, resulting in the augmentation of Aβ. Eventually, increase in Aβ culminated in cognitive impairments in the young rats. Together, data demonstrate that exposure to As+Cd+Pb induces premature manifestation of AD-

like pathology that is synergistic, and oxidative stress and inflammation dependent.

Effect of gestational exposure of cypermethrin on postnatal development of brain cytochrome P450 2D1 and 3A1 and neurotransmitter receptors.

[Singh A, Mudawal A, Shukla RK, Yadav S, Khanna VK, Sethumadhavan R, Parmar D. Mol Neurobiol. 2014 Oct 7. doi.: http://dx.doi.org/10.1007/s12035-014-8903-6]

Oral administration of low doses (1.25, 2.5, or 5 mg/kg) of cypermethrin to pregnant Wistar rats from gestation days 5 to 21 led to dose-dependent differences in the induction of cytochrome P450 2D1 (CYP2D1) and 3A1 messenger RNA (mRNA) and protein in brain regions isolated from the offsprings postnatally at 3 weeks that persisted up to adulthood (12 weeks). Similar alterations were observed in the expression of GABAergic, muscarinic, dopaminergic, and serotonergic neurotransmitter receptors in brain regions of rat offsprings. Rechallenge of the prenatally exposed offsprings at adulthood (12 weeks old) with cypermethrin (p.o., 10 mg/kg for 6 days) led to a greater magnitude of alterations in the expression of CYPs, neurotransmitter receptors, and neurotransmitter receptor binding in the brain regions when compared to the control offsprings treated at adulthood with cypermethrin or prenatally exposed offsprings. A greater magnitude of decrease was also observed in the spontaneous locomotor activity (SLA) in prenatally exposed offsprings rechallenged with cypermethrin. The present data indicating similarities in the alterations in the expression of CYPs (2D1 and 3A1) and neurotransmitter receptors in brain has led us to suggest that endogenous function regulating CYPs is possibly associated with neurotransmission processes. A greater magnitude of alterations in CYP2D1, 3A1, neurotransmitter receptors, and SLA in rechallenged animals has further provided evidence that alterations in CYPs are possibly linked with neurotransmission processes.

Cypermethrin alters the status of oxidative stress in the peripheral blood: Relevance to Parkinsonism.

[Tripathi P, Singh A, Agrawal S, Prakash O, Singh MP. J Physiol Biochem. 2014 Dec;70(4):915-24.]

Parkinson's disease (PD) is a motor scarcity disorder characterized by the striatal dopamine deficiency owing to the selective degeneration of the nigrostriatal dopaminergic neurons. While oxidative stress is implicated in PD, prolonged exposure to moderate dose of cypermethrin induces Parkinsonism. The study aimed to investigate the status of oxidative stress indicators and antioxidant defence system of the polymorphonuclear leukocytes (PMNs), platelets and plasma to delineate the effect of Parkinsonian dose of cypermethrin in the peripheral blood of rats and its subsequent relevance to Parkinsonism. Nitrite content, lipid peroxidation (LPO) and activity of superoxide dismutase (SOD), catalase, glutathione reductase (GR) and glutathione-S-transferase (GST) were measured in the PMNs, platelets and plasma of control and cypermethrin-treated rats in the presence or absence of a microglial activation inhibitor, minocycline or a dopamine precursor containing the peripheral 3,4-dihydroxyphenyla-lanine decarboxylase inhibitor, named syndopa, employing the standard procedures. The striatal dopamine was measured to assess the degree of neurodegeneration/neuroprotection. Cypermethrin increased nitrite and LPO in the plasma, platelets and PMNs while it reduced the striatal dopamine content. Catalase and GST activity were increased in the PMNs and platelets; however, it was reduced in the plasma. Conversely, SOD and GR activities were reduced in the PMNs and platelets but increased in the plasma. Minocycline or syndopa reduced the cypermethrin-mediated changes towards normalcy. The results demonstrate that cypermethrin alters the status of oxidative stress indicators and impairs antioxidant defence system of the peripheral blood, which could be effectively salvaged by minocycline or syndopa. The results could be of value for predicting the nigrostriatal toxicity relevant to Parkinsonism.

Toxicological mode of action of ZnO nanoparticles: Impact on immune cells.

[Roy R, Das M, Dwivedi PD. Mol Immunol. 2015 Feb;63(2):184-92.]

The use of nanoscale materials is growing exponentially as concerns rise about the human hazards to it. It is assumed that living beings are coevolved with nanoparticles ever since the origin of life on earth and therefore, they must have developed the defense and toxicity mitigating mechanisms for nanoparticles. Although having peculiar properties these new materials also present new health risks upon interacting with biological systems. Zinc oxide is the most widely used

nanoparticles among various nanomaterials. Recently, these nanoparticles have been shown to specifically kill cancerous cells; therefore, it is believed that these nanoparticles may be used as an alternative anti-tumor agent. However, it is also known that these nanoparticles pose several deleterious effects to living beings. It is therefore critical to understand the nature and origin of the toxicity imposed by these nanomaterials. Keeping these points in mind the present review provides updated information on various aspects of toxicities induced by these engineered nanoparticles.

Early life arsenic exposure and brain dopaminergic alterations in rats.

[Chandravanshi LP, Shukla RK, Sultana S, Pant AB, Khanna VK. Int J Dev Neurosci. 2014 Nov;38:91-104.]

Recently, authors found that early life exposure to arsenic at low doses resulted to cause brain cholinergic deficits and exhibited a trend of recovery on withdrawal of arsenic exposure. In continuation to this, the present study has been carried out to assess the impact of low level arsenic exposure on brain dopaminergic system and associated behaviour in developing rats and investigate if neurobehavioral changes are recovered or persistent. Early life exposure (PD22-PD59) to arsenic (2 or 4mg/kg body weight, p.o.) in rats resulted to increase the motor activity on PD60, compared to controls. The hyperactivity in arsenic exposed rats was found to be linked with increase in the binding of DA-D2 receptors (38%, 56%), mRNA expression of DAR-D2 receptor gene (68%, 97%) and expression of tyrosine hydroxylase protein (1.93, 2.73-fold) in the corpus striatum as compared to controls on PD60. Exposure to arsenic enhanced generation of ROS (47%, 84%) and was associated with decrease in the mitochondrial membrane potential (13.3%, 15.33%), activity of mitochondrial complexes and increased oxidative stress. Disruption in the expression of pro-apoptotic, anti-apoptotic and stress marker proteins was also distinct in the corpus striatum of arsenic exposed rats. The severity of changes in the behavioral and neurochemical endpoints were found to persist in rats exposed to arsenic at high dose and exhibited a trend of recovery at low dose on withdrawal of arsenic exposure on PD90. Early life arsenic exposure appears to be critical and vulnerable as development of dopamine receptors continues during this period.

Allergic manifestation by black gram (*Vigna mungo*) proteins in allergic patients, BALB/c mice and RBL-2H3 cells.

[Verma AK, Kumar S, Sharma A, Kumar D, Roy R, Gupta RK, Chaudhari BP, Giridhar BH, Das M, Dwivedi PD. Int Immunopharmacol. 2014 Sep 4;23(1):92-103.]

The prevalence of black gram (*Vigna mungo*) induced allergic reactions are reported from several parts of the world including Asia and Australia. But, a thorough exploration of the allergic reactions induced by black gram proteins is still lacking. Therefore, efforts have been made to explore black gram allergy using *in vivo* and *in vitro* approaches. In this study, Simulated Gastric Fluid (SGF) assay and IgE immunoblotting were carried out to identify clinically relevant allergens of black gram. BALB/c mice and RBL-2H3 cells were used for elucidation of allergenic reactions of black gram proteins. Further, this study was extended to screen black gram sensitive patients among nasobronchial allergic patients on the basis of clinical history, skin prick test (SPT), specific IgE levels and IgE immunoblotting. Enhanced levels of specific IgE, IgG1/IgG2a ($p<0.05$), histamine ($p<0.05$), clinical symptoms, pathological indications in the lungs, intestine and spleen were evident in black gram sensitized BALB/c mice. Moreover, the expression of Th2 cytokine transcripts and GATA-3/T-bet ratio was found enhanced in the treated group. *In vitro* studies on RBL-2H3 cells, showed increased release of β-hexosaminidase ($p<0.05$), histamine ($p<0.05$), cysteinyl leukotriene ($p<0.05$) and prostaglandin D2 ($p<0.05$). Further, 8.5% of screened patients were found allergic to black gram and concomitant sensitization with other allergens has shown the possibility of further enhancement in allergenic problem. Conclusively, the present study suggested that black gram consumption may be responsible for inducing immediate type of allergic sensitization in susceptible subjects.

Involvement of EZH2, SUV39H1, G9a and associated molecules in pathogenesis of urethane induced mouse lung tumors: Potential targets for cancer control.

[Pandey M, Sahay S, Tiwari P, Upadhyay DS, Sultana S, Gupta KP. Toxicol Appl Pharmacol. 2014 Oct 15;280(2):296-304.]

In the present study, authors showed the correlation of EZH2, SUV39H1 or G9a expression and histone modifications with the urethane induced mouse lung

tumorigenesis in the presence or absence of antitumor agent, inositol hexaphosphate (IP6). Tumorigenesis and the molecular events involved therein were studied at 1, 4, 12 or 36 weeks after the exposure. There were no tumors at 1 or 4 weeks but tumors started appearing at 12 weeks and grew further till 36 weeks after urethane exposure. Among the molecular events, upregulation of EZH2 and SUV39H1 expressions appeared to be time dependent, but G9a expression was altered significantly only at later stages of 12 or 36 weeks. Alteration in miR-138 expression supports the upregulation of its target, EZH2. H3K9me2, H3K27me3 or H4K20me3 was found to be altered at 12 or 36 weeks. However, ChIP analysis of p16 and MLH1 promoters showed their binding with H3K9me2 and H3K27me3 which was maximum at 36 weeks. Thus, histone modification and their interactions with gene promoter resulted in the reduced expression of p16 and MLH1. IP6 prevented the incidence and the size of urethane induced lung tumors. IP6 also prevented the urethane induced alterations in EZH2, SUV39H1, G9a expressions and histone modifications. Authors' results suggest that the alterations in the histone modification pathways involving EZH2 and SUV39H1 expressions are among the early events in urethane induced mouse lung tumorigenesis and could be exploited for cancer control.

Association of cytochrome P450 2C9 polymorphism with locally advanced head and neck squamous cell carcinoma and response to concurrent cisplatin-based radical chemo-radiation.

[Paul S, Chaudhuri T, Pant MC, Parmar D, Srivastava K. South Asian J Cancer. 2014 Jul;3(3):154-8.]

The aim of the present study is to investigate the association between polymorphism of cytochrome P450 2C9 (CYP2C9) enzyme with head and neck squamous cell carcinoma (HNSCC) and response in patients receiving cisplatin-based radical chemoradiation (CT-RT). Four hundred and sixty patients suffering from locally advanced HNSCC and an equal number of healthy controls were genotyped for CYP2C9*2 and CYP2C9*013, leading to poor metabolizers (PMs) by polymerase chain reaction (PCR)-based restriction fragment length polymorphism (RFLP). Each case was assessed thoroughly for treatment response as per the World Health Organization (WHO) criteria. The frequency of heterozygous genotypes of both CYP2C9*2 (27.8%) and CYP2C9*3 (25%) were found to be significantly higher in the HNSCC cases as compared to the healthy controls. Tobacco intake in the form of chewing or smoking and alcohol intake resulted in several folds increase in the risk to HNSCC in the cases carrying variant genotypes of CYP2C9*2 or CYP2C9*013. Further, majority of the cases assessed for response (n = 436) carrying variant alleles of CYP2C9*2 (69.6%) or CYP2C9*3 (65.2%) were found to respond poorly to cisplatin-based radical CT-RT. The data suggests a significant association of the CYP2C9 polymorphism with HNSCC and treatment outcome underlining the importance of pretherapeutic genotyping in determining the treatment protocol.

FoxO proteins' nuclear retention and BH3-only protein Bim induction evoke mitochondrial dysfunction-mediated apoptosis in berberine-treated HepG2 cells.

[Shukla S, Rizvi F, Raisuddin S, Kakkar P. Free Radic Biol Med. 2014 Nov;76:185-99.]

Mammalian forkhead-box family members belonging to the 'O' category (FoxO) manipulate a plethora of genes modulating a wide array of cellular functions including cell cycle regulation, apoptosis, DNA damage repair, and energy metabolism. FoxO overexpression and nuclear accumulation have been reported to show correlation with hindered tumor growth *in vitro* and size *in vivo*, while FoxO's downregulation via phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt) pathway has been linked with tumor promotion. In this study, authors have explored for the first time intervention of berberine, a plant-derived isoquinoline alkaloid, with FoxO family proteins in hepatoma cells. Authors observed that berberine significantly upregulated the mRNA expression of both FoxO1 and FoxO3a. Their phosphorylation-mediated cytoplasmic sequestration followed by degradation was prevented by berberine-induced downmodulation of the PI3K/Akt/mTOR pathway which promoted FoxO nuclear retention. PTEN, a tumor suppressor gene and negative regulator of the PI3K/Akt axis, was upregulated while phosphorylation of its Ser380 residue (possible mechanism of PTEN degradation) was significantly decreased in treated HepG2 cells. Exposure to berberine induced a significant increase in transcriptional activity of FoxO, as shown by GFP reporter assay. FoxO transcription factors effectively heightened BH3-only protein Bim expression, which in turn, being a direct activator of proapoptotic protein Bax, altered Bax/Bcl-2 ratio, culminating into

mitochondrial dysfunction, caspases activation, and DNA fragmentation. The pivotal role of Bim in berberine-mediated cytotoxicity was further corroborated by knockdown experiments where Bim-silencing partially restored HepG2 cell viability during berberine exposure. In addition, a correlation between oxidative overload and FoxO's nuclear accumulation via JNK activation was evident as berberine treatment led to a pronounced increase in JNK phosphorylation together with enhanced ROS generation, lipid peroxidation, decreased activities of superoxide dismutase and catalase, and diminished glutathione levels. Thus, findings suggest that the antiproliferative effect of berberine may in part be due to mitochondria-mediated apoptosis with Bim acting as a pivotal downstream factor of FoxO-induced transcriptional activation.

ZnO nanoparticles induced adjuvant effect via toll-like receptors and Src signaling in Balb/c mice.

[Roy R, Kumar D, Sharma A, Gupta P, Chaudhari BP, Tripathi A, Das M, Dwivedi PD. Toxicol Lett. 2014 Nov 4;230(3):421-33.]

Authors' previous studies indicated that zinc oxide nanoparticles (ZnO NPs) have adjuvant properties to a known allergen ovalbumin (OVA) in Balb/c mice. Therefore, in this study, authors focused on the mechanisms involved in adjuvant responses induced by ZnO NPs. The eosinophil counts in the Peyers' patches of intestine and ICAM-1, Cox2 protein expressions were enhanced in the ZnO NPs/OVA group. Following screening of toll-like receptors (TLRs), TLR 2, 4 and 6 were found to be increased. Accordingly, authors found that downstream proteins of TLRs such as myeloid differentiation primary response protein-88 (MyD88), IL-1 receptor associated kinase 1 (IRAK 1), and TNFR-associated factor 6 (TRAF 6) were also found to be enhanced in the ZnO NPs/OVA-induced group. These inflammatory responses underlined the critical roles of TLRs in the inflammatory response. ZnO NPs increased the mRNA levels of inflammatory cytokine IL-1β and protein expression of several mediators, including Cox2, PGE2, MMP-9 and finally caspase 1 in macrophages. Another pathway for adjuvant effect is Src which was found to be significantly affected by the activation of p-Lyn, p-Syk, IP3, p-PLC-γ and cAMP. Ca(2+) influx was significantly increased as well in the ZnO NPs/OVA group. These findings demonstrated the differential role of TLRs in regulation of the ZnO NPs-induced adjuvant responses causing the inflammation. Authors therefore, conclude that ZnO NPs have significant adjuvant effect via following Src kinase and TLRs signaling that ascribed to inflammatory responses due to recruitment and activation of adhesion molecules and inflammatory cells. The adjuvant property of ZnO NPs may help in planning strategies for its therapeutic use.

Allergenicity assessment of genetically-modified tobacco expressing salt tolerance cbl gene.

[Verma AK, Kumar S, Chaudhari BP, Tuteja N, Das M, Dwivedi PD. Plant Foods Hum Nutr. 2014 Sep;69(3):209-15.]

It is mandatory to assess the allergenic potential of genetically modified (GM) crops before their commercialization. Recently, a transgene [Calcineurin B-like (CBL) protein] has been introduced into tobacco plant to make the crop salt resistance. Therefore, it was felt necessary to assess the allergenic potential of the cbl gene product, which was introduced and expressed in *Nicotiana tabacum* (tobacco) plant and compared the allergenic effects with the wild-type (WT) counterpart. Bioinformatic analysis revealed that there was no significant sequence homology with known allergens. Also, no difference between the protein digestibility profiles of GM and WT tobacco was found. Rapid digestion of CBL protein (Mol Wt 35 kDa) by simulated gastric fluid (SGF) indicated reduced chances of this protein to induce allergenicity. In addition, BALB/c mice sensitized by intraperitoneal administration of WT and GM tobacco protein showed comparable levels of clinical score, specific IgE, IgG1, histamine level, similar effect on different organs as well as IgE binding proteins. These findings indicate that insertion of cbl gene in tobacco did not cause any additional allergic risk to consumer and the GM and native tobacco proteins behave similarly in both *in vitro* and *in vivo* situations even after genetic modification.

Bisphenol-A impairs myelination potential during development in the hippocampus of the rat brain.

[Tiwari SK, Agarwal S, Chauhan LK, Mishra VN, Chaturvedi RK. Mol Neurobiol. 2014 Aug 2. doi.:http://dx.doi.org/10.1007/s12035-014-8817-3.]

Myelin is the functional implication of oligodendrocytes (OLs), which is involved in insulation of axons and promoting rapid propagation

of action potential in the brain. OLs are derived from oligodendrocyte progenitor cells (OPCs), which proliferate, differentiate, and migrate throughout the central nervous system. Defects in myelination process lead to the onset of several neurological and neurodegenerative disorders. Exposure to synthetic xenoestrogen bisphenol-A (BPA) causes cognitive dysfunction, impairs hippocampal neurogenesis, and causes onset of neurodevelopmental disorders. However, the effects of BPA on OPC proliferation, differentiation and myelination, and associated cellular and molecular mechanism(s) in the hippocampus of the rat brain are still largely unknown. Authors found that BPA significantly decreased bromodeoxyuridine (BrdU)-positive cell proliferation and number and size of oligospheres. Authors observed reduced co-localization of BrdU with myelination markers CNPase and platelet-derived growth factor receptor-α (PDGFR-α), suggesting impaired proliferation and differentiation of OPCs by BPA in culture. Authors studied the effects of BPA exposure during prenatal and postnatal periods on cellular and molecular alteration(s) in the myelination process in the hippocampus region of the rat brain at postnatal day 21 and 90. BPA exposure both *in vitro* and *in vivo* altered proliferation and differentiation potential of OPCs and decreased the expression of genes and levels of proteins that are involved in myelination. Ultrastructural electron microscopy analysis revealed that BPA exposure caused decompaction of myelinated axons and altered g-ratio at both the developmental periods as compared to control. These results suggest that BPA exposure both during prenatal and postnatal periods alters myelination in the hippocampus of the rat brain leading to cognitive deficits.

Phagocytic cells internalize ZnO particles by FcγII/III-receptor pathway.

[Roy R, Chauhan LK, Das M, Tripathi A, Dwivedi PD. Immunobiology. 2014 Oct;219(10):746-55.]

The present study investigates the process of internalization for bulk ZnO particles in macrophages, and further elucidates the underlying mechanism. Since macrophages are active phagocytes and phagocytosis is a size dependent phenomenon, therefore authors hypothesized that bulk ZnO may internalize into macrophages by phagocytic pathways. Interestingly, the phagocytic activity got enhanced in bulk ZnO treated macrophages. Moreover, the bulk ZnO treated macrophages internalized via FcγR-II/III, complement and scavenger-receptor pathways. To confirm the specificity of phagocytic pathway, the uptake was also analyzed in splenocytes where phagocytic (monocytes) and non-phagocytic cells (lymphocytes) are present. It was observed that no significant uptake of bulk ZnO in case of lymphocytes whereas significant uptake in monocytes. Henceforth, our quest for uptake mechanisms also revealed that severe plasma membrane extensions (pseudopodia), FcγR clustering over the surface of macrophages and activation of FcγR signaling were the key players for bulk ZnO uptake; whereas clathrin or caveolae mediated endocytic pathways contributed less. Uptake of these particles was further strengthened by the ZnO-induced activation of the Src-kinase p-Lyn, phospho-tyrosine kinases Syk (spleen tyrosine kinase), p-PLC-γ and PI3K (phosphatidylinositol 3-kinase). Authors' findings illustrate that the phagocytic nature of macrophages could have led to higher uptake of bulk ZnO.

Genetic structure and inter-generic relationship of closed colony of laboratory rodents based on RAPD markers.

[Kumar M, Kumar S. Mol Biol Rep. 2014 Nov;41(11):7273-80.]

Molecular genetic analysis was performed using random amplified polymorphic DNA (RAPD) on three commonly used laboratory bred rodent genera viz. mouse (*Mus musculus*), rat (*Rattus norvegicus*) and guinea pig (*Cavia porcellus*) as sampled from the breeding colony maintained at the Animal Facility, CSIR-Indian Institute of Toxicology Research, Lucknow. In this study, 60 samples, 20 from each genus, were analyzed for evaluation of genetic structure of rodent stocks based on polymorphic bands using RAPD markers. Thirty five random primers were assessed for RAPD analysis. Out of 35, only 20 primers generated a total of 56.88% polymorphic bands among mice, rats and guinea pigs. The results revealed significantly variant and distinct fingerprint patterns specific to each of the genus. Within-genera analysis, the highest (89.0%) amount of genetic homogeneity was observed in mice samples and the least (79.3%) were observed in guinea pig samples. The amount of genetic homogeneity was observed very high within all genera. The average genetic diversity index observed was low (0.045) for mice and high (0.094) for guinea pigs. The inter-generic distances were maximum (0.8775) between mice and guinea pigs; and the minimum (0.5143) between rats and mice.

The study proved that the RAPD markers are useful as genetic markers for assessment of genetic structure as well as inter-generic variability assessments.

Size dependent toxicity of zinc oxide nano-particles in soil nematode *Caenorhabditis elegans.*

[Khare P, Sonane M, Nagar Y, Moin N, Ali S, Gupta KC, Satish A. Nanotoxicology. 2014 Jul 22:1-10.]

Zinc oxide nano-particles (ZnO NPs), with their unique physico-chemical properties conferred by various size formulations, are extensively used in consumer products. The enormous usage coupled with their release to the environment demands risk assessment of ZnO NPs on health and the environment. Toxicity of ZnO NPs is well understood in comparison to the bulk ZnO. However, toxicity in relation to the NP size is poorly understood. In this context, authors examined the adverse effects of different sizes (35nm, 50nm and 100nm) of ZnO NPs in soil nematode *C. elegans* along with bulk ZnO and $ZnCl_2$. Here, authors show that growth, reproduction and behaviour of worms were adversely affected by ZnO NPs in a size dependent manner. Further, exposure to ZnO NPs caused modulation of expression/function of genes associated with Insulin/IGF-like signaling pathway and/or stress response pathway in a size dependent manner in exposed worms. The expression of pro-apoptotic gene and suppression of anti-apoptotic genes, together with increased numbers of cell corpses in the germ line, indicated that apoptosis was also dependent on the size of the ZnO NP. Taken together, study provides evidence that exposure to ZnO NPs disrupts various physiological processes and causes apoptosis in the germ-line even at very low concentration in a size dependent manner. Authors finding suggests the inclusion of size as an additional measure for the cautious monitoring of ZnO NP disposal into the environment.

Quantification of *Salmonella typhi* in water and sediments by molecular-beacon based qPCR.

[Rani N, Vajpayee P, Bhatti S, Singh S, Shanker R, Gupta KC. Ecotoxicol Environ Saf. 2014 Oct;108:58-64.]

A molecular-beacon based qPCR assay targeting staG gene was designed for specific detection and quantification of *S. typhi* and validated against water and sediment samples collected from the river Ganga, Yamuna and their confluence on two days during Mahakumbha mela 2012-2013 (a) 18 December, 2012: before six major religious holy dips (Makar Sankranti, Paush Poornima, Mauni Amavasya, Basant Panchami, Maghi Poornima and Mahashivratri) (b) 10 February, 2013: after the holy dip was taken by over 3,00,00,000 devotees led by ascetics of Hindu sects at Sangam on 'Mauni Amavasya' (the most auspicious day of ritualistic mass bathing). The assay could detect linearly lowest 1 genomic equivalent per qPCR and is highly sensitive and selective for *S. typhi* detection in presence of non specific DNA from other bacterial strains including *S. paratyphi A* and *S. typhimurium*. It has been observed that water and sediment samples exhibit *S. typhi*. The mass holy dip by devotees significantly affected the water and sediment quality by enhancing the number of *S. typhi* in the study area. The qPCR developed in the study might be helpful in planning the intervention and prevention strategies for control of enteric fever outbreaks in endemic regions.

Photosensitized mefloquine induces ROS-mediated DNA damage and apoptosis in keratinocytes under ambient UVB and sunlight exposure.

[Yadav N, Dwivedi A, Mujtaba SF, Verma A, Chaturvedi R, Ray RS, Singh G. Cell Biol Toxicol. 2014 Oct;30(5):253-68.]

The present study illustrates the photosensitizing behavior of mefloquine (MQ) in human skin keratinocytes under ambient doses of UVB and sunlight exposure. Photochemically, MQ generated reactive oxygen species superoxide radical, hydroxyl radical, and singlet oxygen through type I and type II photodynamic reactions, respectively, which caused photooxidative damage to DNA and formed localized DNA lesions cyclobutane pyrimidine dimers. Photosensitized MQ reduced the viability of keratinocytes to 25 %. Significant level of intracellular reactive oxygen species (ROS) generation was estimated through fluorescence probe DCF-H2. Increased apoptotic cells were evident through AO/EB staining and phosphatidyl serine translocation in cell membrane. Single-stranded DNA damage was marked through single-cell gel electrophoresis. Mitochondrial membrane depolarization and lysosomal destabilization were evident. Upregulation of Bax and p21 and downregulation of Bcl-2 genes and corresponding protein levels supported apoptotic cell death of keratinocyte cells. Cyclobutane pyrimidine dimers (CPDs) were confirmed through immunofluores-

cence. In addition, hallmarks of apoptosis and G2/M phase cell cycle arrest were confirmed through flow cytometry analysis. Authors' findings suggest that MQ may damage DNA and produce DNA lesions which may induce differential biological responses in the skin on brief exposure to UVB and sunlight.

Role of oxidative stress in deoxynivalenol induced toxicity.

[Mishra S, Dwivedi PD, Pandey HP, Das M. Food Chem Toxicol. 2014 Oct;72:20-9. doi: 10.1016/j.fct.2014.06.027.]

Deoxynivalenol (DON) is a Fusarium toxin that causes a variety of toxic effects with symptoms such as diarrhoea and low weight gain. To date, no review has addressed the toxicity of DON in relation to oxidative stress. The focus of this article is primarily intended to summarize the information associated with oxidative stress as a plausible mechanism for DON-induced toxicity. The present review shows that over the past two decades, several investigators have documented the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) in oxidative stress as a result of DON treatment and have correlated them with various types of toxicity. The evidence for induction of an oxidative stress response resulting from DON exposure has been more focused on *in vitro* models and is relatively lacking in *in vivo* studies. Hence, more emphasis should be laid on *in vivo* investigations with doses that are commonly encountered in food products. Since DON is commonly found in food and feed, the cellular effects of this toxin in relation to oxidative stress, as well as effective measures to combat its toxicity, are important aspects to be considered for future studies.

Hypersensitivity linked to exposure of broad bean protein(s) in allergic patients and BALB/c mice.

[Kumar D, Kumar S, Verma AK, Sharma A, Tripathi A, Chaudhari BP, Kant S, Das M, Jain SK, Dwivedi PD. Nutrition. 2014 Jul-Aug;30(7-8):903-14.]

Broad bean (*Vicia faba* L.), a common vegetable, belongs to the family Fabaceae and is consumed worldwide. Limited studies have been done on allergenicity of broad beans. The aim of this study was to determine if broad bean proteins have the ability to elicit allergic responses due to the presence of clinically relevant allergenic proteins. Simulated gastric fluid (SGF) assay and immunoglobulin E (IgE) immunoblotting were carried out to identify pepsin-resistant and IgE-binding proteins. The allergenicity of broad beans was assessed in allergic patients, BALB/c mice, splenocytes, and RBL-2H3 cells. Eight broad bean proteins of approximate molecular weight 70, 60, 48, 32, 23, 19, 15, and 10 kDa that remained undigested in SGF, showed IgE-binding capacity as well. Of 127 allergic patients studied, broad bean allergy was evident in 16 (12%). Mice sensitized with broad bean showed increased levels of histamine, total and specific IgE, and severe signs of systemic anaphylaxis compared with controls. Enhanced levels of histamine, prostaglandin D2, cysteinyl leukotriene, and β-hexosaminidase release were observed in the primed RBL-2H3 cells following broad bean exposure. The levels of interleukin IL-4, IL-5, IL-13 and regulated on activation, normal T-cell expressed and secreted were found enhanced in broad bean-treated splenocytes culture supernatant compared with controls. This study inferred that broad bean proteins have the ability to elicit allergic responses due to the presence of clinically relevant allergenic proteins.

TOPIC OF INTEREST

Vishaktata Parikshan: GLP Anuroop Suvidha Toxicity Testing: GLP Test Facility at CSIR-Indian Institute of Toxicology Research, Lucknow

CSIR-IITR received certificate of GLP compliance in June 2014 for toxicity testing and mutagenicity studies. It is noteworthy that CSIR-IITR is the first laboratory in the CSIR family to receive this international accreditation and second in the government sector. The GLP certificate is a testament to high quality research by way of thorough SOP-driven Good Laboratory practices, competent well trained personnel and systematic documentation. The GLP laboratories at CSIR-IITR are designed as per OECD guidelines, which make the integrity and quality of the laboratory data adequate for regulatory submissions across the globe. Our team of 38 members at Vishaktata Parikshan: GLP Anuroop Suvidha is committed to realize its mission towards serving the global needs in the area of toxicology and biosafety. At present we have certification to carry out the following studies:

- Acute toxicity studies
- Sub-acute toxicity studies
- Micronucleus assay *(in vivo)*
- Chromosomal aberration test *(in vivo)*

The types of chemicals for which these studies would be carried out are industrial chemicals, pesticides, pharmaceuticals, cosmetics, food additives and feed additives. The test systems certified for the above studies are Rat (Wistar); Mice (Swiss albino); Rabbit (New Zealand White) and Guinea Pig (Hartley). So far 7 studies have been taken up after receiving the certification and 11 are in the pipeline. India has a full adherence member status of OECD's Working Group on GLP, hence the toxicity/bio-safety data generated for chemicals/ formulations, pesticides, pharmaceuticals, cosmetics, feed and food additives; from GLP Test Facility will be accepted as such by the regulatory authorities in all the thirty four OECD member countries and all other associated non-member countries.

GOVERNMENT OF INDIA
Department of Science and Technology
National Good Laboratory Practice (GLP) Compliance Monitoring Authority (NGCMA)

Certificate of GLP Compliance

Based on the Inspection and the subsequent follow-up actions

Toxicity Testing : GLP Test Facility
CSIR - Indian Institute of Toxicology Research
M. G. Marg, Lucknow - 226001

is certified capable of conducting the below-mentioned tests/studies in compliance with Organization for Economic Co-operation & Development (OECD) Principles of GLP:

- **Toxicity Studies**
- **Mutagenicity Studies**

The specific areas of expertise, types of chemicals and test systems are listed in annexure Below.

Validity: June 5, 2014 – June 4, 2017

This certificate is subject to the condition that the test facility complies with the Terms & Condition of The NGCMA's Document No. GLP-101 and OECD Principles of GLP.

Certificate No.: GLP/C-058/2014
Issue Date : 05-06-2014

(D R PRASADA RAJU)
Head, NGCMA

Research Exemptions in IPR: A Necessity for Researchers

Dr KC Khulbe

Can I perform an innovative research without infringing intellectual properties of others? Unfortunately, the answer of this question is NO.

Introduction

In recent times when technologies are at the crux of science, it is important to see how a researcher could successfully perform any meaningful research without infringing patents of another researcher. A patent excludes others from making and using the invention without permission and it, therefore, creates hindrance in basic research. At the same time, however, patents have become the major source of information. It has become much easier to perform patent landscape analysis to know the current status of research in the specific area of interest. It is, therefore, important to empower "Research Exemptions" or "Safe Harbour Exemption" in the intellectual property rights, particularly in case of process patents, which are generally used as research tools. So far, in some states there are limited research exemptions regulation exists. The research exemptions or rather their interpretation has recently been the subject of policy debate.

Existing research exemptions

Article 30 of the TRIPS Agreement (1) which deals with exceptions to Rights Conferred states "Members may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties." Although, member states have not been able to harmonize the exemptions to patent rights. Article 69 and Protocol of European Patent Convention (2) (EPC) specify that the experimental use exemption in Europe. All the member states of the European Union (EU), except Austria, have introduced research exemption, allowing the use of protected intellectual property for true research purposes, without infringement of patent rights. There is absolute uniformity in the language adopted by EPC member states except Article 53(3) of the Patent Law, 1995 of The Netherlands, which adds the word "solely" to the exemption, which potentially leaves room for a different interpretation. In the United States, one comment of USPTO (3) suggested that patents should "allow for others to learn from and improve the invention." The comment suggested that claims to patented plant varieties should not prohibit others from using the patented plants to develop improved varieties. The comment also stated that uses of plants in speculative manners should not be permitted. Response: By statute, a patent provides the patentee with the right to exclude others from, inter alia, making and using the claimed invention, although a limited research exemption exists.(4) In the United States, this exemption is also technically called § 271(e)(1) exemption or Hatch-Waxman exemption. In Canada, this exemption is known as the Bolar provision or Roche-Bolar provision, named after the case Roche Products vs Bolar Pharmaceutical. India Patents Act, 1970: Section 47(3) states that "…the patent granted may be used, by any person, for the purpose merely of experiment or research, including the imparting of instructions to pupils." Several member states have conducted research into experimental use, leading in many cases to legislative change. For example, in Belgium, amendment to the Patent Act in 2005 included an extension to the scope of the research exception to include research on or with the patented invention. The common law research exemption is an affirmative defense to infringement where the alleged infringer is using a patented invention for research purposes. To prevent the deleterious effects of intellectual property rights including patents on scientific research it has become compelling to harmonise the research exemption in all the member states. At the same time, it is important to consider that it should not adversely affect on the returns on investment of the patent holder. Further to note that the patent rights are not absolute. There are other restrictions on these rights too viz. Competition Law, etc. One major ambiguity about the research exemption is in case of biotechnological patents. Protection of Expressed Sequence Tags (ESTs), Single Nucleotide Polymorphisms (SNPs) and Entire Genomes, which are used as basic tools in modern biotechnology, has raised several issues that are inadequately handled

by the prevailing research exemptions.

Arguments on research exemptions

There are two schools of thought. The opponents of a research exemption say that patents do not prohibit research on the invention and innovation. As per them, the patents only add to the costs of doing research, since the researcher must pay prices in order to use the patent product or process developed by another researcher. In this way, the opponent argues that all research will get the appropriate level of return on investment. If they use knowledge created by another researcher, they should pay the costs associated with it. It is, therefore, the presence of a research exemption may adversely affect on the rate of investment in innovative research. The proponents of the notion argue that it is difficult to keep a watch on every single individual research. Since most of the research is cumulative in nature, therefore, there would be multiple licensing arrangements that need to be negotiated separately before each and every research take place. In this case the transaction costs would be reasonably significant. These payments are deadweight losses and do not augment the incentive to invest for either party. The problem researcher face as a result of increased patenting may be well understood by the case-study of patenting of OncoMouse (5). In the early 1980s, Harvard patented the OncoMouse and licensed it to DuPont, who then commercially exploited the research tool aggressively and enforced their property rights. In recent times, when the open science (6) where information is disseminated and diffused freely, are gearing up to solve the complex problems associated with discovering novel therapies for neglected tropical disease absence of research exemption would cause hindrance to the researchers.

Economic aspects of research exemptions

According to economic theory, innovation policies should be designed to balance the incentives to invest in innovative activity with the promotion of technology transfer. The first-best research exemption policy provides investors with an incentive to invest while not limiting those knowledge spill-over which only have a small effect on this incentive to invest. (7).

(1)Available at URL: http://www.wto.org/ english/ tratop_e/trips_e/t_agm3c_e.htm#5

(2)Available at URL: http://www.epo.org/patents /law/legal-texts/html/epc/2000/e/ar69.html

(3) 1337 CNOG 865 dated December 30, 2008. Available at URL: http://www.uspto.gov/ web/patents/patog/week53/OG/TOCCN/item-160.htm

(4) See 35 U.S.C. 163, 271(a), (e).

(5) The OncoMouse or Harvard mouse is a type of genetically modified mouse with a specific gene making it highly susceptible to cancer.

(6) Open science is to make research accessible to all which help in solving complex global problems. Open Source Drug Discovery (OSDD) of Council of Scientific & Industrial Research (CSIR) is its best example.

(7) Chris Dent, Paul Jensen, Sophie Waller and Beth Webster, STI Working Paper 2006/2, OECD Directorate for Science, Technology and Industry (STI), Research Use of Patented Knowledge: A Review, Available at URL: http://www.oecd.org/ dataoecd/15/16/36311146.pdf

RESEARCH DIGEST

Health: The weighty costs of non-caloric sweeteners

Nature 17 September 2014 doi:10.1038/nature13752

In many parts of the world, obesity is becoming increasingly prevalent. Weight control is important for reducing the risk of metabolic diseases such as type 2 diabetes, which is characterized by high blood-glucose levels and insulin resistance. Limiting calorie intake and replacing dietary fat and sugar with low- or non-caloric alternatives is a common weight-loss strategy. Non-caloric artificial sweeteners (NAS) are often chosen to combat weight problems, because they do not contribute to overall calorie intake and are thought to subvert the rise in blood-glucose levels that occurs in response to food intake. For unknown reasons, however, NAS are not always effective for weight loss. In a paper published on Nature's website, Suez et al. describe an unexpected effect of NAS that may shed some light on this issue.

Suez and colleagues added an NAS supplement (saccharin, sucralose or aspartame) to the diets of mice, and found that the sweeteners altered the animals' metabolism, raising blood glucose to significantly higher levels than those of sugar-consuming mice. This was true both for mice fed a normal diet and for those on a high-fat diet - a model for a situation in which NAS supplements might be used to control weight. Because variations in diet have been shown to directly lead to changes in the populations of bacteria that occupy the gut, the authors examined whether these bacteria were responsible for the metabolic changes that they observed. And, indeed, when they used antibiotics to deplete the gut bacteria, they found that this eliminated NAS-induced glucose intolerance in mice fed either diet. Next, the researchers transplanted faeces from NAS-fed or glucose-fed mice into germ-free mice (those with no gut bacteria of their own) that had never consumed NAS. Transfer from NAS-fed mice induced elevated blood-glucose levels in the transplant recipients. Furthermore, the composition of the recipients' gut bacterial community was different from that of mice receiving transplants from glucose-fed mice, suggesting that changes in this gut microbiota mediate glucose intolerance in NAS-fed mice. Genetic analysis revealed that this altered composition was accompanied by changes in bacterial function. In particular, Suez and co-workers detected an increase in carbohydrate-degradation pathways in the microbiota of NAS-fed mice. This connection parallels a previous report2 that the microbiota of obese mice has a higher carbohydrate-metabolizing capacity than the microbiota of normal-weight mice. What is the relevance of these results for human disease? Suez et al. studied around 400 people, and found that bacterial populations in the guts of those who consumed NAS were significantly different from those who did not. Moreover, NAS consumption correlated with disease markers linked to obesity, such as elevated fasting blood-glucose levels and impaired glucose tolerance. The authors placed seven volunteers who did not normally consume NAS on a seven-day regimen of controlled high NAS intake. After only four days, half the individuals had elevated blood-glucose levels and altered bacterial-community composition, mirroring the results seen in the mice. Transfer of faeces from NAS-fed human donors induced elevated blood-glucose levels in germ-free mouse recipients that had never consumed NAS. Taken together, Suez and colleagues' data indicate that NAS consumption may contribute to, rather than alleviate, obesity-related metabolic conditions, by altering the composition and function of bacterial populations in the gut. Studies examining genetic and diet-induced mouse models of obesity and obesity in humans have demonstrated that the disease is associated with changes in the composition of the gut microbiota. Most bacteria colonizing the gut come from two phyla, Bacteroidetes and Firmicutes. Obese mice and humans both have reduced bacterial diversity, with reduced proportions of Bacteroidetes and increased Firmicutes, when compared to lean littermates or twin controls. Obesity-induced

changes in the microbiota can be reversed by diet - obese mice or humans on fat- or carbohydrate-restricted diets have an increased abundance of Bacteroidetes. It is difficult to directly compare Suez and colleagues' findings with earlier work, because the current report describes changes in a mix of bacteria (including Bacteroidetes and Firmicutes) after NAS treatment. Certain gut bacteria are well adapted to break down dietary components that the human body cannot. It could be that expansion of these populations in response to NAS increases extraction of energy - often stored as fat - from the diet, contributing to obesity. Alternatively, NAS might exert their effect by suppressing the growth of particular bacterial taxa. In obese mice, the growth of certain bacterial species is suppressed, and there is an increased production of metabolites that can contribute to insulin resistance. These two possibilities cannot be distinguished in the current report. Bacterial communities in the gut have been linked to elevated lipid production, and increased storage of lipids and the carbohydrate glycogen, correlating with an increase in adiposity and in cellular energy extraction from food. Furthermore, obesity-induced alterations to the composition of gut microbiota are associated with metabolic changes, including enrichment of pathways related to bacterial growth. This suggests that obesity maintains alterations to the microbiota, allowing for the continued increase in production and storage of lipids and glycogen, further exacerbating the condition. Future work must determine whether the changes in the microbiota brought about by NAS consumption activate any of the same molecular pathways as are active in the obese microbiota. Type 2 diabetes and impaired glucose tolerance have also been linked to alterations in gut microbiota composition. Analysis of gut bacterial genomes shows that microbial-gene signatures differ between patients with and without diabetes, and people with impaired glucose tolerance. Whether the bacterial populations or metabolic pathways altered by the consumption of NAS are similar to those described in people with or developing diabetes remains to be seen. Many diseases associated with Western lifestyles have now been linked to environmentally induced alterations in the composition of the gut microbiota. Questions remain regarding the precise mechanisms by which NAS disrupt the relationship between gut bacteria and their host. Studies to identify specific bacterial populations that promote resistance to weight gain or improve glucose tolerance may prove useful for devising therapies that modulate bacteria or their metabolites.

Vitamin supplement successfully prevents noise-induced hearing loss

http://medicalxpress.com/news/2014-12-vitamin-supplement-successfully-noise-induced-loss.html

Researchers from Weill Cornell Medical College and the Gladstone Institutes have found a way to prevent noise-induced hearing loss in a mouse using a simple chemical compound that is a precursor to vitamin B3. This discovery has important implications not only for preventing hearing loss, but also potentially for treating some aging-related conditions that are linked to the same protein. The researchers used the chemical nicotinamide riboside (NR) to protect the nerves that innervate the cochlea. The cochlea transmits sound information through these nerves to the spiral ganglion, which then passes along those messages to the brain. Exposure to loud noises damages the synapses connecting the nerves and the hair cells in the cochlea, resulting in noise induced hearing loss. The researchers set about trying to prevent this nerve damage by giving mice NR before or after exposing them to loud noises. NR was successful at preventing damage to the synaptic connections, avoiding both short-term and long-term hearing loss. What's more, NR was equally effective regardless of whether it was given before or after the noise exposure. "One of the major limitations in managing disorders of the inner ear, including hearing loss, there are a very limited number of treatments options. This discovery identifies a unique pathway and a potential drug therapy to treat noise-induced hearing loss," says Kevin Brown, MD, PhD, an associate professor of otolaryngology-head and neck surgery at the University of North Carolina School of Medicine and first author on the paper. Brown conducted the research while at Weill Cornell. The researchers chose NR because it is a precursor to the chemical compound nicotinamide adenine dinucleotide (NAD+), which had previously been shown by Dr Brown and co-senior author Samie Jaffrey, MD, PhD, to protect cochlea nerve cells from injury. However, NAD+ is an unstable compound, calling into question whether it could be used out of the petri dish and in a live animal. That led the scientists to use NR instead. Methods for synthesizing NR were recently developed by Anthony Sauve, a professor of pharmacology at Weill Cornell and co-author of the study. This resulted in quantities of NR that were sufficient to test in animals. "NR gets into cells very readily and can

be absorbed when you take it orally. It has all the properties that you would expect in a medicine that could be administered to people," said Dr Jaffrey, a professor of pharmacology at Weill Cornell. Beyond just preventing hearing loss, the researchers think the results may have broader applications because of the underlying way NR protects nerve cells. The scientists showed that NR and NAD+ prevent hearing loss by increasing the activity of the protein sirtuin 3 (SIRT3), which is critically involved in the function of mitochondria, the powerhouses of the cell. The researchers hypothesized that it was this enhancement of SIRT3 that was behind the protective properties of NR. To test this, they manipulated SIRT3 levels independently of NR to see if they could still prevent noise-induced hearing loss by administering NR. Sure enough, deleting the SIRT3 gene in mice abolished any of the protective properties of NR. The researchers also showed that a new strain of mice, generated in the lab of co-senior author Eric Verdin, at the Gladstone Institutes and engineered to express high levels of SIRT3, were inherently resistant to noise induced hearing loss, even without administration of NR. SIRT3 decreases naturally as we age, which could partially explain aging-related hearing loss. Additionally, some individuals carry different versions of the SIRT3 genes that result in reduced enzyme activity, which may make them more susceptible to noise-induced hearing loss. Dr Verdin, an investigator at the Gladstone Institute of Virology and Immunology and professor of medicine at the University of California, San Francisco, says, "The success of this study suggests that targeting SIRT3 using NR could be a viable target for treating all sorts of aging-related disorders-not only hearing loss but also metabolic syndromes like obesity, pulmonary hypertension, and even diabetes."

Giving cities a road map to reducing their carbon footprint

http://news.sciencemag.org/climate/2014/12/giving-cities-road-map-reducing-their-carbon-footprint?utm_campaign=email-news-latest&utm_source=eloqua#main-content

Armed with data from the GPC, Rio de Janeiro expanded public transportation to cut greenhouse gas emissions. Cities are not just where 3.5 billion of us live-they are where more than half of humanity uses electricity, drive cars, and throws out garbage, among myriad other activities that emit greenhouse gases. Now, a global coalition has released the first standardized method for measuring and reporting a given city's greenhouse gas emissions. Called the Global Protocol for Community-Scale Greenhouse Gas Emission Inventories(GPC), the new standards were unveiled today at the United Nations' ongoing climate negotiations in Lima. Cities are responsible for 70% of global carbon dioxide emissions, says Wee Kean Fong, who led development of the GPC at the World Resources Institute-a non-profit based in Washington, D.C.-in partnership with the C40 Cities Climate Leadership Group and Local Governments for Sustainability (ICLEI). But there has been no standardized way to measure and report an individual city's emissions. That has impeded plans to reduce urban climate footprints and track the effectiveness of local policies designed to reduce emissions. "You can't manage what you can't measure," Fong says. A key element of the GPC is its recognition that a city may be responsible for gases emitted far outside its borders. Take power plants that burn fossil fuels to generate electricity, or landfills that receive solid waste, Fong says. Those can be located outside of a city, but their emissions are directly tied to urban activity. Holding cities accountable for such emissions may lead to some pushback when it comes to convincing them to adopt the GPC protocol, but it's important for making sure measurements are accurate as possible, Fong says.

A key selling point is that 35 cities have already benefited from implementing the GPC during its pilot phase in 2012. In the months since, other cities have been test-driving the new standards. David Maleki, a climate change analyst with the Inter-American Development Bank's Emerging and Sustainable Cities Initiative, helps cities in Latin America and the Caribbean use the protocol to figure out which sectors are responsible for most of their greenhouse gas emissions. These "[greenhouse gas] inventories are a very basic building block for taking climate action in cities," he says. Rio de Janeiro, for example, used a draft of the GPC to determine that

transportation was responsible for a whopping 39% of the city's total emissions; that led the government to focus on expanding public transit to more efficiently shrink its carbon footprint. "Building a greenhouse gas emissions inventory enables city leaders to manage their emissions reduction efforts, allocate resources and develop comprehensive climate action plans," said Rio de Janeiro mayor and C40 Chair Eduardo Paes said in a statement.

One lesson Fong and his team learned during the pilot program is that not every city is starting from the same place when it comes to measuring greenhouse gas emissions. Some cities, especially in the developing world, simply don't have access to the kind of data needed for a comprehensive inventory; Maleki says he often works in places where the only emissions data available are on a national scale.

To try to make the GPC accessible to cities that may not have all the right data, Fong's team designed two tiers of reporting. Both incorporate transportation within the city, stationary burning of fossil fuels, consumption of electricity, and emissions related to waste. The more advanced tier adds data about industrial processes, land use change, transportation that brings people into the city, and other indirect sources of emissions. "The GPC is a very inclusive protocol," says Ana Marques, project coordinator of ICLEI's Urban-LEDS project, which will help cities in developing countries apply the GPC. "It enables all cities to participate."

Cannabis extract can have dramatic effect on brain cancer, says new research

http://medicalxpress.com/news/2014-11-cannabis-effect-brain-cancer.html

The new research by specialists at St George's, University of London, studied the treatment of brain cancer tumours in the laboratory and discovered that the most effective treatment was to combine active chemical components of the cannabis plant which are called cannabinoids. Two of these called tetrahydrocannabinol (THC) and cannabidiol (CBD)were tested as part of the research into brain cancer which is particularly difficult to treat and claims the lives of about 5,200 each year. It also has a particularly poor prognosis as the rate of survival after five years of patients' diagnosis is around 10%. Cannabinoids are the active chemicals in cannabis and are also known more specifically as phytocannabinoids. There are 85 known cannabinoids in the cannabis plant. The new research is the first to show a drastic effect when combining THC and CBD with irradiation. Tumours growing in the brains of mice were drastically slowed down when THC/CBD was used with irradiation. Dr Wai Liu, Senior Research Fellow and lead researcher on the project, said: "The results are extremely exciting. The tumours were treated in a variety of ways, either with no treatment, the cannabinoids alone, and irradiation alone or with both the cannabinoids and irradiation at the same time. "Those treated with both irradiation and the cannabinoids saw the most beneficial results and a drastic reduction in size. In some cases, the tumours effectively disappeared in the animals. This augurs well for further research in humans in the future. At the moment this is a mostly fatal disease. "The benefits of the cannabis plant elements were known before but the drastic reduction of brain cancers if used with irradiation is something new and may well prove promising for patients who are in gravely serious situations with such cancers in the future." The research team are discussing the possibility of combining cannabinoids with irradiation in a human clinical trial.

विज्ञान परिक्रमा

(साभार जी न्यूज़ विज्ञान समाचार)

'वायु-प्रदूषण से ताजमहल का सफेद रंग भूरा होता जा रहा है'

भारतीय एवं अमेरिकी अनुसंधानकर्ताओं ने एक अध्ययन में पाया है कि हवा में तैरते कार्बन कणों एवं धूलकणों के चलते ताजमहल बदरंग होता जा रहा है और उसका चमचमाता सफेद रंग भूरा होता जा रहा है। जार्जिया इंस्टीट्यूट ऑफ टेक्नालोजी के स्कूल ऑफ अर्थ एंड एटमोसफेरिक साइंसेज के प्रोफेसर माइकल बर्गिन ने कहा, 'हमारी टीम यह दर्शाने में सफल रही है कि ताजमहल को बदरंग कर रहे प्रदूषक बायोमास, अपशिष्ट, जीवाश्म ईंधन के जलने से निकलने वाले कार्बन कण और धूलकण हैं।' जार्जिया इंस्टीट्यूट ऑफ टेक्नोलॉजी के अलावा कानपुर के भारतीय प्रौद्योगिकी संस्थान, भारतीय पुरातात्विक सर्वेक्षण और विसकोंसिन विश्वविद्यालय के अनुसंधानकर्ताओं ने इस अध्ययन में साथ दिया। सोलहवीं शताब्दी में मुगलशासक शाहजहां द्वारा अपनी पत्नी मुमताज महल की याद में बनाए गए इस ताजमहल में मार्बल का 115 फुट ऊंचा गुबंद और 130 ऊंचे चार मीनार हैं। यहां हर साल लाखों पर्यटक आते हैं और यह 1983 में यूनेस्को के वैश्विक धरोहर स्थल बन गया। अबतक माना जा रहा था कि बदरंग होने के लिए वायु प्रदूषण जिम्मेदार है लेकिन उसके लिए कोई व्यवस्थित अध्ययन नहीं किया गया था। बदरंग होने की वजह जानने के लिए अनुसंधानकर्ताओं ने नवंबर, 2011 से जून, 2012 के बीच एयर सैम्पलिंग उपकरण का इस्तेमाल किया ताकि यह पता चल पाया कि ताजमहल परिसर के वायु में क्या है। उन्होंने अपने इस अध्ययन के दौरान सैम्पल के तौर मूल मार्बल ताजमहल परिसर रख दिए। दो महीने बाद सैम्पल का उन्होंने अध्ययन किया। अनुसंधानकर्ताओं को उपकरण के फिल्टर और मार्बल सैम्पलों पर भूरे आर्गेनिक कार्बन और काले कार्बन के कण मिले।

रात की शिफ्ट में काम करना घटा सकता है आपकी उम्र

लगातार रात की शिफ्ट में बदल-बदल कर काम करना स्वास्थ्य के लिए काफी हानिकारक साबित हो सकता है और इसके कारण फेफड़े का कैंसर और हृदयरोग से जुड़ी समस्याएं हो सकती हैं, जो आपकी जल्द मौत का भी कारण बन सकती है। एक ताजा शोध में बताया गया है कि पांच या इससे अधिक वर्षो तक बदल-बदल कर रात की शिफ्ट में काम करने वाली महिलाओं में हृदयरोग से जुड़ी समस्याओं के कारण मृत्युदर बढ़ी पायी गयी, जबकि 15 वर्ष से अधिक समय तक काम करने वाली महिलाओं में फेफड़े के कैंसर से मृत्यु होने की दर में इजाफा देखा गया। अध्ययन में महीने में

कम से कम तीन शिफ्ट रात में करने वालों को शामिल किया गया। हारवर्ड मेडिकल स्कूल की सहायक प्राध्यापिका इवा शेर्नहैमर ने बताया, इस शोध के परिणाम रात की शिफ्ट में काम करने और स्वास्थ्य या लंबी आयु के बीच संभावित हानिकारक संबंधों के पूर्व सबूतों को प्रमाणित करते हैं। नींद और हमारी दैनिक जैविक क्रियाएं हृदय सर्केडियन सिस्टम दिल के स्वास्थ्य और कैंसर के ट्यूमर को बढ़ने से रोकने में बेहद अहम होती हैं। इवा ने बताया, चूंकि दुनियाभर में रात की शिफ्ट में काम करने वाले कर्मचारियों की संख्या में तेजी से इजाफा हो रहा है, अतः यह अध्ययन संभवतः दुनिया में सबसे बड़े समूह से संबंधित अध्ययन है। अध्ययन के लिए शोधकर्ताओं ने अमेरिका में नर्सो के स्वास्थ्य संबंधी आंकड़ा रखने वाली संस्था नर्सेज हेल्थ स्टडी (एनएचएस) द्वारा दर्ज 22 वर्ष के आंकड़ों का विश्लेषण किया। इस अमेरिकी संस्था से लगभग 75,000 नर्से पंजीकृत हैं। विश्लेषण में पाया गया कि छह से 15 वर्षो तक बदल-बदल कर रात की शिफ्ट में काम करने वाली नर्सो की मृत्यु दर 11 फीसदी अधिक रही। इनमें दिल की बीमारी से होने वाली मृत्यु की दर 19 फीसदी अधिक पाई गई। 15 या इससे भी अधिक वर्षों से रात की शिफ्ट में काम कर करने वाली महिलाओं में फेफड़े के कैंसर से मौत होने का खतरा 25 फीसदी अधिक पाया गया। यह अध्ययन 'अमेरिकन जर्नल आफ प्रीवेंटिव मेडिसिन' के ताजा अंक में प्रकाशित हुआ।

भारत में झुग्गियों को रोशन कर सकती हैं पुराने लैपटाप की बैटरियां

बेकार हो चुके लैपटॉप की बैटरियों में अब भी इतनी क्षमता होती है कि वे भारत एवं अन्य विकासशील देशों में झुग्गियों का अंधेरा दूर कर सकें। आईबीएम इंडिया द्वारा किए गए एक अध्ययन में यह तथ्य सामने आया है। अमेरिका के सैन जोस में एक सम्मेलन में पेश किए गए अध्ययन पत्र में बेकार बैटरियों के नमूनों का विश्लेषण किया गया जिसमें पाया गया कि 70% बैटरियों में एक एलईडी लाइट को एक दिन में चार घंटे से ज्यादा जलाने के लिए पर्याप्त बिजली होती है। आईबीएम इंडिया के अनुसंधानकर्ताओं के मुताबिक, हर साल अनुमानित पांच करोड़ लिथियम-आयन लैपटॉप बैटरियों को रद्दी में डाल दिया जाता है। ये बैटरियां विकासशील देशों में झुग्गियों को रोशन कर सकती हैं। एमआईटी प्रौद्योगिकी

समीक्षा के मुताबिक, एलईडी लाइटों को सोलर पैनल और रीचार्जेबल बैटरियों से जोड़ना संभव है और इस तरह से बहुत सस्ते में इनका बढ़िया इस्तेमाल किया जा सकता है।

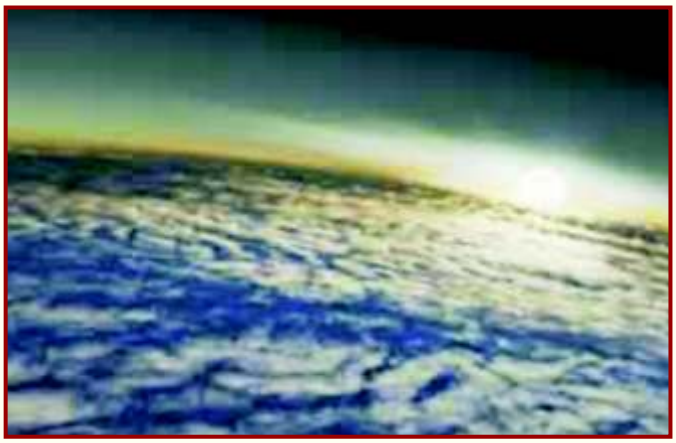
दुनिया में 74.8 करोड़ लोगों को मिलता है गंदा पानीःडब्ल्यू.एच.ओ.

दुनिया में तकरीबन 74.8 करोड़ लोगों को नियमित रूप से साफ पानी नहीं मिल रहा है और करीब 18 लाख लोगों को दूषित पानी से अपनी जरूरतें पूरी करनी पड़ रहीं हैं। यह जानकारी विश्व स्वास्थ्य संगठन (डब्ल्यूएचओ) द्वारा जारी एक रिपोर्ट में सामने आई है। रिपोर्ट में बताया गया है कि 25

लाख लोग सफाई के अभाव में रह रहे हैं और 100 करोड़ लोगों को खुले में शौच जाना पड़ रहा है, वहीं ग्रामीण इलाकों में हर 10 में से नौ लोग खुले में शौच जाने के लिए मजबूर हैं। 'ग्लास-2014' के नाम से जारी की गई इस रिपोर्ट में यह प्रमुख निष्कर्ष सामने आए हैं। यह अध्ययन हर दो साल में डब्ल्यूएचओ द्वारा कराया जाता है। इस अध्ययन के 2014 संस्करण को 'जल और स्वच्छता में निवेश, असमानता को कम करने, उपयोग में वृद्धि' नाम से जारी किया गया है। अध्ययन में बताया गया है कि पिछले दो दशकों में पीने के साफ पानी तक 23 लाख लोगों की पहुंच बढ़ी है। इसी समय चक्र में डायरिया से मरने वाले बच्चों की मौत का कारण काफी हद तक स्वच्छता से जुड़ा हुआ था। 1990 में यह संख्या 15 लाख थी जो कि 2012 में घटकर छह लाख रह गई। डब्ल्यूएचओ में सार्वजनिक स्वास्थ्य और पर्यावरण विभाग की निदेशक मारिया नेरा इन सुधारों की सराहना की, लेकिन उन्होंने कहा कि अभी भी यह आंकड़ा काफी बड़ा है। अध्ययन में साफ-सफाई के महत्व पर ध्यान केंद्रित करते हुए कहा गया कि 75 फीसदी धनराशि का प्रयोग लोगों को पीने का स्वच्छ पानी मुहैया कराने के लिए किया जा रहा है।

ओजोन परत के क्षरण में हो रहा है सुधारः यूएन रिपोर्ट

ओजोन परत के क्षरण में सुधार हो रहा है और अगले कुछ दशकों में इसकी स्थिति दुरूस्त हो सकती है। इसका कारण समन्वित अंतरराष्ट्रीय कदम है जिसके कारण इसमें सुधार जारी है। संयुक्त राष्ट्र पर्यावरण कार्यक्रम तथा विश्व मौसम संगठन ने एक रिपोर्ट में यह बात कही। ओजोन परत गैस का एक नाजुक कवच है जो पृथ्वी की सूर्य से निकलने वाली पराबैंगनी किरणों से रक्षा करता है। दुनिया भर के 300 वैज्ञानिकों द्वारा किए गए ओजोन क्षरण का वैज्ञानिक आकलन, 2014 के अनुसार मांट्रियल प्रोटोकाल के तहत ओजोन परत को नुकसान पहुंचाने वाले तत्वों को लेकर जो कदम उठाये गये, उससे ओजोन परत 1980 के स्तर पर आ सकता है। रिपोर्ट के अनुसार वातावरण में क्लोरोफ्लोरोकार्बन तथा हैलोन जैसे गैसों की उपलब्धता कम हुई है। इन गैसों का उपयोग रेफ्रिजरेटरों, स्प्रे कैन आदि में होता था। इसमें कहा गया है कि 1980 के दशक तथा 1990 की शुरूआत में ओजोन परत में क्षरण पाया गया। यह 2000 से सापेक्षिक रूप से स्थिर था लेकिन हाल के अध्ययन से इसमें सुधार के संकेत हैं।



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