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Inside

CSIR-Indian Institute of Toxicology Research
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EVENTS

NATIONAL SCIENCE DAY

CSIR-Indian Institute of Toxicology Research (IITR), Lucknow celebrated National Science Day on 28th February, 2013. Dr. K.C. Gupta, Director, IITR while welcoming Dr. T.P. Singh, Distinguished Biotechnology Research Professor, AIIMS, New Delhi said that the first National Science Day was celebrated in India in 1987 and since then the scientific fraternity has been celebrating this event to recognize the contributions made by Indian scientists. Dr. Poonam Kakkar, Chief Scientist and Convener of the programme introduced the chief guest, Dr. T.P. Singh to the audience. On this occasion, a publication in Hindi entitled "Vish Vigyan Sandesh" was released by Prof. T.P. Singh. Earlier, Prof. Singh inaugurated an exhibition depicting a few R&D activities of the institute through exhibits. Around 100 students from two schools visited the exhibition. The major exhibits were:

Prof. T.P. Singh visiting the exhibition

(1) Demonstration of colour detection kit (CD-strip), developed by IITR for the detection of a non-permitted, carcinogenic oil soluble dye, butter yellow in mustard oil. Food stuffs coloured with various permitted and non- permitted colours were displayed and the students were made aware of the possible health risk associated with these colours.

(2) The suitability assessment of plastic and polymeric products was explained to the visitors. In addition to this the advantages and disadvantages of synthetic polymers were explained. The need for guidelines and contributions in framing of specifications by regulatory agencies was also elaborated for the benefit of the students.

Guest and students at the exhibition

(3) Noise level monitor for recording of noise levels, air quality monitor for CO, CO_2, PM, Temp. and RH, fine particulate sampler for PM 2.5, respirable dust sampler for monitoring of air pollutants namely, SPM, RSPM, SO_2 and NOx was demonstrated.

(4) Portable water analysis kit for monitoring of water quality.

(5) Herbal Research Section demonstrated:

- Testing of total antioxidant potential of herbal extracts by using four microassays viz-SOD mimetic activity, lipid peroxidation inhibition assay and ABTS, NO quenching decolourization assays.
- Medicinal value and constituents along with safety studies of Mahayogiraj, Gugglu, Arogya Vardhani Vati and Maha Laxmi Vilas Rasa were explained with photographs and microscopic slide shows.
- Chemical finger printing of *Oroxylum indicum* and *Berberis aristata* by HPTLC was displayed through UV visualizer.

(6) Instruments for measuring body fat and for carrying out lung function test were displayed to the students.

Dr K.C. Gupta presenting a memento to Prof. T.P. Singh

Release of Vish Vigyan Sandesh (L-R) Dr Mukul Das, Prof. T.P. Singh, Dr K.C. Gupta and Dr Poonam Kakkar

Prof. T.P. Singh gave a popular lecture entitled "Introducing protein antibiotics as the new weapon against the invading microbes". He said that the pipeline of new antibiotics is drying up. Major drug companies are losing interest in the antibiotics market because;

(1) These drugs may not be profitable as those drugs that treat chronic conditions and lifestyle issues.

(2) Bacteria are developing resistance against antibiotics

Dr. T.P. Singh and his group have demonstrated that peptidoglycan recognition proteins (PGRPs) have the potential to bind to cell wall molecules of bacteria and then kill them. PGRPs can thus be used as an alternative to antibiotics. Dr. Mukul Das, Chairman Organizing Committee proposed the vote of thanks.

WORLD ENVIRONMENT DAY CELEBRATED AT IITR

On the occasion of World Environment Day Dr K.C. Gupta, Director IITR welcoming the guest

Prof. Ganesh Pandey giving prize to a winner of poster painting competition

World Environment Day was celebrated at CSIR-Indian Institute of Toxicology Research (IITR), Lucknow on June 5, 2013. While welcoming the guests, Prof. V.S. Chauhan, Director, International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi and Prof. Ganesh Pandey, Director, Centre for Biomedical Magnetic Resonance (CBMR), SGPGI, Lucknow, Dr. K.C. Gupta, Director, IITR said that ancient wisdom says that one should live in close harmony with Mother Nature and should use the natural resources judiciously. World Environment Day thus symbolizes the occasion of valuing natural wealth and reminds us of revisiting the environmental issues. He further said that CSIR-IITR with its motto "Safety to Environment and Health and Service to Industry" has recently taken an initiative to determine the impact of nanomaterial and nanotechnology products on environment and human health. Dr. Poonam Kakkar, Chief Scientist, IITR gave the genesis of the Dr. C.R. Krishna Murti Memorial oration and introduced the chief guest, Prof. V.S. Chauhan to the audience. In his oration

Goup photograph with poster painting competition winners

entitled "Designed peptide nanosystems: vehicles for targeted and tumor drug delivery", Prof. V.S. Chauhan said that the molecular self-assembly has emerged as a marvelous strategy to construct ensemble of nanomaterials with desired properties. The use of peptides as the building blocks for self assembly offers the ease of design and synthesis, provides the possibility of engineering bio-functionality and biocompatibility into materials making them worthy candidates for potential biological applications. He further said that his work mainly focuses on the synthesis, characterization and potential applications of small self-assembled peptide nanosystems for targeted and effective tumor delivery. Their group has shown that the dipeptides containing the conformational restricting residue α, β-dehydrophenylalanine (ΔPhe), either alone or in hybrid form with small bimolecules (chitosan, cholesterol, small lipids), could self-assemble into nanovesicular, nanotubular or nanogel like structures. Nanostructures could encapsulate various hydrophobic or hydrophilic bioactive molecules as well as important anticancer drugs like doxorubicin, mitoxantrone, curcumin, depending on the constituent dipeptide. These are non-cytotoxic with high cellular uptake. Anticancer drug loaded dipeptide nanostructures showed enhanced toxicity towards cancerous cell lines as compared to free drug molecules. Dipeptide nanostructures could be easily functionalized with different ligands suitable for targeted drug delivery. Folic acid functionalized dipeptide nanostructures showed improved bioavailability and enhanced tumor accumulation and regression in animal tumor models. Prof. V.S. Chauhan released the report on "Assessment of ambient air quality of Lucknow city during pre-monsoon, 2013". A summary of the report is follows:

The study was carried out during the months of March-May, 2013 to assess the status of air quality by monitoring and assessment of some selected air pollutants namely Respirable Particulate Matter (RSPM or PM_{10}), Sulphur dioxide (SO_2), Oxides of Nitrogen (NOx) and Trace metals-Lead (Pb) and Nickel (Ni) and noise level at 9 representative locations, categorized as residential (four), commercial (four) and industrial (one) areas in Lucknow city. The results revealed the 24 hours concentration of PM_{10} to be in the range of 111.6 to 326.7 μg/m^3 with an average of 221.0 μg/m^3. The average values of PM_{10} irrespective of locations were found to be above the permissible limit (100 μg/m^3 prescribed by MoEF). Twenty four hours concentration of SO_2 and NOx were found in the range of 13.2 to 32.9 and 26.8 to 68.5 μg/m^3 with an average concentration of 20.4 and 47.7 μg/m^3 respectively and all the values were below the permissible limits (80 μg/m^3). The mean level of trace metals namely Ni and Pb were 17.7 and 233.5 ng/m^3. Noise levels during day and night time were found in the range of 63.8 to 71.57 dB (A) and 55.9 to 67.4 dB (A) which was above the respective permissible limits except in industrial area.

Lighter moments

Prof. Ganesh Pandey, Director, Centre for Biomedical Magnetic Resonance (CBMR), SGPGI, Lucknow, in his presidential address said that this year the theme for World Environment Day is "Think, eat and save". Think, Eat and Save is an anti-food waste and food loss campaign that encourages us to reduce our food print. Given this enormous imbalance in lifestyles and the resultant devastating effects on the environment, this year's theme – Think.Eat.Save – encourages us to become more aware of the environmental impact of the food choices we make and empowers us to make informed decisions. He further said that we should make the public at large aware of the importance of a cleaner environment by initiating this campaign in the neighbourhood and finally spreading this message to the entire city of Lucknow. A poster painting competition was organized on June 03, 2013. Prof. Ganesh Pandey awarded the trophies and certificates to the winners of the competition. Mr. AH Khan proposed the vote of thanks.

CONFERENCES/WORKSHOPS

International Conference on "Advances in Free Radicals, Redox Signaling and Translational Antioxidant Research" and 12th Annual meeting of Society for Free Radical Research, India.

The International Conference on "Advances in Free Radicals, Redox Signaling and Translational Antioxidant Research" and XII Annual Meeting of the Society for Free Radical Research-India was organized by CSIR-IITR. It was inaugurated at Hotel Clarks Awadh by Dr. Sanjeev Misra, Director, All India Institute of Medical Sciences, Jodhpur on January 30, 2013. In his welcome address Dr. K.C. Gupta, Director, IITR welcomed Dr. Sanjeev Misra, Chief guest of the function; Dr. T.P.A. Devasagayam,

Prof. Sanjiv Misra, Director AIIMS, Jodhpur, Dr K.C. Gupta, Director, CSIR-IITR and Padmashri Dr Nityanand lighting the lamp During inaugural function

President of the Society for Free Radical Research(SFRR)-India; Prof. Young Joon Surh, President, SFRR-Korea. He expressed his delight to see a large congregation of an international community of approximately 350 Free Radical biologists representing 14 countries. He said that while IITR scientists are involved in a variety of programmes pertaining to free radical biology but one particular area that needs a mention is Nanotherapeutics and Nanomaterial toxicology. He further said that in the area of nano-material toxicology, IITR Scientists have shown involvement of free radicals at cellular and sub-cellular levels. He was optimistic that the conference will provide an excellent opportunity for scientists and young researchers in the field for sharing recent developments and innovations along with emerging challenges. While addressing the gathering, Dr. T.P.A. Devasagayam,

Release of the Souvenir of the conference

President SFRR-India said that it is indeed a proud moment for SFRR-India which has completed 12 years of its existence, from a very humble beginning. He appealed to all participants to fully utilize the presence of experts in their area of research for developing contacts and mutually beneficial collaborations.

In his address, Dr. Sanjeev Misra, Director, AIIMS Jodhpur said that as a clinician he is aware that free radicals themselves being unstable incomplete molecules will not rest until they have acquired the missing link. They not only damage a cell to attain their rest full state, but in the advent damage the DNA creating a seat for disease. Cellular oxidative stress disturbs the pro-oxidant-antioxidant balance which leads to potential cellular damage. Their importance is now being recognized in health and disease from new born to geriatric age group.

Session in progress during the conference

Dr K.C. Gupta presenting memento to Prof. Young-Joon Surh

Dr Tobias Stoeger expressing his views about the conference

Dr. Sanjeev Misra released the abstract book. Prof. Young-Joon Surh, welcomed the guests on behalf of SFRR-Korea and released the souvenir of the conference. Dr. Poonam Kakkar, Organizing Secretary & Chief Scientist, CSIR-IITR, thanked the delegates for their participation and encouraged young researchers to avail this opportunity to interact with experts in the area. During all the three days of the conference there were 3 parallel sessions each along with poster presentations. The major areas covered during these sessions were:

i. Cellular and molecular mechanisms involving oxidative stress
ii. Natural and synthetic compounds as modulators of redox signaling
iii. Oxidative damage to macromolecules
iv. Redox mechanism in vascular signalling
v. Translational antioxidant research
vi. Oxidative stress in Cancer
vii. Black tea and health
viii. Nanomaterial toxicology
ix. Redox homeostasis & epigenetics in diseases
x. Angiogenesis
xi. Mitochondrial dysfunction and oxidative stress
xii. Radio-protectors, nutraceuticals & antioxidants
xiii. Free radicals and environmental insults
xiv. Oxidative stress in neurological disorders
xv. Young scientist colloquia
xvi. Nanoparticles and oxidative stress
xvii. Free radicals and inflammation
xviii. Biomarkers of oxidative stress
xix. Plant antioxidants
xx. Oxidative stress and redox signalling in diseases
xxi. Oxidative stress and redox signalling in diabetes

The Valedictory function was held on Feb 1, 2013 where Dr C.M. Gupta, Former Director of CSIR-CDRI and CSIR-IMTECH was the chief guest. In his valedictory address Dr Gupta highlighted the significance of free radical mechanisms in disease and stress conditions. He also spoke on the importance of antioxidants in the management of life style related disorders. Dr K.C. Gupta, Director, CSIR-IITR and chairman of the organizing committee expressed pleasure on the successful organization of the conference, its scientific content and applauded the team work put in by different committees. The awards were given by both Dr C.M. Gupta and Dr K.C. Gupta. There were 3 awards given for each poster session (total 9); three travel awards and 3 Young Investigator awards. Dr Tobias Stoeger, Group Leader, Institute of Lung Biology and Disease, Helmholtz Zentrum Munchen, Germany presented his views about the conference. He praised the high quality of research being done in India in the area of Free Radical biology and excellent hospitality provided by the hosts. At the end of the function Dr P. Kakkar, organizing secretary of SFRR STAR 2013 thanked all the participants for their active participation in the scientific sessions and the organizing team for their whole hearted support. The organizing team received standing ovation from the participants.

IITR RESEARCH HIGHLIGHTS

EGFR-mediated Akt and MAPKs signal pathways play a crucial role in patulin-induced cell proliferation in primary murine keratinocytes via modulation of Cyclin D1 and COX-2 expression.

[Alam S, Pal A, Kumar R, Dwivedi PD, Das M, Ansari KM. Mol Carcinog. 2013 Jun 29. doi: 10.1002/mc.22060. (Epub ahead of print)]

Patulin (PAT), a present day major contaminant of commercial apple and apple products is reported to be carcinogenic, embryotoxic, and immunotoxic. While oral and inhalation are considered to be the most prevalent routes of exposure to this toxin, exposure through skin is now being extensively investigated. Previous study showed that short-term dermal exposure to PAT resulted in toxicological injury to the skin, while long-term exposure induced skin tumorigenesis. In this study, authors explore the mechanism involve in proliferation of mouse keratinocytes by PAT. This study revealed that PAT rapidly induces phosphorylation of EGFR, activation of the Ras/MAPKs, and Akt pathways. This in-turn leads to the activation of NF-κB/AP-1 transcription factors which then binds to the promoter region of the cell growth regulatory genes Cyclin D1 and COX-2 inducing their expression leading ultimately to PMKs proliferation. Inhibition of EGFR or the Ras/MAPKs, PI3/Akt pathways with different pharmacological inhibitors or knockdown of NF-κB, c-jun, c-fos, Cyclin D1, and COX-2 with siRNA inhibited PAT-induced PMKs proliferation.

Role of type-II pathway in apoptotic cell death induction by photosensitized CDRI-97/78 under ambient exposure of UV-B.

[Dwivedi A, Pal MK, Tripathi AK, Yadav N, Mujtaba SF, Pant MC, Singh SK, Mishra DP, Ray RS, Prabhu BH. Toxicol Lett. 2013 Jun 13. pii: S0378-4274(13)01072-2.]

Novel trioxane 97/78, developed by Central Drug Research Institute (CDRI), Lucknow has shown promising antimalarial activity. Clinical experience of anti-malarial drugs registered the occurrence of phototoxicity in patients exposed with sunlight subsequent to medication. Photodegradation study has identified one photo-product up to 4h under UV-B/Sunlight by LC-MS/MS. UV-B irradiated 97/78 compound produced 1O2 via type-II dependent reaction mechanism, corroborated by its specific quencher. 2'-dGua degradation and % tail development in photochemical as well as comet test, advocated the genotoxic potential of 97/78. The photo-cytotoxicity assays (MTT and NRU) on HaCaT cell line revealed the considerable decline in cell viability by 97/78. Cell cycle and AnnexinV/PI double stain along with AO/EB demonstrated the G2/M phase arrest and apoptosis. Significant caspase-3 activity was measured in photoexcited 97/78 by colorimetric assay. Fluorescence stain with AO/JC-1 confirmed the Lysosomal disruption and mitochondrial membrane destabilization by UV-B irradiated 97/78. Gene expression by RT-PCR showed significant upregulation of p21 and pro-apoptotic Bax, but no change observed in Bcl-2. In conclusion, the study highlights ROS mediated DNA damage, lysosomal and mitochondrial destabilization via upregulation of Bax and activation of caspase-3 which further leads to apoptosis.

Simultaneous derivatisation and preconcentration of parabens in food and other matrices by isobutyl chloroformate and dispersive liquid-liquid microextraction followed by gas chromatographic analysis.

[Jain R, Mudiam MK, Chauhan A, Ch R, Murthy RC, Khan HA. Food Chem. 2013 Mar 14.doi: 10.1016/j.foodchem.2013.03.012. (Epub ahead of print)].

A simple, rapid and economical method has been proposed for the quantitative determination of parabens (methyl, ethyl, propyl and butyl paraben) in different samples (food, cosmetics and water) based on isobutyl chloroformate (IBCF) derivatisation and preconcentration using dispersive liquid-liquid microextraction in single step. Under optimum conditions, solid samples were extracted with ethanol (disperser solvent) and 200µL of this extract along with 50µL of chloroform (extraction solvent) and 10µL of IBCF was rapidly injected into 2mL of ultra-pure water containing 150µL of pyridine to induce formation of a cloudy state. After centrifugation, 1µL of the sedimented phase was analysed using gas chromatograph-flame ionization detector (GC-FID) and the peaks were confirmed using gas chromatograph-positive chemical ionization-mass spectrometer (GC-PCI-MS). Method was found to be linear over the range of 0.1-10µgmL(-1) with square of correlation coefficient (R(2)) in the range of 0.9913-0.9992. Limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.029-0.102µgmL(-1) and 0.095-0.336µgmL(-1) with a signal to noise ratio of 3:1 and 10:1, respectively.

Predicting acute aquatic toxicity of structurally diverse chemicals in fish using artificial intelligence approaches.

[Singh KP, Gupta S, Rai P. Ecotoxicol Environ Saf. 2013

Jun 12. doi: 10.1016/j.ecoenv.2013.05.017. (Epub ahead of print)]

The research aims to develop global modeling tools capable of categorizing structurally diverse chemicals in various toxicity classes according to the EEC and European Community directives, and to predict their acute toxicity in fathead minnow using set of selected molecular descriptors. Accordingly, artificial intelligence approach based classification and regression models, such as probabilistic neural networks (PNN), generalized regression neural networks (GRNN), multilayer perceptron neural network (MLPN), radial basis function neural network (RBFN), support vector machines (SVM), gene expression programming (GEP), and decision tree (DT) were constructed using the experimental toxicity data. Diversity and non-linearity in the chemicals' data were tested using the Tanimoto similarity index and Brock-Dechert-Scheinkman statistics. Predictive and generalization abilities of various models constructed here were compared using several statistical parameters. PNN and GRNN models performed relatively better than MLPN, RBFN, SVM, GEP, and DT. Both in two and four category classifications, PNN yielded a considerably high accuracy of classification in training (95.85 percent and 90.07 percent) and validation data (91.30 percent and 86.96 percent), respectively. GRNN rendered a high correlation between the measured and model predicted -log LC_{50} values both for the training (0.929) and validation (0.910) data and low prediction errors (RMSE) of 0.52 and 0.49 for two sets. Efficiency of the selected PNN and GRNN models in predicting acute toxicity of new chemicals was adequately validated using external datasets of different fish species (fathead minnow, bluegill, trout, and guppy). The PNN and GRNN models showed good predictive and generalization abilities and can be used as tools for predicting toxicities of structurally diverse chemical compounds.

Tributyltin induces oxidative damage, inflammation and apoptosis via disturbance in blood-brain barrier and metal homeostasis in cerebral cortex of rat brain: An *in vivo* and *in vitro* study.

[Mitra S, Gera R, Siddiqui WA, Khandelwal S. Toxicology. 2013 Jun 3; 310 C: 39-52.]

Tributyltin (TBT), a member of the organotin family, is primarily used for its biocidal activity. Persistent environmental levels of TBT pose threat to the ecosystem. Since neurotoxic influence of TBT remains elusive, authors therefore, studied its effect on cerebral cortex of male Wistar rats. A single oral dose of Tributyltin-Chloride (TBTC) (10, 20, 30mg/kg) was administered and the animals were sacrificed on day 3 and day 7. Blood-brain barrier permeability remained disrupted significantly till day 7 with all the doses of TBTC. Pro-oxidant metal levels (Fe, Cu) were increased with a concomitant decrease in Zn. ROS generation was substantially raised resulting in oxidative damage (increased protein carbonylation and lipid peroxidation) with marked decline in tissue antioxidant status (GSH/GSSG levels). Protein expression studies indicated astrocyte activation, upregulation of inflammatory molecules (IL-6, Cox-2 and NF-κB) and simultaneous elevation in the apoptotic index (Bax/Bcl2). Neurodegeneration was evident by reduced neurofilament expression and increased calpain cleaved Tau levels. The *in-vitro* study demonstrated involvement of calcium and signaling molecules (p38), with downstream activation of caspase-3 and -8, and apoptotic cell death was evident by nuclear fragmentation, DNA laddering and Annexin V binding experiments. Ca^{2+} inhibitors (BAPTA-AM, EGTA, and RR) and free radical scavengers (NAC and biliprotein [C-PC]) increased cell viability (MTT assay), signifying specific roles of Ca^{2+} and ROS. Significance of p38 signaling was evaluated on pro-apoptotic proteins by using SB203580, a selective p38 inhibitor. This data collectively illustrates that TBTC can disrupt BBB, induce oxidative stress, cause cell death and initiate neurodegeneration in rat brain.

Polycyclic aromatic hydrocarbons and their quinones modulate the metabolic profile and induce DNA damage in human alveolar and bronchiolar cells.

[Gurbani D, Bharti SK, Kumar A, Pandey AK, Ana GR, Verma A, Khan AH, Patel DK, Mudiam MK, Jain SK, Roy R, Dhawan A. Int J Hyg Environ Health. 2013 May 9. doi: 10.1016/j.ijheh.2013.04.001. (Epub ahead of print).]

The release of particulate pollutants into the air through burning of coal, crude oil, diesel, coal tar, etc. raises concerns of potential health hazards to the exposed human population. Polycyclic aromatic hydrocarbons (PAHs) are major toxic constituents of particulate matter (PM), which upon ingestion get metabolized to even more toxic metabolites such as quinones. The PAHs levels were assessed in both respirable particulate matter (RSPM, <10μM size) and suspended particulate matter (SPM, >10μM size) of urban ambient air (UAA) and that of major contributors viz. diesel exhaust particles (DEPs) and coal tar combustions emissions (CTCE). Seven US Environmental Protection Agency (USEPA) prioritized PAHs in RSPM and 10 in SPM were detected in UAA. Ten and 15 prioritized PAHs, respectively, were also detected in diesel exhaust particles (DEP) and coal tar combustion emission (CTCE) evidencing their release in the air. These PM associated PAHs for UAA, DEP and CTCE showed significant increase ($p<0.05$) in mutagenicity and

mammalian genotoxicity in the order CTCE>DEP>UAA. Human lung alveolar (A549) and bronchiolar (BEAS-2B) cells when treated with PAH-metabolites viz. 1,4-benzoquinone (1,4-BQ), hydroquinone (HQ), 1,2-naphthoquinone (1,2-NQ), 1,4-naphthoquinone (1,4-NQ) and 9,10-phenanthroquinone (9,10-PQ) showed metabolic modulation in these cell lines with significant depletion of principal cellular metabolites viz. NADP, uracil, asparagines, glutamine, and histidine and accumulation of di-methyl amine and beta-hydroxybutyrate, identified using (1)H NMR spectroscopy. These results suggest that PAH-quinones induce genotoxic effects by modulating the metabolic machinery inside the cells by a combined effect of oxidative stress and energy depletion. The data for metabolic profiling of human lung cells could also help in understanding the mechanism of toxicity of other xenobiotics.

Synthesis of PLGA nanoparticles of tea polyphenols and their strong *in vivo* protective effect against chemically induced DNA damage.

[Srivastava AK, Bhatnagar P, Singh M, Mishra S, Kumar P, Shukla Y, Gupta KC. Int J Nanomedicine. 2013 ;8:1451-62.]

In spite of proficient results of several phytochemicals in preclinical settings, the conversion rate from bench to bedside is not very encouraging. Many reasons are attributed to this limited success, including inefficient systemic delivery and bioavailability under *in vivo* conditions. To achieve improved efficacy, polyphenolic constituents of black (theaflavin [TF]) and green (epigallocatechin-3-gallate [EGCG]) tea in poly(lactide-co-glycolide) nanoparticles (PLGA-NPs) were entrapped with entrapment efficacy of ~18% and 26%, respectively. Further, their preventive potential against 7,12-dimethylbenzanthracene (DMBA)-induced DNA damage in mouse skin using DNA alkaline unwinding assay was evaluated. Pretreatment (topically) of mouse skin with either TF or EGCG (100 µg/mouse) doses exhibits protection of 45.34% and 28.32%, respectively, against DMBA-induced DNA damage. However, pretreatment with TF-loaded PLGA-NPs protects against DNA damage 64.41% by 1/20th dose of bulk, 71.79% by 1/10th dose of bulk, and 72.46% by 1/5th dose of bulk. Similarly, 51.28% (1/20th of bulk), 57.63% (1/10th of bulk), and 63.14% (1/5th of bulk) prevention was noted using EGCG-loaded PLGA-NP doses. These results showed that tea polyphenol-loaded PLGA-NPs have ~30-fold dose-advantage than bulk TF or EGCG doses. Additionally, TF- or EGCG-loaded PLGA-NPs showed significant potential for induction of DNA repair genes (XRCC1, XRCC3, and ERCC3) and suppression of DNA damage responsive genes (p53, p21, MDM2, GADD45α, and COX-2) as compared with respective bulk TF or EGCG doses. Taken together, TF- or EGCG-loaded PLGA-NPs showed a superior ability to prevent DMBA-induced DNA damage at much lower concentrations, thus opening a new dimension in chemoprevention research.

Anomalies in ovary following oral exposure to oxytocin: Mechanistic studies.

[Mishra M, Mishra V, Chaudhuri BP, Khanna VK, Mehrotra S, Ali S, Das M. Reprod Toxicol. 2013 May 23;40C:24-34.]

Ovarian anomalies following oral oxytocin (OT) (1 and 10ng/100µl) exposure of female Wistar rat pups (10-day old) for 25 days was undertaken as OT injections are illegally used for milk let down in cattle thereby causing oral exposure to human population from early age. OT exposure resulted in increased ovarian weight, γ globulin, total number of follicles, and number of corpus luteum (CLs); indicating higher ovulation. The mechanism may involve over-expression of pEGFR followed by downstream pERK1/2 and subsequently increased ovarian PGE-2 along with enhanced COX-2, HAS-2 & TSG-6 (matrix deposition proteins) and GDF-9 (oocyte factor) proteins, suggesting that oral exposure of OT may affect the physiology and function of the ovary. Further, *in vitro* studies showed increased internalization of OT in IEC-6 cells which further supports that orally administered OT may cause altered manifestations as shown above following internalization in mucosal membrane.

An integrated (nano-bio) technique for degradation of γ-HCH contaminated soil.

[Singh R, Manickam N, Mudiam MK, Murthy RC, Misra V. J Hazard Mater. 2013 Apr 17. doi: 10.1016/j.jhazmat.2013.04.016. (Epub ahead of print).]

Authors have evaluated the effect of an integrated (nano-bio) technique involving the use of stabilized Pd/Fe(0) bimetallic nanoparticles (CMC-Pd/nFe(0)) and a Sphingomonas sp. strain NM05, on the degradation of γ-HCH in soil. Factors affecting degradation such as pH, incubation temperature and γ-HCH initial concentration were also studied. The results revealed that γ-HCH degradation efficiency is ~ 1.7-2.1 times greater in integrated system as compared to system containing either NM05 or CMC-Pd/nFe(0) alone. The integration showed synergistic effect on γ-HCH degradation. Further, cell growth studies indicated that NM05 gets well acclimatized to nanoparticles, showing potential growth in the presence of CMC-Pd/nFe(0) with respect to control system. This study signifies the potential efficacy of integrated technique to become an effective alternative remedial tool for γ-HCH contaminated soil. Further research in this direction could lead to the development of

effective remediation strategies for other isomers of HCH and other chlorinated pesticides as well.

Seasonal variations in cholinesterase activity, nerve conduction velocity and lung function among sprayers exposed to mixture of pesticides.

[Pathak MK, Fareed M, Srivastava AK, Pangtey BS, Bihari V, Kuddus M, Kesavachandran C. Environ Sci Pollut Res Int. 2013 May 1. doi:10.1007/s11356-013-1743-5 (Epub ahead of print)]

Pesticide spraying operation is associated with the increased risk of adverse health effects among sprayers who do not follow safe farm work practices. A study was conducted among pesticide sprayers in North India to evaluate the clinical and subclinical variations in their vital health parameters before and after the pesticide spraying season. Blood cholinesterase levels, pulmonary function test, nerve conduction velocity and self-reported symptoms were studied among 18 eligible and consenting male sprayers. Mean acetylcholinesterase activity was reduced by 55 % in the post-exposure assessment ($P<0.001$) as compared to pre-exposure levels. Mean forced expiratory volume in 1 s was 20 % lower in the post-exposure assessment as compared to the pre-exposure level ($P<0.05$). No significant change was observed in the motor and sensory nerve conduction velocity in the median nerve of sprayers before and after the spraying activity. Also, no significant variation was observed with respect to self-reported symptoms except weakness in arms and legs ($P<0.05$). The significant decline in lung function and acetylcholinesterase level after pesticide exposure reflects the strongly negative effect of exposure to pesticides during spraying activity. More longitudinal studies among pesticide sprayers must be undertaken to further substantiate the cause-effect relationship between pesticide exposure and its subclinical effects. There is a strong necessity to minimise the exposure through the use of personal protective equipment in pesticide sprayers.

Transcriptomic analysis provides insights on hexavalent chromium induced DNA double strand breaks and their possible repair in midgut cells of *Drosophila melanogaster* larvae.

[Mishra M, Sharma A, Shukla AK, Pragya P, Murthy RC, de Pomerai D, Dwivedi UN, Chowdhuri DK. Mutat Res. 2013 Apr 27. doi: 10.1016/j.mrfmmm.2013.04.005. (Epub ahead of print).]

Hexavalent chromium [Cr(VI)] is a well known mutagen and carcinogen. Since genomic instability due to generation of double strand breaks (DSBs) is causally linked to carcinogenesis, authors tested a hypothesis that Cr(VI) causes *in vivo* generation of DSBs and elicits DNA damage response. Authors fed repair proficient *Drosophila melanogaster* (Oregon R(+)) larvae Cr(VI) (20.0µg/ml) mixed food for 24 and 48h and observed a significant ($p<0.05$) induction of DSBs in their midgut cells after 48h using neutral Comet assay. Global gene expression profiling in Cr(VI)-exposed Oregon R(+) larvae unveiled mis-regulation of DSBs responsive repair genes both after 24 and 48h. *In vivo* generation of DSBs in exposed Drosophila was confirmed by an increased pH2Av immunostaining along with the activation of cell cycle regulation genes. Analysis of mis-regulated genes grouped under DSB response by GOEAST indicated the participation of non-homologous end joining (NHEJ) DSB repair pathway. They selected two strains, one mutant (ligIV) and another ku80-RNAi (knockdown of ku80), whose functions are essentially linked to NHEJ-DSB repair pathway. As a proof of principle, authors compared the DSBs generation in larvae of these two strains with that of repair proficient Oregon R(+). Along with this, DSBs generation in spn-A and okr [essential genes in homologous recombination repair (HR) pathway] mutants was also tested for the possible involvement of HR-DSB repair. A significantly increased DSBs generation in the exposed ku80-RNAi and ligIV (mutant) larvae because of impaired repair, concomitant with an insignificant DSBs generation in okr and spn-A mutant larvae indicates an active participation of NHEJ repair pathway. The study, first of its kind to our knowledge, while providing evidences for *in vivo* generation of DSBs in Cr(VI) exposed Drosophila larvae, assumes significance for its relevance to higher organisms due to causal link between DSB generation and Cr(VI)-induced carcinogenesis.

Lipoic acid prevents Cr(6+) induced cell transformation and the associated genomic dysregulation.

[Kumar S, Nigam A, Priya S, Bajpai P, Budhwar R. Environ Toxicol Pharmacol. 2013 Mar 14. doi: 10.1016/j.etap.2013.02.016. (Epub ahead of print).]

Investigation of the transcription profile of cells transformed by Cr(6+) *in vivo* was undertaken. The objective was to elucidate genomic changes underlying the mechanism of action of the carcinogenic dose of Cr(6+) and their prevention using metabolic antioxidant lipoic acid (LA). Cr(6+) was administered intraperitoneally to LPS+TPA challenged Swiss albino mice in host mediated cell transformation assay using peritoneal macrophages *in vivo*. The cell transforming potential of Cr(6+) test doses was validated by gain of anchorage independent growth potential in soft agar and loss of Fc receptor on target cells. LA was administered in equimolar

doses. Compared to non-transformed cells, the gene expression profile of transformed cells was found to be dysregulated substantially and in dose dependent manner. Genes showing down regulation were found to be involved in tumour suppression, apoptosis, DNA repair, and cell-cycle. A similar response was noted in the genes pertaining to immune system, morphogenesis, cell-communication, energy-metabolism, and biosynthesis. The co-administration of lipoic acid prevented the transcription dysregulation and cell transformation by Cr(6+) *in vivo*. The influenced pathways seem to be crucial for progression as well as mitigation of Cr toxicity; and their response to LA indicated their critical role in mechanism of anti-carcinogenic action of LA. Results are of importance to mitigate Cr(6+) induced occupational cancer hazard.

Developmental exposure to As, Cd, and Pb mixture diminishes skeletal growth and causes osteopenia at maturity via osteoblast and chondrocyte malfunctioning in female rats.

[Abbas S, Khan K, Khan MP, Nagar GK, Tewari D, Maurya SK, Dubey J, Ansari NG, Bandyopadhyay S, Chattopadhyay N. Toxicol Sci. 2013 Apr 19. doi: 10.1093/toxsci/kft093. (Epub ahead of print).]

Authors studied the effect of metal mixture (MM), comprising As, Cd, and Pb, in developing female rat skeleton from gestation day 5 until postnatal day 60 (P-60). MM resulted in synergistic inhibition in viability and differentiation of osteoblasts *in vitro*, likely induced by reactive oxygen species. MM, administered at their most frequently occurring concentrations present in the groundwater of India, i.e., As: 0.38 ppm, Pb: 0.22 ppm, and Cd: 0.098 ppm or 10× of the ratio to developing rats, exhibited a synergistic decrease in *ex vivo* mineralization of bone marrow stromal (osteoprogenitor) cells. MM group showed a dose-dependent attenuation in weight and axial lengths and shortening of tibias at P-60. Furthermore, the growth plate was shortened, which was associated with shorter proliferative and hypertrophic zones, decreased parathyroid hormone-related protein and Indian hedgehog expression in the chondrocytes, reduced primary and secondary spongiosa, and hypomineralized osteoids-a major characteristic of osteomalacia. In addition, compared with the control, MM-treated rats were clearly osteopenic based on bone mineral density, microarchitecture, biomechanical strength, and particularly the biochemical profile, that suggested high turnover bone loss. Finally, in comparison to the control, the fracture-healing ability of MM group was delayed and accompanied by inferior quality of the healed bone. Together, these data demonstrated that the mixture of As, Cd, and Pb induced synergistic toxicity to developing skeleton, thereby diminishing modeling-directed bone accrual, inducing osteopenia and dampening fracture healing.

Ultra sound assisted one step rapid derivatization and dispersive liquid-liquid microextraction followed by gas chromatography-mass spectrometric determination of amino acids in complex matrices.

[Mudiam MK, Ratnasekhar Ch J Chromatogr A. 2013 May 24; 1291:10-8.]

A rapid and economical method for the simultaneous determination of 20 amino acids in complex biological and food matrices (hair, urine and soybean seed samples) has been developed using ultrasound assisted dispersive liquid-liquid micro extraction (UA-DLLME). The method involves simultaneous derivatization and extraction followed by gas chromatography-mass spectrometric (GC-MS) analysis of amino acids. The parameters of UA-DLLME were optimized with the aid of design of experiments approach. The procedure involves the rapid injection of mixture of acetonitrile (disperser solvent), trichloroethylene (TCE) (extraction solvent) and ethylchloroformate (derivatization reagent) into the aqueous phase of sample extract containing pyridine. The Plackett-Burman design has indicated that, the factors such as volume of disperser and extraction solvents and pH were found to be significantly affects the extraction efficiency of the method. The optimum conditions of these factors based on central composite design were found to be 250µL of acetonitrile, 80µL of TCE and pH of 10. The limit of detection and limit of quantification were found to be in the range of 0.36-3.68µgL(-1) and 1.26-12.01µgL (-1) respectively. This is the first application of DLLME for the analysis of amino acids in any matrices. The advantages like (i) *in situ* derivatization and extraction of amino acids without any prior lyophilization and cleanup of sample, (ii) low consumption of extraction solvent, (iii) fast and simple, (iv) cost-effective and (iv) good repeatability make the method amenable for the routine analysis of amino acids in clinical, toxicological, nutritional and quality control laboratories.

Mitochondrial diseases of the brain.

[Chaturvedi RK, Flint Beal M. Free Radic Biol Med. 2013 Apr 6;63C:1-29.]

Neurodegenerative disorders are debilitating diseases of the brain, characterized by behavioral, motor and cognitive impairments. Ample evidence underpins mitochondrial dysfunction as a central causal factor in the pathogenesis of neurodegenerative disorders including Parkinson's disease, Huntington's disease, Alzheimer's

disease, Amyotrophic lateral sclerosis, Friedreich's ataxia and Charcot-Marie-Tooth disease. In this review, authors discuss the role of mitochondrial dysfunction such as bioenergetics defects, mitochondrial DNA mutations, gene mutations, altered mitochondrial dynamics (mitochondrial fusion/fission, morphology, size, transport/trafficking, and movement), impaired transcription and the association of mutated proteins with mitochondria in these diseases. Authors highlight the therapeutic role of mitochondrial bioenergetic agents in toxin and in cellular and genetic animal models of neurodegenerative disorders. They also discuss clinical trials of bioenergetics agents in neurodegenerative disorders. Lastly, authors shed light on PGC-1α, TORC-1, AMP kinase, Nrf2-ARE, and Sirtuins as novel therapeutic targets for neurodegenerative disorders.

Minocycline, levodopa and MnTMPyP induced changes in the mitochondrial proteome profile of MPTP and maneb and paraquat mice models of Parkinson's disease.

[Dixit A, Srivastava G, Verma D, Mishra M, Singh PK, Prakash O, Singh MP. Biochim Biophys Acta. 2013 Apr 4. doi: 10.1016/j.bbadis.2013.03.019. (Epub ahead of print).]

Mitochondrial dysfunction is the foremost perpetrator of the nigrostriatal dopaminergic neurodegeneration leading to Parkinson's disease (PD). However, the roles played by majority of the mitochondrial proteins in PD pathogenesis have not yet been deciphered. The present study investigated the effects of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and combined maneb and paraquat on the mitochondrial proteome of the nigrostriatal tissues in the presence or absence of minocycline, levodopa and manganese (III) tetrakis (1-methyl-4-pyridyl) porphyrin (MnTMPyP). The differentially expressed proteins were identified and proteome profiles were correlated with the pathological and biochemical anomalies induced by MPTP and maneb and paraquat. MPTP altered the expression of twelve while combined maneb and paraquat altered the expression of fourteen proteins. Minocycline, levodopa and MnTMPyP, respectively, restored the expression of three, seven and eight proteins in MPTP and seven, eight and eight proteins in maneb- and paraquat-treated groups. Although levodopa and MnTMPyP rescued from MPTP- and maneb- and paraquat-mediated increase in the microglial activation and decrease in manganese-superoxide dismutase expression and complex I activity, dopamine content and number of dopaminergic neurons, minocycline defended mainly against maneb- and paraquat-mediated alterations. The results demonstrate that MPTP and combined maneb and paraquat induce mitochondrial dysfunction and microglial activation and alter the expression of a bunch of mitochondrial proteins leading to the nigrostriatal dopaminergic neurodegeneration and minocycline, levodopa or MnTMPyP variably offset scores of such changes.

Singlet oxygen mediated apoptosis by anthrone involving lysosomes and mitochondria at ambient UV exposure.

[Mujtaba SF, Dwivedi A, Yadav N, Ray RS, Singh G J Hazard Mater. 2013 May 15;252-253:258-71.]

Anthrone a tricyclic aromatic hydrocarbon which is toxic environmental pollutant comes in the environment through photooxidation of anthracene. Authors have studied the photomodification of anthrone under environmental conditions. Anthrone generates reactive oxygen species (ROS) like (1)O2 through Type-II photodynamic reaction. Significant intracellular ROS generation was measured through dichlorohydro-fluorescein fluorescence intensity. The generation of (1)O2 was further substantiated by using specific quencher like sodium azide. UV induced photodegradation of 2-deoxyguanosine and photoperoxidation of linoleic acid accorded the involvement of (1)O2 in the manifestation of anthrone phototoxicity. Phototoxicity of anthrone was done on human keratinocytes (HaCaT) through 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide and neutral red uptake assays. Anthrone induced cell cycle arrest (G2/M-phase) and DNA damage in a concentration dependent manner. They found apoptosis as a pattern of cell death which was confirmed through sub-G1 fraction, morphological changes, caspase-3 activation, acridine orange/ethidium bromide staining and phosphatidylserine translocation. Mitochondrial depolarization and lysosomal destabilization was parallel to apoptotic process. RT-PCR results strongly supports authors view point of apoptotic cell death through up-regulation of pro-apoptotic genes p21 and Bax, and down regulation of anti-apoptotic gene Bcl2. Therefore, much attention should be paid to concomitant exposure of anthrone and UV-R for its total environmental impact.

Molecularly imprinted SPE combined with dispersive liquid-liquid microextraction for selective analysis of telmisartan in biological and formulation samples.

[Mudiam MK, Chauhan A, Singh AK, Sharma VP, Saxena PN. Bioanalysis. 2013 Apr;5(7):847-58.]

The present communication describes the combination of molecularly imprinted SPE and dispersive liquid-liquid microextraction for the selective preconcentration and determination of telmisartan (TEL) in rat urine, plasma and pharmaceutical formulation by HPLC. Various factors

that can affect the extraction efficiency of molecularly imprinted SPE and dispersive liquid-liquid microextraction were optimized. The LOD and LOQ were found to be 0.19 and 0.63 µg ml(-1) in urine, while in plasma it was found to be 0.28 and 0.87 µg ml(-1), respectively. The percentage recovery of TEL in different matrices was found to be in the range of 81-97%. The proposed method may find wide applications in clinical, toxicological and QC laboratories for the routine analysis of TEL.

In matrix derivatization of trichloroethylene metabolites in human plasma with methyl chloroformate and their determination by solid-phase microextraction-gas chromatography-electron capture detector.

[Mudiam MK, Jain R, Varshney M, Ch R, Chauhan A, Goyal SK, Khan HA, Murthy RC J Chromatogr B Analyt Technol Biomed Life Sci. 2013 Apr 15;925:63-9.]

Trichloroethylene (TCE) is a common industrial chemical that has been widely used as metal degreaser and for many industrial purposes. In humans, TCE is metabolized into dichloroacetic acid (DCA), trichloroacetic acid (TCA) and trichloroethanol (TCOH). A simple and rapid method has been developed for the quantitative determination of TCE metabolites. The procedure involves the *in situ* derivatization of TCE metabolites with methyl chloroformate (MCF) directly in diluted plasma samples followed by extraction and analysis with solid-phase microextraction (SPME) coupled to gas chromatography-electron capture detector (GC-ECD). Factors which can influence the efficiency of derivatization such as amount of MCF and pyridine (PYR), ratio of water/methanol were optimized. The factors which can affect the extraction efficiencies of SPME were screened using 2(7-4) Placket-Burman Design (PBD). A central composite design (CCD) was then applied to further optimize the most significant factors for optimum SPME extraction. The optimum factors for the SPME extraction were found to be 562.5mg of NaCl, pH at 1 and an extraction time of 22 min. Recoveries and detection limits of all three analytes in plasma were found to be in the range of 92.69-97.55% and 0.036-0.068 µg mL(-1) of plasma, respectively. The correlation coefficients were found to be in the range of 0.990-0.995. The intra- and inter-day precisions for TCE metabolites were found to be in the range of 2.37-4.81% and 5.13-7.61%, respectively. The major advantage of this method is that MCF derivatization allows conversion of TCE metabolites into their methyl esters in very short time ($\leqslant$ 30 s) at room temperature directly in the plasma samples, thus makes it a solvent less analysis. The method developed was successfully applied to the plasma samples of humans exposed to TCE.

Dysregulation of pathways involved in the processing of cancer and microenvironment information in MCA + TPA transformed C3H/10T1/2 cells.

[Priya S, Nigam A, Bajpai P, Kumar S. In vitro Cell Dev Biol Anim. 2013 Apr;49(4):295-305.]

The two-stage cell transformation assay is an *in vitro* model cell culture system to identify the ability of chemicals to act as initiators or promoters of cell transformation and also to study the cellular and molecular mechanisms of chemically induced morphological and neoplastic cell transformation. The global gene expression profiles of 3-methylcholanthrene (MCA) + 12-O-tetradecanoylphorbol-13-acetate (TPA)-transformed C3H/10T1/2 cells are not known. Therefore, authors have investigated the global transcriptional profile of MCA + TPA-transformed C3H10T1/2 cells using an 8 × 60 k probe microarray. The study revealed a differential regulation of pathways and gene expressions. Multifold dysregulation was seen in pathways of cancer, phagosomal activity, and tumor cell microenvironment information processing systems, notably the neuroactive ligand-receptor interaction, actin cytoskeleton regulation, tight junction, axon guidance, and cell adhesion molecules. The genes FGF1, EIF4E1B, MAGI1, and GRIA3 showed upregulation; these encoded the pluripotent fibroblast growth factor, the translation initiation factor, the tight junction scaffolding protein, and the antiapoptotic as well as the enhancer of proliferation and migration, respectively. The genes CXCL7/CXCL5/CXCL12, H2DMB1, and HSPA1A showed downregulation; these encoded the chemotactic agent protein, the protein involved in MHC class II antigen processing/presentation or participating in cell adhesion/phagosomal activity/autoimmune disorder, and the chaperone protein stabilizing the existing as well as newly translated cytosolic/organelle proteins against aggregation, respectively. By loss or gain of function, these dysregulated genes apparently seem to reprogram cells for apoptosis or proliferation and support their transformation into the tumor cell phenotype. The observed molecular changes can be seen as molecular signatures of transformed cells and can be of use as objective evidences to C3H/10T1/2 cell transformation assay in investigations on the carcinogenic potential of chemicals and their mechanism of actions using *in vitro* carcinogenesis method.

All India survey for analyses of colors in sweets and savories: exposure risk in Indian population.

[Dixit S, Khanna SK, Das M. J Food Sci. 2013 Apr;78(4):T642-7.]

In the present study, an attempt has been made to understand the exposure assessment of food colors through 2 major groups, sweets and savories, at a national level so as to evolve a scientific yardstick to fix levels of colors in commodities based on technological and safety requirement. A vast majority of colored food commodities (83.6%) were found to employ permitted colors and confirmed a marked decline in the trend of use of non permitted colors (NPCs). Of the 4 zones of India, East zone showed the maximum adulteration (80.3%) both by exceeding the prescribed limits of permitted colors (72.3%) and the use of NPCs (28.7%). Tartrazine was the most popular color among the permitted list, which ranged from 12.5 to 1091 mg/kg. Rhodamine B was the most prevalent dye in the NPCs group. On the basis of average consumption of food commodities and average levels of detected colors, the intake of Sunset Yellow FCF saturates the acceptable daily intake limit to a maximum of 47.8% in children, which is a cause of concern. The uniform maximum permissible limit of synthetic colors at 100 mg/kg under the Indian rules thus needs to be reviewed and should rather be governed by the technological necessity and the consumption profiles of food commodities so that the vulnerable population should not unnecessary be exposed to excessive amounts of synthetic colors to pose health risks.

Imprinting of cerebral and hepatic cytochrome p450s in rat offsprings exposed prenatally to low doses of cypermethrin.

[Singh A, Yadav S, Srivastava V, Kumar R, Singh D, Sethumadhavan R, Parmar D. Mol Neurobiol. 2013 Feb 28. Doi: 10.1007/s12035-013-8419-5 (Epub ahead of print)]

Oral administration of low doses (1.25 or 2.5 or 5 mg/kg) corresponding to 1/200th or 1/100th or 1/50th of LD50 of cypermethrin, a synthetic type II pyrethroid, to pregnant Wistar rats from gestation day 5 to 21 produced a dose-dependent increase in the expression of xenobiotic metabolizing cytochrome P450 (CYP) 1A-, 2B- and 2E1 in the brain and liver of offsprings postnatally at 3 weeks that persisted up to 12 weeks. This persistent increase in CYPs was associated with alterations in circulating concentrations of testosterone, luteinizing hormone and follicle stimulating hormone, spontaneous locomotor activity and accumulation of cypermethrin in the brain of exposed offsprings. Rechallenge of exposed offsprings at adulthood (12 weeks old) with cypermethrin (p.o., 10 mg/kg × 6 days) led to a much higher increase in the expression of CYPs in the exposed offsprings when compared to the control offsprings treated with cypermethrin. Further, bioinformatic analysis demonstrating absence of specific short interspersed elements in CYPs suggests that persistence in the increase in CYPs in exposed offsprings could be attributed to the imprinting of the cerebral and hepatic CYPs following prenatal exposure to low doses of cypermethrin. This imprinting could be of toxicological relevance as it may modify the response of drugs or environmental exposures in exposed offsprings particularly for those chemicals which require CYP-mediated metabolism to produce their beneficial or toxic effects.

Temporal distribution of fine particulates ($PM_{2-5}PM_{10}$), potentially toxic metals, PAHs and Metal-bound carcinogenic risk in the population of Lucknow City, India.

[Pandey P, Patel DK, Khan AH, Barman SC, Murthy RC, Kisku GC. J Environ Sci Health A Tox Hazard Subst Environ Eng. 2013;48 (7):730-45.]

Ubiquitous fine particulates can readily be bound to toxic metals and polycyclic aromatic hydrocarbons and are considered to be a great threat to human health. The purpose of this study was to assess the magnitude of air pollution risks to public health by determining four crucial parameters- inhalable particulates, metals in particulates and PAHs which are associated with PM_{10} in the air environment of Lucknow, India during 2007-09. The values of PM_{10} and PM_{2-5} ranged between 102.3-240.5 and 28.0-196.9 µg/m³ whilst the average PM_{10} was 1.7 times and PM was 1.5 times higher than their respective NAAQS of 100 and 60 µg/m³ respectively. The estimated relative death rate and hospital admissions for each increase in the PM_{10} levels of 10 µg/m³ ranged from 1.5-8% and from 3.9-8.0% (as per APHEA2 1990) respectively in persons > 65 yrs. Among the locations; AQ, AQ and AQ (with diversified activities and heavy traffic) recorded higher concentrations of both the particulate fractions than the AQ (residential area with low traffic). The average concentrations of Fe, Pb, Ni, Cu, Cr, Cd in PM_{10} were 219.4, 40.6, 35.1, 27.3, 22.2 and 16.2 ng/m³ and that in PM_{2-5} were 54.3, 33.9, 38.5, 29.4, 8.4, and 1.17 ng/m³ respectively Regression analysis revealed that correlation of metals with PM_{2-5} was stronger than PM. The ratio of metals adsorbed on surface of particles (PM_{2-5} :PM_{10}) reveals that PM_{2-5} has more affinity for Ni, Cu and Pb and PM_{10} for Cd, Fe and Cr. Health risk due to carcinogenic metals bound to respirable particulates was predicted by estimating excess cancer risk (ECR). The highest ECR value was estimated for Cr, 266.70×10^6, which was associated with PM10 and 100.92×10^6 which was associated with PM_{2-5}, whereas lead has the lowest

ECR value. Amongst PAHs, benzo(a)pyrene (51.96 ± 19.71 ng/m) was maximum in PM_{10} samples. Maximum concentrations of PM_{10}, PM_{2-5}, metals and PAHs were detected during winter, and the lowest was during monsoon. The higher prevalence of diseases among the population may be due to high concentration of particulates coated with toxic metals and PAHs present in air environment.

Trans-Resveratrol protects ischemic PC12 Cells by inhibiting the hypoxia associated transcription factors and increasing the levels of antioxidant defense enzymes.

[Agrawal M, Kumar V, Singh AK, Kashyap MP, Khanna VK, Siddiqui MA, Pant AB. ACS Chem Neurosci. 2013 Feb 20;4(2):285-94.]

An *in vitro* model of ischemic cerebral stroke [oxygen-glucose deprivation (OGD) for 6 h followed by 24 h reoxygenation (R)] with PC12 cells increases Ca(2+) influx by upregulating native L-type Ca(2+) channels and reactive oxygen species (ROS) generation. This reactive oxygen species generation and increase in intracellular Ca(2+) triggers the expression of hypoxic homeostasis transcription factors such as hypoxia induced factor-1 alpha (HIF-1α), Cav-beta 3 (Cav β3), signal transducer and activator of transcription 3 (STAT3), heat shock protein 27 (hsp-27), and cationic channel transient receptor potential melastatin 7 (TRPM7). OGD insulted PC12 cells were subjected to biologically safe doses (5, 10, and 25 μM) of trans-resveratrol in three different treatment groups: 24 h prior to OGD (pre-treatment); 24 h post OGD (post-treatment); and from 24 h before OGD to end of reoxygenation period (whole-treatment). Here, authors demonstrated that OGD-R-induced neuronal injury/death is by reactive oxygen species generation, increase in intracellular calcium levels, and decrease in antioxidant defense enzymes. trans-Resveratrol increases the viability of OGD-R insulted PC12 cells, which was assessed by using MTT, NRU, and LDH release assay. In addition, trans-resveratrol significantly decreases reactive oxygen species generation, intracellular Ca(2+) levels, and hypoxia associated transcription factors and also increases the level of antioxidant defense enzymes. Data shows that the whole-treatment group of trans-resveratrol is most efficient in decreasing hypoxia induced cell death through its antioxidant properties.

Clinical complications of kidney bean (*Phaseolus vulgaris* L.) consumption.

[Kumar S, Verma AK, Das M, Jain SK, Dwivedi PD. Nutrition. 2013 Jun;29(6):821-7.]

Kidney beans (*Phaseolus vulgaris* L.), are common legumes, consumed worldwide. The delicacy of kidney beans is highly appreciable but, at the same time, their toxicity has raised an alarming concern. Kidney bean toxicity may be divided into two subcategories: toxicity caused by its lectins, saponins, phytates, and protease inhibitors or allergenicity induced by its allergenic proteins. The purpose of this review is to unravel the facts behind the different aspects of toxicity and allergenicity induced by kidney beans and try to fill the gaps that exist currently.

The activity against Ehrlich's ascites tumors of doxorubicin contained in self assembled, cell receptor targeted nanoparticle with simultaneous oral delivery of the green tea polyphenol epigallocatechin-3-gallate.

[Ray L, Kumar P, Gupta KC. Biomaterials. 2013 Apr;34(12):3064-76.]

Doxorubicin (DOX) is a well-known anticancer drug used for the treatment of a wide variety of cancers. However, undesired toxicity of DOX limits its uses. To address the issue of minimizing toxicity of DOX by making it targeted towards cancer cells, DOX was entrapped in self-assembled 6-O-(3-hexadecyloxy-2-hydroxypropyl)-hyaluronic acid (HDHA) nanoparticles. Authors hypothesized that by encapsulating the drug in biodegradable nanoparticles, its therapeutic efficacy would improve, if targeted against cancer cells. They synthesized cell receptor targeted, DOX loaded HDHA nanoparticles (NPs) and non-targeted DOX loaded O-hexadecylated dextran (HDD) nanoparticles (NPs) and characterized them for their entrapment efficiency, percent yield, drug load, surface morphology, particle size and *in vitro* drug release. The anticancer efficacy of DOX loaded HDHA-NPs was evaluated by measuring the changes in tumor volumes, tumor weights, and mean survival rate of Swiss albino mice grafted with Ehrlich's ascites carcinoma (EAC) cells. For this, the animals were given HDHA-DOX-NPs (1.5 mg/kg b.wt.) intravenously and a green tea polyphenol, Epigallocatechin-3-gallate (EGCG) (20 mg/kg b.wt.), orally through gavage. The targeted NP dose with EGCG significantly increased mean survival time of the animals and enhanced the therapeutic efficacy of the drug compared to the non-targeted NPs and free DOX. Further, authors showed that these NPs (HDD and HDHA) were more active in the presence of EGCG than DOX alone in inducing apoptosis in EAC cells as evident by an increase in sub-G1 cells (percent), Annexin V positive cells and chromatin condensation along with the reduction in mitochondrial membrane potential (MMP). The study demonstrates that DOX loaded HDHA-NPs along with EGCG significantly inhibit the growth of EAC cells with ~ 38-fold dose

advantage compared to DOX alone and thus opens a new dimension in cancer chemotherapy.

Ambient UVA-induced expression of p53 and apoptosis in human skin melanoma A375 cell line by quinine.

[Yadav N, Dwivedi A, Mujtaba SF, Kushwaha HN, Singh SK, Ray RS. Photochem Photobiol. 2013 May-Jun;89(3):655-64.]

This study aimed to analyze the phototoxic mechanism and photostability of quinine in human skin cell line A375 under ambient intensities of UVA (320-400 nm). Photosensitized quinine produced a photoproduct 6-methoxy-quinoline-4-ylmethyl-oxonium identified through LC-MS/MS. Generation of (1)O2, O2(-), and (˙)OH was measured and further substantiated through their respective quenchers. Photosensitized Quinine (Q) caused degradation of 2-deoxyguanosine, the most sensitive nucleotide to UV radiation. The intracellular ROS was increased in a concentration-dependent manner. Significant reduction in metabolic status measured in terms of cell viability (54%) at 25 µg mL(-1) was observed through MTT assay. Results of MTT assay accord NRU assay. Single strand DNA breaks and apoptosis were increased significantly ($P < 0.01$) as observed through comet assay and EB/AO double staining. Photosensitized quinine caused cells to arrest in G2 phase of cell cycle and induced apoptosis (5.08%) as revealed through FACS. Real-Time PCR showed upregulation of p21 (4.56 folds) and p53 (2.811 folds) genes expression. Thus, this study suggests that generation of reactive oxygen species by quinine under ambient intensity of UVA may result into deleterious phototoxic effects among human population.

Sunset yellow FCF, a permitted food dye, alters functional responses of splenocytes at non-cytotoxic dose.

[Yadav A, Kumar A, Tripathi A, Das M. Toxicol Lett. 2013 Mar 13;217(3):197-204.]

Sunset yellow FCF (SY), a permitted food color, is extensively used in various food preparations and quite often exceeds the permissible levels (100-200 mg/kg). Several toxicity studies on SY are reported, however immunomodulatory properties have not been explored yet. To investigate the immunotoxic properties of SY, splenocytes were isolated, cultured and subjected to mitogen stimulated proliferation assay (lipopolysaccharide, LPS or concanavalin A, Con A), mixed lymphocyte reaction (MLR) assay, immunophenotypic analysis of cell surface receptor expression and assay for cytokines release in the culture supernatants were performed in the presence of SY. Since SY did not exhibit any cytotoxicity up to 250 µg/ml, this dose was used for further studies. It was observed that SY (250 µg/ml) significantly ($p<0.05$) suppressed the mitogen induced proliferation of splenocytes and MLR response. Further, immunophenotypic analysis revealed that SY alters the relative expression of CD3e/CD4/CD8 in T cells and CD19 in B-cells. Consistent with the suppression of T-cell and B-cell responses and altered surface receptor expression, SY also lowered the expression of IL2, IL4, IL6, IL-17, IFN-γ and TNF-α cytokines. These results suggest that non-cytotoxic dose of SY may have immunomodulatory effects.

ACHIEVEMENT

Paper with 1000+ Citations Published in CSIR-NISCAIR Journal

A recent study had revealed that there are 36 papers with at least one author from India that have received 1000 or more citations. As of April 2013, such papers have gone up to 38 with two more Indian papers receiving 1000 or more citations.

Incidentally, out of the 38 papers, there is only one paper that has been published in an Indian journal. All the other papers that have received 1000+ citations have been published in foreign journals. The lone Indian paper published in a CSIR-National Institute of Science Communication and Information Resources (NISCAIR) journal is by P. Kakkar, B. Das and P.N. Viswanathan [A modified spectrophotometric assay of superoxide-dismutase, *Indian Journal of Biochemistry and Biophysics*, **21** (2) (1984) 130-132].

The average IF of all the citing journals is 2.148 and the journal with the highest IF that has cited the article is *Biomaterials* (2 citations, IF 7.404) followed by *International Journal of Cardiology* (3 citations, IF 7.078).

The paper has facilitated estimation of superoxide dismutase, an important antioxidant enzyme whose level is found to be altered in many disease conditions. The method has been used even in laboratories where sophisticated equipments are available.

Dr. Poonam Kakkar
CSIR-IITR

TOPIC OF INTEREST

A Glimpse of Research in The Area of Genetically Modified Crops in India

Evaluation of designer crops for biosafety--a scientist's perspective.

[Mehrotra S, Goyal V. Gene. 2013 Feb 25;515(2):241-8. doi: 10.1016/j.gene.2012.12.029. Epub 2012 Dec 22.]

With the advent of transgenic technology, it has become possible to mobilize and express foreign genes into plants and to design crop varieties with better agronomic attributes and adaptability to challenging environmental conditions. Recent advances in transgenic technology have led to concerns about safety of transgenic crops to human and animal health and environment. Biosafety focuses on preventing, minimizing and eliminating risks associated with the research, production, and use of transgenic crops. Food biosafety involves studies of substantial equivalence related to compositional analysis, toxicity and allergenicity. Environmental biosafety involves glasshouse and field trials and study of unintended effects on non-target organisms. Transgenics are characterized at phenotypic and molecular levels for understanding the location of transgene insertion site, ploidy level, copy number, integrated vector sequences, protein expression and stability of the transgene. Various techniques employed for transgene characterization include flow cytometry, southern, northern and western analyses, real-time (qRT) PCR, competitive PCR, FISH, fiber-FISH, DNA micro-arrays, mRNA profiling, 2DE-MS, iTRAQ, FT-MS, NMR, GC-MS, CE-MS and biosensor-based approaches. Evaluation of transgene expression involves the application of integrated phenomics, transcriptomics, proteomics and metabolomics approaches. However, the relevance and application of these approaches may vary in different cases. The elaborate analysis of transgenic crops will facilitate the safety assessment and commercialization of transgenics and lead to global food security for the future.

Expression of phytochelatin synthase from aquatic macrophyte *Ceratophyllum demersum* L. enhances cadmium and arsenic accumulation in tobacco.

[Shukla D, Kesari R, Mishra S, Dwivedi S, Tripathi RD, Nath P, Trivedi PK. Plant Cell Rep. 2012 Sep;31(9):1687-99. doi: 10.1007/s00299-012-1283-3. Epub 2012 May 22.]

Phytochelatin synthase (PCS), the key enzyme involved in heavy metal detoxification and accumulation has been used from various sources to develop transgenic plants for the purpose of phytoremediation. However, some of the earlier studies provided contradictory results. Most of the PCS genes were isolated from plants that are not potential metal accumulators. In this study, we have isolated PCS gene from *Ceratophyllum demersum* cv. L. (CdPCS1), a submerged rootless aquatic macrophyte, which is considered as potential accumulator of heavy metals. The CdPCS1 cDNA of 1,757 bp encodes a polypeptide of 501 amino acid residues and differs from other known PCS with respect to the presence of a number of cysteine residues known for their interaction with heavy metals. Complementation of cad1-3 mutant of Arabidopsis deficient in PC (phytochelatin) biosynthesis by CdPCS1 suggests its role in the synthesis of PCs. Transgenic tobacco plants expressing CdPCS1 showed several-fold increased PC content and precursor non-protein thiols with enhanced accumulation of cadmium (Cd) and arsenic (As) without significant decrease in plant growth. We conclude that CdPCS1 encodes functional PCS and may be part of metal detoxification mechanism of the heavy metal accumulating plant *C. demersum*.

In silico assessment of the potential allergenicity of transgenes used for the development of GM food crops.

[Mishra A, Gaur SN, Singh BP, Arora N. Food Chem Toxicol. 2012 May;50(5):1334-9. doi: 10.1016/j.fct.2012.02.005. Epub 2012 Feb 14.]

Genetically modified (GM) crops require allergenicity and toxicity assessment of the novel protein(s) to ensure complete safety to the consumers. These assessments are performed in accordance with the guidelines proposed by Codex (2003) and ICMR (2008). The guidelines recommend sequence homology analysis as a preliminary step towards allergenicity prediction, later *in vitro* experiments may be performed to confirm allergenicity. In the present study, an *in silico* approach is employed to evaluate the allergenic potential of six transgenes routinely used for the development of GM food crops. Among the genes studied, manganese superoxide dismutase (MnSOD) and osmotin shares greater than 90% identity with Hev b 10 and Cap a 1w, respectively. Chitinase shares greater than 70% identity with allergens namely Pers a 1 and Hev b 11, and fungal chitinase showed significant IgE binding with 7 of 75 patients' sera positive to different food extracts. Glucanases (alfalfa, wheat) and glycine betaine aldehyde

dehydrogenase gene share 50% homology with allergens like - Ole e 9, Cla h 10 and Alt a 10. The results demonstrate the allergenic potential of six genes and can serve as a guide for selection of transgenes to develop GM crops.

Bt brinjal in India: a long way to go.

[Kumar S, Misra A, Verma AK, Roy R, Tripathi A, Ansari KM, Das M, Dwivedi PD. GM Crops. 2011 Apr-Jun;2(2):92-8. doi: 10.4161/gmcr.2.2.16335. Epub 2011 Apr 1.]

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

Glutathione transferase from *Trichoderma virens* enhances cadmium tolerance without enhancing its accumulation in transgenic *Nicotiana tabacum*.

[Dixit P, Mukherjee PK, Ramachandran V, Eapen S. PLoS One. 2011 Jan 21;6(1):e16360. doi: 10.1371/journal.pone.0016360.]

Cadmium (Cd) is a major heavy metal pollutant which is highly toxic to plants and animals. Vast agricultural areas worldwide are contaminated with Cd. Plants take up Cd and through the food chain it reaches humans and causes toxicity. It is ideal to develop plants tolerant to Cd, without enhanced accumulation in the edible parts for human consumption. Glutathione transferases (GST) are a family of multifunctional enzymes known to have important roles in combating oxidative stresses induced by various heavy metals including Cd. Some GSTs are also known to function as glutathione peroxidases. Overexpression/heterologous expression of GSTs is expected to result in plants tolerant to heavy metals such as Cd. Here, we report cloning of a glutathione transferase gene from *Trichoderma virens*, a biocontrol fungus and introducing it into *Nicotiana tabacum* plants by Agrobacterium-mediated gene transfer. Transgenic nature of the plants was confirmed by Southern blot hybridization and expression by reverse transcription PCR. Transgene (TvGST) showed single gene Mendelian inheritance. When transgenic plants expressing TvGST gene were exposed to different concentrations of Cd, they were found to be more tolerant compared to wild type plants, with transgenic plants showing lower levels of lipid peroxidation. Levels of different antioxidant enzymes such as glutathione transferase, superoxide dismutase, ascorbate peroxidase, guiacol peroxidase and catalase showed enhanced levels in transgenic plants expressing TvGST compared to control plants, when exposed to Cd. Cadmium accumulation in the plant biomass in transgenic plants were similar or lower than wild-type plants. The results of the present study suggest that transgenic tobacco plants expressing a *Trichoderma virens* GST are more tolerant to Cd, without enhancing its accumulation in the plant biomass. It should be possible to extend the present results to crop plants for developing Cd tolerance and in limiting Cd availability in the food chain.

Strategies for elimination of cyanogens from cassava for reducing toxicity and improving food safety.

[Nambisan B. Food Chem Toxicol. 2011 Mar;49(3):690-3. doi: 10.1016/j.fct.2010.10.035. Epub 2010 Nov 11.]

Toxicity of cassava arises due to the presence of the cyanoglucosides linamarin and lotaustralin which are hydrolysed by endogenous enzyme linamarase to acetonecyanohydrin (ACN) and cyanide (CN) which are toxic. Major research efforts to eliminate/reduce cyanoglucosides have focused on (i) development of acyanogenic cassava varieties by breeding; (ii) controlling its metabolism; and (iii) processing to remove cyanogens. The cyanoglucoside (CNG) content in cassava is genetically controlled and cultivars may be classified as low (<50 µg/g), medium (50-100 µg/g) and high CN (>100 µg CN eq./g) varieties. Molecular techniques for reducing tuber CNG have focused on development of transgenic plants with reduced expression of cyt P 450 in leaves, or increased expression of hydroxynitrilelyase in tuber. For immediate solution, CNG content can be reduced using several processing methods. Traditional methods used for processing include boiling, drying, parboiling and drying, baking, steaming, frying and preparation of flour. These processes result in CN losses ranging from 25% to 98%.

The cyanogen level in the final product is influenced both by the tuber CNG and the method of processing. In order to achieve safe levels of 10 µg/g in cassava products, new methods of processing, especially for cassava containing more than 250 µg CN eq./g, remains a challenging problem.

Genetic transformation and pyramiding of aprotinin-expressing sugarcane with cry1Ab for shoot borer (*Chilo infuscatellus*) resistance.

[Arvinth S, Arun S, Selvakesavan RK, Srikanth J, Mukunthan N, Ananda Kumar P, Premachandran MN, Subramonian N. Plant Cell Rep. 2010 Apr;29(4):383-95. doi: 10.1007/s00299-010-0829-5. Epub 2010 Feb 24.]

We evaluated the insecticidal toxicity of Cry1Aa, Cry1Ab and Cry1Ac toxins against neonate larvae of sugarcane shoot borer *Chilo infuscatellus* Snellen (Lepidoptera: Crambidae) *in vitro* on diet surface. With the lowest LC(50) value, Cry1Ab emerged as the most effective among the three toxins. Sugarcane cultivars Co 86032 and CoJ 64 were transformed with cry1Ab gene driven by maize ubiquitin promoter through particle bombardment and Agrobacterium-mediated transformation systems. Gene pyramiding was also attempted by retransforming sugarcane plants carrying bovine pancreatic trypsin inhibitor (aprotinin) gene, with cry1Ab. Southern analysis confirmed multiple integration of the transgene in case of particle bombardment and single site integration in Agrobacterium-mediated transformants. The expression of cry1Ab was demonstrated through Western analysis and the toxin was quantified using ELISA. The amount of Cry1Ab protein in different events varied from 0.007 to 1.73% of the total soluble leaf protein; the events transformed by Agrobacterium method showed significantly higher values. In *in vivo* bioassay with neonate larvae of shoot borer, transgenics produced considerably lower percentage of deadhearts despite suffering feeding damage by the borer compared with the untransformed control plants. Expressed Cry1Ab content was negatively related to deadheart damage. Aprotinin-expressing sugarcane pyramided with cry1Ab also showed reduction in damage. The potential of producing sugarcane transgenics with cry1Ab and aprotinin genes resistant to early shoot borer was discussed in the light of the results obtained.

Safety assessment of leaf curl virus resistant tomato developed using viral derived sequences.

[Singh AK, Praveen S, Singh BP, Varma A, Arora N. Transgenic Res. 2009 Dec;18(6):877-87. doi: 10.1007/s11248-009-9274-z. Epub 2009 May 5.]

Genetic engineering of food crops has significantly influenced the agricultural productivity over the past two decades. It has proved a valuable tool, offering crops with higher yields, improved nutritional quality, resistance against pesticides, herbicides and tolerance against abiotic stresses. However, the safety assessment of genetically engineered (GE) crops is prerequisite before introduction into human food chain. The present study was aimed to assess the toxicity and allergenicity of leaf curl virus resistant GE tomato compared to its wild-type species. Balb/c mice fed with genetically engineered or wild-type tomato did not show significant differences in growth, body weight ($P > 0.05$) and food consumption when compared with control mice. Values for serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase, urea and cholesterol were comparable in GE and wild-type tomato fed mice. Mice immunized with GE or wild-type tomato extract showed low IgE response. Lung histology of ovalbumin fed mice showed bronchoconstriction with eosinophilic infiltration whereas GE or wild-type tomato showed no cellular infiltration with normal airways. Genetically engineered and wild-type tomato sensitized mice demonstrated similar IL-4 release in splenic cell culture supernatant. GE and wild tomato extract on ELISA showed comparable IgE binding ($P > 0.05$) with food allergic patients' sera. In conclusion, genetically engineered tomato showed no toxicity in mice and allergenicity is similar to the wild-type tomato.

Safety assessment of bacterial choline oxidase protein introduced in transgenic crops for tolerance against abiotic stress.

[Singh AK, Singh BP, Prasad GB, Gaur SN, Arora N. J Agric Food Chem. 2008 Dec 24;56(24):12099-104. doi: 10.1021/jf8027073.]

Genetically modified crops have resistance to abiotic stress by introduction of choline oxidase protein. In the present study, the safety of choline oxidase protein derived from *Arthrobacter globiformis* was assessed for toxicity and allergenicity. The protein was stable at 90 degrees C for 1 h. Toxicity studies of choline oxidase in mice showed no significant difference ($p > 0.05$) from control in terms of growth, body weight, food consumption, and blood biochemical indices. Histology of gut tissue of mice fed protein showed normal gastric mucosal lining and villi in jejunum and ileum sections. Specific IgE in serum and IL-4 release in splenic culture supernatant were low in choline oxidase treated mice, comparable to control. Intravenous challenge with choline oxidase did not induce any adverse reaction, unlike ovalbumin group mice. Histology of lung tissues from choline oxidase sensitized mice showed normal airways, whereas ovalbumin-sensitized mice showed inflamed airways with eosinophilic infiltration and bronchoconstriction. ELISA carried out with food allergic patients' sera revealed no significant IgE affinity with choline oxidase. Also, choline oxidase did not show any symptoms of toxicity and allergenicity in mice.

RESEARCH DIGEST

Cigarette smoke may increase microbial virulence

[http://ehp.niehs.nih.gov/121-a75/]

Cigarette smoke has long been known to aggravate respiratory infections. A new study expands the potential health effects to a new front, showing that acute *in vitro* exposure of *Staphylococcus aureus* to cigarette smoke promoted biofilm formation and adhesion to human cells. The active agents behind this boost in activity appeared to be reactive oxygen species (such as hydrogen peroxide), which are linked not just to cigarette smoke but also vehicular exhaust and biomass smoke. The research was conducted by Ritwij Kulkarni, a postdoctoral researcher in the laboratory of Adam Ratner at the Columbia University Department of Pediatrics. The new research "may in part explain the strong association between cigarette smoke exposure and respiratory tract infections," says Janet Lee, an associate professor of medicine at the University of Pittsburgh Medical Center, who was not a collaborator on the study. Earlier research had linked cigarette smoke with biofilm formation, but this is the first to examine potential underlying mechanisms, she says. In the current study, the researchers exposed multiple strains of cultured *S. aureus* to various concentrations of cigarette smoke by bubbling the smoke into the growth medium. Biofilm formation increased in exposed *S. aureus* in a dose-dependent fashion. Exposed bacteria also showed increased binding to human fibronectin and lung epithelial cells, compared with controls. Fibronectin is a cell-surface protein that aids in cellular adhesion, among other roles. Bacteria may bind to fibronectin in order to invade human cells. Exposure to hydrogen peroxide alone also induced biofilm production, whereas spiking cigarette smoke with the antioxidant N-acetyl cysteine interrupted its ability to induce biofilm formation. These observations suggest that an oxidant-dependent pathway is triggered by smoke, leading to enhanced biofilm formation. The paper is part of a new but rapidly expanding literature. Noam A. Cohen, an assistant professor in the Department of Otorhinolaryngology, Head and Neck Surgery at the University of Pennsylvania, has investigated cigarette smoke's effect on multiple species of bacteria at once. The bacteria were isolated from sinonasal passages of patients with chronic sinusitis, both smokers and nonsmokers. Cigarette smoke exposure was associated with increased biofilm formation among all species of bacteria, but more so among those isolated from smokers than in those from nonsmokers. Cohen praises the Columbia study and says the new work suggests tobacco smoke may "convert the bacteria to a more aggressive form." But more studies are needed to confirm the findings and determine whether enhanced biofilm formation translates into greater microbial pathogenicity or persistence; Cohen's own data suggest that cessation of smoke exposure reverses the boost in biofilm formation. Furthermore, the use of cigarette smoke extract for *in vitro* studies has not been standardized.

Reactive oxygen species in cigarette smoke may promote biofilm formation by *Staphylococcus aureus* (inset), a common respiratory pathogen

The relevance of all these findings to human environmental health is broad, says Lee, a clinician with

an interest in how cigarette smoke alters immune cell populations. "Cigarette smoke has been linked to a number of diseases, such as oral gingivitis, chronic rhinosinusitis, and chronic lung diseases," she says, and epidemiologic evidence suggests that exposure to secondhand smoke increases the risk of *S. aureus* colonization in children. Other new findings show that cigarette smoke enhances biofilm production of *Pseudomonas aeruginosa* and *Streptococcus pneumoniae*, two very important respiratory pathogens. "But the pathogenic mechanisms are still not well understood," Lee says, calling the new research "an important step in identifying which genes are involved." All this work may have particular relevance for patients with cardiovascular disease. "This could definitely be part of the comorbidities they are seeing with these patients that aren't well explained by the cardiovascular diseases," says Jeff G. Leid, an associate professor of the Center for Microbial Genetics and Genomics at Northern Arizona University. Cohen adds that cigarette smoke exposures go well beyond the respiratory tree. He explains, "Many of the products of tobacco get into the blood stream and can thus affect bacteria in distant locations"—in the joints, heart, and gastrointestinal tract, for example. Concludes Ratner: "Our environmental exposures don't just affect us; they affect our bacteria." Whether this helps us or hurts us, he says, we need to take it into consideration when investigating the health effects of environmental exposures.

Air pollution from industrial swine operations and blood pressure of neighboring residents

[Environ Health Perspect 121:92–96 (2013). http://dx.doi.org/ 10.1289/ehp.1205109]

Industrial swine operations emit odorant chemicals including ammonia, hydrogen sulfide (H_2S), and volatile organic compounds. Malodor and pollutant concentrations have been associated with self-reported stress and altered mood in prior studies. Here authors conducted a repeated-measures study of air pollution, stress, and blood pressure in neighbors of swine operations. For approximately 2 weeks, 101 nonsmoking adult volunteers living near industrial swine operations in 16 neighborhoods in eastern North Carolina sat outdoors for 10 min twice daily at preselected times. Afterward, they reported levels of hog odor on a 9 point scale and measured their blood pressure twice using an automated oscillometric device. During the same 2 to 3 week period, they measured ambient levels of H_2S and PM10 at a central location in each neighborhood. Associations between systolic and diastolic blood pressure (SBP and DBP, respectively) and pollutant measures were estimated using fixed-effects (conditional) linear regression with adjustment for time of day. PM10 showed little association with blood pressure. DBP [β (SE)] increased 0.23 (0.08) mmHg per unit of reported hog odor during the 10 min outdoors and 0.12 (0.08) mmHg per 1 ppb increase of H_2S concentration in the same hour. SBP increased 0.10 (0.12) mmHg per odor unit and 0.29 (0.12) mmHg per 1 ppb increase of H_2S in the same hour. Reported stress was strongly associated with BP; adjustment for stress reduced the odor–DBP association, but the H_2S–SBP association changed little. It was concluded that like noise and other repetitive environmental stressors, malodors may be associated with acute blood pressure increases that could contribute to development of chronic hypertension.

Organic pollutants poison the roof of the world: Accumulation of DDT in Himalayas exceeds that seen in Arctic.

[Nature News 11 April 2013. doi:10.1038/nature. 2013.12776]

Toxic chemicals are accumulating in the ecosystems of the Himalayas and the Tibetan plateau, researchers warn in the the first comprehensive study to assess levels of certain organic pollutants in that part of the world. "The rigour and quality of the work are impressive," says Surendra Singh, an ecologist at the Forest Research Institute in Dehradun. "It's the first study to quantify the accumulation of [persistent organic pollutants] in ecosystems in the region." Persistent organic pollutants (POPs) are carbon-based compounds that are resistant to break-down. Some originate from the burning of fuel or the processing of electronic waste, and others are widely used as pesticides or herbicides or in the manufacture of solvents, plastics and pharmaceuticals. Some POPs,

such as the pesticide dichlorodiphenyltrichloroethane (DDT) and the herbicide Agent Orange, can cause diseases such as cancers, neurological disorders, reproductive dysfunction and birth defects. Many POPs are volatile and insoluble, and can travel a long distance. “They tend to evaporate in hot places, hitch a ride on winds, and then condense in cold regions,” says Xu Baiqing, an environmental scientist at the Institute of Tibetan Plateau Research in Beijing. In 2008, Xu and his colleagues first reported the presence of DDT, hexachlorocyclohexanes (HCHs), and polycyclic aromatic hydrocarbons (PAHs) in the East Rongbuk Glacier near Mount Everest. “Their levels correlate well with human use of those chemicals,” says Wang Xiaoping, an environment scientist at the ITP who was lead author of that study. For instance, the amount of DDT fell sharply during the 1970s, when many European countries started to ban its use, but rose again after 1990s, when its use rose heavily in the Indian subcontinent. Other POPs continue to be commonly used in many developing countries. That was not an isolated incident. At the fourth Third Pole Environment Workshop, held on 1–3 April in Dehradun, India, Xu reported that ice cores from across the Himalayas and Tibetan plateau are rife with those toxic compounds. To trace the sources of those pollutants, Xu and his colleagues correlated meteorological measurements with chemical compositions of air parcels sampled at 16 locations across the region. They found that POPs in the western Tibetan plateau were transported by the westerly winds from Europe and Africa, whereas those in the southern and southeastern regions were brought by the Indian monsoon from South Asia More alarmingly, the researchers also detected large amounts of POPs in various components of the ecosystems such as soil, grass, trees and fish in the Himalayas and in the Tibetan plateau, especially at the highest elevations. “Their levels increase in orders of magnitude as they move further along the food chain,” says Xu. The amounts of DDT in leaves are up to four times higher than those found in boreal forests in the Arctic. “If the trend continues, the forests might reach a critical threshold in the next a few decades,” he says. The results “are another warning of the way we use chemicals”, says David Molden, director of the Integrated Centre for Integrated Mountain Development in Kathmandu. Because some persistent compounds accumulate at the top of the food chain, humans can be exposed to POPs by eating meat and fish. And the mountain communities are hit hardest, researchers say. “They do not emit any of those toxic compounds,” says Xu, “but are forced to shoulder the burden of their impact.

Global warming at your doorstep

Science Now. 30 April 2013

When it comes to reducing carbon footprints, many Americans need look no further than their front yards. The soil beneath those perfectly manicured carpets of green grass—the pride of many suburban homeowners—is pumping surprising amounts of carbon into the atmosphere. That's according to a study published in the Soil Science Society of America Journal, which concludes that the amount of carbon rising from the soil of residential lawns is significantly greater than that from the soil of agricultural land—in this case, irrigated fields of corn. Researchers at Elizabethtown College in Pennsylvania measured weekly carbon emissions from nearby residential lawns and commercial cornfields from October to December 2011. They found that carbon emissions from the soil in suburban lawns were as much as twice as high as those from cornfields. Carbon is naturally deposited into soil by dead plant matter. When those plants begin to decompose, it is released back into the atmosphere as carbon dioxide, where it contributes to climate change. But don't trade in your lawnmower just yet. Moisture, along with warmer temperatures, increases the amount of carbon released from the soil, and the authors say that their findings are due—at least in part—to higher soil temperatures in the lawns rather than the grass itself. Warmer soil temperatures are an unavoidable consequence of urban development, leaving little the typical suburban or urban homeowner can do to reduce the amount of carbon emanating from their lawn. However, trees and other vegetation remove those gases from the atmosphere, so lush landscaping is the best way to mitigate the effects of human warming and achieve a carbon neutral yard.

Silver nanoparticles provide clean water for $2 a year

[http://www.newscientist.com/article/mg21829165.400-silver-nanoparticles-provide-clean-water-for-2-a-year.html]

Sometimes the solution to an enormous problem is tiny. Silver nanoparticles may be the key to supplying clean, affordable drinking water worldwide. Thalappil Pradeep at the Indian Institute of Technology in Chennai and colleagues have developed a filter based on an aluminium composite, embedded with silver nanoparticles. As water flows through the filter, the nanoparticles are oxidised and release ions, which kill viruses and bacteria, and neutralise toxic chemicals such as lead and arsenic. Some nanoparticles leach into the water but at concentrations that pose no threat to health. Pradeep describes the process of making the filter as "water positive": 1 litre of water spent on making nanoparticles gives 500 litres of clean water. In tests, a 50-gram composite filtered 1500 litres of water without needing reactivation, so they estimate that a 120g-filter that costs just $2 would provide safe drinking water for a family of five for one year. The filters are undergoing field trials in India with the aim of preventing waterborne diseases.

More antibiotics may not always be better

[http://www.newscientist.com/article/dn23421-more-antibiotics-may-not-always-be-better.html]

Finish the course of pills: that's what all doctors say when they prescribe antibiotics, and for now, you should heed them. But new research suggests that might not always work as well as they assume, and may even compound the problem of antibiotic-resistant bacteria. Doctors consider it good practice to hit bacterial infections with high doses of antibiotics for days or longer, to make sure all the bacteria are dead. To treat tough infections such as TB, they combine two or more antibiotics in order to prevent the evolution of resistance, so if a bug starts resisting drug A, it will still be killed by drug B. But much of this is based on assumption rather than evidence, says Robert Beardmore at the University of Exeter in the UK. He and his colleagues tested this by treating cultures of *E. coli* with two antibiotics considered synergistic – they kill more bacteria together than separately. They found that bacteria did indeed die off fast on the first day. But any bacteria that survived were those with genes for resisting both drugs, and they boomed as drug-sensitive competitors died. Bacterial loads were higher after treatment than they had been before it, and higher drug doses just quickened the growth of resistant populations. "It's a double-edged sword," says Andrew Read of Pennsylvania State University in University Park, who was not involved in the work. "If you kill all the bacteria with your initial dose, great." But if not – and antibiotics fall to sub-lethal levels at some time or in some part of the body during treatment – then problems arise. Further experiments performed by Beardmore's team suggest that not only synergistic drugs but also longer treatment might not hammer the surviving bacteria as intended. Instead such approaches might make more of the survivors antibiotic-resistant, and may even worsen the infection. "We need to base treatment on better evidence," says Read. "I'm not advocating low dosing," says Beardmore, as this does lead to resistance. But, he says, we need a better understanding of how antibiotics work in different situations instead of going on untested assumptions. He is now testing whether antibiotics that antagonise each other – one may interfere with another's binding to bacteria, for instance – might actually work better than synergistic drugs. This counter-intuitive possibility, thrown up by a mathematical model of bacterial evolution, might work in practice because antibiotics that antagonise each other do not make antibiotic resistance so advantageous.

विज्ञान परिक्रमा

पसीने से बनी एंटीबायोटिक

[PNAS 2013 ; published ahead of print February 20, 2013, doi:10.1073/pnas.1214739110]

मनुष्य के शरीर से निकलने वाले पसीने से वैज्ञानिकों ने एक ऐसा एंटीबायोटिक बनाने का दावा किया है जिससे टीबी और कई अन्य खतरनाक बीमारियों का इलाज संभव हो सकेगा। शोधकर्ताओं के अनुसार, जब शरीर से पसीना निकलता है तो डर्मसीडिन नामक पदार्थ का भी स्त्राव होता है। यह डर्मसीडिन कटने, खरोंच लगने या किसी कीड़े के काटने पर जीवाणुओं से सुरक्षा प्रदान करता है। वैज्ञानिकों ने इस पदार्थ की आणविक संरचना का भी पता लगा लिया है। यूनिवर्सिटी ऑफ एडिनबर्ग के शोधकर्ता यूलरिक जकारी के मुताबिक, एंटीबायोटिक केवल दवा की दुकानों पर ही नहीं मिलते, हमारा शरीर भी कई तरह के एंटीबायोटिक से लैस होता है जो प्राकृतिक रूप से शरीर की रक्षा करते हैं। अब जबकि इनकी संरचना का पता चल गया है तो इसका विभिन्न प्रकार के एंटीबायोटिक बनाने में इस्तेमाल किया जा सकता है। प्रोसीडिंग्स ऑफ द नेशनल एकेडमी ऑफ साइंसेज में

प्रकाशित रिपोर्ट के मुताबिक मानव शरीर में करीब 17 सौ प्राकृतिक एंटीबायोटिक मौजूद हैं। शोधकर्ताओं के मुताबिक ये प्राकृतिक एंटीबायोटिक कृत्रिम एंटीबायोटिक की तुलना में ज्यादा कारगर और प्रभावी होते हैं। इन्हें एंटीमाइक्रोबियल पेप्टाइड्स (एएमपीएस) के नाम से जाना जाता है। यह एएमपीएस जीवाणु पर हमला करके उसे नष्ट कर देता है, जिससे जीवाणु के विकास की संभावना लगभग समाप्त हो जाती है।

लाल नदी का लाल पानी

[http://serc.carleton.edu/microbelife/topics/riotinto/index.html]

नदियों का नीला साफ पानी शायद सभी को अच्छा लगता होगा। इस नीले साफ पानी में कई बार आपने दोस्तों संग मस्ती भी की होगी। इसके ठंडे–नीले पानी में तैरना, घुटनों तक पानी में खड़े होकर दूर आसमान देखना लगभग हर किसी को लुभाता है। पहाड़ी इलाकों में नदियों का पानी इतना शुद्ध और साफ होता है कि लोग इसे पीते भी हैं। कहते हैं कि यह पानी बहुत मीठा होता है। पर क्या कभी आपने तेजाबी पानी वाली नदी का नाम सुना है? क्या लाल नदी या लाल पानी वाली तेजाबी नदी देखी है? स्पेन में एक नदी है जिसका पानी लाल रंग का और तेजाबी है। न आप इसका पानी पी सकते हैं, ना इसमें खड़े होकर आसमान निहार सकते हैं, न ही दोस्तों के साथ इसके पानी से खेल सकते हैं। दक्षिण–पश्चिमी स्पेन में स्थित रिओ तिन्तो नदी में सिर्फ कुछ जलीय सूक्ष्मजीव ही रहते हैं जो इसके तेजाबी पानी को सहन कर सकते हैं। यह स्पेन के सिएर्रा मोरेना पहाड़ श्रृंखला से निकलकर अन्ध महासागर में गिरती है। यह अपने लाल–नारंगी पानी के लिए पूरे विश्व में मशहूर है। कहते हैं नदी के निकटवर्ती प्रदेशों में 3000 ई.पू. से ही तांबे, सोने, चांदी तथा अन्य खनन पदार्थों की खानें चलाई जाती रही हैं। बीच में कुछ समय के लिए इसे बंद किया गया था पर 1724 ई. में स्पेन सरकार ने वापस यह खनन कार्य शुरू करवा दिया। इन खनन कार्यों के कारण यहां का पानी तेजाबी हो गया है। लोहे के खनन प्रदेश में होने के कारण इसके पानी में लोहा की मात्रा भी बहुत होती है। इसी लोहे की मात्रा के कारण इसका पानी लाल–नारंगी रंग का दिखता है। वास्तव में इस नदी का नाम रिओ तिन्तो भी इसके लाल रंग के पानी के कारण ही पड़ा। तिन्तो का अर्थ होता है लाल और रिओ का मतलब नदी अर्थात लाल रंग की नदी।

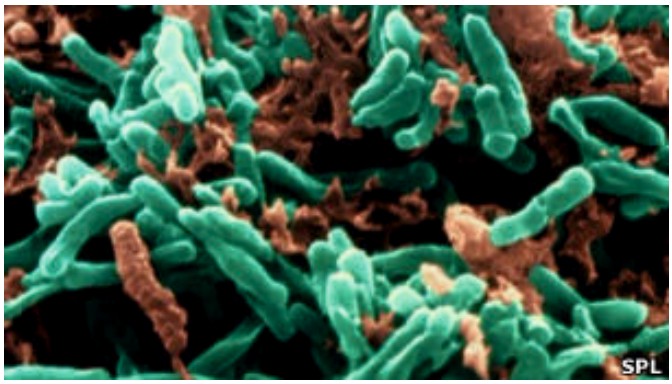
विटामिन 'सी' से हो सकता है लाइलाज टीबी का इलाज?

[http://www.nature.com/ncomms/journal/v4/n5/full/ncomms2898.html#abstract]

वैज्ञानिकों ने दावा किया है कि विटामिन 'सी' से टीबी या तपेदिक के उस स्वरूप का भी इलाज किया जा सकता है जिनपर कुछ ताकतवर दवाएं भी कारगर नहीं हो पाती हैं। येशिवा युनिवर्सिटी के अमरीकी शोधकर्ताओं ने अपनी रिपोर्ट में कहा है कि चौंका देने वाली यह खोज टीबी के संक्रमण से निपटने के एक नए तरीके पर रोशनी डालती है। 'नेचर कम्युनिकेशन्स' में प्रकाशित इस रिपोर्ट के मुताबिक 'मल्टीड्रग रेजिस्टेंट टीबी' का यह संक्रमण दिन पर दिन लाइलाज होता जाता है। 'मल्टीड्रग रेजिस्टेंट टीबी' की वह अवस्था है जब इसके शुरुआती इलाज के काम आने वाली कुछ असरदार दवाएं भी नाकाम हो जाती हैं। एक अनुमान के मुताबिक दुनिया भर में इस तरह की टीबी या तपेदिक के तकरीबन साढ़े छह लाख मरीज हैं। इन नतीजों के बाद अब

इस बात के अध्ययन की और अधिक जरूरत महसूस की जा रही है कि क्या इलाज के इस तरीके में विटामिन सी का इस्तेमाल मनुष्यों में टीबी की दवा के तौर पर किया जाना फायदेमंद रहेगा। प्रयोगशाला में किए गए अध्ययनों में यह बात सामने आई कि विटामिन सी शरीर में कुछ ऐसे तत्वों के उत्पादन को सक्रिय करता है जो टीबी को खत्म करती हैं।

ये तत्व फ्री रैडिकल्स के नाम से जाने जाते हैं और यह टीबी के उस स्वरूप में भी कारगर होता है जब पारंपरिक एंटीबायोटिक्स दवाएं भी नाकाम हो जाती हैं।



माइक्रोस्कोप से ली गई तपेदिक के जीवाणु की तस्वीर

डॉक्टर विलियम जैकब्स येशिवा युनिवर्सिटी में अलबर्ट आइंसटीन कॉलेज ऑफ मेडिसिन के प्रोफेसर हैं और उन्होंने इस शोध की अगुवाई भी की है। वह कहते हैं, ''हम इसे अभी तक एक टेस्ट ट्यूब में ही दिखा पाने में कामयाब हुए हैं और हमें नहीं पता कि यह मनुष्यों या जानवरों पर कारगर होगा या नहीं।'' डॉक्टर विलियम ने बताया, ''इस बात पर विचार करने के लिए यह एक महत्वपूर्ण अध्ययन होगा क्योंकि हमारे पास टीबी का नमूना है, इनके लिए हमारे पास कोई दवा नहीं है और हमने प्रयोगशाला में देखा कि टीबी के इन नमूनों को विटामिन सी असरहीन कर देता है।'' वह बताते हैं, ''सब को पता है कि विटामिन सी सस्ता है, आसानी से उपलब्ध है और इसे इस्तेमाल करना सुरक्षित भी है। और आखिर में सबसे अच्छी बात ये है कि टेस्ट से हमें यह पता चलता है कि इस तरीके से हम टीबी के इलाज की संभावनाओं का पता लगा सकते हैं।''

कार्बन डाई ऑक्साइड खतरनाक स्तर पर

[http://www.noaa.gov/newsarchive.html]

वैज्ञानिकों ने दुनिया भर के नेताओं को चेतावनी दी है कि वायुमंडल में बढ़ते कार्बन डाई ऑक्साइड के स्तर के देखते

माउना लोआ ज्वालामुखी के शिखर पर कार्बन डाइऑक्साइड गैस की माप की जाती है

हुए इस पर नियंत्रण करने के लिए तुरंत कदम उठाएं। हवाई में मौजूद अमरीकी प्रयोगशाला में रोजाना होने वाले कार्बन डाई ऑक्साइड (CO_2) के उत्सर्जन की माप से अंदाजा मिला है कि पहली बार इस गैस का उत्सर्जन 400 पार्ट्स प्रति 10 लाख के स्तर पर पहुंच गया है। ब्रिटेन की रॉयल सोसायटी के मौसम परिवर्तन विभाग के प्रमुख ब्रायन हस्किंस का कहना है कि कार्बन डाइ ऑक्साइड गैस के आंकड़े यह संकेत दे रहे हैं कि दुनिया की सरकारों को इसके लिए उचित कदम उठाना चाहिए। साल 1958 से लेकर अब तक माउना लोआ ज्वालामुखी पर मौजूद गैस मापक स्टेशन में दर्ज किए जाने वाले आंकड़े दर्शाते हैं कि इस गैस की मात्रा लगातार बढ़ रही है। दिलचस्प है कि मानव जीवन के अस्तित्व से करीब 30 से 50 लाख साल पहले नियमित तौर पर कार्बन डाई ऑक्साइड (CO_2) की मात्रा 400 पीपीएम से ऊपर थी। वैज्ञानिकों का कहना है कि उस वक्त का मौसम आज के मुकाबले काफी गर्म हुआ करता था। कार्बन डाई ऑक्साइड को सबसे प्रमुख मानव जनित ग्रीनहाउस गैस माना जाता है और उसे पिछले कुछ दशकों से धरती के तापमान को बढ़ाने के लिए जिम्मेदार माना जाता है। जीवाश्म ईंधन मसलन कोयला, तेल और गैस के जलने से मुख्यतौर पर कार्बन का उत्सर्जन होता है। ज्वालामुखी के आसपास आमतौर पर यह रुझान देखा जाता है CO_2 की मात्रा ठंड के मौसम में बढ़ती है लेकिन उत्तरी गोलार्द्ध में मौसम बदलने के साथ ही इसकी मात्रा कम हो जाती है। वैसे जंगलों, दूसरे पौधों और वनस्पतियों की वजह से वातावरण को नुकसान पहुंचाने वाले गैस की मात्रा कम होती है। इसका मतलब यह है कि आने वाले हफ्तों में CO_2 की मात्रा 400 पीपीएम में कुछ कमी आ सकती है। लेकिन आने वाले लंबे समय तक इसकी मात्रा में तेजी के रुझान हैं। माउना लोआ में नैशनल ओसनिक ऐंड एटमॉस्फेरिक एडमिनिस्ट्रेशन (एनओएए) से जुड़े अर्थ सिस्टम रिसर्च

लैबोरेटरी को स्थापित करने में जेम्स बटलर का मुख्य योगदान है। यहां CO_2 की औसत दैनिक सांद्रता का आंकड़ा 400.03 था। डॉ बटलर ने बीबीसी न्यूज से कहा, "CO_2 में घंटे, दैनिक और साप्ताहिक आधार पर परिवर्तनशीलता का रुझान देखा जाता है इसलिए हम इसका कोई एक आंकड़ा बताने में सहज नहीं हैं। सबसे कम आंकड़ा रोजाना औसत आधार पर तय होता है जिसे इस मामले में भी देखा जा रहा है।" "माउना लोआ और दक्षिणी ध्रुव की वेधशालाएं दो ऐसी प्रतिष्ठित जगहें हैं जहां साल 1958 से ही CO_2 की मात्रा मापी जा रही है। पिछले साल पहली बार आर्कटिक क्षेत्र की सभी जगहों पर CO_2 की मात्रा 400 पीपीएम के स्तर पर पहुंच गई।" माउना लोआ ज्वालामुखी के शिखर के नजदीक मौजूद कार्बन डाइऑक्साइड की मात्रा पर निगरानी रखने वाले मॉनीटर दुनिया के सबसे सुदूर इलाके में मौजूद वैज्ञानिक उपकरणों में शामिल हैं। "ऐसा पहली बार है कि माउना लोआ में भी CO_2 की दैनिक औसत मात्रा ने 400 पीपीएम के स्तर को पार कर लिया है।" माउना लोआ पर लंबी अवधि की माप की शुरुआत स्क्रिप्स इंस्टीट्यूशन ऑफ ओशनोग्राफी के वैज्ञानिक चार्ल्स कीलिंग ने कराई थी। उन्होंने अपनी खोज में यह पाया कि ज्वालामुखी के शीर्ष पर CO_2 की सघनता करीब 315 पीपीएम है। स्क्रिप्स, एनओएए के साथ–साथ पहाड़ों की चोटी पर CO_2 की मात्रा मापने की कोशिश में जुटा है। हाल के दिनों में इसने CO_2 की मात्रा 400 पीपीएम दर्ज की है और शुक्रवार को इसने 399.73 दैनिक औसत रिकॉर्ड किया। डॉ बटलर का कहना है, "संभवतः अगले साल तक या उसके बाद औसत सालाना रीडिंग 400 पीपीएम के स्तर को पार कर लेगी।" "कुछ सालों बाद दक्षिणी ध्रुव की रीडिंग 400 पीपीएम होगी और अगले आठ से नौ सालों में CO_2 की रीडिंग शायद ही 400 पीपीएम से कम होगी।" CO_2 के स्तर को तय करने से वैज्ञानिकों को प्रॉक्सी मापन का इस्तेमाल जरूर करना पड़ता है। इसके तहत अंटार्कटिक के बर्फ में मौजूद प्राचीन काल के हवा के बुलबुले का अध्ययन किया जाता है। इस तरीके का इस्तेमाल कर पिछले 800,000 सालों के CO_2 के स्तर को बताया जा सकता है। इस अध्ययन से यह नतीजे भी निकले कि इस लंबी अवधि में CO_2 की मात्रा 200 पीपीएम से 300 पीपीएम के बीच रही। ब्रिटेन के वायुमंडलीय भौतिकशास्त्री प्रोफेसर जोएना हेग का कहना है, "मौसम तंत्र की भौतिकी के लिए 400 पीपीएम CO_2 की कोई खास अहमियत नहीं है। लंबे समय तक इस गैस की सांद्रता का स्तर 300 तक रहा था और अब हमने 400 के स्तर को पार कर लिया है। हालांकि इससे हमें CO_2 की लगातार बढ़ रही मात्रा और मौसम के लिए आखिर यह एक समस्या क्यों है, इस पर सोचने को मौका मिल रहा है।"

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