

# Bulletin Board

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## Technical

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## CHEMICAL EFFECTS

## Exploring novel insights into the molecular mechanisms underlying Bisphenol A-induced toxicity: A persistent threat to human health

2024-05-17

Bisphenol A (BPA) is a ubiquitous industrial chemical used in the production of polycarbonate plastics and epoxy resins, found in numerous consumer products. Despite its widespread use, its potential adverse health effects have raised significant concerns. This review explores the molecular mechanisms and evidence-based literature underlying BPA-induced toxicities and its implications for human health. BPA is an endocrine-disrupting chemical (EDC) which exhibits carcinogenic properties by influencing various receptors, such as ER, AhR, PPARs, LXR, and RARs. It induces oxidative stress and contributes to cellular dysfunction, inflammation, and DNA damage, ultimately leading to various toxicities including but not limited to reproductive, cardiotoxicity, neurotoxicity, and endocrine toxicity. Moreover, BPA can modify DNA methylation patterns, histone modifications, and non-coding RNA expression, leading to epigenetic changes and contribute to carcinogenesis. Overall, understanding molecular mechanisms of BPA-induced toxicity is crucial for developing effective strategies and policies to mitigate its adverse effects on human health.

Authors: Israel Ahmad, Mandeep Kaur, Devansh Tyagi, Tejinder Bir Singh, Gurpreet Kaur, Shaikh Mohammad Afzal, Mohsin Jauhar

Full Source: Environmental toxicology and pharmacology 2024 May 17:104467. doi: 10.1016/j.etap.2024.104467.

## Microplastic coupled with soil dissolved organic matter mediated changes in the soil chemical and microbial characteristics

2024-05-16

The abundance of microplastics (MPs) in soil environments has attracted significant attentions, due to their impact on soil physico-chemical properties. However, limited information is available on the influences of MPs on soil carbon composition and microbial utilization characteristics. Therefore, a two-month incubation experiment was conducted to add polyethylene microplastics (PE-MPs) with different levels (1%, 10%) and sizes (150-300  $\mu\text{m}$  and 75-150  $\mu\text{m}$ ) into different soils. After that, soil chemical properties including the dissolved organic carbon (DOC),

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spectral characteristics of dissolved organic matter (DOM) and soil microbial characteristics were analyzed. Results revealed that PE-MPs addition caused significant differences in soil chemical properties between farmland and woodland soils, particularly in soil pH, DOM composition, and soil phosphatase activity. Woodland soil always exhibited higher levels of DOC content, microbial diversity, and soil carbon source utilization compared to farmland soil, leading to increased humification in the DOM of woodland soil. PE-MPs with a larger particle size significantly increased both the soil DOC content and enzyme activity. Addition of PE-MPs altered the soil DOM composition, and the fluorescence parameters like the biological index (BIX) and humification degree. Moreover, the carbon source utilization intensity of microorganisms on PE-MPs-contaminated soils is higher in woodland soils. Various analyses confirmed that compared to other soil properties, characteristics of soil DOM had a more significant impact on soil microbial community composition. Thus, PE-MPs in conjunction with soil DOM spectral characteristics regulated soil microbial diversity, which is crucial for understanding soil carbon sequestration.

Authors: Zhiwang Feng, Ningyuan Zhu, Hanzhou Wu, Ming Li, Jian Chen, Xuyin Yuan, Jizhou Li, Yimin Wang

Full Source: Chemosphere 2024 May 16:142361. doi: 10.1016/j.chemosphere.2024.142361.

## ENVIRONMENTAL RESEARCH

## Exploring the abundance of microplastics in Indian landfill leachate: An analytical study

2024-05-17

Landfills are a major source of many emerging pollutants, including microplastics (MPs). This makes them a potential threat to human and environmental health and calls for a more detailed analysis of their hazard potential. India is a developing country with multiple unscientific waste dumping sites. In spite of their hazardous nature, detailed studies on the abundance of microplastics in landfills in India are scanty. Current work investigates the abundance and diversity of MPs in two landfills of India, Uruli Devachi in Pune (S1) and Deonar in Mumbai (S2). MPs collected from landfill leachate using multiple filters were analyzed using an optical microscope and categorized on the basis of shape, color and size to give information on their distribution. MP abundance in S1 was  $1473 \pm 273.01$  items/L while  $2067 \pm 593.75$  items/L were found in leachate from S2. Film and fragment were the dominant shape and black was the dominant color

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of MP found in both the landfills. Maximum number of MPs were in the size range below 100  $\mu\text{m}$  in both the landfills necessitating the study of small sized particles. Chemical characterization revealed the prevalence of four types of MPs (polyethylene terephthalate, polypropylene, cellulose acetate and polyvinyl chloride). This study sheds light on the prevalence, characteristics, abundance and distribution of MPs in landfill leachate in Western India, sparking more research into the processes followed for capturing the factual small sized microplastic abundance data. This study is vital for a detailed management of landfill leachate enabling a sustainable waste management and targeted actions for ecosystem preservation.

Authors: Meenakshi Verma, Pooja Singh, Manikprabhu Dhanorkar  
Full Source: Journal of environmental management 2024 May 17:360:121181. doi: 10.1016/j.jenvman.2024.121181.

### A review of occurrence, bioaccumulation, and fate of novel brominated flame retardants in aquatic environments: A comparison with legacy brominated flame retardants

2024-05-17

Novel brominated flame retardants (NBFRs) have been developed as replacements for legacy brominated flame retardants (BFRs) such as polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecanes (HBCDs). The prevalence of NBFRs in aquatic environments has initiated intense concerns that they resemble to BFRs. To comprehensively elucidate the fate of NBFRs in aquatic environments, this review summarizes the physico-chemical properties, distribution, bioaccumulation, and fates in aquatic environments. 1,2-Bis(2,3,4,5,6-pentabromophenyl) ethane (DBDPE) as the major substitute for PBDEs is the primary NBFR. The release from industrial point sources such as e-waste recycling stations is the dominant way for NBFRs to enter the environment, which results in significant differences in the regional distribution of NBFRs. Sediment is the major sink of NBFRs attributed to the high hydrophobicity. Significantly, there is no decreasing trend of NBFRs concentrations, while PBDEs achieved the peak value in 1970-2000 and decreased gradually. The bioaccumulation of NBFRs is reported in both field studies and laboratory studies, which is regulated by the active area, lipid contents, trophic level of aquatic organisms, and the log KOW of NBFRs. The biotransformation of NBFRs showed similar metabolism patterns to that of BFRs, including debromination, hydroxylation, methoxylation, hydrolysis, and glycosylation. In addition, NBFRs show great potential in trophic magnification along the aquatic food chain, which could pose a higher risk

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to high trophic-level species. The passive uptake by roots dominates the plant uptake of NBFRs, followed by acropetal and basipetal bidirectional transportation between roots and leaves in plants. This review will provide the support to understand the current pollution characteristics of NBFRs and highlight perspectives for future research.

Authors: Mao Li, Xinying Gong, Qinwen Tan, Yonghong Xie, Yuanjun Tong, Junyi Ma, Dongmei Wang, Lian Ai, Zhengjun Gong  
Full Source: The Science of the total environment 2024 May 17:173224. doi: 10.1016/j.scitotenv.2024.173224.

### Microplastic Pollution in Surface Sediments of Coromandel Coastline, South-East Coast, India: Diversity Index, Carbonyl Index, Pollution Load Index, Risk Fraction and MPs Inventory

2024-05-17

The investigation along the Coromandel coastline of South-east India focused on assessing microplastics abundance using Simpson's diversity index, Degradation-carbonyl index (), Pollution load index and Ecological risk fraction. These indices evaluated the dissemination and transportation of MPs across a 1076 km stretch divided into five zones from Chennai to Kanyakumari. During the wet season, average microplastics abundance ( $101 \pm 36.6$  items/kg dw) was lower compared to the dry season ( $143 \pm 56.2$  items/kg dw). Notably, 54% and 45% of microplastics were found in the 0.1 to 0.5 mm size range, with 45% and 64% being colored microplastics, and 80% and 71% being fibers during the wet and dry seasons respectively. Micro-Fourier-transform infrared spectroscopy ( $\mu\text{FTIR}$ ) analysis showed rayon (34%) and PE (64%) dominance in ports and estuaries during both seasons. Kottaiappattinam Port exhibited higher diversity indices (compared to other zones, with an overall diversity index of 0.57. Notably, among the values ( $n=96$ ), only 12 fell within the moderate photo-chemical oxidation range (0.16-0.35), while the majority ( $n=60$ ) surpassed 0.35 indicating higher oxidation levels, with some ( $n=24$ ) exceeding 0.50, signifying extreme oxidation. revealed that 42% of sampling stations had very low to negligible MP contamination levels in ports and estuaries. However, ecological risk fraction values ranged from 10.2 to 13,670, with 27% of values exceeding 1500, indicating higher coastal ecological risk in 13 sampling stations.

Authors: Mrunmayee Manjari Sahoo  
Full Source: Environmental pollution (Barking, Essex : 1987) 2024 May 17:124179. doi: 10.1016/j.envpol.2024.124179.

The investigation along the Coromandel coastline of South-east India focused on assessing microplastics abundance using Simpson's diversity index, Degradation-carbonyl index (), Pollution load index and Ecological risk fraction.

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## PHARMACEUTICAL/TOXICOLOGY

## Elevated level of urinary tellurium is a potential risk for increase of blood pressure in humans and mice

2024-05-12

Background: People worldwide are routinely exposed to tellurium mainly via dietary ingestion. There has been no study to clarify the contribution of tellurium to blood pressure in humans or animals.

Methods: In this cross-sectional study conducted in a general population of 2592 residents in Japan, the associations of urinary tellurium levels with blood pressure and prevalence of hypertension were investigated. The potential sources of tellurium were also investigated. An interventional study in mice confirmed the effect of tellurium exposure on blood pressure.

Results: Linear and logistic regression analyses with consideration of confounders including urinary sodium-potassium ratio showed significant positive associations of urinary tellurium level with prevalence of hypertension and blood pressure. Cereals/beans and vegetables/fruits were determined to be potential dietary sources of tellurium exposure. Intermediary analysis suggested that increased intake of cereals/beans, but not that of vegetables/fruits, is positively associated with the tellurium-mediated risk of hypertension. Correspondingly, the mouse study showed that exposure to a putative human-equivalent dose of tellurium via drinking water increased blood pressure with an elevated level of urinary tellurium. The temporally increased blood pressure was decreased to the normal level by a break of tellurium exposure with a reduced level of urinary tellurium.

Conclusions: The interdisciplinary approach provided the first evidence that tellurium exposure is a potential risk for increase of blood pressure. Since the human urinary tellurium level in this study is comparable with the levels in general populations in other Asian and European countries in previous studies, exposure to tellurium may be a latent universal risk for hypertension.

Authors: Tomoko Misawa, Takumi Kagawa, Nobutaka Ohgami, Akira Tazaki, Shoko Ohnuma, Hisao Naito, Dijie Chen, Yishuo Gu, Takashi Tamura, Kenji Wakai, Kimitoshi Nishiwaki, Masashi Kato

Full Source: Environment international 2024 May 12;188:108735. doi: 10.1016/j.envint.2024.108735.

Background: People worldwide are routinely exposed to tellurium mainly via dietary ingestion.

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## Technical

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## Assessment of TROP2, CEACAM5 and DLL3 in metastatic prostate cancer: Expression landscape and molecular correlates

2024-05-17

Therapeutic approaches targeting proteins on the surface of cancer cells have emerged as an important strategy for precision oncology. To capitalize on the potential impact of drugs targeting surface proteins, detailed knowledge about the expression patterns of the target proteins in tumor tissues is required. In castration-resistant prostate cancer (CRPC), agents targeting prostate-specific membrane antigen (PSMA) have demonstrated clinical activity. However, PSMA expression is lost in a significant number of CRPC tumors. The identification of additional cell surface targets is necessary to develop new therapeutic approaches. Here, we performed a comprehensive analysis of the expression heterogeneity and co-expression patterns of trophoblast cell-surface antigen 2 (TROP2), delta-like ligand 3 (DLL3), and carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5) in CRPC samples from a rapid autopsy cohort. We show that DLL3 and CEACAM5 exhibit the highest expression in neuroendocrine prostate cancer (NEPC), while TROP2 is expressed across different CRPC molecular subtypes, except for NEPC. We further demonstrated that AR alterations were associated with higher expression of PSMA and TROP2. Conversely, PSMA and TROP2 expression was lower in RB1-altered tumors. In addition to genomic alterations, we show a tight correlation between epigenetic states, particularly histone H3 lysine 27 methylation (H3K27me3) at the transcriptional start site and gene body of TACSTD2 (encoding TROP2), DLL3, and CEACAM5, and their respective protein expression in CRPC patient-derived xenografts. Collectively, these findings provide insights into patterns and determinants of expression of TROP2, DLL3, and CEACAM5 with implications for the clinical development of cell surface targeting agents in CRPC.

Authors: Azra Ajkunic, Erolcan Sayar, Martine P Roudier, Radhika A Patel, Ilsa M Coleman, Navonil De Sarkar, Brian Hanratty, Mohamed Adil, Jimmy Zhao, Samir Zaidi, Lawrence D True, Jamie M Sperger, Heather H Cheng, Evan Y Yu, Robert B Montgomery, Jessica E Hawley, Gavin Ha, Thomas Persse, Patricia Galipeau, John K Lee, Stephanie A Harmon, Eva Corey, Joshua M Lang, Charles L Sawyers, Colm Morrissey, Michael T Schweizer, Roman Gulati, Peter S Nelson, Michael C Haffner

Full Source: NPJ precision oncology 2024 May 17;8(1):104. doi: 10.1038/s41698-024-00599-6.

Therapeutic approaches targeting proteins on the surface of cancer cells have emerged as an important strategy for precision oncology.

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## Capmatinib plus nivolumab in pretreated patients with EGFR wild-type advanced non-small cell lung cancer

2024-05-10

**Introduction:** Dysregulated MET is an established oncogenic driver in non-small cell lung cancer (NSCLC). MET signaling may also suppress anticancer immune responses. Concomitant MET inhibition with capmatinib (a MET inhibitor) synergistically enhanced the efficacy of immunotherapies in murine cancer models, regardless of tumor dependency to MET signaling. Here, we report results of a multicenter, open-label, phase 2 study of capmatinib plus nivolumab (a PD-1 inhibitor) in patients with EGFR wild-type advanced NSCLC, previously treated with platinum-based chemotherapy.

**Methods:** Patients were allocated into high-MET or low-MET groups according to MET expression determined by immunohistochemistry, MET gene copy number as assessed by fluorescence in-situ hybridization, and presence of MET exon 14 skipping mutation, then received capmatinib 400 mg, oral, twice daily in combination with nivolumab 3 mg/kg intravenously every 2 weeks. The primary endpoint was investigator-assessed 6-month progression-free survival (PFS) rate per RECIST v1.1. **Results:** The primary endpoint was met in both the high-MET (N = 16) and low-MET (N = 30) groups. In the high-MET and low-MET groups, respectively, the estimated mean 6-month PFS rate (95 % credible interval) by Bayesian analysis was 68.9 % (48.5-85.7) and 50.9 % (35.6-66.4). The Kaplan-Meier median PFS (95 % CI) was 6.2 months (3.5-19.2) and 4.2 months (1.8-7.4). The overall response rate (95 % CI) was 25.0 % (7.3-52.4) and 16.7 % (5.6-34.7). Most frequent treatment-related adverse events ( $\geq 30$  % any grade, N = 46) were nausea (52.2 %), peripheral edema (34.8 %), and increased blood creatinine (30.4 %).

**Conclusions:** Capmatinib plus nivolumab showed clinical activity and manageable safety in pretreated patients with advanced EGFR wild-type NSCLC, independent of MET status.

**Trial registration:** ClinicalTrials.gov NCT02323126.

**Authors:** Enriqueta Felip, Giulio Metro, Daniel S W Tan, Juergen Wolf, Michael Mark, Michael Boyer, Brett G M Hughes, Alessandra Bearz, Denis Moro-Sibilot, Xiuning Le, Javier Puente, Bartomeu Massuti, Ralph Tiedt, Yingying Wang, Chao Xu, Feby I Mardjuadi, Manuel Cobo

**Full Source:** Lung cancer (Amsterdam, Netherlands) 2024 May 10:192:107820. doi: 10.1016/j.lungcan.2024.107820.

**Introduction: Dys-regulated MET is an established oncogenic driver in non-small cell lung cancer (NSCLC).**

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## OCCUPATIONAL

## Epidemiology of work-related injuries, musculoskeletal disorders and dermatitis among hospital food service workers in a tertiary hospital in Asia

2024-05-17

**Background:** Despite the relative importance, the prevalence of workplace safety and health issues in hospital food service workers is not well studied. This study describes the epidemiology of work-related injuries and occupational diseases among hospital food service workers (FSWs) in a tertiary hospital in Singapore.

**Methods:** Using a total population sampling approach, a cross-sectional self-administered questionnaire was distributed to all FSWs employed at a major tertiary hospital in Singapore.

**Results:** The response rate was 98.4% (n = 125). The overall prevalence of workplace injuries and musculoskeletal symptoms was 35% (n = 43) and 53% (n = 65) respectively. The most common workplace injuries were cuts/lacerations (35.8%), muscle strain (25.4%) and burns (19.4%). The prevalence of workplace injuries among staff performing food preparation duties was higher at 56.3% as compared to 21.6% among staff with no food preparation duties (p < 0.01). The prevalence of workplace injuries among staff performing cooking duties was also higher at 47.5%, compared to 29.3% among staff with no cooking duties (p = 0.05). Staff performing food preparation duties had a higher prevalence of musculoskeletal symptoms at 66.7% as compared to 44.6% among staff with no food preparation duties (p = 0.02). Obese staff had a higher prevalence of musculoskeletal symptoms at 78.9%, compared to overweight staff at 53.8% and staff with normal weight at 43.1% (p = 0.03). **Conclusion:** FSWs with jobs involving cooking and preparation of food, and those with obesity, are at higher risk of sustaining workplace injuries or musculoskeletal symptoms. Targeted interventions should be implemented for injury prevention and to mitigate these risks.

**Authors:** Kenneth Bao Ren Leong, Qin Xiang Ng, Wee Hoe Gan, Wee Tong Ng, John Wah Lim

**Full Source:** Journal of occupational medicine and toxicology (London, England) 2024 May 17;19(1):18. doi: 10.1186/s12995-024-00413-w.

**Background: Despite the relative importance, the prevalence of workplace safety and health issues in hospital food service workers is not well studied.**

# Bulletin Board

## Technical

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### Application and demonstration of meso-activity exposure factors to advance estimates of incidental soil ingestion among agricultural workers

2024-05-17

**Background:** Soil is an understudied and underregulated pathway of chemical exposure, particularly for agricultural workers who cultivate food in soils. Little is known about how agricultural workers spend their time and how they may contact soil while growing food. Exposure factors are behavioral and environmental variables used in exposure estimation.

**Objectives:** Our study aimed to derive exposure factors describing how growers engage in different tasks and use those factors to advance the use of time-activity data to estimate soil ingestion exposures among agricultural workers.

**Methods:** We administered a meso-activity-based, season-specific soil contact activity questionnaire to 38 fruit and vegetable growers. We asked growers to estimate the frequency and duration of six meso-activities and describe how they completed them. We used questionnaire data to derive exposure factors and estimate empirical and simulated exposures to a hypothetical contaminant in soil via incidental ingestion using daily, hourly, and hourly-task-specific ingestion rates.

**Results:** We generated exposure factors characterizing the frequency and duration of six meso-activities by season, and self-reported soil contact, glove use, and handwashing practices by meso-activity and season. Seasonal average daily doses (ADDs) were similar across all three forms of ingestion rates. No consistent patterns regarding task-specific contributions to seasonal or annual ADDs were observed.

**Authors:** Sara N Lupolt, Brent F Kim, Jacqueline Agnew, Gurumurthy Ramachandran, Thomas A Burke, Ryan David Kennedy, Keeve E Nachman

**Full Source:** Journal of exposure science & environmental epidemiology 2024 May 17. doi: 10.1038/s41370-024-00671-0.

**Background:** Soil is an understudied and underregulated pathway of chemical exposure, particularly for agricultural workers who cultivate food in soils.