# CHEMWATCH

# Bulletin Board

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## CONTACT US

subscribers@chemwatch.net
tel +61 3 9572 4700
fax +61 3 9572 4777

1227 Glen Huntly Rd
Glen Huntly
Victoria 3163 Australia

## CHEMICAL EFFECTS

### Reproductive and transgenerational toxicity of bisphenol S exposure in pregnant rats: Insights into hormonal imbalance and steroid biosynthesis pathway disruption

2024-04-11

Bisphenol S (BPS) is an alternative chemical to bisphenol A commonly used in food packaging materials. It raises concerns due to potential adverse effects on human health. However, limited evidence exists regarding reproductive toxicity from BPS exposure, and the mechanism of associated transgenerational toxicity remains unclear. In this study, pregnant SD rats were exposed to two different doses of BPS (0.05 or 20 mg/kg) from GD6 to PND21. The objective was to investigate reproductive and transmissible toxicity induced by BPS, explore endocrine effects, and uncover potential underlying mechanisms in rats. Perinatal exposure to BPS in the F0 generation significantly decreased the rate of body weight, ovarian organ coefficient, and growth and development of the F1 generation. Notably, these changes included abnormal increases in body weight and length, estrous cycle disruption, and embryonic dysplasia in F1. 4D-DIA proteomic and PRM analyses revealed that exposure to 20 mg/kg group significantly altered the expression of proteins, such as Lhcgr and Akr1c3, within the steroid biosynthetic pathway. This led to elevated levels of FSH and LH in the blood. The hypothalamic-pituitary-ovarian (HPO) axis, responsible for promoting fertility through the cyclic secretion of gonadotropins and steroid hormones, was affected. RT-qPCR and Western blot results demonstrated that the expression of GnRH in the hypothalamus was decreased, the GnRHR in the pituitary gland was decreased, and the expression of FSHβ and LHβ in the pituitary gland was increased. Overall, BPS exposure disrupts the HPO axis, hormone levels, and steroid biosynthesis in the ovaries, affecting offspring development and fertility. This study provides new insights into the potential effects of BPS exposure on the reproductive function of the body and its relevant mechanisms of action.

Authors: Min Zhao, Ying Xie, Xiuqin Xu, Zequan Zhang, Can Shen, Xianglin Chen, Biran Zhu, Lihua Yang, Bingsheng Zhou

Full Source: The Science of the total environment 2024 Apr 11:927:172379. doi: 10.1016/j.scitotenv.2024.172379.

> Bisphenol S (BPS) is an alternative chemical to bisphenol A commonly used in food packaging materials.

### Specific CpG sites methylation is associated with hematotoxicity in low-dose benzene-exposed workers

2024-04-10

Benzene is a broadly used industrial chemicals which causes various hematologic abnormalities in human. Altered DNA methylation has been proposed as epigenetic biomarkers in health risk evaluation of benzene exposure, yet the role of methylation at specific CpG sites in predicting hematological effects remains unclear. In this study, we recruited 120 low-level benzene-exposed and 101 control male workers from a petrochemical factory in Maoming City, Guangdong Province, China. Urinary S-phenylmercapturic acid (SPMA) in benzene-exposed workers was 3.40-fold higher than that in control workers ($P < 0.001$). Benzene-induced hematotoxicity was characterized by reduced white blood cells counts and nuclear division index (NDI), along with an increased DNA damage and urinary 8-hydroxy-2'-deoxyguanosine (all $P < 0.05$). Methylation levels of TRIM36, MGMT and RASSF1a genes in peripheral blood lymphocytes (PBLCs) were quantified by pyrosequencing. CpG site 6 of TRIM36, CpG site 2, 4, 6 of RASSF1a and CpG site 1, 3 of MGMT methylation were recognized as hot CpG sites due to a strong correlation with both internal exposure and hematological effects. Notably, integrating hot CpG sites methylation of multiple genes reveal a higher efficiency in prediction of integrative damage compared to individual genes at hot CpG sites. The negative dose-response relationship between the combined methylation of hot CpG sites in three genes and integrative damage enabled the classification of benzene-exposed individuals into high-risk or low-risk groups using the median cut-off value of the integrative index. Subsequently, a prediction model for integrative damage in benzene-exposed populations was built based on the methylation status of the identified hot CpG sites in the three genes. Taken together, these findings provide a novel insight into application prospect of specific CpG site methylation as epi-biomarkers for health risk assessment of environmental pollutants.

Authors: Feier Wang, Lizhu Ye, Xinhang Jiang, Rui Zhang, Shen Chen, Liping Chen, Hongyao Yu, Xiaowen Zeng, Daochuan Li, Xiumei Xing, Yongmei Xiao, Wen Chen

Full Source: Environment international 2024 Apr 10:186:108645. doi: 10.1016/j.envint.2024.108645.

> Benzene is a broadly used industrial chemicals which causes various hematologic abnormalities in human.

## Technical

### 8-OHdG mediates the association of co-exposure to fifty-five typical endocrine-disrupting chemicals with renal function: a cross-section investigation in Southern Chinese adults

2024-04-13

Individual typical endocrine-disrupting chemicals (EDCs), including organophosphate triesters (OPEs), parabens, triclosan (TCS), bisphenols, benzophenones (BPs), phthalates (PAEs), and synthetic phenolic antioxidants (SPAs), are associated with renal dysfunction. However, the combined effects and underlying mechanisms of mixed EDC exposure on renal function remain unclear. Two hundred ninety-nine adult participants were enrolled in the cross-sectional survey conducted in Guangzhou, China. Urinary levels of 7 OPEs, 6 parabens, TCS, 14 bisphenols, 8 BPs, 15 PAEs, 4 SPAs, and 8-hydroxy-2'-deoxyguanosine (8-OHdG) were determined, and estimated glomerular filtration rate (eGFR) was served as the outcome index. We found elevated levels of diphenyl phosphate (DPP), bisphenol A (BPA), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), and mono-butyl phthalate (MBP) showed dose-responsive associations with eGFR decline, However, nonlinear associations were observed for bis(2-butoxyethyl) hydrogen phosphate (BBOEP), TCS, 4-hydroxybenzophenone (HBP), mono-n-pentyl phthalate (MnPP), and mono-benzyl phthalate (MBzP). The quantile-based g-computation model demonstrated that a quartile increase in the EDC mixture corresponded to a 0.383-SD decrease (95% CI - 0.658 ~ - 0.108, P = 0.007) in eGFR. Notably, BPA was identified as the primary contributor to this effect. Moreover, 8-OHdG mediated the eGFR decline associated with EDC mixtures with a mediation proportion of 25.49%. A sex-modified effect was also observed (P = 0.004), indicating that exposure to the mixture of EDC was linked to more pronounced renal dysfunction in females. Our novel findings suggest that exposure to a typical mixture of EDCs is associated with renal dysfunction in the general adult population of Southern China. Furthermore, 8-OHdG may play a role in the pathogenesis of EDC mixture-related renal dysfunction.

Authors: Qingfei Chen, Qifei Deng, Qilong Liao, Yan Liu, Zhaorui Zhang, Dehua Wu, Yanrong Lv, Jingyao Qin, Qing Liu, Shuangqi Li, Zihao Long, Xiumei Xing, Qing Wang, Xiaowen Zeng, Guanghui Dong, Mengjun Hou, Yongmei Xiao

Full Source: Environmental science and pollution research international 2024 Apr 13. doi: 10.1007/s11356-024-33266-1.

> Individual typical endocrine-disrupting chemicals (EDCs), including organophosphate triesters (OPEs), parabens, triclosan (TCS), bisphenols, benzophenones (BPs), phthalates (PAEs), and synthetic phenolic antioxidants (SPAs), are associated with renal dysfunction.

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## Technical

### ENVIRONMENTAL RESEARCH

### Polycyclic aromatic compounds in a northern freshwater ecosystem: patterns, sources, and the influences of environmental factors

2024-04-11

Polycyclic aromatic compounds (PACs) - a large group of organic chemicals naturally present in petroleum deposits (i.e., petrogenic) or released into the environment by incomplete combustion of organic materials (i.e., pyrogenic) - represent a potential risk to the health of aquatic ecosystems. In high latitude freshwater ecosystems, concentrations of PACs may be increasing, yet there are limited studies in such systems to assess change and to understand threats. Using 10 years of contemporary data from passive samplers deployed across five regions (n = 43 sites) in the Mackenzie River Basin, we (i) describe baseline levels of PACs, (ii) assess spatiotemporal patterns, and (ii) evaluate the extent to which environmental factors (fire, snowmelt, and proximity to oil infrastructure) influence concentrations in this system. Measured concentrations were low, relative to those in more southern systems, with mixtures primarily being dominated by non-alkylated, low molecular weight compounds. Concentrations were spatially consistent, except for two sites near Norman Wells (an area of active oil extraction) with increased levels. Similarly, observed annual variation was minimal, with 2014 having generally higher levels of PACs. We did not detect effects of fire, snowmelt, or oil infrastructure on concentrations. Taken together, our findings suggest that PACs in the Mackenzie River are currently at low levels and are primarily petrogenic in origin. They further indicate that ongoing monitoring and testing of environmental drivers (especially at finer spatial scales) are needed to better predict how ecosystem change will influence PACs levels in the Basin and in other northern systems.

Authors: Jordyn A Stalwick, Kristin M Eccles, Gila Somers, Philippe J Thomas, Kirsty Gurney

Full Source: Environmental pollution (Barking, Essex : 1987) 2024 Apr 11:123962. doi: 10.1016/j.envpol.2024.123962.

### Unveiling the hidden risks: Pesticide residues in aquaculture systems

2024-04-11

The present study systematically assessed the presence and ecological risks of 79 pesticides in various aquaculture systems, namely pond

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aquaculture (PA), greenhouse aquaculture (GA), and raceway aquaculture (RA) at different aquaculture stages, along with evaluating the pesticide removal of four tailwater treatment systems. Sixteen herbicides and two fungicides were identified, with the total concentrations ranging from 8.33 ng/L to 3248.45 ng/L. The PA system demonstrated significantly higher concentrations ($p < 0.05$) and a wider range of pesticide residues compared to the GA and RA systems. Prometryn, simetryn, atrazine, and thifluzamide were found to be the predominant pesticides across all three aquaculture modes, suggesting their significance as pollutants that warrant monitoring. Additionally, the findings indicated that the early aquaculture stage exhibits the highest levels of pesticide concentration, underscoring the importance of heightened monitoring and regulatory interventions during this phase. Furthermore, among the four tailwater treatment systems analyzed, the recirculating tailwater treatment system exhibited the highest efficacy in pesticide removal. A comprehensive risk assessment revealed minimal ecological risks in both the aquaculture and tailwater environments. However, the pesticide mixtures present high risks to algae and low to medium risks to aquatic invertebrates and fish, particularly during the early stages of aquaculture. Simetryn and prometryn were identified as high-risk pesticides. Based on the prioritization index, simetryn, prometryn, diuron, and ametryn are recommended for prioritization in risk assessment. This study offers valuable data for pesticide control and serves as a reference for the establishment of a standardized pesticide monitoring and management system at various stages of aquaculture.
Authors: Weijia Gan, Rongrong Zhang, Zhi Cao, Hao Liu, Wentao Fan, Aili Sun, Suquan Song, Zeming Zhang, Xizhi Shi
Full Source: The Science of the total environment 2024 Apr 11:172388. doi: 10.1016/j.scitotenv.2024.172388.

## PHARMACEUTICAL/TOXICOLOGY

### Gut Microbiome and Transcriptomic Changes in Cigarette Smoke-Exposed Mice Compared to COPD and CD Patient Datasets

2024-04-05
Chronic obstructive pulmonary disease (COPD) patients and smokers have a higher incidence of intestinal disorders. The aim of this study was to gain insight into the transcriptomic changes in the lungs and intestines, and the fecal microbial composition after cigarette smoke exposure. Mice

Chronic obstructive pulmonary disease (COPD) patients and smokers have a higher incidence of intestinal disorders.

were exposed to cigarette smoke and their lung and ileum tissues were analyzed by RNA sequencing. The top 15 differentially expressed genes were investigated in publicly available gene expression datasets of COPD and Crohn's disease (CD) patients. The murine microbiota composition was determined by 16S rRNA sequencing. Increased expression of MMP12, GPNMB, CTSK, CD68, SPP1, CCL22, and ITGAX was found in the lungs of cigarette smoke-exposed mice and COPD patients. Changes in the intestinal expression of CD79B, PAX5, and FCRLA were observed in the ileum of cigarette smoke-exposed mice and CD patients. Furthermore, inflammatory cytokine profiles and adhesion molecules in both the lungs and intestines of cigarette smoke-exposed mice were profoundly changed. An altered intestinal microbiota composition and a reduction in bacterial diversity was observed in cigarette smoke-exposed mice. Altered gene expression in the murine lung was detected after cigarette smoke exposure, which might simulate COPD-like alterations. The transcriptomic changes in the intestine of cigarette smoke-exposed mice had some similarities with those of CD patients and were associated with changes in the intestinal microbiome. Future research could benefit from investigating the specific mechanisms underlying the observed gene expression changes due to cigarette smoke exposure, focusing on identifying potential therapeutic targets for COPD and CD.
Authors: Lei Wang, Pim J Koelink, Johan Garssen, Gert Folkerts, Paul A J Henricks, Saskia Braber
Full Source: International journal of molecular sciences 2024 Apr 5;25(7):4058. doi: 10.3390/ijms25074058.

### Clinical investigator perspectives on patient outcomes in children with neuronopathic mucopolysaccharidosis II during intrathecal idursulfase-IT treatment

2024-04-12
Background: Mucopolysaccharidosis II (MPS II) is a rare lysosomal storage disease characterized by iduronate-2-sulfatase gene (IDS) deficiency and downstream glycosaminoglycan accumulation. Two-thirds of patients present with neuronopathic disease and evaluating cognitive function in these patients is challenging owing to limitations of currently available tests. During the clinical development of intrathecal idursulfase (idursulfase-IT), regulatory authorities requested qualitative data to further understand the neurocognitive changes observed by the investigators through the clinical trials.
Results: This qualitative study consisted of semi-structured interviews with all nine of the principal investigators who participated in the idursulfase-

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IT phase 2/3 (NCT02055118) and extension (NCT02412787) trials. These investigators enrolled the 56 patients with neuronopathic MPS II who qualified for the extension phase of the trial. The investigators were asked to rate the disease status of their patients. Of the 56 patients, 49 (88%) were rated as having disease that was improved/improving, stabilized or slowing progression compared with the expected outcomes with no treatment. Three patients were rated as worsening, while the remaining four patients were considered to have slowing progression or worsening disease. Similar results were demonstrated for patients aged from 3 to under 6 years at baseline, with 33 of 39 patients (85%) rated as having disease that was improved/improving, stabilized or slowing progression. Of the seven patients rated with slowing progression/worsening or worsening disease, five of them had an IDS variant other than missense, while two had a missense class variant. All the assigned improved/improving ratings were in patients receiving idursulfase-IT from the start of the phase 2/3 trial. Moreover, patients under 3 years of age at baseline were all rated as either improved/improving or stabilized disease. In a blinded review of patient profiles, investigators were requested to assign a disease status rating to 18 patients with large IDS deletions; 67% of these patients were rated as improved/improving or stabilized disease. Conclusions: This qualitative analysis provides a snapshot of clinicians' considerations when evaluating treatment in patients with neuronopathic MPS II, compared with the expected decline in cognitive function in the absence of treatment. The results highlight the importance of robust assessment tools in treatment evaluation.
Authors: Karen S Yee, David Alexanderian, Susan Martin, Bimpe Olayinka-Amao, David A H Whiteman
Full Source: Orphanet journal of rare diseases 2024 Apr 12;19(1):158. doi: 10.1186/s13023-024-03147-4.

## The impact of indoor air pollution on children's health and well-being: the experts' consensus

2024-04-14
Background: Pollution of the indoor environment represents a concern for human health, mainly in case of prolonged exposure such as in the case of women, children, the elderly, and the chronically ill, who spend most of their time in closed environments.
Main body: The aim of the study is to organize a group of experts in order to evaluate the evidence and discuss the main risk factors concerning indoor air and the impact on human health as well as challenging factors regarding preventive strategies to reduce pollution. The experts

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highlighted the main risk factors concerning indoor air, including poor ventilation, climatic conditions, chemical substances, and socio-economic status. They discussed the impact on human health in terms of mortality and morbidity, as well as challenging factors regarding preventive strategies to reduce pollution.
Conclusion: The experts identified strategies that can be reinforced to reduce indoor pollution and prevent negative consequences on human health at national and local levels.
Authors: Elena Bozzola, Rino Agostiniani, Laura Pacifici Noja, Jibin Park, Paolo Lauriola, Tiziana Nicoletti, Domenica Taruscio, Giovanni Taruscio, Alberto Mantovani
Full Source: Italian journal of pediatrics 2024 Apr 14;50(1):69. doi: 10.1186/s13052-024-01631-y.

## OCCUPATIONAL

### Harnessing technology to improve sleep in frontline healthcare workers: A pilot study of electronic noise-masking earbuds on subjective and objective sleep measures

2024-04
Objective: This pilot study assessed the effects of electronic noise-masking earbuds on subjective sleep perception and objective sleep parameters among healthcare workers (HCWs) reporting sleep difficulties during the COVID-19 pandemic. Methods: Using a pre-post design, 77 HCWs underwent 3 nights of baseline assessment followed by a 7-night intervention period. Participants wore an at-home sleep monitoring headband to assess objective sleep measures and completed subjective self-report assessments. The difference in mean sleep measures from baseline to intervention was estimated in linear mixed models. Results: Compared to baseline assessments, HCWs reported significant improvements in sleep quality as measured by the Insomnia Severity Index (ISI) (Cohen's d = 1.74, p < 0.001) and a significant reduction in perceived sleep onset latency (SOL) during the intervention (M = 17.2 minutes, SD = 7.7) compared to baseline (M = 24.7 minutes, SD = 16.1), (Cohen's d = -0.42, p = 0.001). There were no significant changes in objective SOL (p = 0.703). However, there was a significant interaction between baseline objective SOL (<20 minutes vs >20 minutes) and condition (baseline vs intervention) (p = 0.002), such that individuals with objective SOL >20 minutes experienced a significant decrease in objective SOL during the

> Objective: This pilot study assessed the effects of electronic noise-masking earbuds on subjective sleep perception and objective sleep parameters among healthcare workers (HCWs) reporting sleep difficulties during the COVID-19 pandemic.

intervention period compared to baseline (p = 0.015). Conclusions: HCWs experienced a significant improvement in perceived SOL and ISI scores after using the electronic noise-masking earbuds. Our data provide preliminary evidence for a nonpharmacological intervention to improve the sleep quality of HCWs which should be confirmed by future controlled studies.

Authors: Heinrich C Haller, Susan L Moore, Katherine K Green, Rachel L Johnson, Mary D Sammel, C Neill Epperson, Andrew M Novick
Full Source: Science progress 2024 Apr-Jun;107(2):368504241242276. doi: 10.1177/00368504241242276.

## Biomarker profiling in plants to distinguish between exposure to chlorine gas and bleach using LC-HRMS/MS and chemometrics

2024-04-09

Since its first employment in World War I, chlorine gas has often been used as chemical warfare agent. Unfortunately, after suspected release, it is difficult to prove the use of chlorine as a chemical weapon and unambiguous verification is still challenging. Furthermore, similar evidence can be found for exposure to chlorine gas and other, less harmful chlorinating agents. Therefore, the current study aims to use untargeted high resolution mass spectrometric analysis of chlorinated biomarkers together with machine learning techniques to be able to differentiate between exposure of plants to various chlorinating agents. Green spire (Euonymus japonicus), stinging nettle (Urtica dioica), and feathergrass (Stipa tenuifolia) were exposed to 1000 and 7500 ppm chlorine gas and household bleach, pool bleach, and concentrated sodium hypochlorite. After sample preparation and digestion, the samples were analyzed by liquid chromatography high resolution tandem mass spectrometry (LC-HRMS/MS) and liquid chromatography tandem mass spectrometry (LC-MS/MS). More than 150 chlorinated compounds including plant fatty acids, proteins, and DNA adducts were tentatively identified. Principal component analysis (PCA) and linear discriminant analysis (LDA) showed clear discrimination between chlorine gas and bleach exposure and grouping of the samples according to chlorine concentration and type of bleach. The identity of a set of novel biomarkers was confirmed using commercially available or synthetic reference standards. Chlorodopamine, dichlorodopamine, and trichlorodopamine were identified as specific markers for chlorine gas exposure. Fenclonine (Cl-Phe), 3-chlorotyrosine (Cl-Tyr), 3,5-dichlorotyrosine (di-Cl-Tyr), and 5-chlorocytosine (Cl-Cyt) were more abundantly present in plants after chlorine contact. In contrast, the

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DNA adduct 2-amino-6-chloropurine (Cl-Ade) was identified in both types of samples at a similar level. None of these chlorinated biomarkers were observed in untreated samples. The DNA adducts Cl-Cyt and Cl-Ade could clearly be identified even three months after the actual exposure. This study demonstrates the feasibility of forensic biomarker profiling in plants to distinguish between exposure to chlorine gas and bleach.

Authors: Mirjam de Bruin-Hoegée, Marcel J van der Schans, Jan P Langenberg, Arian C van Asten
Full Source: Forensic science international 2024 Apr 9:358:112022. doi: 10.1016/j.forsciint.2024.112022.