

Bulletin Board

Contents

MAR. 24, 2023

(click on page numbers for links)

CHEMICAL EFFECTS

Controlled Diesel Exhaust Exposure Induces a Concentration-Dependent Increase in Airway Inflammation 3

Association of polycyclic aromatic hydrocarbons exposure with child neurodevelopment and adult emotional disorders: A meta-analysis study..... 4

ENVIRONMENTAL RESEARCH

The generation of environmentally persistent free radicals on photoaged microbeads from cosmetics enhances the toxicity via oxidative stress..... 5

Pesticide residues in nectar and pollen of melon crops: Risk to pollinators and effects of a specific pesticide mixture on *Bombus terrestris* (Hymenoptera: Apidae) micro-colonies 6

Spatial prediction and influencing factors identification of potential toxic element contamination in soil of different karst landform regions using integration model 7

PHARMACEUTICAL/TOXICOLOGY

Application of physiologically-based pharmacokinetic modeled toluene blood concentration in the assessment of short term exposure limits 8

Associations between exposure to a mixture of phenols and sex steroid hormones among pre- and postmenopausal women: evidence from NHANES 2015-2016 8

OCCUPATIONAL

Clinical manifestation score and characterization of cytokines and lymphocytes of dimethylacetamide-induced toxic hepatitis in spandex workers..... 10

Electronic-waste-associated pollution of per- and polyfluoroalkyl substances: Environmental occurrence and human exposure..... 10

Non-negligible health risks caused by inhalation exposure to aldehydes and ketones during food waste treatments in megacity Shanghai..... 11

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Bulletin Board

Technical

MAR. 24, 2023

CHEMICAL EFFECTS

Controlled Diesel Exhaust Exposure Induces a Concentration-Dependent Increase in Airway Inflammation

2023-03-17

Rationale: Air Pollution exposure is harmful to human airways and its impacts are best studied using concentration-response relationships. However, most concentration-response research on airway health has investigated chronic exposures, with less known about acute effects, which can be robustly studied using controlled human exposures.

Objectives: To investigate the concentration-relationship between airway health measures and diesel exhaust (DE).

Methods: We conducted a double-blinded crossover study with 17 healthy non-smokers exposed to filtered air (FA) and DE standardized to 20, 50 and 150 $\mu\text{g}/\text{m}^3$ of particulate matter $<2.5\mu\text{m}$ (PM_{2.5}) for 4h. Before, during and up to 24h from the exposure start, we measured lung function, airway responsiveness and airway inflammation using spirometry, methacholine challenge and fractional exhaled nitric oxide (FeNO) respectively.

Additionally, we measured nasal airway inflammation using differential cell counts and cytokines in nasal lavage and epithelial lining fluid at 24h. We assessed DE concentration-responses and associations between outcomes using linear mixed effects models and repeated measures correlations respectively, thereafter adjusting for multiple comparisons.

Results: DE exposure increased % ΔFeNO at 4h ($\beta=0.16\pm0.06$). Compared to FA, % ΔFeNO trended towards an increase at concentrations of 20 $\mu\text{g}/\text{m}^3$ ($\beta=18.66\pm8.76$) and 50 $\mu\text{g}/\text{m}^3$ ($\beta=19.33\pm8.92$) and increased significantly at 150 $\mu\text{g}/\text{m}^3$ ($\beta=34.43\pm8.92$). Additionally, DE exposure induced a trend towards increased nasal IL-6 at 24h (% difference = 0.88 (95% CI: 0.08, 1.70)). There were no effects of DE exposure on FeNO at 24h, lung function, airway responsiveness, or nasal cell counts.

Conclusions: DE induces a concentration-dependent increase in FeNO, indicating that it may be a sensitive marker of an acute inflammatory response in the airways. We report responses at concentrations below those in previous controlled DE exposure studies, and document PM_{2.5} concentration-response estimates at exposure levels routinely experienced in the community and occupational settings. Clinical trial registered with ClinicalTrials.gov (NCT03234790).

Authors: Juma Orach, Christopher Francis Rider, Agnes Che Yan Yuen, Carley Schwartz, Neeloffer Mookherjee, Christopher Carlsten

Full Source: Annals of the American Thoracic Society 2023 Mar 17. doi: 10.1513/AnnalsATS.202209-762OC.

Rationale: Air Pollution exposure is harmful to human airways and its impacts are best studied using concentration-response relationships.

Bulletin Board

Technical

MAR. 24, 2023

Association of polycyclic aromatic hydrocarbons exposure with child neurodevelopment and adult emotional disorders: A meta-analysis study

2023-03-15

Background: Polycyclic aromatic hydrocarbons (PAHs) have been demonstrated to be neurotoxic.

Objectives: To summarize the existing epidemiological studies to quantify the effects of PAHs exposure on child neurodevelopment and adult emotional disorders.

Data sources and study eligibility criteria: We conducted a systematic literature search for studies of child neurodevelopment and adult emotional disorders published in English up to April 2022 in the databases of PubMed, Web of Science and Embase using combinations of MeSH terms and Entry terms, and the articles were filtered out according to data availability. A variety of common PAHs were included in the meta-analysis: 1-hydroxynaphthalene, 2-hydroxynaphthalene, 2-hydroxyfluorene, 3-hydroxyfluorene, 9-hydroxyfluorene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene, 3-hydroxyphenanthrene, 4-hydroxyphenanthrene, 9-hydroxyphenanthrene, 1-hydroxypyrene and benzoapyrene (BaP).

Study evaluation and synthesis methods: We extracted the content of each article, summarized its design characteristics and performed quality evaluation. We combined the odds ratio (OR) available in various studies to obtain the risk of PAHs exposure and adaptive, language, social, attention, motor skills and child depression/anxiety in children ≤ 15 years old. In addition, we also conducted a meta-analysis on the relationship between PAHs exposure and the risk of depression in adults.

Results: We included a total of 16 epidemiological studies (4 cross-sectional studies and 12 cohort studies). The sample size of all included studies ranged from 110 to 9625. Prenatal exposure to PAHs was found to be associated with increased risk of social behavior (OR = 1.60, 95% CI: 1.00-2.54), attention (OR = 2.99, 95% CI: 1.48-6.02), motor skill problems (OR = 1.91, 95% CI: 1.27-2.86) and any adverse neurodevelopmental outcome in children (OR = 2.10, 95% CI: 1.69-2.62). In addition, we found that PAHs exposure could increase the risk of adult depression, with 2-hydroxyfluorene exposure showing the highest combined OR (OR = 1.48, 95% CI: 1.10-2.00).

Conclusions: The results suggested that PAHs exposure are associated with increased risk of child neurodevelopment and adult depression. The neurotoxic effects of PAHs exposure in human being should be paid more attention. The results suggested that PAHs exposure are associated

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Bulletin Board

Technical

MAR. 24, 2023

with increased risk of child neurodevelopment and adult depression. The neurotoxic effects of PAHs exposure in human being should be paid more attention. Steps should be taken to enhance the biomonitoring of PAHs and to reduce the exposure in general population.

Authors: Hualong Zhen, Fan Zhang, Hengshun Cheng, Fengying Hu, Yunfei Jia, Yanyan Hou, Mengqing Shang, Huan Yu, Minmin Jiang
Full Source: Ecotoxicology and environmental safety 2023 Mar 15;255:114770. doi: 10.1016/j.ecoenv.2023.114770.

ENVIRONMENTAL RESEARCH

The generation of environmentally persistent free radicals on photoaged microbeads from cosmetics enhances the toxicity via oxidative stress

2023-03-13

Microbeads used in personal care products have been one of the important sources of microplastics (MPs), and little has been reported on their environmental behaviors and health risks. The characteristics of environmentally persistent free radicals (EPFRs) and the toxicity assessment of MPs (environmentally relevant concentrations) from cosmetics during photoaging remains largely unknown. In this study, the formation of EPFRs on polyethylene (PE) microbeads from facial scrubs under light irradiation and their toxicity were investigated using *C. elegans* as a model organism. The results suggested that light irradiation induced the generation of EPFRs, which accelerates the aging process and alters the physicochemical properties of PE microbeads. Acute exposure to PE (1 mg/L) at photoaged times of 45-60 d significantly decreased the physiological indicators (e.g., head thrashes, body bends, and brood size). The oxidative stress response and stress-related gene expression were also enhanced in nematodes. The addition of N-acetyl-L-cysteine induced significant inhibition of toxicity and oxidative stress in nematodes exposed to 45-60 d of photoaged PE. The Pearson correlation results showed that the concentration of EPFRs was significantly correlated with physiological indicators, oxidative stress, and related-genes expression in nematodes. The data confirmed that the generation of EPFRs combined with heavy metals and organics contributed to toxicity induced by photoaged PE, and oxidative stress might be involved in regulating adverse effects in *C. elegans*. The study provides new insight into the potential risks of microbeads released into the environment during photoaging. The

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Bulletin Board

Technical

MAR. 24, 2023

findings also highlight the necessity for considering the role of EPFRs formation in evaluating the impacts of microbeads.

Authors: Haibo Chen, Yongqi Jiang, Yulun Gu, Ping Ding, Chen Wang, Ruolin Pan, Chongli Shi, Lingjun Zeng, Xiaoxia Chen, Hui Li
Full Source: Environment international 2023 Mar 13;174:107875. doi: 10.1016/j.envint.2023.107875.

Pesticide residues in nectar and pollen of melon crops: Risk to pollinators and effects of a specific pesticide mixture on *Bombus terrestris* (Hymenoptera: Apidae) micro-colonies

2023-03-16

Residues detected in pollen collected by honey bee are often used to estimate pesticide exposure in ecotoxicological studies. However, for a more accurate assessment of pesticides effect on foraging pollinators, residues found directly on flowers are a more realistic exposure approximation. We conducted a multi-residue analysis of pesticides on pollen and nectar of melon flowers collected from five fields. The cumulative chronic oral exposure Risk Index (RI) was calculated for *Apis mellifera*, *Bombus terrestris* and *Osmia bicornis* to multiple pesticides. However, this index could underestimate the risk since sublethal or synergistic effects are not considered. Therefore, a mixture containing three of the most frequently detected pesticides in our study was tested for synergistic impact on *B. terrestris* micro-colonies through a chronic oral toxicity test. According to the result, pollen and nectar samples contained numerous pesticide residues, including nine insecticides, nine fungicides, and one herbicide. Eleven of those were not applied by farmers during the crop season, revealing that melon agroecosystems may be pesticide contaminated environments. The primary contributor to the chronic RI was imidacloprid and *O. bicornis* is at greatest risk for lethality resulting from chronic oral exposure at these sites. In the bumblebee micro-colony bioassay, dietary exposure to acetamiprid, chlorpyrifos and oxamyl at residue level concentration, showed no effects on worker mortality, drone production or drone size and no synergies were detected when pesticide mixtures were evaluated. In conclusion, our findings have significant implications for improving pesticide risk assessment schemes to guarantee pollinator conservation. In particular, bee pesticide risk assessment should not be limited to acute exposure effects to isolated active ingredients in honey bees. Instead, risk assessments should account for long-term pesticide exposure effects in both pollen and nectar on

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Bulletin Board

Technical

MAR. 24, 2023

a range of bees that reflect the diversity of natural ecosystems and the synergistic potential among pesticide formulations.

Authors: Celeste Azpiazu, Pilar Medina, Fabio Sgolastra, Ana Moreno-Delafuente, Elisa Viñuela

Full Source: Environmental pollution (Barking, Essex : 1987) 2023 Mar 16;121451. doi: 10.1016/j.envpol.2023.121451.

Spatial prediction and influencing factors identification of potential toxic element contamination in soil of different karst landform regions using integration model

2023-03-15

The prediction of contamination distribution of potentially toxic elements (PTEs) in soils of Guangxi province, China and the identification of their controlling factors pose great challenges due to diverse bedrock types, intense leaching and weathering, and discontinuous terrain distributions. Herein, we integrated the random forest (RF) and empirical Bayesian kriging (EBK) to interpret and predict complex PTEs contamination distribution from three different karst landform regions (fenglin, fengcong, isolated peak plain) in Guangxi province. The modeling results are compared with the commonly used ordinary kriging and regression-kriging. In this study, our developed RF-EBK model combines the advantages of the RF and EBK model to promote the prediction accurately and efficiently. In this study, it was shown that the integration RF-EBK model exhibited desirable for Cd and As concentrations, with R² of 0.89 and 0.83, respectively. The average RMSE and MAE of integration RF-EBK model decreased by 39% and 44%, respectively, relative to the regression-kriging with the second highest accuracy. Furthermore, the modeling results showed that approximately 41.96% and 18.96% of total area was classified as Cd and As polluted and above regions ($I_{geo} > 0$) in Guangxi province, respectively. Higher Cd concentration was observed in the soil of fenglin and fengcong regions than that in isolated peak plain region due to the secondary enrichment and parent rock inheritance, while the As concentration exhibited no significant difference among the three regions. The modeling results indicated that the elevated Cd concentration might be associated with soil CaO concentration and alkaline soil environment, whereas As concentration tended to be increased with the elevating Fe₂O₃ concentrations in weakly acidic soil environment. This result confirmed the applicability and effectiveness of integration model in

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Bulletin Board

Technical

MAR. 24, 2023

predicting complex spatial patterns of soil PTEs and identifying their controlling factors.

Authors: Bolun Zhang, Hong Hou, Lingling Liu, Zhanbin Huang, Long Zhao

Full Source: Chemosphere 2023 Mar 15;138404. doi: 10.1016/j.chemosphere.2023.138404.

PHARMACEUTICAL/TOXICOLOGY

Application of physiologically-based pharmacokinetic modeled toluene blood concentration in the assessment of short term exposure limits

2023-03-17

Toluene is a volatile hydrocarbon with solvent applications in several industries. Acute neurological effects in workers exposed to toluene have been reported in various publications. To inform the basis for a toluene Short Term Exposure Limit (STEL), studies of toluene-exposed workers were modeled using customized exposure scenarios within an existing physiologically-based pharmacokinetic (PBPK) model to simulate blood concentrations during individual studies. Maximum simulated blood concentration ranged from 0.3 to 1.7 (mean = 0.74 mg/L, median = 0.73, upper 95th percentile = 1.07) at the studies identified No Observed Adverse Effect Concentration (NOAEC). Maximum simulated blood concentration ranged from 0.7 to 4.1 mg/L (mean = 1.81, median = 1.63, lower 95th percentile = 0.92) at the studies identified Lowest Observed Adverse Effect Concentration (LOAEC). The maximum blood concentration for a 100 ppm STEL-like simulation was 0.4 mg/L, at the lower end of the NOAEC range and below the 95th percentile of the LOAEC. Therefore, it appears that a STEL <100 ppm would be unnecessary to protect workers due to peak occupational exposures to toluene.

Authors: Colin M North, Martijn Rooseboom, Neslihan Aygun Kocabas, Nicolas Synhaeve, James Radcliffe, Lawrence Segal

Full Source: Regulatory toxicology and pharmacology : RTP 2023 Mar 17;105380. doi: 10.1016/j.yrtph.2023.105380.

Associations between exposure to a mixture of phenols and sex steroid hormones among pre- and postmenopausal women: evidence from NHANES 2015-2016

2023-03-17

Environmental phenols are well known as emerging endocrine-disrupting chemicals; however, their impacts on sex hormone homeostasis among

Toluene is a volatile hydrocarbon with solvent applications in several industries.

Bulletin Board

Technical

MAR. 24, 2023

pre- and postmenopausal women remain unknown. Our objective was to evaluate independent and combined relationships between phenol levels in urine and sex steroid hormones among 323 premenopausal women and 263 postmenopausal women from National Health and Nutrition Examination Survey (NHANES) 2015-2016. A total of 10 phenol concentrations in urine were quantified using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Serum concentrations of estradiol and total testosterone were measured by LC-MS/MS and serum sex hormone-binding globulin (SHBG) concentrations were measured using an immunofluorometric assay. Multivariable linear regression models were conducted to explore associations of individual phenol concentration in urine with natural logarithm-transformed serum hormone levels. Bayesian kernel machine regression (BKMR) model was conducted to evaluate phenol mixtures exposure in association with sex hormones among pre- and postmenopausal women, respectively. Considering both single-chemical models and multiple-chemical models, each doubling of urinary BPS concentration was significantly inversely related to serum SHBG concentration in premenopausal women (percent change: -6.70%, 95% confidence interval, CI: -11.12%, -2.73%; $P = 0.002$). Moreover, every doubling of urinary BP-3 concentration was significantly positively associated with SHBG level in serum (percent change: 3.53%, 95%CI: 0.70%, 5.70%; $P = 0.008$). Regarding postmenopausal women, inverse associations between urinary BPS levels and serum estradiol concentrations were observed (percent change: -8.62%, 95% CI: -15.33%, -2.06%; $P = 0.012$). The results revealed that BPS and BP-3 exposure may adversely disrupt sex hormone homeostasis at the current exposure levels among women in the USA. The findings and their underlying mechanisms are warranted to be confirmed and comprehensively interpreted in further epidemiological and experimental studies.

Authors: Menglu Guo, Changlin Zhu

Full Source: Environmental science and pollution research international 2023 Mar 17. doi: 10.1007/s11356-023-26421-7.

Environmental phenols are well known as emerging endocrine-disrupting chemicals.

Bulletin Board

Technical

MAR. 24, 2023

OCCUPATIONAL

Clinical manifestation score and characterization of cytokines and lymphocytes of dimethylacetamide-induced toxic hepatitis in spandex workers

2023-03-19

Occupational exposure to dimethylacetamide (DMAc) has been reported to cause toxic hepatitis. Sixty spandex workers were included in this study to research the clinical manifestations and expression of cytokines and lymphocytes in DMAc-induced toxic hepatitis. Chinese drugs (reduced glutathione and Huga tablets) were used to treat them. The manifestations including jaundice, asthenia, appetite, nausea, emesis, abdominal distension, yellow urine, and dizziness were scored. The percentages of patients rated as 0-3, 4-6, 7-9, and 10-12 points were 33.3%, 43.3%, 21.7%, and 1.7%, respectively, before treatment, and all patients showed 0-3 points after the treatment. The ultrasonic and CT imaging revealed diffuse intrahepatic hypodensity, intrahepatic calcification, signs of liver injury, and splenomegaly, which improved after therapy. Blood analysis showed that ALT, AST, TBIL, IL-6, IL-10, TNF- α , IFN- γ , CD3+%, and CD4+/CD8+ statistically decreased after drug treatment. Correlation analysis demonstrated positive linear correlations between ALT and TBIL, AST and TBIL, IL-10 and ATL, IL-10 and AST, IL-10 and TBIL, IFN- γ and IL-6, IFN- γ and TNF- α , and CD3+% and ALT. Pro-inflammatory cytokines and lymphocytes in DMAc-induced toxic hepatitis reflected an active immune state that decreased after treatment. IL-10 may inhibit the immune response in this disease, as a protective mechanism.

Authors: Jinglei Wang, Kai Tang, Caiping Wang, Shengzhi Xu, Yaqin Wang, Qinya Zhu

Full Source: Toxicology and industrial health 2023 Mar 19;7482337231162762. doi: 10.1177/07482337231162762.

Electronic-waste-associated pollution of per- and polyfluoroalkyl substances: Environmental occurrence and human exposure

2023-03-13

Occupational exposure to per- and polyfluoroalkyl substances (PFASs) is of serious concern because their adverse health effects. Nevertheless, knowledge regarding contamination in e-waste dismantling regions is rather scarce. We therefore analysed seven neutral PFASs (n-PFASs) and forty ionized PFASs (i-PFASs) in dust and hand wipes collected from

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Bulletin Board

Technical

MAR. 24, 2023

an e-waste dismantling plant and homes. Both dust (1370 ng/g) and workers' hand wipe (1100 ng/m²) in e-waste dismantling workshops contained significantly higher median levels of Σ PFASs than those from homes (684 ng/g and 444 ng/m²) ($p < 0.01$). Σ PFAS concentrations in dust and on workers' hand wipes from workshops were significantly higher than those from storage area. 8:2 fluorotelomer alcohol was the dominant n-PFAS in workshop dust (70.7%) and on worker's hand wipes (46.6%). Perfluoroalkyl carboxylic acids (C2 -C3) were the significant components (based on concentration) of i-PFASs in dust (57.9%) and on hand wipes (89.6%). A significant positive correlation ($p < 0.001$) of Σ PFAS concentrations between workshop dust and workers' hand wipes was observed, indicating that they come from common sources. Compared to dust ingestion, hand-to-mouth contact was highlighted as a vital exposure route, accounting for 68.8% for workers and 72.2% for residential population, respectively, of the sum of two exposure doses.

Authors: Leicheng Zhao, Zhipeng Cheng, Hongkai Zhu, Hao Chen, Yiming Yao, Mujtaba Baqar, Hao Yu, Biting Qiao, Hongwen Sun

Full Source: Journal of hazardous materials 2023 Mar 13;451:131204. doi: 10.1016/j.jhazmat.2023.131204.

Non-negligible health risks caused by inhalation exposure to aldehydes and ketones during food waste treatments in megacity Shanghai

2023-03-15

Aldehydes and ketones in urban air continue to receive regulatory and scientific attention for their environmental prevalence and potential health hazard. However, current knowledge of the health risks and losses caused by these pollutants in food waste (FW) treatment processes is still limited, especially under long-term exposure. Here, we presented the first comprehensive assessment of chronic exposure to 21 aldehydes and ketones in urban FW-air environments (e.g., storage site, mechanical dewatering, and composting) by coupling substantial measured data (383 samples) with Monte Carlo-based probabilistic health risk and impact assessment models. The results showed that acetaldehyde, acetone, 2-butanone and cyclohexanone were consistently the predominant pollutants, although the significant differences in pollution profiles across treatment sites and seasons (Adonis test, $P < 0.001$). According to the risk assessment results, the estimated cancer risk (CR; mean range: 1.6×10^{-5} - 1.12×10^{-4}) and non-cancer risk (NCR; mean range: 2.98-22.7) triggered by aldehydes and ketones were both unacceptable in most cases (CR: 37.8%-99.3%; NCR: 54.2%-99.8%), and even reached the limit of concern

Aldehydes and ketones in urban air continue to receive regulatory and scientific attention for their environmental prevalence and potential health hazard.

Bulletin Board

Technical

MAR. 24, 2023

to CR (1×10^{-4}) in some exposure scenarios (6.18%-16.9%). Application of DALYs (disability adjusted life years) as a metric for predicting the damage suggested that exposure of workers to aldehydes and ketones over 20 years of working in FW-air environments could result in 0.02-0.14 DALYs per person. Acetaldehyde was the most harmful constituent of all targeted pollutants, which contributed to the vast majority of health risks (>88%) and losses (>90%). This study highlights aldehydes and ketones in FW treatments may be the critical pollutants to pose inhalation risks.

Authors: Liangmao Zhang, Binghan Wang, Kaiyi Li, Zijiang Wang, Dan Xu, Yinglong Su, Dong Wu, Bing Xie

Full Source: Environmental pollution (Barking, Essex : 1987) 2023 Mar 15;325:121448. doi: 10.1016/j.envpol.2023.121448.