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CHEMICAL EFFECTS

Characterization of adipogenic, PPAR γ , and TR β activities in house dust extracts and their associations with organic contaminants

2020-11-14

In this study, we sought to expand our previous research on associations between bioactivities in dust and associated organic contaminants. Dust samples were collected from central NC homes (n = 188), solvent extracted, and split into two fractions, one for analysis using three different bioassays (nuclear receptor activation/inhibition and adipocyte development) and one for mass spectrometry (targeted measurement of 124 organic contaminants, including flame retardants, polychlorinated biphenyls, perfluoroalkyl substances, pesticides, phthalates, and polycyclic aromatic hydrocarbons). Approximately 80% of dust extracts exhibited significant adipogenic activity at concentrations that are comparable to estimated exposure for children and adults (e.g. ~20 $\mu\text{g}/\text{well}$ dust) via either triglyceride accumulation (65%) and/or pre-adipocyte proliferation (50%). Approximately 76% of samples antagonized thyroid receptor beta (TR β), and 21% activated peroxisome proliferator activated receptor gamma (PPAR γ). Triglyceride accumulation was significantly correlated with TR β antagonism. Sixty-five contaminants were detected in at least 75% of samples; of these, 26 were correlated with adipogenic activity and ten with TR β antagonism. Regression models were used to evaluate associations of individual contaminants with adipogenic and TR β bioactivities, and many individual contaminants were significantly associated. An exploratory g-computation model was used to evaluate the effect of mixtures. Contaminant mixtures were positively associated with triglyceride accumulation, and the magnitude of effect was larger than for any individually measured chemical. For each quartile increase in mixture exposure, triglyceride accumulation increased by 212% (RR = 3.12 and 95% confidence interval: 1.58, 6.17). These results suggest that complex mixtures of chemicals present in house dust may induce adipogenic activity in vitro at environmental concentrations and warrants further research.

Authors: Christopher D Kassotis, Kate Hoffman, Allison L Phillips, Sharon Zhang, Ellen M Cooper, Thomas F Webster, Heather M Stapleton

Full Source: The Science of the total environment 2020 Nov 14;143707. doi: 10.1016/j.scitotenv.2020.143707.

In this study, we sought to expand our previous research on associations between bioactivities in dust and associated organic contaminants.

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Research progress on toxicity, function, and mechanism of metal oxide nanoparticles on vascular endothelial cells

2020-11-26

Metal oxide nanoparticles present stable and unique performance that makes them suitable for various biomedical applications. There are four common exposure ways that nanoparticles enter our body: injection, inhalation, skin penetration, and ingestion. Among them, injection, ingestion, and skin routes may become significant ways for nano-scale treatment and cosmetics, and inhalation is the essential way for occupational exposure. All those nanoparticles could pass through the exposure routes and enter the circulation, which could cause damage on the cardiovascular system. So it is necessary to evaluate the toxicity of metal oxide nanoparticles and to explore the mechanism. This review chose four commonly used nanometal oxides to discuss about the toxicity they produced, the function they affected, and the mechanisms on cardiovascular endothelial cells. First, we discussed the toxicity they caused. These nanoparticles are less toxic when applied in low doses, but owing to the small particle size and large specific surface area, acute exposure or the metal ions released by nanoparticles will lead to phenotypic changes of endothelial cells, oxidative stress, and apoptosis. An endothelial cell is an essential part of blood vessels and could act as a barrier, maintain vascular tension, and keep the balance between coagulation and anticoagulation. Once vascular endothelium is injured or exposed to vascular risk factors, it would cause endothelial activation, endothelial dysfunction, and nitric oxide (NO) synthase (NOS) dysfunction, which are closely related to the cardiovascular disease. Finally, we talked about the mechanisms by four levels, and we especially mentioned inflammation, the production of reactive oxygen species, and NO.

Authors: Zhihui Wang, Meng Tang

Full Source: Journal of applied toxicology : JAT 2020 Nov 26. doi: 10.1002/jat.4121.

A review of 1,2-dibromo-4-(1,2-dibromoethyl)cyclohexane in the environment and assessment of its persistence, bioaccumulation and toxicity

2020-11-21

Following the ban of many historically-used flame retardants (FRs), numerous replacement chemicals have been produced and used in products, with some being identified as environmental contaminants. One of these replacement flame retardants is 1,2-dibromo-4-(1,2-

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dibromoethyl)-cyclohexane (DBE-DBCH; formerly abbreviated as TBECH), which to date has not been identified for risk assessment and potential regulation. DBE-DBCH technical mixtures consist largely of α - and β -diastereomers with trace amounts of γ - and δ -DBE-DBCH. The α - and β -isomers are known contaminants in various environmental media. While current global use and production volumes of DBE-DBCH are unknown, recent studies identified that DBE-DBCH concentrations were among the highest of the measured bromine-based FRs in indoor and urban air in Europe. Yet our mass balance fugacity model and modeling of the physical-chemical properties of DBE-DBCH estimated only 1% partitioning to air with a half-life of 2.2 d atmospherically. In contrast, our modeling characterized DBE-DBCH adsorbing strongly to suspended particulates in the water column (12%), settling onto sediment (2.5%) with minimal volatilization, but with most partitioning and adsorbing strongly to soil (85%) with negligible volatilization and slow biodegradation. Our modeling further predicted that organisms would be exposed to DBE-DBCH through partitioning from the dissolved aquatic phase, soil, and by diet, and given its estimated logKow (5.24) and a half-life of 1.7 d in fish, DBE-DBCH is expected to bioaccumulate into lipophilic tissues. Low concentrations of DBE-DBCH are commonly measured in biota and humans, possibly because evidence suggests rapid metabolism. Yet toxicological effects are evident at low exposure concentrations: DBE-DBCH is a proven endocrine disruptor of sex and thyroid hormone pathways, with in vivo toxic effects on reproductive, metabolic, and other endpoints. The objectives of this review are to identify the current state of knowledge concerning DBE-DBCH through an evaluation of its persistence, potential for bioaccumulation, and characterization of its toxicity, while identifying areas for future research.

Authors: Sarah C Marteinson, Anjelica Bodnaryk, Mark Fry, Nicole Riddell, Robert J Letcher, Chris Marvin, Gregg T Tomy, Kim J Fernie

Full Source: Environmental research 2020 Nov 21;110497. doi: 10.1016/j.envres.2020.110497.

ENVIRONMENTAL RESEARCH

Modified Ziziphus spina-christi stones as green route for the removal of heavy metals

2020-11-25

Green routes for remediation of heavy metals are worldwide challenges to overcome pollution problems on one hand and control the adverse impact of chemicals on the other hand. Biosorption is one of the most

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effective methods for removing lower level of heavy metals. The idea to apply natural resources as a green method for removal of heavy metals, this route has no adverse impacts on the environment. This study investigated the ability of chemically modified Ziziphus spina-christi stones (ZSCs) as agriculture by-products to perform the biosorption of Pb(II), Zn(II) and Cd(II) ions from wastewater in a single and ternary metal system. The characteristic functional groups of chemically modified ZSCs were analyzed by Fourier transform infrared. In comparison with acidic ZSCs, alkali-modified ZSCs by KOH was more effective and enhanced the removal efficiency of ZSCs. Using Langmuir isotherm, the maximum adsorption capacity on the modified ZSCs for Pb(II) was 9.06 mg/g, for Zn(II) obtained by using ZSC-citric acid was 4.19 mg/g and 5.38 mg/g for Cd(II) as obtained by using ZSC-H₂O₂. The molecular electrostatic potential, which was calculated at B3LYP/6-31G(d,p), indicated that each metal is di-hydrated, forming a complex with two units of amino acids. This mechanism demonstrated the uptake process by ZSCs.

Authors: Eman A Assirey, Shadia M Sirry, Hayfaa A Burkani, Medhat A Ibrahim

Full Source: Scientific reports 2020 Nov 25;10(1):20557. doi: 10.1038/s41598-020-76810-y.

Birth Defects and Unconventional Natural Gas Developments in Texas, 1999-2011

2020-11-24

Unconventional natural gas developments (UNGD) may release air and water pollutants into the environment, potentially increasing the risk of birth defects. We conducted a case-control study evaluating 52,955 cases with birth defects and 642,399 controls born between 1999 to 2011 to investigate the relationship between UNGD exposure and the risk of gastroschisis, congenital heart defects (CHD), neural tube defects (NTDs), and orofacial clefts in Texas. We calculated UNGD densities (number of UNGDs per area) within 1, 3, and 7.5 km of maternal address at birth and categorized exposure by density tertiles. For CHD subtypes with large case numbers, we also performed time-stratified analyses to examine temporal trends. We calculated adjusted odds ratios (aOR) and 95% confidence intervals (CI) for the association with UNGD exposure, accounting for maternal characteristics and neighborhood factors. We also included a bivariable smooth of geocoded maternal location in an additive model to account for unmeasured spatially varying risk factors. Positive associations were observed between the highest tertile of UNGD density within 1 km of maternal address and risk of anencephaly (aOR: 2.44, 95% CI: 1.55,

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3.86), spina bifida (aOR: 2.09, 95% CI: 1.47, 2.99), gastroschisis among older mothers (aOR: 3.19, 95% CI: 1.77, 5.73), aortic valve stenosis (aOR: 1.90, 95% CI: 1.33, 2.71), hypoplastic left heart syndrome (aOR: 2.00, 95% CI: 1.39, 2.86), and pulmonary valve atresia or stenosis (aOR: 1.36, 95% CI: 1.10, 1.66). For CHD subtypes, results did not differ substantially by distance from maternal address or when residual confounding was considered, except for atrial septal defects. We did not observe associations with orofacial clefts. Our results suggest that UNGDs were associated with some CHDs and possibly NTDs. In addition, we identified temporal trends and observed presence of spatial residual confounding for some CHDs.

Authors: Ian W Tang, Peter H Langlois, Verónica M Vieira

Full Source: Environmental research 2020 Nov 24;110511. doi: 10.1016/j.envres.2020.110511.

Climate Change, Air Pollution, and Biodiversity in Asia Pacific and Impact on Respiratory Allergies

2021-02

Allergic diseases are increasing globally. Air pollution, climate change, and reduced biodiversity are major threats to human health with detrimental effects on chronic noncommunicable diseases. Outdoor and indoor air pollution and climate change are increasing. Asia has experienced rapid economic growth, a deteriorating environment, and an increase in allergic diseases to epidemic proportions. Air pollutant levels in Asian countries are substantially higher than in developed countries. Moreover, industrial, traffic-related, and household biomass combustion and indoor pollutants from chemicals and tobacco are major sources of air pollutants. We highlight the major components of pollutants and their impacts on respiratory allergies.

Authors: Ruby Pawankar, Jiu-Yao Wang

Full Source: Immunology and allergy clinics of North America 2021 Feb;41(1):63-71. doi: 10.1016/j.iac.2020.09.008.

OCCUPATIONAL

Methyl siloxanes in road dust from a large silicone manufacturing site in China: implications of human exposure

2020-11-27

Methyl siloxanes are becoming increasingly prevalent in the environment because of their extensive use in various consumer products. Little is

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known about the distribution of these chemicals around factories or their presence in road dust. We conducted a survey of four cyclic (D3-D6) and 13 linear (L4-L16) siloxanes in road dusts around a manufacturing site and found a total siloxane concentration range of 47.3-3.16 × 10³ ng/g (median 372). The predominant siloxanes in the road dust samples were D3, D4, D5, and D6, with median contributions of 65.3%, 17.9%, 6.36%, and 2.16% of the total siloxane concentrations, respectively. Our reported concentrations were comparable to those found in household dusts in previous studies. No high concentrations of siloxanes were observed in the road dust samples from the manufacturing site, which suggests that siloxanes in outdoor dusts are likely affected by many factors. Under a high exposure scenario, the daily intakes of total siloxanes via road dust ingestion at the 95th percentile were 2.13 and 0.313 ng/kg-bw/day for children and adults, respectively. Although the estimated exposure to siloxanes in outdoor dust for humans was low, more studies on the distributions and risks of siloxanes released from manufacturing sites are needed.

Authors: Jiali Cheng, Zhenwu Tang, Yan Ma, Hongmin Yin, Tong Meng, Jiazheng Sun

Full Source: Environmental science and pollution research international 2020 Nov 27. doi: 10.1007/s11356-020-11773-1.

Estimation of lymphocyte subsets and cytokine levels in workers occupationally exposed to cadmium

2020-11-12

Introduction: Occupational exposure to Cadmium (Cd) may have serious health effect on workers. However, little is known about its effect on immune system. Moreover, previous studies have been inconclusive in stating the effect of Cd on immune system. The aim of our study was to estimate immune parameters in workers occupationally exposed to Cd. Material and methods: 110 individuals occupationally exposed to Cd and 97 apparently healthy non-exposed individuals were recruited for this study. Blood Cadmium levels were determined by AAS. Lymphocyte subset were analyzed using flow cytometry and the cytokine levels were determined by ELISA.

Results: Exposed group have significantly higher levels of B-Cd. % of CD8 cells were higher in exposed while % of CD4 cells showed a decreasing trend in the exposed group. Among the CD3CD4 T cell subsets Th1 (%) and Tregs (%) cells were lower while Th17 (%) were higher in exposed group. Increased levels of IL-4 (Th2), IL-6 (Th2) and TNF- α (Th1) and decreased levels of IL-2 (Th1) and IL-10 (Tregs) were observed in Cd

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exposed workers which is indicative of a predominant pro-inflammatory response in Cd exposed workers. IL-17 (Th17) levels did not show any significant difference between the two groups. Increased Th17/Tregs ratio in the exposed group is also suggestive of an increased pro-inflammatory immune response in exposed group.

Conclusion: To conclude, even low level of exposure to Cd in occupational settings is associated with alterations in Th17 cells, which may further predispose an individual to other systemic abnormalities.

Authors: Taru Goyal, Prasenjit Mitra, Preeti Singh, Raghunoy Ghosh, Malavika Lingeswaran, Shailja Sharma, Purvi Purohit, Praveen Sharma
Full Source: Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS) 2020 Nov 12;64:126681. doi: 10.1016/j.jtemb.2020.126681.

Occupational exposure to antimony trioxide: a risk assessment

2020-11-26

Objectives: The US National Toxicology Program (NTP) recently recommended in its Report on Carcinogens Monograph for Antimony Trioxide that antimony trioxide be listed as 'reasonably anticipated to be a human carcinogen' based on sufficient evidence of carcinogenicity in experimental animals and supporting evidence from mechanistic studies. Our goal was to estimate the possible human cancer risk from occupational exposure to antimony trioxide.

Methods: We selected data from 2-year inhalation studies in male and female mice conducted by the NTP and performed cancer dose-response analyses using cancer models and benchmark dose methods developed by the US Environmental Protection Agency. In these analyses, we generated benchmark doses and cancer slope factors for antimony trioxide, and then estimated human cancer risk under various exposure scenarios. Typical and worst-case inhalation scenarios in multiple occupational settings were used in risk estimation.

Results: In typical case scenarios, the occupational cancer risk from antimony trioxide was estimated to be 0.025 (25 in 1000) for persons working with flame retardants in plastics and textiles for 40 years. Under worst-case scenarios, the occupational cancer risk was estimated to be 0.11 (110 in 1000) for persons working with flame retardants in plastics and textiles. At the current Occupational Safety and Health Administration Permissible Exposure Limit, the cancer risk for occupational inhalation exposure of antimony trioxide was estimated to be 0.096 (96 in 1000).

Objectives: The US National Toxicology Program (NTP) recently recommended in its Report on Carcinogens Monograph for Antimony Trioxide that antimony trioxide be listed as 'reasonably anticipated to be a human carcinogen' based on sufficient evidence of carcinogenicity in experimental animals and supporting evidence from mechanistic studies.

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Conclusion: The risk estimates calculated in this study suggest that exposure to antimony trioxide at levels present in certain occupational settings results in a large increase in the risk of developing cancer.

Authors: Samantha Schildroth, Gwendolyn Osborne, Anna R Smith, Caryn Yip, Caroline Collins, Martyn T Smith, Martha S Sandy, Luoping Zhang
Full Source: Occupational and environmental medicine 2020 Nov 26;oemed-2020-106980. doi: 10.1136/oemed-2020-106980.

PHARMACEUTICAL/TOXICOLOGY

Associations between Urinary, Dietary, and Water Fluoride Concentrations among Children in Mexico and Canada

2020-11-20

Fluoride, which may be toxic to the developing brain, is added to salt in Mexico and drinking water in Canada to prevent dental caries. We compared childhood urinary fluoride (CUF) concentrations in Mexico City and Canada to characterize patterns of fluoride exposure in these two populations. We also examined associations of CUF with dietary and water fluoride levels in Mexico City and Canada respectively. We included 561 children (ages 4-6; mean age 4.8 years) from the Programming Research in Obesity, Growth, Environment, and Social Stress (PROGRESS) cohort in Mexico City, and 626 children (ages 2-6; mean age 3.7 years) from the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort in Canada. We applied Spearman correlations, T-tests, ANOVA or covariate-adjusted linear regression to examine associations of CUF (mg/L; adjusted for specific gravity) with demographics and dietary or water fluoride concentrations. We used Welch equivalence testing to compare means across cohorts. Mean (SD) CUF was equivalent in PROGRESS: 0.74 (0.42) and fluoridated Canadian communities: 0.79 (0.71), but lower in non-fluoridated Canadian communities: 0.55 (0.60), $t(276) = -6.02$, $p < 0.001$. In MIREC, mean (SD) CUF was higher in males: 0.79 (0.74) than females: 0.54 (0.58), $p < 0.001$; no sex differences were observed in PROGRESS ($p = 0.97$). Water fluoride concentrations were significantly associated with CUF after covariate adjustment for age and sex in MIREC ($B = 0.36$, 95% CI: 0.11, 0.61, $p = 0.005$). In contrast, daily food and beverage fluoride intake was not associated with CUF in PROGRESS ($p = 0.82$). We found that CUF levels are comparable among children in Mexico City and fluoridated Canadian communities, despite distinct sources of exposure. Community water fluoridation is a major source of fluoride exposure for Canadian children. Further studies are needed to clarify whether higher CUF in older children

Fluoride, which may be toxic to the developing brain, is added to salt in Mexico and drinking water in Canada to prevent dental caries.

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reflects different exposure patterns, sources of exposure, or age-related toxicokinetics.

Authors: Rivka Green, Christine Till, Alejandra Cantoral, Bruce Lanphear, E Angeles Martinez-Mier, Pierre Ayotte, Robert O Wright, Martha M Tellez-Rojo, Ashley J Malin

Full Source: *Toxics* 2020 Nov 20;8(4):E110. doi: 10.3390/toxics8040110.