

# Bulletin Board

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## Technical

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## CHEMICAL EFFECTS

## The potential toxicity of microplastics on human health

2023-12-01

Microplastics are plastic particles, films, and fibers with a diameter of <5 mm. Given their long-standing existence in the environment and terrible increase in annual emissions, concerns were raised about the potential health risk of microplastics on human beings. In particular, the increased consumption of masks during the COVID-19 pandemic has dramatically increased human contact with microplastics. To date, the emergence of microplastics in the human body, such as feces, blood, placenta, lower airway, and lungs, has been reported. Related toxicological investigations of microplastics were gradually increased. To comprehensively illuminate the interplay of microplastic exposure and human health, we systematically reviewed the updated toxicological data of microplastics and summarized their mode of action, adverse effects, and toxic mechanisms. The emerging critical issues in the current toxicological investigations were proposed and discussed. Our work would facilitate a better understanding of MPs-induced health hazards for toxicological evaluation and provide helpful information for regulatory decisions.

Authors: Bosen Zhao, Palizhati Rehati, Zhu Yang, Zongwei Cai, Caixia Guo, Yanbo Li

Full Source: The Science of the total environment 2023 Dec 1:168946. doi: 10.1016/j.scitotenv.2023.168946.

## The role of estrogen receptors (ERs)-Notch pathway in thyroid toxicity induced by Di-2-ethylhexyl phthalate (DEHP) exposure: Population data and in vitro studies

2023-12-01

Background: This study aimed to assess the exposure level and risk of Di-2-ethylhexyl Phthalate (DEHP) among adults in Jilin Province, China, clarify the impact of DEHP on human thyroid function, and to explore the role of estrogen receptors (ERs)-Notch signaling pathway in the effect of DEHP metabolites on thyroid hormones based on population data and in vitro experiments.

Methods: 312 adults participated in this study. Urinary DEHP metabolites were determined by high performance liquid chromatography coupled to a tandem mass spectrometer (HPLC-MS/MS). Two pharmacokinetic models were used to evaluate the estimated daily intake (EDI) and hazard quotient (HQ) of the adults. Multiple linear regression and mediating effect models

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were used to evaluate the target associations. In cell experiments, thyroid follicular epithelial (Nthy-ori3-1) cells were exposed to mono (2-ethylhexyl) phthalate (MEHP) for testing. The inhibitions of ER $\alpha$  and Notch pathway were conducted by siRNA and Notch pathway inhibitor DAPT. Results: The detection rate of five DEHP metabolites was 97.1–100.0%. The HQ value of 0.3% of adults was higher than 1. The levels of urinary DEHP metabolites were significantly correlated with thyrotropin (TSH), thyrotropin-releasing hormone (TRH), total triiodothyronine (TT3), total thyroxine (TT4), free triiodothyronine (FT3) and free thyroxine (FT4) and gene (estrogen receptor  $\alpha$  (ER $\alpha$ ), Notch1, Dll4) levels. The ER $\alpha$ -Notch pathway played a mediating role in the association between DEHP metabolite levels and FT4. The cell results showed, the levels of FT3 and FT4 in cell supernatant decreased after MEHP exposure, and the downward trend was reversed after ER $\alpha$  and notch pathways were inhibited, notch pathway genes also decreased after ER $\alpha$  inhibition. Conclusion: Adults in the Jilin Province of China were widely exposed to DEHP. ERs-Notch pathway played an important role in the effect of DEHP metabolites on thyroid hormones.

Authors: Xueting Zhang, Yuezhu Zhang, Xin Feng, Haotang Zhao, Hui Ye, Xiaoqi Fang, Jianwei Cui, Wen Qi, Lin Ye

Full Source: Ecotoxicology and environmental safety 2023 Dec 1:269:115727. doi: 10.1016/j.ecoenv.2023.115727.

## ENVIRONMENTAL RESEARCH

## Comparative studies on radon seasonal variations in various underground environments: Cases of abandoned Beshtaugorskiy uranium mine and Kungur Ice Cave

2023-12-02

It is well known that one of the most important risk factors in underground environment is the harmful effects of radon. The reasons for strong seasonal fluctuations in radon content in underground environments remain not fully understood. The purpose of this article is to improve existing ideas about this phenomenon. The article presents the results of a study of radon transport in two different underground spaces - the Beshtaugorskiy uranium mine (North Caucasus) and the Kungur Ice Cave (Middle Ural). We have used the direct measurements of the equilibrium equivalent concentration (EEC) of radon progeny in air, as well as the air flow velocity. A very wide range and strong seasonal variations in the radon levels have been recorded in both cases. The EEC has a range of

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11-6653 by Bq m-3 and 10-89,020 Bq m-3 in the Kungur cave and the Beshtaugorskiy mine, respectively. It has been established that seasonal fluctuations in radon levels both in the mine and in the cave are caused by the same process - convective air circulation in the underground space due to the temperature difference between the mountain massif and the atmosphere (so called chimney effect). Overall, these results indicate that due to convective air circulation, underground spaces are periodically intensively ventilated with atmospheric air, and then, on the contrary, they are filled with radon-enriched air that seeps into caves or adits from rocks and ores. In both cases, the EEC of radon progeny exceeds the permissible level for the population and workers. The results of this study highlight the need for the development of measures to limit the presence of people in the surveyed underground spaces.

Authors: Petr S Miklyaev, Tatiana B Petrova, Nikolay G Maksimovich, Alexey V Krasikov, Aleksey V Klimshin, Dmitriy V Shchitov, Pavel A Sidyakin, Dmitriy N Tsebro, Olga Yu Meshcheriakova

Full Source: Journal of environmental radioactivity 2023 Dec 2:272:107346. doi: 10.1016/j.jenvrad.2023.107346.

### Surface interaction of vancomycin with polystyrene microplastics and its effect on human serum albumin

2023-12-01

Microplastics have a well-documented ability to adsorb various chemicals and contaminants found in the environment. By similar mechanisms, when medicines are stored in plastic packaging, the leaching of plastics into the contents poses the risk of possible toxicity and decreased drug efficacy. The work thus examines the presence of two categories of anthropogenic materials - microplastics (MPs) and medications - with their possible combined effects and fate in biological systems. A study on the kinetics and isotherm of the adsorption of vancomycin hydrochloride on the surface of polystyrene microspheres is performed, and the best-fitting models are obtained respectively as the pseudo-second-order model and the Temkin isotherm. Further, the interaction of each of, the drug, MPs and drug-adsorbed MPs with human serum albumin (HSA), the model protein chosen to validate the potential toxicity in humans, is determined by fluorescence spectroscopy. A thermodynamic analysis of this protein-ligand interaction shows that the process is spontaneous, endothermic and entropically favoured, and that hydrophobic forces operate between the interacting species. An unfolding of HSA is observed, disrupting its functions like the esterase activity. Competitive binding experiments with

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Warfarin and Ibuprofen as specific site markers on HSA reveal that all the studied ligands bind non-specifically to HSA.

Authors: Lydia Ann Vinod, Durgalakshmi Rajendran, Muruges Shivashankar, Natarajan Chandrasekaran

Full Source: International journal of biological macromolecules 2023 Dec 1:128491. doi: 10.1016/j.ijbiomac.2023.128491.

### PHARMACEUTICAL/TOXICOLOGY

#### Use of personal care product mixtures and incident hormone-sensitive cancers in the Sister Study: A U.S.-wide prospective cohort

2023-11-02

Background: Personal care products (PCPs), a source of endocrine-disrupting chemical exposure, may be associated with the risk of hormone-sensitive cancers. Few studies have investigated associations for PCP use with the incidence of hormone-sensitive cancers or considered the joint effect of multiple correlated PCPs. We examined associations between frequently used, or "everyday", PCPs and incident cancers of the breast, ovary, and uterus with a focus on the joint effect of multiple product exposure.

Methods: Sister Study participants (n=49 899) self-reported frequency of use in the year before enrollment (2003-2009) for 41 PCPs. Using five-level frequency categories based on questionnaire options, hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated for the associations between multiple PCP use and incident breast, ovarian, and uterine cancer using quantile-based g-computation with Cox proportional hazards regression as the underlying model. Multiple PCP use was examined using groupings (beauty, hygiene, and skincare products) determined by both a priori knowledge and Spearman correlation coefficients for co-occurring product use. Associations between individual PCPs and the three cancers were also examined using Cox proportional hazards models coupling with Benjamini-Hochberg procedure for multiple comparisons.

Results: Over an average of 11.6 years, 4 226 breast, 277 ovarian, and 403 uterine cancer cases were identified. Positive associations were observed between the hygiene mixture and ovarian cancer (HR=1.35, 95%CI=1.00, 1.83) and the beauty mixture with postmenopausal breast cancer (HR=1.08, 95%CI=1.01, 1.16). Additionally, we observed an inverse association between the skincare mixture and breast cancer (HR=0.91,

Background: Personal care products (PCPs), a source of endocrine-disrupting chemical exposure, may be associated with the risk of hormone-sensitive cancers.

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95%CI=0.83, 0.99). No significant associations were observed for individual products after corrected for multiple comparison.

Conclusions: Findings from this multi-product, joint-effect approach contribute to the growing body of evidence for associations between PCPs and breast cancer and provides novel information on ovarian and uterine cancer.

Authors: Che-Jung Chang, Katie M O'Brien, Alexander P Keil, Mandy Goldberg, Kyla W Taylor, Dale P Sandler, Alexandra J White  
Full Source: Environment international 2023 Nov 2:183:108298. doi: 10.1016/j.envint.2023.108298.

### Associations between metals and metabolomic profiles related to diabetes among adults in a rural region

2023-12-01

Introduction: Exposure to metals is associated with increased risk of type 2 diabetes (T2D). Potential mechanisms for metals-T2D associations involve biological processes including oxidative stress and disruption of insulin-regulated glucose uptake. In this study, we assessed whether associations between metal exposure and metabolite profiles relate to biological pathways linked to T2D.

Materials and methods: We used data from 29 adults rural Colorado residents enrolled in the San Luis Valley Diabetes Study. Urinary concentrations of arsenic, cadmium, cobalt, lead, manganese, and tungsten were measured. Metabolic effects were evaluated using untargeted metabolic profiling, which included 61,851 metabolite signals detected in serum. We evaluated cross-sectional associations between metals and metabolites present in at least 50% of samples. Primary analyses adjusted urinary heavy metal concentrations for creatinine. Metabolite outcomes associated with each metal exposure were evaluated using pathway enrichment to investigate potential mechanisms underlying the relationship between metals and T2D.

Results: Participants had a mean age of 58.5 years (standard deviation = 9.2), 48.3% were female, 48.3% identified as Hispanic/Latino, 13.8% were current smokers, and 65.5% had T2D. Of the detected metabolites, 455 were associated with at least one metal, including 42 associated with arsenic, 22 with cadmium, 10 with cobalt, 313 with lead, 66 with manganese, and two with tungsten. The metabolic features were linked to 25 pathways including linoleate metabolism, butanoate metabolism, and arginine and proline metabolism. Several of these pathways have been previously associated with T2D, and our results were similar when including only participants with T2D.

Introduction: Exposure to metals is associated with increased risk of type 2 diabetes (T2D).

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Conclusions: Our results support the hypothesis that metals exposure may be associated with biological processes related to T2D, including amino acid, co-enzyme, and sugar and fatty acid metabolism. Insight into biological pathways could influence interventions to prevent adverse health outcomes due to metal exposure.

Authors: Julia G Debertin, Elizabeth A Holzhausen, Douglas I Walker, Brismar Pinto Pacheco, Katherine A James, Tanya L Alderete, Laura Corlin  
Full Source: Environmental research 2023 Dec 1:117776. doi: 10.1016/j.envres.2023.117776.

### OCCUPATIONAL

#### Occupational asthma, rhinitis and contact urticaria from greenhouse work

2023-12-02

Background: The current knowledge about occupational allergic diseases among greenhouse workers is scant.

Aims: To describe greenhouse workers' occupational allergic diseases.  
Methods: We identified 28 greenhouse workers with occupational allergic diseases in 2002-2020 by conducting a systematic search in the patient register of the Finnish Institute of Occupational Health. All the patients worked in tomato- or cucumber-growing greenhouses and showed immunoglobulin-E-mediated sensitization to occupational agents. Specific inhalation challenges or workplace peak expiratory flow monitoring confirmed occupational asthma (OA), nasal allergen challenges confirmed occupational rhinitis (OR) and open skin tests confirmed occupational contact urticaria (OCU).

Results: Most patients had more than one occupational disease and were sensitized to several workplace agents. Tomato plants were the most common cause of occupational diseases and induced 22 allergic diseases in 14 patients. Cucumber plants caused occupational diseases in 10 patients (3 OA, 7 OR and 6 OCU). The pest control mite *Amblyseius swirskii* and a mixture of parasitic wasps *Encarsia formosa* and *Eretmocerus eremicus* both induced two OA cases. Three patients had an occupational disease caused by storage mites and three others had a work-related systemic reaction to a bumblebee sting.

Conclusions: The greenhouse workers typically suffered from several occupational allergic diseases and were sensitized to cultivated plants, various pest control organisms and storage mites. All these can cause OA and OR, but in this study, OCU was only induced by cultivation plants.

Background: The current knowledge about occupational allergic diseases among greenhouse workers is scant.

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Cucumber plant is a novel cause of OA and OR, and *A. swirskii* is a novel cause of OA.

Authors: I Lindström, P Hölttä, L Airaksinen, K Suuronen, S Suomela, H Suojalehto

Full Source: Occupational medicine (Oxford, England) 2023 Dec 2:kqad099. doi: 10.1093/occmed/kqad099.

### Exposure, bioaccumulation, and risk assessment of organophosphate flame retardants in crayfish in the middle and lower reaches of the Yangtze River

2023-11-29

Organophosphate flame retardants (OPFRs), a novel class of persistent pollutants, are widely distributed in the environment, and their potential health risks have garnered significant global attention in recent years. Crayfish is a popular freshwater crustacean product in China primarily sourced from the middle and lower reaches of the Yangtze River. The purpose of this study was to investigate the exposure levels of OPFRs in crayfish, assess the health and safety risks associated with crayfish consumption, and explore the bioaccumulation of OPFRs in environmental water and sediment on crayfish. Ultra-high performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS) was employed to analyze 7 common OPFRs in 106 crayfish samples and 76 environmental samples. The results revealed that OPFRs were detected at a high frequency of 100 % in crayfish, with tripropyl phosphate (TPP) being the predominant pollutant found in edible portions while also exhibiting secondary contamination within the crayfish food chain. Monte Carlo modeling combined with @risk risk assessment software demonstrated that TPP present in crayfish muscles had the most substantial impact on health effects, however, overall OPFR exposure did not pose significant risks to human health. Furthermore, analysis of OPFRs bioenrichment ability indicated that crayfish predominantly accumulated these compounds within their edible parts from surrounding environmental water sources, particularly highlighting TPP's potential for bioaccumulation.

Authors: Qihong Peng, Lingfeng Peng, Jin Liu, Yan Liu, Xin Liu, Jiaojiao Yin, Shuo Duan, Xiaofang Liu, Yuzhi Li, Zhiyong Gong, Qiao Wang

Full Source: The Science of the total environment 2023 Nov 29:168859. doi: 10.1016/j.scitotenv.2023.168859.

Organophosphate flame retardants (OPFRs), a novel class of persistent pollutants, are widely distributed in the environment, and their potential health risks have garnered significant global attention in recent years.

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### Prevalence of pulmonary hypertension in chronic simple silicosis patients and its correlation with smoking history, occupation type, age and duration of silica exposure

2023-11-30

Silicosis is a preventable occupational health hazard with potential for permanent physical disability and increased socio-economic burden. Pulmonary hypertension (PH) secondary to chronic respiratory diseases signifies poorer prognosis and transthoracic echocardiography (TTE) has proven its usefulness as a screening tool for PH diagnosis. The objectives were to determine PH prevalence in chronic simple silicosis patients through TTE screening and correlate PH prevalence with smoking status, occupation type, age and duration of silica exposure (DSE). We enrolled 104 patients in the study based on occupational exposure to silica dust and radiologic confirmation of chronic simple silicosis. The study sample was divided into significant smokers (SS group) and insignificant smokers (InS group) on the basis of  $\geq 10$  pack years smoking history, and into drillers and dressers based on occupation type. TTE examination was performed to measure resting mean pulmonary artery pressure (mPAP) and the patients were classified into: no PH (mPAP $\leq 20$  mm Hg), borderline PH (mPAP $> 20$  and  $< 25$  mmHg), and PH (mPAP $\geq 25$ ). PH prevalence was 25% in study subjects (26/104); 29.6% (16/54) among SS group versus 20% (10/50) among InS group (.52) ; and 34.2% (14/41) among drillers versus 19.1% (12/63) among dressers (p=.024). Mean age and mean duration of silica exposure among SS and InS groups were comparatively similar, while they had lower values among drillers against dressers with no statistical significance. Logistic regression analysis established a significant association of PH prevalence with higher age in the study sample, SS group and drillers group, while a significant association of PH prevalence with longer DSE was only seen in the study sample. PH prevalence was significantly associated (p=.007) with SS-driller group on comparing TTE findings with combined smoking and occupation type based groups. This study has shown PH prevalence in chronic simple silicosis patients at alarming levels, having associations with driller occupation, older age and longer DSE with varying results among groups and complex interplay with smoking exposure, suggesting the need for large sample-based molecular and genetic studies. Including TTE in the initial work-up of silicosis patients will promote timely intervention and reduce morbidity and mortality with a high benefit-cost ratio.

Authors: Jyoti Kumari, Manish Advani, Gopal Purohit

Full Source: Monaldi archives for chest disease = Archivio Monaldi per le malattie del torace 2023 Nov 30. doi: 10.4081/monaldi.2023.2719.

Silicosis is a preventable occupational health hazard with potential for permanent physical disability and increased socio-economic burden.

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### Understanding the pathogenesis of engineered stone-associated silicosis: The effect of particle chemistry on the lung cell response

2023-12-03

**Background and objective:** The resurgence of severe and progressive silicosis among engineered stone benchtop industry workers is a global health crisis. We investigated the link between the physico-chemical characteristics of engineered stone dust and lung cell responses to understand components that pose the greatest risk.

**Methods:** Respirable dust from 50 resin-based engineered stones, 3 natural stones and 2 non-resin-based materials was generated and analysed for mineralogy, morphology, metals, resin, particle size and charge. Human alveolar epithelial cells and macrophages were exposed in vitro to dust and assessed for cytotoxicity and inflammation. Principal component analysis and stepwise linear regression were used to explore the relationship between engineered stone components and the cellular response.

**Results:** Cutting engineered stone generated fine particles of <600 nm. Crystalline silica was the main component with metal elements such as Ti, Cu, Co and Fe also present. There was some evidence to suggest differences in cytotoxicity ( $p = 0.061$ ) and IL-6 ( $p = 0.084$ ) between dust samples. However, IL-8 (CXCL8) and TNF- $\alpha$  levels in macrophages were clearly variable ( $p < 0.05$ ). Quartz explained 11% of the variance ( $p = 0.019$ ) in macrophage inflammation while Co and Al accounted for 32% of the variance ( $p < 0.001$ ) in macrophage toxicity, suggesting that crystalline silica only partly explains the cell response. Two of the reduced-silica, non-engineered stone products induced considerable inflammation in macrophages.

**Conclusion:** These data suggest that silica is not the only component of concern in these products, highlighting the caution required as alternative materials are produced in an effort to reduce disease risk.

**Authors:** Chandnee Ramkissoon, Yong Song, Seiha Yen, Katherine Southam, Simone Page, Dino Pisaniello, Sharyn Gaskin, Graeme R Zosky  
**Full Source:** *Respirology* (Carlton, Vic.) 2023 Dec 3. doi: 10.1111/resp.14625.

**Background and objective:** The resurgence of severe and progressive silicosis among engineered stone benchtop industry workers is a global health crisis.