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CHEMICAL EFFECTS

Nickel-based nanomaterials: a comprehensive analysis of risk assessment, toxicity mechanisms, and future strategies for health risk prevention

2025-03-14

Nickel-based nanomaterials (NBNs) have seen a surge in usage across a variety of applications. However, the widespread use of NBNs has led to increased human exposure, raising questions about their associated health risks, both in the short and long term. Additionally, the spread of NBNs in the environment has attracted considerable attention, emerging as a vital focus for research and development. This review aims to provide an in-depth assessment of the current understanding of NBNs toxicity, the mechanisms underlying their toxicological effects, and the strategies for mitigating associated health risks. We begin by examining the physicochemical properties of NBNs, such as particle size, composition and surface functionalization, which are key determinants of their biological interactions and toxicity. Then, through an extensive analysis of in vitro and in vivo studies, we highlight the adverse effects of NBNs exposure, including the generation of reactive oxygen species (ROS), oxidative stress, inflammation, cytotoxicity, genotoxicity, and immunotoxicity. To address the potential health risks associated with NBNs, we propose future strategies for risk prevention, including the development of safer nanomaterial designs, implementation of stringent regulatory guidelines, and advancement of novel toxicity testing approaches.

Authors: Xiaoting Zhou, Jiaqi Liao, Zipeng Lei, Huiqin Yao, Le Zhao, Chun Yang, Yan Zu, Yuliang Zhao

Full Source: Journal of nanobiotechnology 2025 Mar 14;23(1):211. doi: 10.1186/s12951-025-03248-7.

Prediction of acute toxicity of organic contaminants to fish: Model development and a novel approach to identify reactive substructures

2025-03-12

In this study, count-based Morgan fingerprints (CMF) were employed to represent the fundamental chemical structures of contaminants, and a neural network model ($R^2 = 0.76$) was developed to predict acute fish toxicity (AFT) of organic compounds. Models based on CMF consistently outperformed those based on binary Morgan fingerprints (BMF), likely due to the latter's inefficiency in describing homologous

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structures. The similarity of CMF was calculated using an improved method based on Tanimoto distance, which was used for calculation of dataset partition and application domain. The similarity-based dataset partitioning method ensured structural diversity within the training set and improved performance on the validation set, demonstrating its potential for toxicological structure analysis and priority screening. Toxic substructures identified by Shapley additive explanation (SHAP) method were substituted benzenes, long carbon chains, unsaturated carbons and halogen atoms. By incorporating Kow and monitoring shifts in feature importance, the influence of substructures on AFT was further delineated, revealing their roles in facilitating exposure (e.g.: long carbon chains) and reactive toxicity (e.g.: methyl). Additionally, we compared the toxicity of similar substructures and the same substructure in different chemical environments as well. To address SHAP's insensitivity to low-variance features, this study introduced a novel metric termed the toxicity index (TI), designed to pinpoint substructures that are present in minimal quantities yet potentially exhibit high toxicity. With TI, we identified several important substructures, such as parathion and polycyclic substituents. Finally, prevalent toxic substructures and potential highly toxic substances were identified in two external datasets.

Authors: Shangyu Li, Mingming Zhang, Peizhe Sun

Full Source: Journal of hazardous materials 2025 Mar 12:491:137917. doi: 10.1016/j.jhazmat.2025.137917.

Ammonia-rich sediment: Practical issues about embryotoxicity as endpoint supporting challenges in dredging activities

2025-03-13

Regulations for dredging and sediment management often require the use of toxicity tests to support sediment classification, together with chemical characterization; among available bioassays, embryotoxicity tests (conducted on aqueous phase prepared from sediment) are commonly applied to evaluate sub-chronic toxicity, as in the case of Italian legislation. However, toxicity tests can be influenced by several confounding factors, such as ammonia that, in the context of sediment management, generally is not considered as a "traditional" contaminant of concern due to its low persistence. In order to better address and optimize sediment management, it is therefore essential to understand the influence of ammonia on the observed sediment toxicity. The scope of this work is to provide an overview of the toxic effects of ammonia focusing on embryotoxicity endpoints, enabling a proper evaluation of sediment

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toxicity, discussing the role of ammonia on sediment quality classification, and contributing to improve the management options. The paper presents the results of an experimental activity aimed at evaluating the role of ammonia on sediment toxicity, jointly to a literature review delineating the range of ammonia toxicity thresholds on larval development evaluated in embryotoxicity tests for oysters, mussels and sea urchins. Results from this study demonstrated the influence of ammonia on sediment toxicity from a case-study (Venice lagoon), testing methods for toxicity identification evaluation and providing recommendation to support scientific discussion to pursue the most sustainable sediment management, especially when just the embryotoxicity endpoint is responding concomitantly to high ammonia levels, considering that; impacts primarily due to nonpersistent contaminants should be managed differently than persistent ones.

Authors: Elisa Chiara Bizzotto, Giovanni Libralato, Lorenzo Saviano, Marta Citron, Petra Scanferla, Fabio Russo, Antonio Marcomini

Full Source: Environmental pollution (Barking, Essex: 1987) 2025 Mar 13:372:126058. doi: 10.1016/j.envpol.2025.126058.

ENVIRONMENTAL RESEARCH

Environmental low-dose nanosized carbon black exposure aggravates lung fibrosis-induced by radiation in vivo and in vitro

2025-03-15

The question of whether the emerging nano-material, nanosized carbon black (CB) could influence the lung damage-induced by radiation exposure in cancer patients or in acute nuclear accident population remains incompletely uncovered. Therefore, our study investigated potential health risk from environmental low-dose CB exposure level (0.1 mg/kg/d, once per three days, for 12 weeks) via nasal instillation using a lung fibrosis mouse model induced by radiation. Compared to either CB or radiation single exposure, low-dose CB plus radiation exposure showed an aggravated risk of lung damage in mice, which was embodied in more increased collagen, reactive oxygen species (ROS) concentrations, and inflammation cytokines levels including IL-1 β and TNF- α , as well as promoted epithelial-mesenchymal transition (EMT) progress through increasing relative biomarkers such as N-cadherin and α -SMA. Mechanistically, CB triggered the cGAS-STING signaling pathway to aggravation of radiation-induced lung injury. Furthermore, knocking down the GAS or STING expression would suppress the EMT

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process and inflammation reaction, resulting in significantly attenuating the combination effects of low-dose CB plus radiation on lung damage. Overall, our study indicates that environmental CB exposure may increase the lung damage in certain special population cannot be ignored. It sheds light on possible molecular mechanisms from cGAS-STING inflammation perspective and providing valuable basic understanding for future study on radiation-induced lung damage. Synopsis State of exposure of environmentally relevant nanosized carbon black may exacerbate the lung injury among cancer patients undergoing radiotherapy.

Authors: Can Qu, Chenjun Bai, Jinhua Luo, Dafei Xie, Huiji Pan, Lihui Xuan, Jingjing Yang, Yongyi Wang, Hua Guan, Pingkun Zhou, Ruixue Huang
Full Source: The Science of the total environment 2025 Mar 15:972:179119. doi: 10.1016/j.scitotenv.2025.179119.

PHARMACEUTICAL/TOXICOLOGY

Maternal di(2-ethylhexyl) phthalate exposure increases the risk of congenital heart disease in mice offspring

2025-03-15

BACKGROUND: Epidemiological data suggest that maternal occupational exposure to mixed phthalates comprising di(2-ethylhexyl) phthalate (DEHP) increases the risk of congenital heart disease (CHD). In this study, we used mice as an animal model to validate impact of first-trimester DEHP exposure on the risk of CHD in offspring, to elucidate the possible mechanisms and to provide a potential feasible intervention. Methods and results: Eight-week-old C57BL/6J pregnant mice were randomly divided into standard and DEHP diet groups. The incidence of CHD in DEHP diet group offspring was up to 14.41% observed via Hematoxylin-eosin (HE) staining. Quantitative PCR analysis revealed that expression of key genes involved in cardiogenesis were suppressed at the transcriptional level, which may be due to decreased nuclear translocation of p65. The inhibition of DEHP on key genes was rescued to some extent by choline through driving p65 into nuclear. In the mice, supplementation of choline during DEHP exposure reduced the incidence of CHD in offspring from 14.41% to 4.63%.

Conclusions: Our study demonstrates that mice first-trimester DEHP exposure significantly increases the risk of CHD in the offspring via inhibiting mRNA levels of key genes in cardiogenesis, and choline could protect against the pathogenesis.

Impact: Our study provides key mechanistic insights into the risk of CHD by DEHP exposure during early pregnancy, and provides choline as a

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potentially effective intervention. DEHP suppressed the expression of key genes involved in embryonic cardiac septum development at the transcriptional level via inhibiting nuclear translocation of p65. Choline can play a role in rescuing the inhibition of DEHP on cardiogenesis genes via driving p65 translocate into the nuclear.

Authors: Haiqun Shi, Zehua Zhang, Anna Shen, Tong Ding, Rui Zhao, Yan Shi, Jianyuan Zhao, Ke Cai, Feng Wang
Full Source: Pediatric research 2025 Mar 15. doi: 10.1038/s41390-025-03997-z.

Exploring the Activation of the Keap1-Nrf2-ARE Pathway by PAHs in Children's Toys

2025-03-15

Background: Children are particularly susceptible to environmental pollutants. This study assessed the skin sensitisation risk associated with polycyclic aromatic hydrocarbons (PAHs), prevalent in toys.

Objectives: To evaluate the skin sensitisation potential of PAHs using the KeratinoSens assay.

Methods: Individual PAHs (acenaphthylene, anthracene, benzo[a]anthracene, benzo[a]pyrene (B[a]P), benzo[b]fluoranthene (B[b]F), benzo[e]pyrene, benzo[g,h,i]perylene, benzo[k]fluoranthene (B[k]F), chrysene, fluoranthene, fluorene, naphthalene, phenanthrene, pyrene and triphenylene) and ternary mixtures containing B[a]P were assessed for their ability to activate the Keap1-Nrf2-ARE pathway in human keratinocytes. The concentration addition model and additive index were used to predict and analyse mixture effects.

Results: Among the individual PAHs, B[k]F demonstrated the most potent activation of the pathway, exhibiting a 34-fold higher potency relative to B[a]P. B[b]F, chrysene and B[a]P also exhibited significant activation, while the remaining PAHs displayed negligible or weak activation. Notably, PAH mixtures exhibited synergistic effects, except for those composed solely of potent sensitizers.

Conclusions: This study provides the first assessment of the skin sensitization potential of these PAHs. The findings suggest that B[k]F, B[b]F and chrysene may pose a higher risk of skin sensitisation than previously thought. Additionally, the synergistic effects observed in mixtures highlight the importance of considering combined exposures when assessing PAH exposure risk.

Authors: Jonas Lauenstein, Simon van de Weyer, Rasha Alsaleh, Christoph Wiedmer, Andrea Buettner, Christian Kersch, Simone Schmitz-Spanke
Full Source: Contact dermatitis 2025 Mar 15. doi: 10.1111/cod.14792.

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Dissociation-dependent kinetics and distinct pathways for direct photolysis and $\cdot\text{OH}/\text{SO}_4^{\cdot-}$ radical dominated photodegradation of ionizable antiviral drugs in aquatic systems

2025-03-09

Advanced oxidation processes (AOPs), such as UV, UV/H₂O₂ and UV/persulfate, are widely used to remove emerging organic contaminants from wastewater streams. However, knowledge on chemical degradation pathways, reaction kinetics as well as formation and toxicity of key degradates is limited. We investigated the direct photolysis and $\cdot\text{OH}/\text{SO}_4^{\cdot-}$ dominated kinetics, intermediates and toxicity evolution of three ionizable antiviral drugs (ATVs): tenofovir (TFV), didanosine (DDI), and nevirapine (NVP). Their transformation kinetics were found to depend on the dominant protonated states. Under UV-Vis irradiation ($\lambda > 290 \text{ nm}$), TFV and DDI photolyzed the fastest in the cationic forms (H₂TFV⁺ and H₂DDI⁺), whereas NVP exhibited the fastest photodegradation in the anionic forms (NVP⁻). The anionic forms (TFV⁻ and NVP⁻) demonstrated the highest reactivities towards $\cdot\text{OH}$ in most cases, while the cationic forms (H₂DDI⁺ and H₂NVP⁺) reacted the fastest with $\text{SO}_4^{\cdot-}$ for most of the ATVs. The dissociation-dependent kinetics can be attributed to the discrepancies in deprotonation degrees, quantum yields, electron densities and coulombic repulsion with $\text{SO}_4^{\cdot-}$ in their dissociated forms. Based on the key product identification via HPLC-MS/MS, the pathways involved hydroxylation, dehydroxylation, oxidation, reduction, cyclopropyl cleavage, C-N breaking, elimination, cyclization and deamidation reactions, which can be prioritized based on the specific compound and the photochemical process. Furthermore, a bioassay showed the photomodified toxicity of the ATVs to *Vibrio fischeri* (bioluminescent bacteria) during the three processes, which was also demonstrated by ECOSAR model assessment. Nearly half of the chemical intermediates were demonstrably more toxic than their respective parent ATVs. These results provide new insights into understanding the persistence, fate and hazards associated with applying the UV-assisted AOPs to treat wastewater containing ATVs.

Authors: Nannan Cui, Linke Ge, Crispin Halsall, Junfeng Niu, Jinshuai Zheng, Peng Zhang
Full Source: Water research 2025 Mar 9:279:123452. doi: 10.1016/j.watres.2025.123452.

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Fractional exhaled nitric oxide (FeNO) among elementary school children in Stockholm: Associations with asthma, allergies, and home and school environment

2025-03-15

Objective: Few studies have investigated links between fraction exhaled nitric oxide (FeNO), the home and the school environment. FeNO is a biomarker of T helper 2 (Th2) airway inflammation. We investigated associations between FeNO and airway symptoms, allergies, household and classroom exposure among pupils in ten primary schools in Stockholm (N = 415).

Methods: Information on health and household environment was obtained by a questionnaire. FeNO was measured at school. Particle mass (PM1, PM2.5, PM10), carbon dioxide (CO2), temperature, and relative air humidity (RH) were measured in the classrooms. Microbial DNA and 3-hydroxy fatty acids (3-OHs) from endotoxin in Gram-negative bacteria were analysed in vacuumed dust from floors and upper surfaces. Three-level linear mixed models were used to analyse associations.

Results: In total, 9.7 % of the pupils had elevated FeNO (>20 ppb), 15.2 % doctor diagnosed asthma, 10.7 % current asthma, 17.8 % reported allergy and 9.6 % doctor diagnosed allergy. Reported allergy (p = 0.02), diagnosed allergy (p = 0.002), and current asthma (p = 0.007) were associated with elevated FeNO. Children living in single-family houses with basement had higher FeNO than those in self-owned apartments (p = 0.001). In the classrooms, PM10 (p = 0.008), RH (p = 0.004) and DNA copies from Gram-negative bacteria in vacuumed floor dust (p = 0.008) were associated with higher FeNO. C16 3-OH in floor dust (p = 0.046) and C10 (p = 0.02) and C11 3-OHs (p = 0.04) in upper surface dust were associated with higher FeNO. The association between Gram-negative bacteria at school and FeNO was stronger among girls. Children with parental asthma and allergy, and among those with dampness and mould at home and in single-family houses with basement.

Conclusions: FeNO is associated with reported asthma and allergy. In the school environment, PM10 and exposure to some subpopulations of Gram-negative bacteria can increase FeNO. Sex, parental asthma or allergy, dampness at home and type of housing can modify associations between classroom exposure and FeNO.

Authors: Erica Bloom, Martin Taubel, Gulli Saeidyfar, Gunilla Wieslander, Chengju Wang, Francesco Sacco, Dan Norbäck

Full Source: The Science of the total environment 2025 Mar 15:972:179113. doi: 10.1016/j.scitotenv.2025.179113.

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OCCUPATIONAL

Long-term exposure to low-level crystalline silica and risk assessment of silicosis: a cohort study

2025-03-16

Background: High-level exposure to crystalline silica dust is the key factor in silicosis. Long-term exposure to low-level silica dust, for example, lower than that in occupational exposure limits, still needs to be studied for their risk of silicosis.

Methods: A total of 30 697 workers were included from a cohort in China. Low-level silica dust exposure was defined as those having a lifetime mean silica dust concentration equal to or under permissible exposure limits, including 0.05 mg/m³, 0.10 mg/m³ and 0.35 mg/m³. Cumulative respirable silica dust exposure (CDE) for individual workers was assessed by linking a job-exposure matrix to personal work history.

Results: Among those with average exposure level equal to or lower than 0.05 mg/m³, compared with the lowest quartile CDE (Q1), the HRs of silicosis were 1.32 (95% CI 0.82 to 2.10) for Q2, 1.87 (95% CI 1.22 to 2.88) for Q3 and 2.00 (95% CI 1.30 to 3.09) for Q4. Among those exposed to 0.10 mg/m³ or less exposure level, compared with Q1, the HRs were 2.52 (95% CI 1.88 to 3.38) for Q2, 4.08 (95% CI 3.09 to 5.39) for Q3 and 4.02 (95% CI 3.04 to 5.32) for Q4. Among those exposed to 0.35 mg/m³ or less exposure level, compared with Q1, the HRs were 2.80 (95% CI 2.38 to 3.28) for Q2, 5.76 (95% CI 4.93 to 6.73) for Q3 and 7.14 (95% CI 6.07 to 8.40) for Q4, respectively. Stratified analysis showed that the results and trends did not change with facilities and smoking status.

Conclusion: Long-term exposure to low-level silica dust is still associated with a higher risk of silicosis. Control measurements and personal protective equipment should be emphasised to protect the health of workers.

Authors: Dongming Wang, Wenzhen Li, Min Zhou, Jixuan Ma, Yanjun Guo, Weihong Chen

Full Source: Thorax 2025 Mar 16:thorax-2024-222660. doi: 10.1136/thorax-2024-222660.

Gender-specific effects of prenatal polystyrene nanoparticle exposure on offspring lung development

2025-03-13

Nanoplastics are widely present in the environment. Exposure to environmental pollutants during pregnancy can have adverse effects on

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fetal development and health. Establishing a link between nanoplastics and Bronchopulmonary Dysplasia (BPD) requires further investigation. In this study, we examined the impact of prenatal exposure to 80 nm polystyrene nanoparticles (PS-NPs) on offspring lung development, taking into account potential gender-specific effects. Pregnant female mice were exposed to PS-NPs through oropharyngeal aspiration, and critical data on lung development were collected at postnatal days 1, 7, and 21. We found that exposure to PS-NPs reduced birth weight in female offspring and significantly increased lung weight in both male and female offspring by PND 21. Maternal exposure led to a reduction in alveolar numbers across offspring, with distinct underlying mechanisms observed between sexes. In female offspring, the reduction in alveolar numbers was linked to disrupted surfactant protein expression, significant inflammation, and increased apoptosis and fibrosis. In male offspring, impaired angiogenesis was the primary factor contributing to the increased risk of BPD. The impact on alveolar development was substantial in both genders. This study underscores the gender-specific impacts of prenatal nanoplastic exposure on lung development and offers new evidence and direction for future research on the cross-generational respiratory toxicity of PS-NPs.

Authors: Wenxia Bu, Mengjiao Yu, Xinyi Ma, Zhaoping Shen, Jialing Ruan, Yi Qu, Ruiyao Huang, Peng Xue, Yuanyuan Ma, Juan Tang, Xinyuan Zhao

Full Source: Toxicology letters 2025 Mar 13;407:1-16. doi: 10.1016/j.toxlet.2025.03.001.