

# Bulletin Board

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## Technical

MAR. 19, 2021

## CHEMICAL EFFECTS

The selective toxicity of superparamagnetic iron oxide nanoparticles (SPIONs) on oral squamous cell carcinoma (OSCC) by targeting their mitochondria

2021-03-11

In recent years, many researchers have made tremendous efforts into using nanotechnology in biomedical applications and science, such as magnetic resonance imaging, drug delivery, and in particular, oncological therapeutic via superparamagnetic iron oxide nanoparticles (SPIONs). Head and neck squamous cell carcinoma (HNSCC) and especially oral squamous cell carcinoma (OSCC) have been a serious and ongoing concern. There are many strong emphases on the importance of toxic mechanisms due to oxidative stress and specifically, the changed cellular response. Therefore, our study was designed to evaluate the effects of SPIONs on OSCC mitochondria because of the usefulness of the application of these nanoparticles in cancer treatment and diagnosis. An increased level of reactive oxygen species (ROS) is one of the substantial mechanisms found for SPIONs in this study, and initially originated from disruption of the electron transfer chain shown by a decrease in mitochondrial succinate dehydrogenase activity. Increased ROS formation subsequently followed a decline of mitochondrial membrane potential, the release of mitochondrial cytochrome complex, and mitochondrial swelling in the OSCC mitochondria compared with almost no effect in normal mitochondria. In addition, the SPIONs decreased cell viability and increased lipid peroxidation level and caspase-3 activity in OSCC cells. The results represented that the exposure to the SPIONs induced selective toxicity only on the OSCC but not normal mitochondria. Based on our findings, we finally concluded that the SPIONs may be considered as a potential therapeutic candidate for the treatment of OSCC.

Authors: Mona Afrasiabi, Enayatollah Seydi, Shabnam Rahimi, Ghazaleh Tahmasebi, Jahanfar Jahanbani, Jalal Pourahmad

Full Source: Journal of biochemical and molecular toxicology 2021 Mar 11;e22769. doi: 10.1002/jbt.22769.

In recent years, many researchers have made tremendous efforts into using nanotechnology in biomedical applications and science, such as magnetic resonance imaging, drug delivery, and in particular, oncological therapeutic via superparamagnetic iron oxide nanoparticles (SPIONs).

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Synthetic organic chemicals (flame retardants and pesticides) with neurotoxic potential induced behavioral impairment on zebrafish (*Danio rerio*): a non-invasive approach for neurotoxicology

2021-03-13

Behavior responses of organisms can be used as a non-invasive method for neurotoxicology studies since it directly links the nervous system's functioning and biochemical activities. Among different behavioral activities, aquatic organisms' swimming behavior (fitness) is the essential factor for health assessment; thus, it is practiced routinely in neurotoxicological studies. Zebrafish (*Danio rerio*) are excellent models for neurotoxicology studies. Based on the above information, we hypothesized that zebrafish's swimming behavior is a potential biomarker for neurotoxic effect assessment. We exposed zebrafish (length, 3-4 cm; weight, 0.2-0.3 g) to different synthetic organic chemicals (organophosphorus flame retardants (tri-cresyl phosphate and cresyl diphenyl phosphate) and neurotoxic pesticides (cypermethrin and methomyl) for 15 days. For each test chemical, we chose two different concentrations (Treatment-I 5  $\mu\text{L/L}$  and Treatment-II 25  $\mu\text{L/L}$ ) to study their eco-toxicity. The swimming strength of zebrafish was quantified using an online monitoring system. The swimming strength of zebrafish decreased under different treatments (Treatment-I (5  $\mu\text{L/L}$ ) and -II (25  $\mu\text{L/L}$ )) of target chemicals. The circadian rhythm of zebrafish was predominantly not affected in this study. Higher neurotoxic effect (behavioral impairment) was observed in Treatment-II when compare to Treatment-I of organophosphorus flame retardants and pesticides groups. Responses of zebrafish under organophosphorus flame retardant (tri-cresyl phosphate and cresyl diphenyl phosphate) treatments were identical with pesticide (cypermethrin and methomyl) treatments. Based on the results, we conclude that swimming behavior could be an ideal non-invasive biomarker to assess waterborne contaminants' neurotoxic effect.

Authors: Zongming Ren, Rama-Krishnan Poopal, Mathan Ramesh

Full Source: Environmental science and pollution research international 2021 Mar 13. doi: 10.1007/s11356-021-13370-2.

Behavior responses of organisms can be used as a non-invasive method for neurotoxicology studies since it directly links the nervous system's functioning and biochemical activities.

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## Organophosphate Flame Retardants, Highly Fluorinated Chemicals, and Biomarkers of Placental Development and Disease during Mid-Gestation

2021-03-02

Perfluoroalkyl and polyfluoroalkyl substances (PFASs) and organophosphate flame retardants (OPFRs) are chemicals that may contribute to placenta-mediated complications and adverse maternal-fetal health risks. Few studies have investigated these chemicals in relation to biomarkers of effect during pregnancy. We measured 12 PFASs and four urinary OPFR metabolites in 132 healthy pregnant women during mid-gestation and examined a subset with biomarkers of placental development and disease (n = 62). Molecular biomarkers included integrin alpha-1 (ITGA1), vascular endothelial-cadherin (CDH5), and matrix metalloproteinase-1 (MMP1). Morphological endpoints included potential indicators of placental stress and the extent of cytotrophoblast (CTB)-mediated uterine artery remodeling. Serum PFASs and urinary OPFR metabolites were detected in 50-100% of samples. The most prevalent PFASs were perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA), and perfluorooctane sulfonic acid (PFOS), with geometric mean (GM) levels of 1.3-2.8 (95% confidence limits from 1.2-3.1) ng/mL compared to  $\leq 0.5$  ng/mL for other PFASs. Diphenyl phosphate (DPhP) and bis(1,3-dichloro-2-propyl) phosphate (BDCIPP) were the most prevalent OPFR metabolites, with GMs of 2.9 (95% CI: 2.5-3.4) and 3.6 (95% CI: 2.2-3.1) ng/mL, respectively, compared to  $< 1$  ng/mL for bis(2-chloroethyl) phosphate (BCEP) and bis(1-chloro-2-propyl) phosphate (BCIPP). We found inverse associations of PFASs or OPFRs with ITGA1 or CDH5 immunoreactivity and positive associations with indicators of placental stress in multiple basal plate regions, indicating these chemicals may contribute to abnormal placentation and future health risks. Associations with blood pressure and lipid concentrations warrant further examination. This is the first study of these chemicals with placental biomarkers measured directly in human tissues and suggests specific biomarkers are sensitive indicators of exposure during a vulnerable developmental period.

Authors: Julia R Varshavsky, Joshua F Robinson, Yan Zhou, Kenisha A Puckett, Elaine Kwan, Sirirak Buarpung, Rayyan Aburajab, Stephanie L Gaw, Saunak Sen, Songmei Gao, Sabrina Crispo Smith, June-Soo Park, Igor Zakharevich, Roy R Gerona, Susan J Fisher, Tracey J Woodruff  
Full Source: Toxicological sciences : an official journal of the Society of Toxicology 2021 Mar 2;kfab028. doi: 10.1093/toxsci/kfab028.

Perfluoroalkyl and polyfluoroalkyl substances (PFASs) and organophosphate flame retardants (OPFRs) are chemicals that may contribute to placenta-mediated complications and adverse maternal-fetal health risks.

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## ENVIRONMENTAL RESEARCH

## Prediction of organic compounds adsorbed by polyethylene and chlorinated polyethylene microplastics in freshwater using QSAR

2021-03-10

Microplastics (MPs), a growing class of emerging pollutants in the environment, have attracted widespread attention due to their adsorption properties. Recent research on MPs has mainly concentrated on seawater, and little work has been conducted on freshwater. Investigating and predicting the adsorption behavior of organic pollutants by MPs are necessary in freshwater. In this study, the adsorption behavior of 13 organic chemicals by polyethylene (PE) and chlorinated polyethylene (CPE) MPs was determined under freshwater conditions. Results shows the majority of the organic chemicals exhibit no distinctive differences in their adsorption on two MPs. However, the adsorption of polycyclic aromatic hydrocarbons and chlorobenzene on CPE is obviously stronger than that on PE, and the result is a counter for two pesticides. Quantitative structure activity relationship (QSAR) analysis was performed for the prediction of adsorption capacity. A QSAR model with acceptable performance ( $R^2 = 0.8586$ ) was built to predict the adsorptive affinity (expressed as  $\log K_d$ ) of organic compounds on the PE MPs via multivariable linear regression (MLR) on forty-nine determined and collected data. The octanol/water partition coefficient ( $\log K_{ow}$ ) and excess molar refractive index (E) play dominant roles in the model. A QSAR model with satisfactory performance ( $R^2 = 0.9302$ ) was also established for  $\log K_d$  values from CPE MPs in freshwater by using 13 adsorption data determined. The  $\log K_{ow}$  and most negative charge on Cl atom (Q-max,cl) play decisive roles in the adsorption. The findings can provide a scientific basis for the risk assessment of waters contaminated by MPs and organic pollutants.

Authors: Bingxin Gui, Xiaotian Xu, Shengnan Zhang, Yue Wang, Chao Li, Dongmei Zhang, Limin Su, Yuanhui Zhao  
Full Source: Environmental research 2021 Mar 10;111001. doi: 10.1016/j.envres.2021.111001.

## Estimating climate change-related impacts on outdoor air pollution infiltration

2021-03-08

Background: Rising temperatures due to climate change are expected to impact human adaptive response, including changes to home cooling

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and ventilation patterns. These changes may affect air pollution exposures via alteration in residential air exchange rates, affecting indoor infiltration of outdoor particles. We conducted a field study examining associations between particle infiltration and temperature to inform future studies of air pollution health effects.

**Methods:** We measured indoor fine particulate matter (PM<sub>2.5</sub>) in Atlanta in 60 homes (810 sampling-days). Indoor-outdoor sulfur ratios were used to estimate particle infiltration, using central site outdoor sulfur concentrations. Linear and mixed-effects models were used to examine particle infiltration ratio-temperature relationships, based on which we incorporated projected meteorological values (Representative Concentration Pathways intermediate scenario RCP 4.5) to estimate particle infiltration ratios in 20-year future (2046-2065) and past (1981-2000) scenarios.

**Results:** The mean particle infiltration ratio in Atlanta was  $0.70 \pm 0.30$ , with a 0.21 lower ratio in summer compared to transition seasons (spring, fall). Particle infiltration ratios were 0.19 lower in houses using heating, ventilation, and air conditioning (HVAC) systems compared to those not using HVAC. We observed significant associations between particle infiltration ratios and both linear and quadratic models of ambient temperature for homes using natural ventilation and those using HVAC. Future temperature was projected to increase by 2.1 °C in Atlanta, which corresponds to an increase of 0.023 (3.9%) in particle infiltration ratios during cooler months and a decrease of 0.037 (6.2%) during warmer months.

**Discussion:** We estimated notable changes in particle infiltration ratio in Atlanta for different 20-year periods, with differential seasonal patterns. Moreover, when stratified by HVAC usage, increases in future ambient temperature due to climate change were projected to enhance seasonal differences in PM<sub>2.5</sub> infiltration in Atlanta. These analyses can help minimize exposure misclassification in epidemiologic studies of PM<sub>2.5</sub>, and provide a better understanding of the potential influence of climate change on PM<sub>2.5</sub> health effects.

**Authors:** Donghai Liang, Wan-Chen Lee, Jiawen Liao, Joy Lawrence, Jack M Wolfson, Stefanie T Ebelt, Choong-Min Kang, Petros Koutrakis, Jeremy A Sarnat

**Full Source:** Environmental research 2021 Mar 8;196:110923. doi: 10.1016/j.envres.2021.110923.

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## OCCUPATIONAL

## Effects of long-term high-level lead exposure on the immune function of workers

2021-03-10

This work was undertaken to study the immunomodulatory effects of long-term exposure to varying levels of lead (Pb) in workers. A total of 49 people who underwent occupational health examinations from 2009 to 2018 were selected as study subjects. Differences between the two group populations regarding the levels of T-lymphocytes, B-lymphocytes, natural killer (NK) cells, and granulocytes, as well as the levels of TH1/TH2/TH17 cytokines, were evaluated. The results indicated that the percentages of CD3+ cells in the high-Pb group were significantly higher than those in the low-Pb counterparts ( $p < .05$ ). In contrast, the percentages of CD3-CD16+CD56+ cells were significantly lower in the high-Pb workers. There were no significant differences in other immunomy cells and TH1/TH2/TH17 cytokine between the groups. CD3+ cell levels in workers positively correlated with blood Pb levels ( $R_s = 0.378$ ,  $p = .007$ ), while the expression of CD3-CD16+CD56+ cells was negatively correlated ( $R_s = -0.320$ ,  $p = .025$ ). There was no significant correlation between blood Pb concentration and the other immune endpoints evaluated here.

**Authors:** Jianrui Dou, Le Zhou, Yi Zhao, Wu Jin, Huanxi Shen, Feng Zhang  
**Full Source:** Archives of environmental & occupational health 2021 Mar 10;1-8. doi: 10.1080/19338244.2021.1893632.

This work was undertaken to study the immunomodulatory effects of long-term exposure to varying levels of lead (Pb) in workers.

## Methyl siloxanes in soils from a large silicone-manufacturing site, China: concentrations, distributions and potential human exposure

2021-03-12

Methyl siloxanes are widely found in the environment, but little is known about the distributions of these chemicals in soils especially in areas where they are manufactured. We determined the concentrations of four cyclic (D3-D6) and 13 linear methyl siloxanes (L4-L16) in the soils from a siloxane-manufacturing site in China; the total concentrations of these 17 siloxanes (TSi) in the soils were 17.1-3,191 (median, 134) ng/g. We did not find extremely high concentrations of siloxanes in the soils. The median concentrations of total cyclic siloxanes (TCSi) were approximately sevenfold higher than those of total linear congeners. Hexamethylcyclotrisiloxane and octamethylcyclotetrasiloxane contributed a median of 59.7% and 20.3% of the TSi concentrations,

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respectively. Higher concentrations of soil TCSi were found in the silicone-manufacturing area relative to the other study areas. Source analysis indicated that industrial activities contributed substantially to soil siloxanes, in addition to the contribution of the siloxane emissions from specific consumer products. We calculated that the median values of daily TSi intakes through soil ingestion were 0.021 and 0.138 ng/kg-body weight/day for adults and children, respectively, under high exposure scenarios. Although our estimated daily intakes of the chemicals from soils were low, more research is required to improve our understanding of the health risks posed to humans exposed to siloxanes through other pathways.

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

Full Source: Environmental geochemistry and health 2021 Mar 12. doi: 10.1007/s10653-021-00873-7.

### Epidemiological Study of Mortality Among Workers Exposed to Tritium in France

2021-03-01

Workers of the Commissariat for Atomic Energy and Alternative Energy (CEA) may be potentially exposed to tritium over long periods. We aimed to assess the effect of tritium exposure on mortality in a cohort of employees followed by radiotoxicological monitoring. A total of 1,746 employees who worked for at least six months at one of three CEA centers were included between 1962 and 2011 (median follow-up 29.6 years). The cumulative dose of tritium was based on the quantification of tritium present from urinary excretion monitoring data from the beginning of occupational exposure to the end of such exposure or December 2011. Mortality was first compared to that in the French population using the standardized mortality ratio (SMR). Then, mortality risk ratios (RRs) per category of cumulative dose of tritium were estimated using categorical Poisson models adjusted for age at the onset of exposure, age, calendar period, sex, smoking, employment status, CEA center, and taking into account the number of person-years. The main causes of mortality were tumors (48%) and cardiovascular diseases (20%). The comparison of mortality within the cohort to that in the French population highlighted a lower rate for all-cause mortality and that due to cancer, related to the healthy worker effect bias. The regression model showed no effect of cumulative dose on all-cause mortality. The risk of death for most malignancies was positive, but not significant for the higher classes of doses relative to the reference class. The highest risk (not significant) was

Workers of the Commissariat for Atomic Energy and Alternative Energy (CEA) may be potentially exposed to tritium over long periods.

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present for the class of higher doses for tumors of the larynx, trachea, bronchi and lung. The risk was significant for the higher doses for tumors of the pancreas and bladder (based on a limited number of cases: five and six deaths, respectively). Significantly more smokers died from tumors of the respiratory system than non-smokers, as expected. We were unable to show an effect of cumulative tritium dose due to the small size of the cohort and the low exposure level. However, our study underlines the need to continue following tritium-exposed workers and conducting multicenter studies.

Authors: Sylvie Martin, Claire Ségala

Full Source: Radiation research 2021 Mar 1;195(3):284-292. doi: 10.1667/RR15353.1.

### Assessment of respiratory exposure to cypermethrin among farmers and farm workers of Shiraz, Iran

2021-03-13

Cypermethrin, a member of the synthetic pyrethroids group, is a popular insecticide used to eliminate a broad range of common bugs in agricultural lands and households. However, studies of farmers' exposure to this insecticide are limited. The present study aimed to measure the respiratory exposure to cypermethrin among farmers and farm workers of Shiraz, as one of the biggest cities in Fars province, Iran. Totally, nine target regions were selected, where 42 individual samples were taken using XAD-2 sorbents and were analyzed by gas chromatography-electron capture detector (GC-ECD). This is the first study on farmers' exposure to insecticides during spraying in Iran. The average concentration of cypermethrin vapor in farmers' respiratory area during spraying was  $0.982 \pm 0.421$  mg/m<sup>3</sup>, which was lower than the permitted threshold value for cypermethrin recommended by the Occupational Safety and Health Administration (OSHA). The mean time-weighted average (TWA) was also evaluated in two distinct occupational groups (tree operators and field operators). The exposure was significantly higher in tree operators than in field operators. A direct correlation was also found between the height of the workers and the amount of cypermethrin (Spearman's  $r = 0.555$ ). Findings support that farm workers' respiratory exposure to cypermethrin was within the permissible range, but this situation cannot guarantee

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workers' safety. Total respiratory exposure and skin exposure studies are recommended in future research.

Authors: Farnaz Behnami, Saeed Yousefinejad, Saeed Jafari, Masoud Neghab, Esmaeel Soleimani

Full Source: Environmental monitoring and assessment 2021 Mar 13;193(4):187. doi: 10.1007/s10661-021-08964-9.

### PHARMACEUTICAL/TOXICOLOGY

#### Pentachlorophenol and nine other chlorophenols in urine of children and adolescents in Germany - Human biomonitoring results of the German Environmental Survey 2014-2017 (GerES V)

2021-03-04

Chlorophenols comprise of a large group of chemicals used inter alia for the production of biocides, pharmaceuticals, other industrial products and are used e.g. as antiseptics or wood preservatives due to their biocidal properties. Several of them are classified as toxic to aquatic life and harmful to humans by ingestion, inhalation, or dermal contact, causing skin and eye irritation. Moreover, chlorophenols are possibly carcinogenic to humans. The most prominent chlorophenol - pentachlorophenol - is carcinogenic to humans, was banned in Germany in 1989 and further regulated by the European Commission in 2006 and included in the Stockholm Convention in 2017. Some chlorophenols are persistent in the environment and are also biodegradation products of precursor substances. To evaluate the health-relevance of recent exposure and monitor the effectiveness of regulatory measures, chlorophenols were analysed in the population-representative German Environmental Survey on Children and Adolescents 2014-2017 (GerES V). First-morning void urine samples of 485 3-17-year-old children and adolescents were analysed for ten chlorophenols. Pentachlorophenol was still quantified in 87% of the children and adolescents with a geometric mean (GM) concentration of 0.19 µg/L (0.16 µg/gcrea) and a maximum concentration of 6.7 µg/L (5.4 µg/gcrea). The maximum concentration was well below the health-based guidance value HBM-I of 25 µg/L (20 µg/gcrea). 4-Monochlorophenol was quantified in all samples with a GM concentration of 1.38 µg/L (1.14 µg/gcrea). 2-Monochlorophenol, 2,4-dichlorophenol, and 2,5-dichlorophenol were quantified in 97%, 98%, and 95% of the samples, with GMs of 0.26 µg/L (0.21 µg/gcrea), 0.24 µg/L (0.20 µg/gcrea), and 0.26 µg/L (0.21 µg/gcrea). 2,6-dichlorophenol,

Chlorophenols comprise of a large group of chemicals used inter alia for the production of biocides, pharmaceuticals, other industrial products and are used e.g.

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2,3,4-trichlorophenol, and 2,4,5-trichlorophenol were quantified in 17-25% of the samples with GMs below the limit of quantification (LOQ) of 0.1 µg/L. 2,4,6-trichlorophenol was quantified in 72% of the samples (GM: 0.13 µg/L, 0.11 µg/gcrea), 2,3,4,6-tetrachlorophenol in 44% of the samples (GM < LOQ). Comparison to previous cycles of GerES revealed substantially lower exposure to most of the chlorophenols in GerES V. Exposure levels found in Germany were comparatively low in contrast to North American results.

Authors: Maria I H Schmied-Tobies, Aline Murawski, Lukas Schmidt, Enrico Rucic, Gerda Schwedler, Petra Apel, Thomas Göen, Marike Kolossa-Gehring  
Full Source: Environmental research 2021 Mar 4;196:110958. doi: 10.1016/j.envres.2021.110958.