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CHEMICAL EFFECTS

In vitro prediction of clinical signs of respiratory toxicity in rats following inhalation exposure

2021-05-21

To date there are no OECD validated alternative approaches to study toxicity following inhalation exposure to airborne chemicals. The available OECD test guidelines for acute inhalation toxicity aim to estimate a value of the lethal air concentration of the test chemical leading to the death of 50% of the exposed animals (LC50), to satisfy hazard classification and labelling requirements. This paper explores the view that alternative approaches must compare to outcomes of existing guideline methods to become accepted and implemented in a regulatory context. This case study describes the initiatives taken to validate the lung surfactant bioassay, an in vitro cell-free method, and discusses the challenges faced. While the lung surfactant bioassay could not predict the GHS classification for acute inhalation toxicity of 26 chemicals, the assay successfully predicted the clinical signs of respiratory toxicity observed during or shortly after exposure in vivo as reported in registration dossiers. The lung surfactant bioassay is a promising alternative approach to assess the potential of chemicals to cause changes to respiration remaining after exposure (indicating decreased lung function), and can be combined with other test methods in an integrated approach to testing and assessment of inhaled substances.

Authors: E Da Silva, C Hickey, G Ellis, K S Hougaard, J B Sørli

Full Source: Current research in toxicology 2021 May 21;2:204-209. doi: 10.1016/j.crttox.2021.05.002.

Suspension array for multiplex immunoassay of five common endocrine disrupter chemicals

2021-08-06

A low cost and effective indirect competitive method is reported to detect five EDCs, 17-beta-estradiol (E2), estriol (E3), bisphenol A (BPA), diethylstilbestrol (DES), and nonylphenol (NP) simultaneously, based on suspension array technology (SAT). Five kinds of complete antigens (E2-BSA, E3-BSA, BPA-BSA, DES-BPA, NP-BSA) were coupled to different encoding microspheres using purpose-made solutions in our laboratory instead of commercially available amino coupling kits; the method was further optimized for determination and reducing the cost. Encoding and signaling fluorescence of the particles are determined at 635/532 nm

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emission wavelengths. High-throughput curves of five EDCs were drawn and the limit of detection (LOD) were between 0.0010 ng mL⁻¹ ~ 0.0070 ng mL⁻¹. Compared with traditional ELISA methods, the SAT exhibited better specificity and sensitivity. Experiments using spiked milk and tap water samples were also carried out, and the recovery was between 85 and 110%; the results also confirmed good repeatability and reproducibility. It illustrated great potential of the present strategy in the detection of EDCs in actual samples.

Authors: Xue-Xia Jia, Zi-Yi Yao, Sha Liu, Zhi-Xian Gao

Full Source: Mikrochimica acta 2021 Aug 6;188(9):290. doi: 10.1007/s00604-021-04905-y.

In utero exposure to endocrine disruptors and developmental neurotoxicity: Implications for behavioural and neurological disorders in adult life

2021-08-03

Endocrine disrupting chemicals (EDCs) are a class of environmental toxicants that interfere with the endocrine system, resulting in developmental malformations, reproductive disorders, and alterations to immune and nervous system function. The emergence of screening studies identifying these chemicals in fetal developmental matrices such as maternal blood, placenta and amniotic fluid has steered research focus towards elucidation of in utero effects of exposure to these chemicals, as their capacity to cross the placenta and reach the fetus was established. The presence of EDCs, a majority of which are estrogen mimics, in the fetal environment during early development could potentially affect neurodevelopment, with implications for behavioural and neurological disorders in adult life. This review summarizes studies in animal models and human cohorts that aim to elucidate mechanisms of action of EDCs in the context of neurodevelopment and disease risk in adult life. This is a significant area of study as early brain development is heavily mediated by estrogen and could be particularly sensitive to EDC exposure. A network analysis presented using genes summarized in this review, further show a significant association with disorders such as major depressive disorder, alcoholic disorder, psychotic disorders and autism spectrum disorder. Functional outcomes such as alterations in memory, behaviour, cognition, learning memory, feeding behaviour and regulation of ion transport are also highlighted. Interactions between genes, receptors and signaling pathways like NMDA glutamate receptor activity, 5-hydroxytryptamine receptor activity, Ras-activated Ca²⁺ influx and Grin2A interactions, provide further potential mechanisms of action of EDCs in mediating

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brain function. Taken together with the growing pool of human and animal studies, this review summarizes current status of EDC neurotoxicity research, limitations and future directions of study for researchers.

Authors: Glancis Luzeena Raja, K Divya Subhashree, Kamalini Esther Kantayya

Full Source: Environmental research 2021 Aug 3;203:111829. doi: 10.1016/j.envres.2021.111829.

ENVIRONMENTAL RESEARCH

Are your shoes safe for the environment? - Toxicity screening of leachates from microplastic fragments of shoe soles using freshwater organisms

2021-07-29

This study investigated the toxic effects of leachates from microplastic fragments of soles from four different types of shoes (slippers, trekking shoes, running shoes, and sneakers) on three aquatic organisms (*Chlamydomonas reinhardtii*, *Daphnia magna*, and *Danio rerio*). The chemical components in each leachate were identified; furthermore, chlorophyll a contents of *C. reinhardtii* were measured, and immobilization of *D. magna* and deformities in *D. rerio* were observed. The abnormalities observed in the test species exposed to the leachates were compared and chemical compounds majorly influencing the species were determined by principal component analysis (PCA). Sneaker leachate showed growth inhibitions in *C. reinhardtii*, immobility and mortality in *D. magna*, and severe abnormalities in *D. rerio*. Consequently, aquatic toxicity was majorly associated with benzothiazole, carbon disulfide, ethyl acetate, and p-xylene. The results showed that toxic chemicals could leach from load-originated microplastics when exposed to aquatic media, and consequently, induce significant negative effects on aquatic organisms. Since microplastics from shoe soles discharge the above-mentioned toxic chemicals, regulating the chemical use during plastic production is critical to prevent severe effects of microplastic toxicity in aquatic organisms, and to maintain the health of aquatic environments.

Authors: Lia Kim, Dokyung Kim, Sang A Kim, Haemi Kim, Tae-Yang Lee, Youn-Joo An

Full Source: Journal of hazardous materials 2021 Jul 29;421:126779. doi: 10.1016/j.jhazmat.2021.126779.

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The EU chemicals strategy for sustainability: in support of the BfR position

2021-08-07

The EU chemicals strategy for sustainability (CSS) asserts that both human health and the environment are presently threatened and that further regulation is necessary. In a recent Guest Editorial, members of the German competent authority for risk assessment, the BfR, raised concerns about the scientific justification for this strategy. The complexity and interdependence of the networks of regulation of chemical substances have ensured that public health and wellbeing in the EU have continuously improved. A continuous process of improvement in consumer protection is clearly desirable but any initiative directed towards this objective must be based on scientific knowledge. It must not confound risk with other factors in determining policy. This conclusion is fully supported in the present Commentary including the request to improve both, data collection and the time-consuming and bureaucratic procedures that delay the publication of regulations.

Authors: Frank A Barile, Sir Colin Berry, Bas Blaauboer, Alan Boobis, Herrmann M Bolt, Christopher Borgert, Wolfgang Dekant, Daniel Dietrich, Jose L Domingo, Corrado L Galli, Gio Batta Gori, Helmut Greim, Jan G Hengstler, Pat Heslop-Harrison, Sam Kacew, Hans Marquardt, Angela Mally, Olavi Pelkonen, Kai Savolainen, Emanuela Testai, Aristides Tsatsakis, Nico P Vermeulen

Full Source: Archives of toxicology 2021 Aug 7. doi: 10.1007/s00204-021-03125-w.

Investigation of long-term hazards of chemical weapon agents in the environment of Sardasht area, Iran

2021-07-31

The present study aimed to investigate the persistence and existence of chemical warfare agents (CWAs) and related dissipation products in the environment of Sardasht area, Iran. Three types of environmental samples including water, soil, and native local plant materials were collected and analyzed. Gas chromatography-mass spectrometry in the electron impact ionization mode has been developed for the separation, screening, identification, and qualification of chemicals after the sample preparation methods. The initial results revealed that no trace of related compounds or CWAs was detected in the soil and water samples. However, trace amounts of some degradation products of blistering agents like mustard gas (HD) and lewisite were found in a tree wood from a house subjected

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to chemical attack as well as in barley samples (a mixture of leaves and root) collected from an agricultural field in the area indicating chronic low exposure to the environment and people. In order to validate the applied extraction procedures, ethylene glycol was spiked to some of the samples including groundwater, surface soil, grape, and alfalfa plants. All the recoveries were in the range of 83.6-107.4% with the relative standard deviations varying from 4.9% to 12.4% (n = 3) successfully.

Authors: Abdorreza Vaezehir, Asra Pirkhezranian, Negar Sehati, Mohammad Reza Hosseinzadeh, Seyed Yahya Salehi-Lisar, Hans Sanderson

Full Source: Environmental science and pollution research international 2021 Jul 31. doi: 10.1007/s11356-021-15593-9.

OCCUPATIONAL

Urinary toluene levels and adverse health symptoms among automotive garage workers, Nakhon Si Thammarat province, Thailand

2021-09

To determine their urinary toluene levels, to describe the workers' hygiene behaviors and the prevalence of adverse health symptoms among automotive garage workers exposed to chemical substances. A cross-sectional descriptive study was conducted by interviewing among automotive garages located in the Nakhon Si Thammarat province, Thailand. During between 1 November 2020 and 31 December 2020. A total of 140 automotive garages workers were selected using a purposive sampling method. The questionnaire was conducted via face-to-face interview and the toluene was quantified using gas chromatography. Descriptive statistics were computed for the variables. Risk factors were evaluated using multiple logistic regression analysis. Adjusted odds ratio (OR_{adj}) and 95% confidence interval (CI) were presented as statistically significant when the p value was < 0.05. The Mann-Whitney U test was used to compare the medians of continuous variables of the two groups. The prevalence of skin effects (60.71%); respiratory tract irritation (49.29%); nausea (46.43%); and dizziness (40.71%) was remarkable in the automotive garage workers. Several socio-demographic variables were significantly associated with increased skin effects, respiratory tract irritant, nausea, and dizziness. The median urinary toluene level of the automotive garage workers was 145 µg/L (range, 12.0-958.0 µg/L) which the median urinary levels and demographic

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characteristics, occupational lifestyle, personal protective equipment used, hygiene behavior, and adverse health symptoms had significantly different ($p < 0.05$). Urine is one of the most useful a sample for biomonitoring of occupational exposure to toluene. Personal hygiene is important for the automotive garage workers, and it should be emphasized in education programs.

Authors: Somsiri Decharat

Full Source: Environmental analysis, health and toxicology 2021 Sep;36(3):e2021018-0. doi: 10.5620/eaht.2021018.

Occupational mortality in the New Mexico oil and gas industry

2021-08-07

New Mexico's oil and natural gas industry has the second highest occupational fatality rate among oil and gas workers in the nation. There is currently limited data available regarding the top contributing factors to occupational mortality specific to the state's oil and gas industry. This study seeks to understand causes of mortality among oil and gas workers in New Mexico between 2008 and 2018. To facilitate this study, case reports were obtained from the New Mexico Office of the Medical Investigator, and population data was acquired from the US Department of Labor. In this 11-year span, there were 73 cases, with an average annual mortality rate of 37 deaths per 100,000 oil and gas workers. Leading causes of death were vehicle accidents (36%), cardiovascular incidents (22%), and crush injuries (19%). The majority of vehicle accidents involved single vehicle accidents, and correct seat belt use was only documented 23% of the time. The majority of cardiovascular deaths were due to arteriosclerotic and atherosclerotic cardiovascular disease. Alcohol was present in 18% of cases, and drugs were present in 19% of cases with methamphetamine present in 10% of investigated deaths. This is the first study to directly include cardiovascular incidents in the leading causes of death; otherwise, this study reflects national data reporting vehicle accidents and crush injuries as the leading causes of death. Going forward, prevention measures should effectively target safe driving practices focusing on seatbelt use, and mitigation of workplace drug and alcohol consumption.

Authors: Andrew Faturos, Garon Bodor, Lori Proe, Sarah Lathrop

Full Source: Journal of forensic sciences 2021 Aug 7. doi: 10.1111/1556-4029.14831.

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PHARMACEUTICAL/TOXICOLOGY

The use of human induced pluripotent stem cells to screen for developmental toxicity potential indicates reduced potential for non-combusted products, when compared to cigarettes

2020-11-15

devTOX quickPredict (devTOX qP) is a metabolomics biomarker-based assay that utilises human induced pluripotent stem (iPS) cells to screen for potential early stage embryonic developmental toxicity in vitro. Developmental toxicity potential is assessed based on the assay endpoint of the alteration in the ratio of key unrelated biomarkers, ornithine and cystine (o/c). This work aimed to compare the developmental toxicity potential of tobacco-containing and tobacco-free non-combustible nicotine products to cigarette smoke. Smoke and aerosol from test articles were produced using a Vitrocell VC10 smoke/aerosol exposure system and bubbled into phosphate buffered saline (bPBS). iPS cells were exposed to concentrations of up to 10% bPBS. Assay sensitivity was assessed through a spiking study with a known developmental toxicant, all-trans-retinoic acid (ATRA), in combination with cigarette smoke extract. The bPBS extracts of reference cigarettes (1R6F and 3R4F) and a heated tobacco product (HTP) were predicted to have the potential to induce developmental toxicity, in this screening assay. The bPBS concentration at which these extracts exceeded the developmental toxicity threshold was 0.6% (1R6F), 1.3% (3R4F), and 4.3% (HTP) added to the cell media. Effects from cigarette smoke and HTP aerosol were driven largely by cytotoxicity, with the cell viability and o/c ratio dose-response curves crossing the developmental toxicity thresholds at very similar concentrations of added bPBS. The hybrid product and all the electronic cigarette (e-cigarette) aerosols were not predicted to be potential early developmental toxicants, under the conditions of this screening assay.

Authors: Liam Simms, Kathryn Rudd, Jessica Palmer, Lukasz Czekala, Fan Yu, Fiona Chapman, Edgar Trelles Sticken, Roman Wieczorek, Lisa Maria Bode, Matthew Stevenson, Tanvir Walele

Full Source: Current research in toxicology 2020 Nov 15;1:161-173. doi: 10.1016/j.crttox.2020.11.001.

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Placental Transfer and Composition of Perfluoroalkyl Substances (PFASs): A Korean Birth Panel of Parent-Infant Triads

2021-07-14

Exposure to perfluoroalkyl substances (PFASs) is of public concern due to their persistent exposure and adverse health effects. Placental transfer of PFASs is an important excretion pathway of these chemicals in pregnant women and exposure route in fetuses. We measured PFAS concentrations in maternal, paternal, and umbilical cord serum collected from 62 pregnant Korean women and matched biological fathers of the fetuses. Placental transfer rates (cord to maternal serum ratio) of PFASs were also calculated. Demographics and pregnancy-related factors determining the placental transfer rates were identified using linear regression models. Maternal, paternal, and cord serum showed different PFASs compositions. Among the PFASs, perfluorooctane sulfonate (PFOS) showed the highest concentrations in maternal and paternal serum, while perfluorooctanoic acid (PFOA) showed the highest concentration in cord serum. There was a higher proportion of perfluoroalkyl carboxylic acids (PFCAs) with 9-12 carbon chains than those with 13-14 carbon chains in maternal and paternal serum, but this proportion was in the opposite direction in cord serum. PFOA and perfluorohexane sulfonate (PFHxS) had higher placental transfer rates (means of 0.32 and 0.36, respectively) than PFOS (mean of 0.12), which is in line with the results of previous studies. Gestational age and birth weight were positively associated with placental transfer rate of PFOA, PFHxS, and PFOS, while pre-pregnant BMI and weight were inversely associated with PFOS. This study showed that placental transfer of PFASs differs by compounds and is associated with pregnancy-related factors. Further studies on novel PFASs are warranted for Korean pregnant women.

Authors: Habyeong Kang, Hee-Sun Kim, Yeong Sook Yoon, Jeongsun Lee, Younglim Kho, Jisun Lee, Hye Jin Chang, Yoon Hee Cho, Young Ah Kim
Full Source: Toxics 2021 Jul 14;9(7):168. doi: 10.3390/toxics9070168.
and two human body media (human milk and blood) in China from 2010 to 2020. In addition, this study conducted multi-pathway exposure health risk assessments of populations of different ages in urban, rural, key regions, and industrial factories using the Monte-Carlo simulation. Finally, the human health ambient water quality criteria (AWQC) of eight PBDEs were derived using Chinese exposure parameters and bioaccumulation factors (BAFs). The results showed that the eastern and southeastern coastal regions of China were heavily polluted by PBDEs, and the variation trends of the PBDEs concentrations in the different exposure media were

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not consistent. PBDEs did not pose a risk to urban and rural residents in ordinary regions, but the hazard indexes (HIs) for residents in key regions and occupational workers exceeded the safety threshold. Dust exposure was the primary exposure pathway for urban and rural residents in ordinary regions, but for residents in key regions and occupational workers, dietary exposure was the primary exposure pathway. BDE-209 was found to be the most serious individual PBDE congener in China. The following human health AWQC values of the PBDEs were derived: drinking water exposure: 0.233-65.2 $\mu\text{g}\cdot\text{L}^{-1}$; and drinking water and aquatic products exposure: 8.51×10^{-4} -1.10 $\mu\text{g}\cdot\text{L}^{-1}$.

Authors: Jing Wang, Zhenguang Yan, Xin Zheng, Shuping Wang, Juntao Fan, Qianhang Sun, Jiayun Xu, Shuhui Men

Full Source: The Science of the total environment 2021 Jul 30;799:149353. doi: 10.1016/j.scitotenv.2021.149353.