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CHEMICAL EFFECTS

Metal Toxicity and Speciation: A Review

2021-03-24

Background: Essential metal ions play a specific and fundamental role in human metabolism. Their homeostasis is finely tuned and any concentration imbalance in form of deficiency or excess could lead to a progressive reduction and failure of normal biological function, to severe physiological and clinical outcomes till death. Conversely, non-essential metals are not necessary for life and only noxious effects could arise after their exposure. Large environmental amounts of such chemicals come from both natural and anthropogenic sources, with the latter being predominant because of human activities. The dissipation of toxic metals contaminates water, air, soil, and food, causing a series of chronic and acute syndromes.

Objective: This review discusses the toxicity of non-essential metals considering their peculiar chemical characteristics such as different forms, hard-soft character, oxidation states, binding capabilities and solubility, which can influence their speciation in biological systems, and subsequently, the main cellular targets. Particular focus is given to selected toxic metals, major non-essential metals or semimetals related to toxicity such as mercury, lead, cadmium, chromium, nickel and arsenic. In addition, we provide indications on the possible treatments/interventions on metal poisoning based on chelation therapy.

Conclusion: Toxic metal ions can exert their peculiar harmful effects in several ways. They strongly coordinate to important biological molecules on the basis of their chemical-physical characteristics (mainly HSAB properties) or replace essential metal ions from their natural locations in proteins, enzymes or in hard structures such as bones or teeth. Metals with redox properties could be key inducers of reactive oxygen species, leading to oxidative stress and cellular damage. Therapeutic detoxification, through complexation of toxic metal ions by specific chelating agents, appears an efficacious clinical strategy mainly in acute cases of metal intoxication.

Authors: Massimiliano Peana, Alessio Pelucelli, Serenella Medici, Rosita Cappai, Valeria Marina Nurchi, Maria Antonietta Zoroddu

Full Source: Current medicinal chemistry 2021 Mar 24. doi: 10.2174/0929867328666210324161205.

Background:
Essential metal ions play a specific and fundamental role in human metabolism.

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Development of a Comprehensive Toxicity Pathway Model for 17 β -Ethinylestradiol in Early Life Stage Fathead Minnows (*Pimephales promelas*)

2021-03-23

There is increasing pressure to develop alternative ecotoxicological risk assessment approaches that do not rely on expensive, time-consuming, and ethically questionable live animal testing. This study aimed to develop a comprehensive early life stage toxicity pathway model for the exposure of fish to estrogenic chemicals that is rooted in mechanistic toxicology. Embryo-larval fathead minnows (FHM; *Pimephales promelas*) were exposed to graded concentrations of 17 β -ethinylestradiol (water control, 0.01% DMSO, 4, 20, and 100 ng/L) for 32 days. Fish were assessed for transcriptomic and proteomic responses at 4 days post-hatch (dph), and for histological and apical end points at 28 dph. Molecular analyses revealed core responses that were indicative of observed apical outcomes, including biological processes resulting in overproduction of vitellogenin and impairment of visual development. Histological observations indicated accumulation of proteinaceous fluid in liver and kidney tissues, energy depletion, and delayed or suppressed gonad development. Additionally, fish in the 100 ng/L treatment group were smaller than controls. Integration of omics data improved the interpretation of perturbations in early life stage FHM, providing evidence of conservation of toxicity pathways across levels of biological organization. Overall, the mechanism-based embryo-larval FHM model showed promise as a replacement for standard adult live animal tests.

Authors: Alper James G Alcaraz, David Potůšil, Kamil Mikulášek, Derek Green, Bradley Park, Connor Burbridge, Kerstin Bluhm, Othman Soufan, Taylor Lane, Marek Pipal, Markus Brinkmann, Jianguo Xia, Zbyněk Zdráhal, David Schneider, Doug Crump, Niladri Basu, Natacha Hogan, Markus Hecker

Full Source: Environmental science & technology 2021 Mar 23. doi: 10.1021/acs.est.0c05942.

An annotation database for chemicals of emerging concern in exposome research

2021-03-24

Background: Chemicals of Emerging Concern (CECs) include a very wide group of chemicals that are suspected to be responsible for adverse effects on health, but for which very limited information is available. Chromatographic techniques coupled with high-resolution

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mass spectrometry (HRMS) can be used for non-targeted screening and detection of CECs, by using comprehensive annotation databases. Establishing a database focused on the annotation of CECs in human samples will provide new insight into the distribution and extent of exposures to a wide range of CECs in humans.

Objectives: This study describes an approach for the aggregation and curation of an annotation database (CECscreen) for the identification of CECs in human biological samples.

Methods: The approach consists of three main parts. First, CECs compound lists from various sources were aggregated and duplications and inorganic compounds were removed. Subsequently, the list was curated by standardization of structures to create "MS-ready" and "QSAR-ready" SMILES, as well as calculation of exact masses (monoisotopic and adducts) and molecular formulas. The second step included the simulation of Phase I metabolites. The third and final step included the calculation of QSAR predictions related to physicochemical properties, environmental fate, toxicity and Absorption, Distribution, Metabolism, Excretion (ADME) processes and the retrieval of information from the US EPA CompTox Chemicals Dashboard.

Results: All CECscreen database and property files are publicly available (DOI: <https://doi.org/10.5281/zenodo.3956586>). In total, 145,284 entries were aggregated from various CECs data sources. After elimination of duplicates and curation, the pipeline produced 70,397 unique "MS-ready" structures and 66,071 unique QSAR-ready structures, corresponding with 69,526 CAS numbers. Simulation of Phase I metabolites resulted in 306,279 unique metabolites. QSAR predictions could be performed for 64,684 of the QSAR-ready structures, whereas information was retrieved from the CompTox Chemicals Dashboard for 59,739 CAS numbers out of 69,526 inquiries. CECscreen is incorporated in the in silico fragmentation approach MetFrag.

Discussion: The CECscreen database can be used to prioritize annotation of CECs measured in non-targeted HRMS, facilitating the large-scale detection of CECs in human samples for exposome research. Large-scale detection of CECs can be further improved by integrating the present database with resources that contain CECs (metabolites) and meta-data measurements, further expansion towards in silico and experimental (e.g., MassBank) generation of MS/MS spectra, and development of bioinformatics approaches capable of using correlation patterns in the measured chemical features.

Authors: Jeroen Meijer, Marja Lamoree, Timo Hamers, Jean-Philippe Antignac, Sébastien Hutinet, Laurent Debrauwer, Adrian Covaci, Carolin

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Huber, Martin Krauss, Douglas I Walker, Emma L Schymanski, Roel Vermeulen, Jelle Vlaanderen

Full Source: Environment international 2021 Mar 24;152:106511. doi: 10.1016/j.envint.2021.106511.

Cytotoxicity of mesoporous silica modified by amino and carboxyl groups on vascular endothelial cells

2021-03-25

Mesoporous silica is widely used because of its unique and excellent properties, especially it can be used as a drug carrier and gene carrier in the biomedical field. After the mesoporous silica is put into clinical use, it is more likely to be exposed in human body. Therefore, the effect of mesoporous silica on human body cannot be ignored. The injury of vascular endothelial cells is a prerequisite for the occurrence of many cardiovascular diseases. As a drug and gene carrier, mesoporous silica increases its contact with vascular endothelial cells, so its toxic effect on cardiovascular system cannot be ignored. In this study, amino (-NH_2) and carboxyl (-COOH) were modified on mesoporous silica SBA-15 by post-grafting. The results showed that it still maintained the one-dimensional hexagonal mesoporous structure of SBA-15 and had typical mesoporous structure. Then human umbilical vein endothelial cells (HUVECs) were infected with SBA-15, -NH_2 -SBA-15, and -COOH -SBA-15. The results showed that the functionalized mesoporous silica SBA-15 had cytotoxicity to HUVECs and damaged the cell membrane, but compared with the unmodified mesoporous silica SBA-15 the cytotoxicity of functionalized mesoporous silica SBA-15 was lower and the toxicity of carboxyl modified group was the lowest. By comparing the cell inhibition rate and the expression level of lactate dehydrogenase and reactive oxygen species induced by the three materials, oxidative damage and cell membrane damage may be two mechanisms of cytotoxicity. Mesoporous silica SBA-15 has an effect on cardiovascular system by inducing the high expression of nitric oxide, intercellular adhesive molecule-1 and vascular cell adhesive molecule-1 in HUVECs. In summary, our results show that mesoporous silica is toxic to vascular endothelial cells.

Authors: Ji Zhao, De-Yun Bu, Na Zhang, Da-Nian Tian, Li-Ya Ma, Hui-Fang Yang

Full Source: Environmental toxicology 2021 Mar 25. doi: 10.1002/tox.23138.

Mesoporous silica is widely used because of its unique and excellent properties, especially it can be used as a drug carrier and gene carrier in the biomedical field.

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ENVIRONMENTAL RESEARCH

Emerging pollutants in Nigeria: A systematic review

2021-03-20

Emerging pollutants represent a group of synthetic or naturally occurring compounds that are not normally monitored within the environment but can enter into the environment and cause different adverse ecological and health effects. This systematic review identified the various emerging pollutants in Nigeria. The following databases, ScienceDirect, PubMed, Google Scholar, and African Journals OnLine (AJOL) were searched to identify studies on pollutants of emerging concerns in Nigeria. A total of 933 articles were identified out of which 30 articles were selected to be eligible for the study. Over 250 emerging pollutants were identified and divided into 9 major groups which are personal care products, pharmaceuticals, industrial chemicals, polycyclic aromatic hydrocarbons, volatile organic compounds, pesticides, mycotoxins, radionuclides and electromagnetic radiations (Gamma radiation) and other pollutants of emerging concerns such as microbes, microplastics, and particulate matter. These pollutants are found in water bodies and underground waters, soils and sediments, biological systems, and ambient air at different concentrations with seasonal variations. Some of these pollutants act as endocrine disruptors, β -adrenergic receptors agonist blockers, oxidative stress inducers and can cause genetic alterations in DNA and epigenetic reprogramming through global DNA methylation, gene-specific CpG methylation and microRNA expression. Emerging pollutants of public health concern in Nigeria are on the increase and are threat to both ecological and human health.

Authors: Chukwuebuka Egbuna, Cecilia N Amadi, Kingsley C Patrick-Iwuanyanwu, Shahira M Ezzat, Chinaza Godswill Awuchi, Peter Okechukwu Ugonwa, Orish E Orisakwe

Full Source: Environmental toxicology and pharmacology 2021 Mar 20;85:103638. doi: 10.1016/j.etap.2021.103638.

An investigation into the leaching of micro and nano particles and chemical pollutants from disposable face masks - linked to the COVID-19 pandemic

2021-03-10

The production of disposable plastic face masks (DPFs) in China alone has reached to approximately 200 million a day, in a global effort to tackle the spread of the new SARS-CoV-2 virus. However, improper and unregulated

Emerging pollutants represent a group of synthetic or naturally occurring compounds that are not normally monitored within the environment but can enter into the environment and cause different adverse ecological and health effects.

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disposals of these DPFs has been and will continue to intensify the plastic pollution problem we are already facing. This study focuses on the emission of pollutants from 7 DPF brands that were submerged in water to simulate environmental conditions if these DPFs were littered. The DPF leachates were filtered by inorganic membranes, and both particle-deposited organic membranes and the filtrates were characterized using techniques such as FTIR, SEM-EDX, Light Microscopy, ICP-MS and LC-MS. Micro and nano scale polymeric fibres, particles, siliceous fragments and leachable inorganic and organic chemicals were observed from all of the tested DPFs. Traces of concerning heavy metals [i.e. lead up to 6.79 $\mu\text{g/L}$] were detected in association with silicon containing fragments. ICP-MS also confirmed the presence of other leachable metals like cadmium (up to 1.92 $\mu\text{g/L}$), antimony (up to 393 $\mu\text{g/L}$) and copper (up to 4.17 $\mu\text{g/L}$). LC-MS analysis identified polar leachable organic species related to plastic additives and contaminants; polyamide-66 monomer and oligomers (nylon-66 synthesis), surfactant molecules, dye-like molecules and polyethylene glycol were all tentatively identified in the leachate. The toxicity of some of the chemicals found and the postulated risks of the rest of the present particles and molecules, raises the question of whether DPFs are safe to be used on a daily basis and what consequences are to be expected after their disposal into the environment.

Authors: G L Sullivan, J Delgado-Gallardo, T M Watson, S Sarp

Full Source: Water research 2021 Mar 10;196:117033. doi: 10.1016/j.watres.2021.117033.

Microplastics in the human digestive environment: A focus on the potential and challenges facing in vitro gut model development

2021-03-11

Plastic pollution is a major issue worldwide, generating massive amounts of smaller plastic particles, including microplastics (MPs). Their ubiquitous nature in the environment but also in foodstuff and consumer packaged goods has revealed potential threats to humans who can be contaminated mainly through air, food and water consumption. In this review, the current literature on human exposure to MPs is summarized with a focus on the gastrointestinal tract as portal of entry. Then, we discuss the vector effect of MPs, in their pristine versus weathered forms, with well-known contaminants as heavy metals and chemicals, or more emerging ones as antibiotics or microbial pathogens, like *Pseudomonas* spp., *Vibrio* spp., *Campylobacter* spp. and *Escherichia coli*. Comprehensive knowledge on MP fate in the gastrointestinal tract and their potential impact on gut

Plastic pollution is a major issue worldwide, generating massive amounts of smaller plastic particles, including microplastics (MPs).

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homeostasis disruption, including gut microbiota, mucus and epithelial barrier, is reported in vitro and in vivo in mammals. Special emphasis is given on the crucial need of developing robust in vitro gut models to adequately simulate human digestive physiology and absorption processes. Finally, this review points out future research directions on MPs in human intestinal health.

Authors: Elora Fournier, Lucie Etienne-Mesmin, Charlotte Grootaert, Lotte Jelsbak, Kristian Syberg, Stéphanie Blanquet-Diot, Muriel Mercier-Bonin
Full Source: Journal of hazardous materials 2021 Mar 11;415:125632.
doi: 10.1016/j.jhazmat.2021.125632.

OCCUPATIONAL

Prenatal Exposure to Pesticides and Risk of Preeclampsia among Pregnant Women: Results from the ELFE Cohort

2021-03-22

Background: Preeclampsia is a pregnancy-specific syndrome caused by abnormal placentation. Although environmental chemicals, including some pesticides, are suspected of impairing placentation and promoting preeclampsia, its relationship with preeclampsia has been insufficiently explored. Objectives: We aimed to investigate the relation between non-occupational exposure to pesticides during pregnancy and the risk of preeclampsia.

Methods: The study cohort comprised 195 women with and 17,181 without preeclampsia from the ELFE birth cohort. We used toxicogenomic approaches to select 41 pesticides of interest for their possible influence on preeclampsia. We assessed household pesticide use (self-reported data), environmental exposure to agricultural pesticides (geographic information systems), and dietary exposure (food-frequency questionnaire with data from monitoring pesticide residues in food and water). Dietary exposures to pesticides were grouped into clusters of similar exposures to resolve collinearity issues. For each exposure source, pesticides were mutually adjusted, and odds ratios estimated with logistic regression models.

Results: The quantity of prochloraz applied within a kilometer of the women's homes was higher in women with than without preeclampsia (fourth quartile vs. others; adjusted odds ratio [aOR]=1.54; 95%CI: 1.02, 2.35), especially when preeclampsia was diagnosed before 34 weeks of gestation (aOR=2.25; 95%CI: 1.01, 5.06). The reverse was observed

Background:
Preeclampsia is a pregnancy-specific syndrome caused by abnormal placentation.

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with nearby cypermethrin application (aOR=0.59, 95%CI: 0.36, 0.96). In sensitivity analyses, women with preeclampsia receiving antihypertensive treatment had a significantly higher probability of using herbicides at home during pregnancy than women without preeclampsia (aOR=2.20; 95%CI: 1.23, 3.93). No statistically significant association was found between dietary exposure to pesticide residues and preeclampsia. Discussion: While the most of the associations examined remained statistically non-significant, our results suggest the possible influence on preeclampsia of residential exposures to prochloraz and some herbicides. These estimations are supported by toxicological and mechanistic data.

Authors: Isabelle Enderle, Nathalie Costet, Noriane Cogne, Cécile Zaros, Julien Caudeville, Ronan Garlantezec, Cécile Chevrier, Alexandre Nougadere, Blandine DE Lauzon-Guillain, Maela LE Lous, Rémi Beranger
Full Source: Environmental research 2021 Mar 22;111048. doi: 10.1016/j.envres.2021.111048.

A PRELIMINARY ASSESSMENT OF PHYSICAL WORK EXPOSURES AMONG ELECTRONIC WASTE WORKERS AT AGBOGBLOSHIE, ACCRA GHANA

2021-03

Occupational exposure associated with unstructured, informal e-waste recycling has received very limited attention. This study aimed to quantify the occupational physical exposures among informal e-waste workers at the largest e-waste site in Africa. A cross-sectional field survey of 163 male e-waste workers was conducted using a self-report occupational physical activity questionnaire, along with direct work observations, and pedometer estimates of walking activity for a subset of workers (n = 42). Results indicated significant differences in self-reported 7-day work exposures among the three main e-waste job categories, namely, collectors (n = 70), dismantlers (n = 73) and burners (n = 20). Prolonged walking, sitting and standing on five or more days in the workweek was frequently reported by collectors (87%), dismantlers (82%) and burners (60%), respectively. Nearly 90% of collectors and burners and 60% of dismantlers reported lifting and carrying on five or more days in the workweek. The exposure combinations identified suggest a risk for musculoskeletal disorders (MSDs). Findings call attention to the need for research examining potential associations between physical exposures and MSDs affecting e-waste workers in Agbogbloshie. The high exposure

Occupational exposure associated with unstructured, informal e-waste recycling has received very limited attention.

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variability both between and within workers has implications for future exposure assessments conducted in unregulated, informal work settings.

Authors: Augustine A Acquah, Clive D'Souza, Bernard J Martin, John Arko-Mensah, Paul K Botwe, Prudence Tettey, Duah Dwomoh, Afua Amoabeng Nti, Lawrencina Kwarteng, Sylvia Takyi, Isabella A Quakyi, Thomas G Robins, Julius N Fobil

Full Source: International journal of industrial ergonomics 2021 Mar;82:103096. doi: 10.1016/j.ergon.2021.103096.

PHARAMACEUTICAL/TOXICOLOGY

Flufenoxuron suppresses the proliferation of testicular cells by targeting mitochondria in mice

2021-03

Flufenoxuron is a benzoylurea pesticide that is used to eradicate insects and acarids in the farmland. Even though it specifically works on target animals, the possibilities of its bioaccumulation and harmful effects on non-target animals cannot be denied. As the usage and application of pesticides increases, exposure to them also increases through ingestion of food residues, inhalation, or dermal contact. Pesticides could also be considered as endocrine disruptor chemicals; however, the reproductive toxicity and cellular mechanisms of flufenoxuron have not been identified. Our results indicate that flufenoxuron inhibits cellular proliferation and hampers calcium homeostasis, especially by targeting mitochondria. We also confirmed the induction of endoplasmic reticulum (ER) stress and ER-mitochondrial contact signaling. Using pharmacological inhibitors, we also observed that the mitogen-activated protein kinase and Akt signaling pathways were upregulated by flufenoxuron. Further, by oral administration of flufenoxuron (100 mg/kg/bw) to C57BL/6 male mice, we observed transcriptional changes in the testis-related genes. Collectively, we demonstrated that flufenoxuron inhibits cell proliferation and alters gene expression in mouse testis cells and induces testicular dysfunction in mice. These results indicate that flufenoxuron may be harmful to male reproduction and fertility in the early stages of pregnancy.

Authors: Jiyeon Ham, Whasun Lim, Gwonhwa Song

Full Source: Pesticide biochemistry and physiology 2021 Mar;173:104773. doi: 10.1016/j.pestbp.2021.104773.

Flufenoxuron is a benzoylurea pesticide that is used to eradicate insects and acarids in the farmland.