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CHEMICAL EFFECTS

Uncovering Evidence for Endocrine-Disrupting Chemicals That Elicit Differential Susceptibility through Gene-Environment Interactions

2021-04-06

Exposure to endocrine-disrupting chemicals (EDCs) is linked to myriad disorders, characterized by the disruption of the complex endocrine signaling pathways that govern development, physiology, and even behavior across the entire body. The mechanisms of endocrine disruption involve a complex system of pathways that communicate across the body to stimulate specific receptors that bind DNA and regulate the expression of a suite of genes. These mechanisms, including gene regulation, DNA binding, and protein binding, can be tied to differences in individual susceptibility across a genetically diverse population. In this review, we posit that EDCs causing such differential responses may be identified by looking for a signal of population variability after exposure. We begin by summarizing how the biology of EDCs has implications for genetically diverse populations. We then describe how gene-environment interactions (GxE) across the complex pathways of endocrine signaling could lead to differences in susceptibility. We survey examples in the literature of individual susceptibility differences to EDCs, pointing to a need for research in this area, especially regarding the exceedingly complex thyroid pathway. Following a discussion of experimental designs to better identify and study GxE across EDCs, we present a case study of a high-throughput screening signal of putative GxE within known endocrine disruptors. We conclude with a call for further, deeper analysis of the EDCs, particularly the thyroid disruptors, to identify if these chemicals participate in GxE leading to differences in susceptibility.

Authors: Dylan J Wallis, Lisa Truong, Jane La Du, Robyn L Tanguay, David M Reif

Full Source: Toxics 2021 Apr 6;9(4):77. doi: 10.3390/toxics9040077.

Endocrine-Disrupting Chemicals and Infectious Diseases: From Endocrine Disruption to Immunosuppression

2021-04-11

Endocrine-disrupting chemicals (EDCs) are hormonally active compounds in the environment that interfere with the body's endocrine system and consequently produce adverse health effects. Despite persistent public health concerns, EDCs remain important components of common

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consumer products, thus representing ubiquitous contaminants to humans. While scientific evidence confirmed their contribution to the severity of Influenza A virus (H1N1) in the animal model, their roles in susceptibility and clinical outcome of the coronavirus disease (COVID-19) cannot be underestimated. Since its emergence in late 2019, clinical reports on COVID-19 have confirmed that severe disease and death occur in persons aged ≥65 years and those with underlying comorbidities. Major comorbidities of COVID-19 include diabetes, obesity, cardiovascular disease, hypertension, cancer, and kidney and liver diseases. Meanwhile, long-term exposure to EDCs contributes significantly to the onset and progression of these comorbid diseases. Besides, EDCs play vital roles in the disruption of the body's immune system. Here, we review the recent literature on the roles of EDCs in comorbidities contributing to COVID-19 mortality, impacts of EDCs on the immune system, and recent articles linking EDCs to COVID-19 risks. We also recommend methodologies that could be adopted to comprehensively study the role of EDCs in COVID-19 risk.

Authors: Elikanah Olusayo Adegoke, Md Saidur Rahman, Yoo-Jin Park, Young Ju Kim, Myung-Geol Pang

Full Source: International journal of molecular sciences 2021 Apr 11;22(8):3939. doi: 10.3390/ijms22083939.

Environmental occurrence, toxicity concerns, and remediation of recalcitrant nitroaromatic compounds

2021-04-27

Nitroaromatic compounds (NACs) are considered important groups of chemicals mainly produced by human and industrial activities. The large-scale application of these xenobiotics creates contamination of the water and soil environment. Despite applicability, NACs have been caused severe hazardous side effects in animals and human systems like different cancers, anemia, skin irritation, liver damage and mutagenic effects. The effective remediation of the NACs from the environment is a significant concern. Researchers have implemented physicochemical and biological methods for the remediation of NACs from the environment. Most of the applied methods are based on adsorption and degradation approaches. Among these methods, degradation is considered a versatile method for the subsequent removal of NACs due to its exceptional properties like simplicity, easy operation, cost-effectiveness, and availability. Most importantly, the degradation process does not generate hazardous side products and wastes compared to other methods. Hence, the importance of NACs, their remediation, and supreme attributes of the

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degradation method have encouraged us to review the recent progress and development for the removal of these perilous materials using degradation as a versatile method. Therefore, in this review, (i) NACs, physicochemical properties, and their hazardous side effects on humans and animals are discussed; (ii) Physicochemical methods, microbial, anaerobic bioremediation, mycoremediation, and aerobic degradation approaches for the degradation of NACs were thoroughly vetted; (iii) The possible mechanisms for degradation of NACs were investigated and discussed. (iv) The applied kinetic models for evaluation of the rate of degradation were also assessed and discussed. Finally, (vi) current challenges and future prospects of proposed methods for degradation and removal of NACs were also directed.

Authors: Muhammad Bilal, Ahmad Reza Bagheri, Pankaj Bhatt, Shaohua Chen

Full Source: Journal of environmental management 2021 Apr 27;291:112685. doi: 10.1016/j.jenvman.2021.112685.

ENVIRONMENTAL RESEARCH

Aquatic toxicity of waterpipe wastewater chemicals

2021-04-28

Introduction: The recent increase in U.S. popularity and use prevalence of water pipe (WP) tobacco smoking raises concerns about the potential environmental impacts of WP waste disposal and the need for strategies to reduce such impacts. The U.S. Food and Drug Administration (FDA) is required to assess the environmental impacts of its tobacco regulatory actions per the U.S. National Environmental Policy Act (NEPA). The purpose of this study was to identify and quantify specific chemical constituents in WP wastewater and to determine their potential aquatic toxicity.

Methods: Using a modified Beirut smoking regimen, five different WP charcoal brands (n=70) and ten WP tobacco brands (n=35) were smoked separately using a WP smoking machine in which smoke was passed through the WP base water. We analyzed and quantified specific chemical constituents in the WP bowl wastewater through standardized U.S. Environmental Protection Agency's (EPA) Hazardous Waste Test Methods. We then characterized the ecological hazard for acute and chronic aquatic toxicity posed by the specific chemicals through compilations of Globally Harmonized System of Classification and Labelling of Chemicals (GHS) and hazardous concentration values (concentration affecting 50% of the species).

Introduction: The recent increase in U.S.

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Results: Among the list of 31 specific chemicals analyzed, we detected 22 and 11 chemicals in wastewater from WP tobacco and WP charcoal smoking, respectively. Nearly half of the 22 WP wastewater chemicals were classified as "very toxic" or "toxic" for acute and chronic aquatic toxicity per GHS classification. The most hazardous compounds with acute and chronic toxicity in aquatic organisms include acrolein, acrylonitrile, and metals (cadmium, lead, chromium, nickel, cobalt) found in both WP tobacco and charcoal wastewater, and N-nitrosonornicotine, nicotine, crotonaldehyde and selenium were additionally found in WP tobacco wastewater. All the identified chemicals are considered harmful or potentially harmful constituents in tobacco products and tobacco smoke per FDA's list, and seventeen of them represent hazardous waste per EPA's list.

Conclusion: Our study expands the identification and quantifies several WP wastewater chemical constituents. It characterizes the ecological hazard of these chemicals and identifies chemicals of concern, aiding our evaluation of the environmental impacts of WP waste products. Our results add to the existing evidence that WP wastewater is a source of toxins that could affect water quality and aquatic organisms, and bioaccumulate in the environment if disposed of into public sewers, on the ground, or in an onsite septic system. These findings highlight the importance of concerted efforts to raise awareness of appropriate WP waste disposal practices in both retail and residential settings, and applicable regulatory compliance requirements for WP retailer establishments, thereby limiting hazards from WP wastewater.

Authors: Ronald L Edwards Jr, P Dilip Venugopal, Jason R Hsieh

Full Source: Environmental research 2021 Apr 28;111206. doi: 10.1016/j.envres.2021.111206.

The reasons behind the extensive use of pesticides include the need to destroy vector organisms and promote agricultural production in order to sustain population growth.

An Experimental Approach to Study the Effects of Realistic Environmental Mixture of Linuron and Propamocarb on Zebrafish Synaptogenesis

2021-04-27

The reasons behind the extensive use of pesticides include the need to destroy vector organisms and promote agricultural production in order to sustain population growth. Exposure to pesticides is principally occupational, even if their persistence in soil, surface water and food brings the risk closer to the general population, hence the demand for risk assessment, since these compounds exist not only as individual chemicals but also in form of mixtures. In light of this, zebrafish represents a suitable model for the evaluation of toxicological effects. Here, zebrafish embryos were exposed for 96 h post fertilization (hpf) to sublethal

concentrations (350 µg/L) of linuron and propamocarb, used separately and then combined in a single solution. We investigated the effects on morphological traits and the expression of genes known to be implicated in synaptogenesis (neurexin1a and neuroligin3b). We observed alterations in some phenotypic parameters, such as head width and interocular distance, that showed a significant reduction ($p < 0.05$) for the mixture treatment. After individual exposure, the analysis of gene expression showed an imbalance at the synaptic level, which was partially recovered by the simultaneous administration of linuron and propamocarb. This preliminary study demonstrates that the combined substances were responsible for some unpredictable effects, diverging from the effect observed after single exposure. Thus, it is clear that risk assessment should be performed not only on single pesticides but also on their mixtures, the toxicological dynamics of which can be totally unpredictable.
Authors: Giulia Caioni, Carmine Merola, Monia Perugini, Michele d'Angelo, Anna Maria Cimini, Michele Amorena, Elisabetta Benedetti
Full Source: International journal of environmental research and public health 2021 Apr 27;18(9):4664. doi: 10.3390/ijerph18094664.

National-scale down-the-drain environmental risk assessment of oxybenzone in the United States

2021-04-29
Organic ultraviolet (UV) filters are used in cosmetic and personal care products (CPCPs) and over-the-counter (OTC) sunscreens, due to their ability to absorb solar radiation. OTC and CPCP ingredients are washed down-the-drain and can then enter freshwaters that receive wastewater treatment plant (WWTP) effluents. This paper presents a freshwater environmental safety assessment of a key UV filter, oxybenzone, used in OTC sunscreens and CPCPs in the United States. Exposure was characterized using iSTREEM®, a spatially resolved aquatic exposure model developed for chemicals disposed of down-the-drain. It provides a comprehensive exposure assessment of oxybenzone concentrations in U.S. receiving waters through predicted environmental concentration (PEC) distributions representative of conditions across the region. A review of available hazard data was used to derive a predicted no-effect concentration (PNEC) using aquatic toxicity data and assessment factors. A safety assessment was conducted by comparing the PEC distribution to the PNEC. The results indicate that oxybenzone is of low concern and there is a significant margin of safety; even the 90th percentile PEC is two orders of magnitude below the PNEC. These results are instrumental in demonstrating the environmental safety of key organic UV filters in the

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U.S. freshwater environment and will help prioritize future work. This article is protected by copyright. All rights reserved.
Authors: Emily E Burns, Susan A Csiszar, Kyle Roush, Iain A Davies
Full Source: Integrated environmental assessment and management 2021 Apr 29. doi: 10.1002/ieam.4430.

OCCUPATIONAL

Use of Contact Lenses in an Industrial Environment

2021-05-01
Industrial workers can come into contact with harmful agents that are transmitted via the eye in the form of an aerosol droplet or splash. Contact lenses do not provide ocular protection from hazards. This guidance from the American College of Occupational and Environmental Medicine addresses the use of contact lenses and personal protective equipment by the industrial worker and provides recommendations for contact lens use in an eye-hazardous environment.
Authors: Kenji Saito, Jeff K Hovis
Full Source: Journal of occupational and environmental medicine 2021 May 1;63(5):e298-e300. doi: 10.1097/JOM.0000000000002132.

Industrial workers can come into contact with harmful agents that are transmitted via the eye in the form of an aerosol droplet or splash.

Public health risks associated with chronic, low-level domoic acid exposure: A review of the evidence

2021-04-27
Domoic acid (DA), the causative agent for the human syndrome Amnesic Shellfish Poisoning (ASP), is a potent, naturally occurring neurotoxin produced by common marine algae. DA accumulates in seafood, and humans and wildlife alike can subsequently be exposed when consuming DA-contaminated shellfish or finfish. While strong regulatory limits protect people from the acute effects associated with ASP, DA is an increasingly significant public health concern, particularly for coastal dwelling populations, and there is a growing body of evidence suggesting that there are significant health consequences following repeated exposures to levels of the toxin below current safety guidelines. However, gaps in scientific knowledge make it difficult to precisely determine the risks of contemporary low-level exposure scenarios. The present review characterizes the toxicokinetics and neurotoxicology of DA, discussing results from clinical and preclinical studies after both adult and developmental DA exposure. The review also highlights crucial areas for future DA research and makes the case that DA safety limits need to be

reassessed to best protect public health from deleterious effects of this widespread marine toxin.
Authors: Rebekah Petroff, Alicia Hendrix, Sara Shum, Kimberly S Grant, Kathi A Lefebvre, Thomas M Burbacher
Full Source: Pharmacology & therapeutics 2021 Apr 27;107865. doi: 10.1016/j.pharmthera.2021.107865.

Occupational physical activity and longevity in working men and women in Norway: a prospective cohort study

2021-04-28
Background: Studies suggest that high occupational physical activity increases mortality risk. However, it is unclear whether this association is causal or can be explained by a complex network of socioeconomic and behavioural factors. We aimed to examine the association between occupational physical activity and longevity, taking a complex network of confounding variables into account.
Methods: In this prospective cohort study, we linked data from Norwegian population-based health examination surveys, covering all parts of Norway with data from the National Population and Housing Censuses and the Norwegian Cause of Death Registry. 437 378 participants (aged 18-65 years; 48·7% men) self-reported occupational physical activity (mutually exclusive groups: sedentary, walking, walking and lifting, and heavy labour) and were followed up from study entry (between February, 1974, and November, 2002) to death or end of follow-up on Dec 31, 2018, whichever came first. We estimated differences in survival time (death from all causes, cardiovascular disease, and cancer) between occupational physical activity categories using flexible parametric survival models adjusted for confounding factors.
Findings: During a median of 28 years (IQR 25-31) from study entry to the end of follow-up, 74 203 (17·0%) of the participants died (all-cause mortality), of which 20 111 (27·1%) of the deaths were due to cardiovascular disease and 29 886 (40·3%) were due to cancer. Crude modelling indicated shorter mean survival times among men in physically active occupations than in those with sedentary occupations. However, this finding was reversed following adjustment for confounding factors (birth cohort, education, income, ethnicity, prevalent cardiovascular disease, smoking, leisure-time physical activity, body-mass index), with estimates suggesting that men in occupations characterised by walking, walking and lifting, and heavy labour had life expectancies equivalent to 0·4 (95% CI -0·1 to 1·0), 0·8 (0·3 to 1·3), and 1·7 (1·2 to 2·3) years longer, respectively, than men in the sedentary referent category. Results for

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mortality from cardiovascular disease and cancer showed a similar pattern. No clear differences in survival times were observed between occupational physical activity groups in women. Interpretation: Our results suggest that moderate to high occupational physical activity contributes to longevity in men. However, occupational physical activity does not seem to affect longevity in women. These results might inform future physical activity guidelines for public health.
Funding: The Norwegian Research Council (grant number 249932/F20).
Authors: Knut Eirik Dalene, Jakob Tarp, Randi Marie Selmer, Inger Kristine Holtermann Ariansen, Wenche Nystad, Pieter Coenen, Sigmund Alfred Anderssen, Jostein Steene-Johannessen, Ulf Ekelund
Full Source: The Lancet. Public health 2021 Apr 28;S2468-2667(21)00032-3. doi: 10.1016/S2468-2667(21)00032-3.

PHARAMACEUTICAL/TOXICOLOGY

Perfluoroalkyl Chemicals and Male Reproductive Health: Do PFOA and PFOS Increase Risk for Male Infertility?

2021-04-05
Poly- and perfluoroalkyl substances (PFAS) are manmade synthetic chemicals which have been in existence for over 70 years. Though they are currently being phased out, their persistence in the environment is widespread. There is increasing evidence linking PFAS exposure to health effects, an issue of concern since PFAS such as perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) bioaccumulate in humans, with a half-life of years. Many epidemiological studies suggest that, worldwide, semen quality has decreased over the past several decades. One of the most worrying effects of PFOS and PFOA is their associations with lower testosterone levels, similar to clinical observations in infertile men. This review thus focuses on PFOS/PFOA-associated effects on male reproductive health. The sources of PFAS in drinking water are listed. The current epidemiological studies linking increased exposure to PFAS with lowered testosterone and semen quality, and evidence from rodent studies supporting their function as endocrine disruptors on the reproductive system, exhibiting non-monotonic dose responses, are noted. Finally, their mechanisms of action and possible toxic effects on the Leydig, Sertoli, and germ cells are discussed. Future research efforts must consider utilizing better human model systems for exposure, using more accurate PFAS exposure susceptibility windows, and improvements

Poly- and perfluoroalkyl substances (PFAS) are manmade synthetic chemicals which have been in existence for over 70 years.

in statistical modeling of data to account for the endocrine disruptor properties of PFAS.
Authors: Pheruza Tarapore, Bin Ouyang
Full Source: International journal of environmental research and public health 2021 Apr 5;18(7):3794. doi: 10.3390/ijerph18073794.