

# Bulletin Board

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## CHEMICAL EFFECTS

**In vivo neurophysiological assessment of in silico predictions of neurotoxicity: Citronellal, 3,4-dichloro-1-butene, and benzyl bromoacetate**

2022-02-25

Neurotoxicants may be widespread in the environment and can produce serious health impacts in the human population. Screening programs that use in vitro methods have generated data for thousands of chemicals. However, these methods often do not evaluate repeated or prolonged exposures, which are required for many neurotoxic outcomes. Additionally, the data produced by such screening methods may not include mechanisms which play critical biological roles necessary for in vivo neurotoxicity. The Hard and Soft Acids and Bases (HSAB) in silico model focuses on chemical structure and electrophilic properties which are important to the formation of protein adducts. A group of structurally diverse chemicals have been evaluated with an in silico screening approach incorporating HSAB parameters. However, the predictions from the expanded chemical space have not been evaluated using in vivo methods. Three chemicals predicted to be cumulative toxicants were selected for in vivo neurotoxicological testing. Adult male Long-Evans rats were treated orally with citronellal (CIT), 3,4-dichloro-1-butene (DCB), or benzyl bromoacetate (BBA) for 8 weeks. Behavioral observations were recorded weekly to assess motor function. Peripheral neurophysiological measurements were derived from nerve excitability (NE) tests which involved compound muscle action potentials (CMAPs) in the tail and foot, and mixed nerve action potentials (MNAPs) in the tail. Compound nerve action potentials (CNAPs) and nerve conduction velocity (NCV) in the tail were also quantified. Peripheral inputs into the central nervous system were examined using somatosensory evoked potentials recorded from the cortex (SEPCTX) and cerebellum (SEPCEREB). CIT or BBA did not result in significant alterations to peripheral nerve or somatosensory function. DCB reduced grip-strength and altered peripheral nerve function. The MNAPs required less current to reach 50% amplitude and had a lower calculated rheobase, suggesting increased excitability. Increased CNAP amplitudes and greater NCV were also observed. Novel changes were found in the SEPCTX with an abnormal peak forming in the early portion of the waveforms of treated rats, and decreased latencies and increased amplitudes were observed in SEPCEREB recordings. These data contribute to testing an expanded chemical space from an in silico HSAB model

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for predicting cumulative neurotoxicity and may assist with prioritizing chemicals to protect human health.

Authors: Garyn L Jung, Katherine L McDaniel, Richard M LoPachin, Brian C Geohagen, Alicia Smith, Mitchell Huffstickler, David W Herr

Full Source: Neurotoxicology 2022 Feb 25;90:48-61. doi: 10.1016/j.neuro.2022.02.008.

**Impact of Contaminants on Microbiota: Linking the Gut-Brain Axis with Neurotoxicity**

2022-01-26

Over the last years, research has focused on microbiota to establish a missing link between neuronal health and intestine imbalance. Many studies have considered microbiota as critical regulators of the gut-brain axis. The crosstalk between microbiota and the central nervous system is mainly explained through three different pathways: the neural, endocrine, and immune pathways, intricately interconnected with each other. In day-to-day life, human beings are exposed to a wide variety of contaminants that affect our intestinal microbiota and alter the bidirectional communication between the gut and brain, causing neuronal disorders. The interplay between xenobiotics, microbiota and neurotoxicity is still not fully explored, especially for susceptible populations such as pregnant women, neonates, and developing children. Precisely, early exposure to contaminants can trigger neurodevelopmental toxicity and long-term diseases. There is growing but limited research on the specific mechanisms of the microbiota-gut-brain axis (MGBA), making it challenging to understand the effect of environmental pollutants. In this review, we discuss the biological interplay between microbiota-gut-brain and analyse the role of endocrine-disrupting chemicals: Bisphenol A (BPA), Chlorpyrifos (CPF), Diethylhexyl phthalate (DEHP), and Per- and polyfluoroalkyl substances (PFAS) in MGBA perturbations and subsequent neurotoxicity. The complexity of the MGBA and the changing nature of the gut microbiota pose significant challenges for future research. However, emerging in-silico models able to analyse and interpret meta-omics data are a promising option for understanding the processes in this axis and can help prevent neurotoxicity.

Authors: Jordina Balaguer-Trias, Deepika Deepika, Marta Schuhmacher, Vikas Kumar

Full Source: International journal of environmental research and public health 2022 Jan 26;19(3):1368. doi: 10.3390/ijerph19031368.

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### The abundance of endocrine-disrupting chemicals (EDCs) in downstream of the Bengawan Solo and Brantas rivers located in Indonesia

2022-03-01

Numerous chemical substances used for daily life activities have an effect on the endocrine system and are frequently classed as endocrine-disrupting chemicals (EDCs). The present study investigated the fact and distribution of EDCs type (estrogen, plasticizer, and preservative). In particular, EDCs such as estriol, 1,2,4 triazole, 17 $\alpha$ -ethinylestradiol, methyl paraben, estrone, 3,4,4 trichlorocarbanilide, 17 $\beta$ -estradiol, and bisphenol A (BPA) were selected as the target EDCs for the detection in the Bengawan Solo and Brantas rivers located in Indonesia. Among the targeted EDCs, BPA is found to be highest in the water samples of Bengawan Solo (1070 ng/L and mean at 219 ng/L) and Brantas (556 ng/L and mean at 222 ng/L) rivers. The EDCs concentration is higher in both rivers during the dry season compared to the wet season due to the dilution effect caused by heavy rainfall. The entry of municipal wastewater is the primary sources of EDCs contamination in both rivers. Finally, this study suggests that the contamination level of EDCs in river water could pose an environmental threat, particularly during dry seasons.

Authors: Aris Ismanto, Tony Hadibarata, Risky Ayu Kristanti, Lilik Maslukah, Novia Safinatunnajah, Palanivel Sathishkumar

Full Source: Chemosphere 2022 Mar 1;134151. doi: 10.1016/j.chemosphere.2022.134151.

### Aggregating exposures and toxicity equivalence approach into an integrated probabilistic dietary risk assessment for perchlorate, nitrate, and thiocyanate: Results from the National food monitoring study and National Food Consumption Database

2022-02-26

Perchlorate, nitrate, and thiocyanate, namely thyroid disrupting chemicals (TDCs), are found ubiquitously in the environment, leading to broad human exposure and primary uptake through the food web and drinking water. TDCs are all competitive inhibitors of thyroid iodide uptake activity, but limited studies have assessed the cumulative risk of dietary exposure to multiple TDCs. Thus, in this study, we analyzed the individual exposure risk from 310 food samples in 11 categories, and also assessed the cumulative health risks from TDCs for the Taiwanese population using

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a perchlorate equivalent concentration (PEC) approach. Consequently, this study not only demonstrated the non-carcinogenic health risks from individual exposure but also highlighted that the cumulative exposure to these TDCs may adversely affect human thyroid functioning. Vegetables, livestock, fruits, and dairy products are the most susceptible to PEC exposure. We highlighted nitrate as the main contributor to PEC exposure. Finally, controlling the overall TDC concentrations from vegetables, livestock, fruits, and dairy products is emphasized in this study. This is the first study to conduct a cumulative risk assessment of dietary exposure to TDCs using the PEC approach for the Taiwanese population through probabilistic and sensitivity analyses.

Authors: Wei-Hsiang Chang, Pei-Hsuan Chen, Samuel Herianto, Hsiu-Ling Chen, Ching-Chang Lee

Full Source: Environmental research 2022 Feb 26;211:112989. doi: 10.1016/j.envres.2022.112989.

## ENVIRONMENTAL RESEARCH

### Effects of African BaP emission from wildfire biomass burning on regional and global environment and human health

2022-03-02

The vegetation burning caused by wildfires can release significant quantities of aerosols and toxic chemicals into the atmosphere and result in health risk. Among these emitted pollutants, Benzo(a)pyrene (BaP), the most toxic congener of 16 parent PAHs (polycyclic aromatic hydrocarbons), has received widespread concerns because of its carcinogenicity to human health. Efforts have been made to investigate the environmental and health consequences of wildfire-induced BaP emissions in Africa. Still, uncertainties remain due to knowledge and data gaps in wildfire incidences and biomass burning emissions. Based on a newly-developed BaP emission inventory, the present study assesses quantitatively the BaP environment cycling in Africa and its effects on other continents from 2001 to 2014. The new inventory reveals the increasing contribution of BaP emission from African wildfires to the global total primarily from anthropogenic sources, accounting for 48% since the 2000 s. We identify significantly higher BaP emissions and concentrations across sub-Saharan Africa, where the annual averaged BaP concentrations were as high as 5-8 ng/m<sup>3</sup>. The modeled BaP concentrations were implemented to estimate the lifetime cancer risk (LCR) from the inhalation exposure to

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BaP concentrations. The results reveal that the LCR values in many African countries exceeded the acceptable risk level at  $1 \times 10^{-6}$ , some of which suffer from very high exposure risk with the  $LCR > 1 \times 10^{-4}$ . We show that the African BaP emission from wildfires contributed, to some extent, BaP contamination to Europe as well as other regions, depending on source proximity and atmospheric pathways under favorable atmospheric circulation patterns.

Authors: Min Wu, Jinmu Luo, Tao Huang, Lulu Lian, Tianlei Chen, Shijie Song, Zhanxiang Wang, Shuxin Ma, Chaoran Xie, Yuan Zhao, Xiaoxuan Mao, Hong Gao, Jianmin Ma

Full Source: Environment international 2022 Mar 2;162:107162. doi: 10.1016/j.envint.2022.107162.

### Environmental disruption of reproductive rhythms

2022-02-25

Reproduction is a key biological function requiring a precise synchronization with annual and daily cues to cope with environmental fluctuations. Therefore, humans and animals have developed well-conserved photoneuroendocrine pathways to integrate and process circadian and seasonal light signals within the hypothalamic-pituitary-gonadal axis. However, in the past century, industrialization and the modern 24h/7d human lifestyle have imposed detrimental changes in natural habitats and rhythms of life. Indeed, the excessive amount of artificial light exposure at inappropriate timing because of shift work and nocturnal urban lighting, as well as the ubiquitous environmental contamination by endocrine-disrupting chemicals threaten the integrity of the daily and seasonal timing of biological functions. Here we review recent epidemiological, field and experimental studies, to discuss how light and chemical pollution of the environment can disrupt reproductive rhythms by interfering with the photoneuroendocrine timing system.

Authors: Marie-Az lie Moralia, Clarisse Quignon, Marine Simonneaux, Val rie Simonneaux

Full Source: Frontiers in neuroendocrinology 2022 Feb 25;100990. doi: 10.1016/j.yfrne.2022.100990.

### Towards a toxic-free environment: perspectives for chemical risk assessment approaches

2022-02-22

Regulatory frameworks to control chemical exposure in general living and occupational environments have changed exposure scenarios towards a widely spread contamination at relatively low doses in

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developed countries. In such evolving context, some critical aspects should be considered to update risk assessment and management strategies. Risk assessment in low-dose chemical exposure scenarios should take advantage of: toxicological investigations on emerging substances of interest, like those recognised as endocrine disruptors or increasingly employed nanoscale materials; human biological monitoring studies aimed to identify innovative biomarkers for known chemical exposure; "omic" technologies useful to identify hazards of chemicals and their modes of action. For updated risk assessment models, suitable toxicological studies, analyses of dose-responses at low-concentrations, environmental and biological monitoring of exposure, together with exposome studies, and the proper definition of susceptible populations may all provide helpful contributions. These may guide defining preventive measures to control the exposure and develop safe and sustainable chemicals by design. Occupational medicine can offer know-how and instruments to understand and manage such evolution towards a toxic-free environment to protect the safety and health of the workforce and, in turn, that of the general population.

Authors: Matteo Bonzini, Veruscka Leso, Ivo Iavicoli

Full Source: La Medicina del lavoro 2022 Feb 22;113(1):e2022004. doi: 10.23749/mdl.v113i1.12748.

### PHARMACEUTICAL/TOXICOLOGY

#### The influences of perfluoroalkyl substances on the rheumatoid arthritis clinic

2022-03-04

Background: The effect of environmental factors on genetically susceptible individuals is a basic link in the pathogenesis of rheumatoid arthritis. Perfluoroalkyl substances (PFASs) are a class of synthetic organic fluorine chemicals, which have been mass-produced and widely used in the past 60 years, and also have been shown to be one of the major pollutants affecting human health. The impact of fluoride on the development of Rheumatoid Arthritis (RA) is unclear. This study explored the relationship between common fluoride and clinical manifestations of rheumatoid arthritis.

Results: A cohort of 155 patients with RA and 145 health controls in Second Affiliated Hospital of Zhejiang University School of Medicine were investigated. Serum concentrations of all fluoride detected were higher in RA patients than in healthy controls. There were 43 male patients and 112 female patients in the RA cohort. Some of perfluoroalkyl

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substances (perfluorooctanoate (PFOA), perfluorononanoate (PFNA), perfluorodecanoate (PFTrA), perfluorooctanesulfonate (PFOS)) were correlated negatively with the Body Mass Index (BMI); some of them (PFOA, PFNA, PFTrA, PFOS, 8:2 Chlorinated polyfluorinated ether sulfonate (8:2Cl-PFESA)) were correlated positively with the Disease Activity Score 28 (DAS28); two (PFOA, PFOS) of them were correlated positively with the white blood cell count, and one (Perfluoroundecanoate (PFUnA)) of them was correlated negatively with the hemoglobin; two (Perfluorodecanoate (PFDA), PFUnA) of them were correlated negatively with the presence of interstitial lung disease.

Conclusion: These data suggest that exposure to perfluoroalkyl substances may promote the disease activity of rheumatoid arthritis and the visceral lesions.

Authors: Yun Zhao, Hangbiao Jin, Jianli Qu, Sunzhao Zhang, Shilei Hu, Jing Xue, Meirong Zhao

Full Source: BMC immunology 2022 Mar 4;23(1):10. doi: 10.1186/s12865-022-00483-7.

## OCCUPATIONAL

## Occupational exposure in the work process of radiology technologists with 68 Ga-labeled radiopharmaceuticals

2022-02-10

The study identified occupational exposure in the work of radiology technologists with 68Ga radiopharmaceuticals, in a Nuclear Medicine service in southern Brazil, by means of observation and document analysis. The occupational exposure related the factors, distance, time and shielding. Thus, it was observed high times during handling of the material, small distances between sources and radiosensitive structures, such as the eye lens and the thyroid gland. It is recommended to reassess and standardize the work, once that critical moments should not be restricted only to dosimetric reading.

Authors: Tayana Portela, Tatiane Sabriela Cagol Camozzato, Rita de Cássia Flor, Gerusa Ribeiro, Juliana Almeida Coelho de Melo, Caroline Scalabrin de Oliveira Alves

Full Source: Applied radiation and isotopes : including data, instrumentation and methods for use in agriculture, industry and medicine 2022 Feb 10;183:110104. doi: 10.1016/j.apradiso.2022.110104.

The study identified occupational exposure in the work of radiology technologists with 68Ga radiopharmaceuticals, in a Nuclear Medicine service in southern Brazil, by means of observation and document analysis.

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## Perceptions of Occupational Cancer Risk and Prevention Among Dominican Republic Firefighters: A Qualitative Study

2022-03-01

Objectives: Characterize occupational cancer risk perceptions and attitudes toward cancer prevention practices among firefighters in the Dominican Republic.

Methods: Focus group discussions and key informant interviews were conducted in June 2019 among firefighters from three fire departments.

Themes were inductively created using a qualitative descriptive approach.

Results: Thirty-seven firefighters were interviewed with a group mean age of  $36.2 \pm 10.3$  years, of which 97.3% were male, and 37.1% worked at least 10 years. Six themes emerged: 1) availability of personal protective equipment (PPE); 2) toxic exposure during fire suppression; 3) work-related stress; 4) lack of workplace health promotion activities; 5) Dominican culture impacts medical checkups; and 6) expensive medical copays limits healthcare access. Conclusion: Dominican firefighters are willing to adopt cancer prevention practices, however organizational barriers (ie, PPE availability, cultural barriers, and health promotion practices) limit engagement.

Authors: Paola Louzado-Feliciano, Katerina M Santiago, Laura Paule, Geovanny Rivera, Natasha Schaefer Solle, Marija Miric, Eddy Perez-Then, Alberto J Caban-Martinez

Full Source: Journal of occupational and environmental medicine 2022 Mar 1;64(3):e131-e135. doi: 10.1097/JOM.0000000000002466.

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