# **Bulletin Board**

## Contents

(click on page numbers for links)

#### CHEMICAL EFFECTS

The occurrence of selected endocrine-disrupting chemicals in water and sediments from an urban lagoon in Southern Italy	3
Endocrine-disrupting chemicals and child health	3
Development of a new needle trap-based method for the determination of some volatile organic compounds in the indoor	Λ
environment	.4

#### ENVIRONMENTAL RESEARCH

Confronting plastic pollution to protect environmental and public health 5

#### OCCUPATIONAL

Occupations and exposure events in acute and subacute irritant- induced asthma	5
Association of microsomal epoxide hydrolase gene (fast genotype) with lung functions impairment in wood workers	6
Respiratory health and silicosis in artisanal mine workers in southern Brazil	7
The presence of radioactive heavy minerals in prospecting trenches and concomitant occupational exposure	8

#### PHARAMACEUTICAL/TOXICOLOGY

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## **Bulletin Board**

### **Technical**

APR. 09, 2021

#### CHEMICAL EFFECTS

The occurrence of selected endocrine-disrupting chemicals in water and sediments from an urban lagoon in Southern Italy

#### 2021-04-01

Endocrine disrupting chemicals (EDCs) are agents able to exert perturbation toward the endocrine system via a broad array of signalling pathways. Some EDCs are released into the environment as a result of antropogenic activities. Analytical surveillance plays a critical role in investigating the prevalence of such chemicals in environmental samples. A study was carried out in a lagoon in Southern Italy, a water basin relates to the sea through a mouth channel, making this water body a "dynamic environment". The screening of fourteen EDCs in surface waters and sediments, includes a fast and cost-effective sample preparation, based on a solid-liquid (sediments) and liquid-liquid (surface waters) extraction and a chromatographic analysis by liquid chromatography tandem UV and fluorescence detection. Only four chemicals out the fourteen investigated EDCs were detected in both matrices with a frequency higher than 60%. The average concentrations of the single EDC were higher in sediments (730 - 155.000 ng Kg-1 dw) than in surface waters (132 - 28.000 ng L-1). Limited to the assayed EDCs, the ecosystem has a low risk regarding to the conservation of biodiversity of the animal species living thereby, since the total estrogenic activity does not exceed 1 ng L-1.

Authors: Giacomo Russo, Sonia Laneri, Ritamaria Di Lorenzo, Luciano Ferrara, Lucia Grumetto

Full Source: Water environment research : a research publication of the Water Environment Federation 2021 Apr 1. doi: 10.1002/wer.1566.

#### Endocrine-disrupting chemicals and child health

#### 2021-03-10

Endocrine-disrupting chemicals (EDCs) are chemicals which are introduced into the environment by human activities. In many cases it has been proven that EDCs can cause adverse health effects in the human. EDCs are classified by their chemical structure, putative direct or indirect effects on endocrine glands and systems, may accumulate and persist in organisms and in the environment, and/or they may exert clinically observable and measurable effects. Often, EDCs may act in concert and as mixtures. Legislation to ban EDCs and protect especially pregnant women and children at young age are needed and needs to be revised and Endocrine disrupting chemicals (EDCs) are agents able to exert perturbation toward the endocrine system via a broad array of signalling pathways.

### Technical

CHEMWATCH

adjusted to new developments on a regular basis. Putative associations, in spite of sometimes conflicting results, have to be analyzed in in vitro model systems be it in cell biology, in vitro settings or animal studies in more detail. This chapter depicts the mainly positive albeit detrimental epidemiological findings for EDC-caused effects in the fields of growth and metabolism, neurocognitive development and sexual development and reproduction.

Authors: Wieland Kiess, Gabriele Häussler, Mandy Vogel Full Source: Best practice & research. Clinical endocrinology & metabolism 2021 Mar 10;101516. doi: 10.1016/j.beem.2021.101516.

## Development of a new needle trap-based method for the determination of some volatile organic compounds in the indoor environment

#### 2021-03-19

Volatile Organic Compounds (VOCs) are a large group of chemicals mostly found in indoor environments such as homes and workplaces. Long term exposure to certain VOCs can cause symptoms in some individuals and therefore, monitoring and controlling air quality can help better manage chronic respiratory diseases. In this study, we aimed to develop an easyto-use, economical, in house needle trap-based methodology to detect certain VOCs to be used for public and occupational health. For this purpose, a multi-bed (packed with PDMS/Carbopack-X/Carboxen-1000) needle trap device (NTD) was utilized for sampling, enrichment, and injection of the VOCs into the gas chromatography. The performance of the developed method was investigated for the analysis of the group known as BTEX (benzene, toluene, ethylbenzene and xylene). Operational and instrumental parameters such as sampling flow rate and relative humidity, desorption time and temperature were optimized, and the analytical figures of merit of the proposed method have indicated that very low levels of BTEX in air samples can be easily determined by this new method. Overall results have shown that multi-bed NTD offers a high sensitive procedure for sampling and analysis of BTEX in concentration range of 0.002-0.298 mg/m3 in indoor air.

Authors: Ertan Baysal, Umut Can Uzun, Fatma Nil Ertaş, Ozlem Goksel, Levent Pelit

Full Source: Chemosphere 2021 Mar 19;277:130251. doi: 10.1016/j. chemosphere.2021.130251.

## Bulletin Board

APR. 09, 2021

Volatile Organic Compounds (VOCs) are a large group of chemicals mostly found in indoor environments such as homes and workplaces.

# **Bulletin Board**

## **Technical**

APR. 09. 2021

#### **ENVIRONMENTAL RESEARCH**

#### Confronting plastic pollution to protect environmental and public health

#### 2021-03-30

A new collection of evidence-based commentaries explores critical challenges facing scientists and policymakers working to address the potential environmental and health harms of microplastics. The commentaries reveal a pressing need to develop robust methods to detect, evaluate, and mitigate the impacts of this emerging contaminant, most recently found in human placentas.

Authors: Liza Gross, Judith Enck

Full Source: PLoS biology 2021 Mar 30;19(3):e3001131. doi: 10.1371/ journal.pbio.3001131.

#### OCCUPATIONAL

#### Occupations and exposure events in acute and subacute irritant-induced asthma

#### 2021-03-31

Background: Exposures leading to irritant-induced asthma (IIA) are poorly Methods: We retrospectively screened the medical documented. records of patients with IIA diagnosed in an occupational medicine clinic during 2000-2018. We classified the cases into acute (onset after single exposure) and subacute (onset after multiple exposures) IIA. We analysed in detail, occupations, causative agents and their air levels in the workplace, exposure events and the root causes of high exposure. Results: Altogether 69 patients were diagnosed with IIA, 30 with acute and 39 with subacute IIA. The most common occupational groups were industrial operators (n=23, 33%), metal and machinery workers (n=16, 11%) and construction workers (n=12, 8%). Among industrial operators significantly more cases had subacute IIA than acute IIA (p=0.002). Forty cases (57%) were attributable to some type of corrosive acidic or alkaline chemical. Acute IIA followed accidents at work in different types of occupation, while subacute IIA was typical among industrial operators performing their normal work tasks under poor work hygiene conditions. The most common root cause was lack of information or false guidance in acute IIA (n=11, 36%) and neglect of workplace hygiene measures in Conclusions: Accidents are the main subacute IIA (n=29, 74%). causes of acute IIA, whereas subacute IIA can develop in normal work in

A new collection of evidence-based commentaries explores critical challenges facing scientists and policymakers working to address the potential environmental and health harms of microplastics.

### Technical

CHEMWATCH

risk trades with poor work hygiene. Airborne strong acids or bases seem to be the most important causative agents of acute and subacute IIA. The different risk profiles of acute and subacute IIA should be considered in the prevention and identification of the cases.

Authors: Irmeli Lindström, Jussi Lantto, Kirsi Karvala, Satu Soini, Katriina Ylinen, Hille Suojalehto, Katri Suuronen

Full Source: Occupational and environmental medicine 2021 Mar 31;oemed-2020-107323. doi: 10.1136/oemed-2020-107323.

#### Association of microsomal epoxide hydrolase gene (fast genotype) with lung functions impairment in wood workers

#### 2021-04-01

Objectives: Exposure to wood dust may lead to impairment of the lung functions. Microsomal epoxide hydrolase enzyme (EPHX1) was shown to take part in protection against oxidative stress. An alteration in enzyme activity might be associated with its gene polymorphisms. In vitro polymorphisms in exons 3 (His113Tyr) and 4 (Arg139His) lead to reduced activity (slow allele) and increased activity (fast allele). Macrophage inflammatory protein 2 (MIP-2) is produced in rat lung epithelial cells after exposure to fine particles. We aimed to investigate the associations between mEPHX1 polymorphisms (in exon 3 and 4) and lung function in furniture workers and assessment of MIP-2 effect. Methods: Our study was performed on 70 wood dust exposed male workers and 70 matched normal controls subjects. Ventilatory function tests were measured by spirometer, MIP-2 was performed by ELISA methods and EPHX gene was done by polymerase chain reactionrestriction fragment length polymorphism (PCR-RFLP) methods for each participant.

Results: Significant reduction in forced vital capacity (FVC%) and forced expiratory volume in the first second (FEV1) levels in Tyr-Tyr and Tyr-Hist genotypes of EPHX (exon 3) was observed. Reduced peak expiratory flow (PEF) levels and significant rise in MIP-2 levels were detected in Tyr-Tyr genotype. While high significant reduction in FVC% and FEV1 levels were shown in different genotypes in exon 4. Significant rise was observed in MIP-2 levels in Hist-Hist genotype of exon 4. An increase in duration of exposure showed positive correlation with fall in ventilatory functions.

## **Bulletin Board**

APR. 09

**Objectives: Exposure** to wood dust may lead to impairment of the lung functions.

## Bulletin Board

### Technical

APR. 09. 202

Conclusions: It was concluded that in Hist139Arg of EPHX gene, fast genotype (Arg-Arg) was associated with impaired ventilatory functions. Authors: Mona M Taha, Amal Saad-Hussein, Heba Mahdy-Abdallah Full Source: Journal of complementary & integrative medicine 2021 Apr 1. doi: 10.1515/jcim-2020-0085.

#### Respiratory health and silicosis in artisanal mine workers in southern Brazil

#### 2021-03-28

Background: Artisanal and small-scale mining (ASM) are an important source of employment in southern Brazil. Mining workers are frequently exposed to unhealthy work conditions which increase the risk of occupational diseases. In this study, we assessed the association of sociodemographic factors and the occupational history of artisanal mining workers with the risk of adverse respiratory outcomes. Methods: The study was conducted with 258 artisanal mining workers in southern Brazil, who were exposed to dust (mainly crystalline silica) in their work. Information on sociodemographic variables and occupational histories was collected between 2017 and 2018. To estimate the worker's exposure to inhalable dust we use the Advanced REACH (Registration, Evaluation, and Authorization of Chemicals) Tool (ART).

Results: Study participants were all men, with an average age of 40 years. Median crude dust exposure estimated by ART was 13.2 mg/m<sup>3</sup> and median crude crystalline silica exposure was 1.6 mg/m3. The prevalence ratio (PR) for self-reported silicosis was 3.08 (95% confidence interval, 1.39-7.17) in workers with 20 years or more of mining work. Factors associated with silicosis were age, pack-years of tobacco use, and body mass index. Smokers were over twice as likely to report respiratory symptoms. Conclusions: Our findings indicate that a high prevalence of silicosis and other associated diseases in mining workers is associated with both unhealthy work environment conditions and the health profile of workers. This study is an important step for understanding health outcomes from work in ASM.

Authors: Tamires P Souza, Martie van Tongeren, Inês Monteiro Full Source: American journal of industrial medicine 2021 Mar 28. doi: 10.1002/ajim.23242.

**Background: Artisanal** and small-scale mining (ASM) are an important source of employment in southern Brazil.

### Technical

CHEMWATCH

The presence of radioactive heavy minerals in prospecting trenches and concomitant occupational exposure 2021-03-31

Uranium, perhaps the most strategically important component of heavy minerals, finds particular significance in the nuclear industry. In prospecting trenches, the radioactivity of 238U and 232Th provides a good signature of the presence of heavy minerals. In the work herein, the activity concentrations of several key primordial radionuclides (238U, 232Th, and 40K) were measured in prospecting trenches (each of the latter being of approximately the same geometry and physical situation). All of these are located in the Seila area of the South Eastern desert of Egypt. A recently introduced industry standard, the portable hand-held RS-230 BGO gamma-ray spectrometer (1024 channels) was employed in the study. Based on the measured data, the trenches were classified as either non-regulated (U activity less than 1000 Bq kg-1) or regulated (with 238U activity more than 1000 Bq kg-1). Several radiological hazard parameters were calculated, statistical analysis also being performed to examine correlations between the origins of the radionuclides and their influence on the calculated values. While the radioactivity and hazard parameters exceed United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) guided limits, the mean annual effective doses of 0.49 and 1.4 mSv y-1 in non-regulated and regulated trenches respectively remain well below the International Commission on Radiological Protection (ICRP) recommended 20 mSv/y maximum occupational limit. This investigation reveals that the studied area contains high uranium content, suitable for extraction of U-minerals for use in the nuclear fuel cycle.

Authors: Mohamed Youssef Mohamed Hanfi, Masoud Salah Masoud, M I Sayyed, Mayeen Uddin Khandaker, Mohammed Rashed Igbal Farugue, D A Bradley, Mostafa Yuness Abdelfatah Mostafa Full Source: PloS one 2021 Mar 31;16(3):e0249329. doi: 10.1371/journal. pone.0249329.

## **Bulletin Board**

APR. 09

Uranium, perhaps the most strategically important component of heavy minerals, finds particular significance in the nuclear industry.

## **Bulletin Board**

### **Technical**

APR. 09, 2021

#### PHARAMACEUTICAL/TOXICOLOGY

Development of a strategic approach for comprehensive detection of organophosphate pesticide metabolites in urine: Extrapolation of cadusafos and prothiofos metabolomics data of mice to humans

#### 2021-01

Objectives: The comprehensive detection of environmental chemicals in biospecimens, an indispensable task in exposome research, is advancing. This study aimed to develop an exposomic approach to identify urinary metabolites of organophosphate (OP) pesticides, specifically cadusafos and prothiofos metabolites, as an example chemical group, using an original metabolome dataset generated from animal experiments. Methods: Urine samples from 73 university students were analyzed using liquid chromatography-high-resolution mass spectrometry. The metabolome data, including the exact masses, retention time (tR), and tandem mass spectra obtained from the human samples, were compared with the existing reference databases and with our original metabolome dataset for cadusafos and prothiofos, which was produced from mice to whom two doses of these OPs were orally administered. Results: Using the existing databases, one chromatographic peak was annotated as 2,4-dichlorophenol, which could be a prothiofos metabolite. Using our original dataset, one peak was annotated as a putative cadusafos metabolite and three peaks as putative prothiofos metabolites. Of these, all three peaks suggestive of prothiofos metabolites, 2,4-dichlorophenol, 3,4,5-trihydroxy-6-(2,4-dichlorophenoxy) oxane-2carboxylic acid, and (2,4-dichlorophenyl) hydrogen sulfate were confirmed as authentic compounds by comparing their peak data with both the original dataset and peak data of the standard reagents. The putative cadusafos metabolite was identified as a level C compound (metabolite candidate with limited plausibility).

Conclusions: Our developed method successfully identified prothiofos metabolites that are usually not a target of biomonitoring studies. Our approach is extensively applicable to various environmental contaminants beyond OP pesticides.

Authors: Karin Nomasa, Naoko Oya, Yuki Ito, Takehito Terajima, Takahiro Nishino, Nayan Chandra Mohanto, Hirotaka Sato, Motohiro Tomizawa, Michihiro Kamijima

Full Source: Journal of occupational health 2021 Jan;63(1):e12218. doi: 10.1002/1348-9585.12218.

**Objectives:** The comprehensive detection of environmental chemicals in biospecimens, an indispensable task in exposome research, is advancing.

### Technical

CHEMWATCH

Chronic peptide-based GIP receptor inhibition exhibits modest glucose metabolic changes in mice when administered either alone or combined with GLP-1 agonism

#### 2021-03-31

Combinatorial gut hormone therapy is one of the more promising strategies for identifying improved treatments for metabolic disease. Many approaches combine the established benefits of glucagon-like peptide-1 (GLP-1) agonism with one or more additional molecules with the aim of improving metabolic outcomes. Recent attention has been drawn to the glucose-dependent insulinotropic polypeptide (GIP) system due to compelling pre-clinical evidence describing the metabolic benefits of antagonising the GIP receptor (GIPR). We rationalised that benefit might be accrued from combining GIPR antagonism with GLP-1 agonism. Two GIPR peptide antagonists, GIPA-1 (mouse GIP(3-30)NH2) and GIPA-2 (NaAc-K10[yEyE-C16]-Arg18-hGIP(5-42)), were pharmacologically characterised and both exhibited potent antagonist properties. Acute in vivo administration of GIPA-1 during an oral glucose tolerance test (OGTT) had negligible effects on glucose tolerance and insulin in lean mice. In contrast, GIPA-2 impaired glucose tolerance and attenuated circulating insulin levels. A mouse model of diet-induced obesity (DIO) was used to investigate the potential metabolic benefits of chronic dosing of each antagonist, alone or in combination with liraglutide. Chronic administration studies showed expected effects of liraglutide, lowering food intake, body weight, fasting blood glucose and plasma insulin concentrations while improving glucose sensitivity, whereas delivery of either GIPR antagonist alone had negligible effects on these parameters. Interestingly, chronic dual therapy augmented insulin sensitizing effects and lowered plasma triglycerides and free-fatty acids, with more notable effects observed with GIPA-1 compared to GIPA-2. Thus, the coadministration of both a GIPR antagonist with a GLP1 agonist uncovers interesting beneficial effects on measures of insulin sensitivity, circulating lipids and certain adipose stores that seem influenced by the degree or nature of GIP receptor antagonism.

Authors: Jason A West, Anastasia Tsakmaki, Soumitra S Ghosh, David G Parkes, Rikke V Grønlund, Philip J Pedersen, David Maggs, Harith Rajagopalan, Gavin A Bewick

Full Source: PloS one 2021 Mar 31;16(3):e0249239. doi: 10.1371/journal. pone.0249239.

## **Bulletin Board**

APR. 09

**Combinatorial gut** hormone therapy is one of the more promising strategies for identifying improved treatments for metabolic disease.