CHEMWATCH

Bulletin Board

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OCCUPATIONAL

ENVIRONMENTAL RESEARCH

Annual release of selected UV filters via effluent from wastewater treatment plants in Australia

2020-01-10

Studies conducted globally have identified wastewater effluent as a key source of UV filters released into the aquatic environment. We assessed the annual release of UV filters from wastewater treatment plant effluent in Australia and evaluated the removal of these chemicals during wastewater treatment. Effluent samples were collected from 33 sites alongside matching influent samples. Sample collection predominately occurred during the Australian Census in August 2016, which allowed for accurate per capita normalisation of the results. A subset of sites was also sampled over the Southern Hemisphere summer (December-February) period. Five UV filters were detected with at least one detected in 95% of effluent samples. The summed concentration of UV filters ranged from 130 ng L^{-1} to 8400 ng L^{-1} and averaged 2800 (±1900) ng L^{-1}. Of the target UV filters, 2-phenylbenzimidazole-5-sulfonic acid (PBSA) and benzophenone 4 (BP4) showed the lowest removal efficiencies (11 ± 36% and 51 ± 43%, respectively) across all sites and were the most abundant in effluent. Average estimated removal efficiencies of the other compounds were between 59 (±24) % (4-methylbenzylidene camphor (4-MBC)) and 74 (±22) % (benzophenone 1 (BP1)). We did not find a trend in seasonal differences in the per capita release of UV filters in effluent samples. We estimate that approximately 40% of UV filter loads measured in influent are breaking through to the effluent resulting in the release of approximately 20 kg day^{-1} of the selected UV filters into the aquatic environment from treated wastewater effluent in Australia.

The summed concentration of UV filters ranged from 130 ng L-1 to 8400 ng L-1 and averaged 2800 (±1900) ng L-1

Authors: O'Malley E, O'Brien JW, Verhagen R, Mueller JF

Full Source:Chemosphere. 2020 Jan 10;247:125887. doi: 10.1016/j.chemosphere.2020.125887. [Epub ahead of print]

Seasonal distribution, risks, and sources of endocrine disrupting chemicals in coastal waters: Will these emerging contaminants pose potential risks in marine environment at continental-scale?

2020-02-14

Coastal waters are the critical ecologically fragile regions under the influence of the fastest economic developing pace and the extensive anthropogenic activities in coastal zone. Little information on the seasonal

distribution, risks, and sources of endocrine disrupting chemicals (EDCs) which are emerging contaminants to pose potential risks at very low concentrations in coastal waters at continental-scale is available. This study investigated the coastline-based distribution, risks, and sources of target EDCs in coastal water of China. EDCs in coastal waters of China showed significant spatio-temporal variation with phenolic compounds serving as predominant EDCs. Bisphenol A (BPA) was detected in all water samples with average concentration of 449.2/186.3 ng/L in winter/summer while estrone was the main steroidal estrogen with the average concentration of 87.2/2.7 ng/L in winter/summer. EDCs in coastal waters of South China Sea Area showed higher concentrations. EDCs in coastal waters exerted high ecological risks and estrone/BPA averagely accounted for over 61%/71% of total risk quotient in winter/summer. Average estradiol equivalent concentration of all target EDCs reached 68.87/1.76 ng/L in winter/summer. EDCs in coastal waters did not pose potential non-cancer health risks for humans. The positive matrix factorization (PMF) model was firstly used to identify and quantify possible sources of EDCs. The PMF analysis showed that wastewater and sewage might be the main source for EDCs in coastal waters. EDCs in coastal waters showed high estradiol equivalent concentration and ecological risks at continental-scale, highlighting that EDCs contamination has become a crucial stress affecting the sustainable development of coastal regions.

Authors: Lu J, Zhang C, Wu J, Zhang Y, Lin Y

Full Source:Chemosphere 2020 Jan 14;247:125907. doi: 10.1016/j.chemosphere.2020.125907. [Epub ahead of print]

Indoor polybrominateddiphenyl ethers in urban China: An exposure and risk assessment based on settled dust from selected urban regions.

2020-01-20

In this study, measurements of seven typical polybrominateddiphenyl ethers (PBDEs) in indoor settled dust were summarized in selected urban regions of China. BDE-209 was the most dominant congener in settled dust (1.4-101 μg/g), with a mean contribution of 95%. Indoor exposures to PBDEs were estimated via inhalation, dust ingestion, and dermal absorption. The average daily intake of ΣPBDE was 4.9 to 19.1 ng/day/kg for all the population groups, with >80% of the total exposures from dust ingestion. Exposures in commuting environments (contributing 60%-80% of the total exposures) were higher than those in other microenvironments. The means of hazard indexes ranged from 1.66×10^{-3} to 5.26×10^{-3}, which were mainly as a result of exposure to

The average daily intake of ΣPBDE was 4.9 to 19.1 ng/day/kg for all the population groups, with >80% of the total exposures from dust ingestion.

BDE-209, BDE-47, and BDE-99. The average lifetime cancer risks were from 0.03×10^{-9} to 2.37×10^{-9}, which indicated the acceptable health risks resulting from indoor PBDE exposure for the Chinese population. The present study could provide valuable information that could be helpful for decision-makers, analysts and researchers to develop, implement and evaluate the effectiveness of interventions for the reduction of exposures to semi-volatile organic compounds (SVOCs) for large population groups in China.

Authors: Bu Z, Xu Z, Xu Q, Mmereki D, Wang J, Cheng Z, Li K, Dong C
Full Source: The Science of the total environment. 2020 Jan 20;714:136808. doi: 10.1016/j.scitotenv.2020.136808. [Epub ahead of print]

Biocomponent-based microalgal transformations into biofuels during the pretreatment and fermentation process.

2020-01-25

Microalgal cell wall integrity and composition have a significant impact on the fermentation process and biofuel recovery. In this study, various biofuels (bioethanol, higher alcohols (C3-C5), and biodiesel) were produced by the fermentation of carbohydrates and proteins, and transesterification of lipids from three different microalgal strains (Pseudochlorella sp., Chlamydomonasmexicana, and Chlamydomonaspitschmannii), each possessing different proportions of bioconstituents (carbohydrates, proteins, and lipids). Changes in the cell wall structure and thickness were observed before and after fermentation using transmission electron microscopy. Pseudochlorella sp. showed the highest yields of bioethanol (0.45 g-ethanol/g-carbohydrates), higher alcohols (0.44 g-higher alcohols/g-proteins), and biodiesel (0.55 g-biodiesel/g-lipids), which consequently revealed a maximum energy recovery (42%) from whole constituents. This study suggests that different physiological properties, including cell wall thickness and the proportion of bioconstituents in microalgae, could have a significant impact on the pretreatment and fermentation efficiencies for biofuels production.

Changes in the cell wall structure and thickness were observed before and after fermentation using transmission electron microscopy.

Authors: Ha GS, El-Dalatony MM, Kim DH, Salama ES, Kurade MB, Roh HS, El-Fatah Abomohra A, Jeon BH
~Full Source: Biosource Technology. 2020 Apr;302:122809. doi: 10.1016/j.biortech.2020.122809. Epub 2020 Jan 15.

The Toxicity and valorization options of cigarette butts

2020-01-21

Cigarette butts, one of the most abundant forms of waste in the world, contain more than 4000 toxic chemicals and pose serious risks to the health of wildlife, humans, and marine and freshwater organisms. Although trivial in size, trillions of cigarettes are produced every year worldwide, resulting in the accumulation of tonnes of toxic waste litter. In 2016, a world production of over 5.7 trillion cigarettes was reported with the majority comprising cellulose acetate filters - a polymer with poor biodegradability. Depending on the environmental conditions, cellulose acetate filters can take up to 10 years to decompose during which time they leach heavy metals and toxic chemicals into the environment. Although possible disposal methods for collected cigarette butt waste include incineration and landfilling, both techniques may result in the release of hazardous fumes and can be costly. However, recycling CBs in different materials could be a possible solution for this concurrent environmental pollution. A number of novel studies have been publicized on recycling cigarette butts with encouraging results, and several methods have been studied, including recycling of cigarette butts in asphalt concrete and fired clay bricks, as a carbon source, sound absorbing material, corrosion inhibitor, biofilm carrier, and many more. Hence, this paper provides a comprehensive review and discussion of various studies that have been carried out on the toxicity and valorization of cigarette butt waste and investigates the feasibility and sustainability of recycling methods adopted. Further research and developments are essential for the widespread application of recycling cigarette butts.

Authors: Kurmus H, Mohajerani A

Full Source:Waste Management (New York, N.Y.). 2020 Mar 1;104:104-118. doi: 10.1016/j.wasman.2020.01.011. Epub 2020 Jan 21.

To safeguard current and future generations from the increasing number of chemicals polluting our environment, a systematic and agnostic approach is needed.

CHEMICAL EFFECTS

The exposome and health: Where chemistry meets biology

2020-01-24

Despite extensive evidence showing that exposure to specific chemicals can lead to disease, current research approaches and regulatory policies fail to address the chemical complexity of our world. To safeguard current and future generations from the increasing number of chemicals polluting our environment, a systematic and agnostic approach is needed. The "exposome" concept strives to capture the diversity and range of exposures to synthetic chemicals, dietary constituents, psychosocial

stressors, and physical factors, as well as their corresponding biological responses. Technological advances such as high-resolution mass spectrometry and network science have allowed us to take the first steps toward a comprehensive assessment of the exposome. Given the increased recognition of the dominant role that nongenetic factors play in disease, an effort to characterize the exposome at a scale comparable to that of the human genome is warranted.
Authors: Vermeulen R, Schymanski EL, Barabási AL, Miller GW
Full Source: Science (New York, N.Y.). 2020 Jan 24;367(6476):392-396. doi: 10.1126/science.aay3164.

Lethal Hydrogen Sulfide poisoning in open space: An atypical case of asphyxiation of two workers

2019-12-31
Hydrogen sulfide is one of the most dangerous toxic gases that has led to the deaths in confined spaces of many workers. We report an atypical case of a fatal accident of H_2S poisoning in an open space when two workers died during the opening of a hatch on a tanker truck filled with leachate water. Despite being outdoors, the two workers, were suddenly and quickly overwhelmed by a lethal cloud of H_2S, which escaped like a geyser from the hatch and hovered over the top of the tanker making it impossible for them to survive. The first operator was engulfed by the sudden flow of lethal gas near the hatch while the second worker, who came to his aid, immediately lost consciousness and fell off the tanker onto the ground. Environmental toxicological analyses were carried out on the air near the hatch and inside the tanker 2h, 20 days and 70 days after the accident. Toxicological analyses on the blood were also carried out but unfortunately, no urine sample was available. The thiosulfate, detected by GC/MS analysis after derivatization of PFBBr, was found to be 0.01 and 0.04mM/L. These values are included in the medium-low lethal values of occupational fatalities involving H_2S reported in the literature.
Authors: Aventaggiato L, Colucci AP, Strisciullo G, Favalli F, Gagliano-Candela R
Full Source: Forensic Science International. 2019 Dec 31;308:110122. doi: 10.1016/j.forsciint.2019.110122. [Epub ahead of print]

We report an atypical case of a fatal accident of H2S poisoning in an open space when two workers died during the opening of a hatch on a tanker truck filled with leachate water.

Wheat Extract Oil (WEO) Attenuates UVB-Induced Photoaging via Collagen Synthesis in Human Keratinocytes and Hairless Mice.

2020-01-22
The efficacy of wheat extract oil (WEO), standardized to glucosylceramides, for protecting against ultraviolet B (UVB)-induced damage of skin barrier function was assessed using the SHK-1 hairless mouse model and two human skin cell lines, namely, CCD-986sk and HeCaT. The ability of repeated oral administration of 30, 60, and 120 mg of WEO/kg/day for 12 weeks to prevent skin damage of SKH-1 hairless mice induced by UVB irradiation was evaluated. The results demonstrated that UVB-induced water evaporation (transepidermal water loss, TEWL) was significantly decreased by WEO. Similarly, UVB-induced losses in moisture and skin elasticity were improved by WEO supplementation. WEO attenuated the tissue procollagen type I, hyaluronic acid (HA), and ceramide reductions induced by UVB treatment as well. Collagen concentrations in skin tissue were increased in the WEO-treated mice, while UVB-induced epidermal thickening was reduced. In vitro studies using HeCaT human keratinocytes confirmed increased HA and collagen synthesis in response to WEO treatment. This may occur via WEO suppression of matrix metallopeptidase-1 (MMP-1), since its induction by UVB treatment was diminished in treated CCD-986sk cells. Oral administration of WEO improves skin barrier function in UVB-irradiated mice by attenuating damage typically observed in photoaging. This research further clarifies the clinical benefits previously observed by dietary WEO consumption.
Authors: Son DJ, Jung JC, Choi YM, Ryu HY, Lee S, Davis BA
Full Source: Nutrients. 2020 Jan 22;12(2). pii: E300. doi: 10.3390/nu12020300.

Overall, patients without co-morbidities had lower hepatotoxicity risk (0.1% versus 1.0%).

PHARMACEUTICAL/TOXICITY

Treatment with Isoniazid or Rifampin for Latent Tuberculosis Infection: Population-Based Study of Hepatotoxicity, Completion, and Costs.

2020-01-24
BACKGROUND:
Clinical trials suggest less hepatotoxicity and better adherence with 4 months rifampin (4R) versus 9 months isoniazid (9H) for treating latent tuberculosis infection (LTBI). Our objectives were to compare frequencies of severe hepatic adverse events and treatment completion, and direct

health system costs of LTBI regimens 4R and 9H, in the general population of the province of Quebec, Canada, using provincial health administrative data.
METHODS:
Our retrospective cohort included all patients starting rifampin or isoniazid regimens between 2003 and 2007. We estimated hepatotoxicity from hospitalisation records, treatment completion from community pharmacy records, and direct costs from billing records and fee schedules. We compared rifampin to isoniazid using logistic (hepatotoxicity), log-binomial (completion), and gamma (costs) regression, with adjustment for age, co-morbidities, and other confounders.
RESULTS:
10559 individuals started LTBI treatment (9684 isoniazid; 875 rifampin). Rifampin patients were older with more baseline co-morbidities. Severe hepatotoxicity risk was higher with isoniazid (n=15) than rifampin (n=1), adjusted OR=2.3 (95%CI: 0.3,16.1); there were 2 liver transplants and 1 death with isoniazid and none with rifampin. Overall, patients without co-morbidities had lower hepatotoxicity risk (0.1% versus 1.0%). 4R completion (53.5%) was higher than 9H (36.9%), adjusted RR=1.5 (95%CI:1.3,1.7). Mean costs per patient were lower for rifampin than isoniazid: adjusted Cost Ratio=0.7 (95%CI:0.5,0.9).
CONCLUSION:
Risk of severe hepatotoxicity and direct costs were lower, and completion was higher, for 4R than 9H, after adjustment for age and co-morbidities. Severe hepatotoxicity resulted in death or liver transplant in three patients receiving 9H, compared to no patients receiving 4R.
Authors: Ronald LA, FitzGerald JM, Bartlett-Esquilant G, Schwartzman K, Benedetti A, Boivin JF, Menzies D
Full Source: The European Respiratory Journal. 2020 Jan 24. pii: 1902048. doi: 10.1183/13993003.02048-2019. [Epub ahead of print]

Safety, tolerability and effectiveness of transition to eslicarbazepine acetate from carbamazepine or oxcarbazepine in clinical practice.

2019-12-23
PURPOSE:
To assess the efficacy, safety and tolerability of eslicarbazepine acetate (ESL) in patients transitioning from carbamazepine or oxcarbazepine to ESL in clinical practice, by analysing data from the Euro-Esli study.
METHODS:

Euro-Esli included 2058 patients, of whom 233 (11.3 %) transitioned from carbamazepine to ESL and 134 (6.5 %) transitioned from oxcarbazepine to ESL.

Euro-Esli was a pooled analysis of 14 European clinical practice studies. Effectiveness assessments included responder rate (≥50 % seizure frequency reduction) and seizure freedom rate (seizure freedom at least since prior visit), assessed after 3, 6 and 12 months of ESL treatment, and at the last visit. Safety and tolerability were assessed throughout follow-up by evaluating adverse events (AEs) and ESL discontinuation due to AEs, respectively. Data were analysed for cohorts of patients who transitioned from carbamazepine and oxcarbazepine to ESL either due to lack of efficacy or poor tolerability.
RESULTS:
Euro-Esli included 2058 patients, of whom 233 (11.3 %) transitioned from carbamazepine to ESL and 134 (6.5 %) transitioned from oxcarbazepine to ESL. After 12 months of ESL treatment, responder and seizure freedom rates for patients transitioning from carbamazepine due to lack of efficacy (n = 163) were 70.0 % and 30.9 %, respectively. Corresponding values for patients transitioning from oxcarbazepine due to lack of efficacy (n = 90) were 57.1 % and 25.0 %, respectively. Among patients who transitioned from carbamazepine and oxcarbazepine to ESL due to poor tolerability (n = 64 and n = 61, respectively), 26.6 % and 39.5 % experienced AEs, and 8.3 % and 6.8 % discontinued ESL due to AEs, respectively.
CONCLUSION:
ESL was efficacious and generally well tolerated in patients transitioning from carbamazepine or oxcarbazepine in clinical practice due to inadequate seizure control or intolerable AEs with these agents.
Authors: Rocamora R, Peltola J, Assenza G, McMurray R, Villanueva V
Full Source: Seizure. 2020 Feb;75:121-128. doi: 10.1016/j.seizure.2019.12.022. Epub 2019 Dec 23.

Several animal studies showing analgesic effects of carvacrol indicate potential of carvacrol as a new medication for patients with refractory pain.

Carvacrol inhibits the neuronal voltage-gated sodium channels $Na_v1.2$, $Na_v1.6$, $Na_v1.3$, $Na_v1.7$, and $Na_v1.8$ expressed in Xenopus oocytes with different potencies.

2020-01-07
Carvacrol is the predominant monoterpene in essential oils from many aromatic plants. Several animal studies showing analgesic effects of carvacrol indicate potential of carvacrol as a new medication for patients with refractory pain. Voltage-gated sodium channels (Na_v) are thought to have crucial roles in the development of inflammatory and neuropathic pain, but there is limited information about whether the analgesic mechanism of carvacrol involves Na_v. We used whole-cell, two-electrode, voltage-clamp techniques to examine the effects of carvacrol on sodium currents in Xenopus oocytes expressing α subunits of $Na_v1.2$, $Na_v1.3$,

$Na_v1.6$, $Na_v1.7$, and $Na_v1.8$. Carvacrol dose-dependently suppressed sodium currents at a holding potential that induced half-maximal current. The half-maximal inhibitory concentration values for $Na_v1.2$, $Na_v1.3$, $Na_v1.6$, $Na_v1.7$, and $Na_v1.8$ were 233, 526, 215, 367, and 824 µmol/L, respectively, indicating that carvacrol had more potent inhibitory effects towards $Na_v1.2$ and $Na_v1.6$ than $Na_v1.3$, $Na_v1.7$, and $Na_v1.8$. Gating analysis showed a depolarizing shift of the activation curve and a hyperpolarizing shift of the inactivation curve in all five α subunits following carvacrol treatment. Furthermore, carvacrol exhibits a use-dependent block for all five α Na_v subunits. These findings provide a better understanding of the mechanisms associated with the analgesic effect of carvacrol.

Authors: Horishita T, Ogata Y, Horishita R, Fukui R, Moriwaki K, Ueno S, Yanagihara N, Uezono Y, Sudo Y, Minami K

~Full Source: Journal of Pharmacological Sciences. 2020 Jan 7. pii: S1347-8613(19)35745-7. doi: 10.1016/j.jphs.2019.12.009. [Epub ahead of print]

A urinary metabolomic study from subjects after long-term occupational exposure to low concentration acrylamide using UPLC-QTOF/MS

2020-01-23

his study identifies important related metabolic changes in the bodies of workers after long-term occupational exposure to low concentration ACR and suggests new biomarkers of nervous system injury caused by ACR.

Because long-term occupational exposure to low concentrations of acrylamide (ACR) has the potential to cause neurological damage, it is important to identify biomarkers that can be used to evaluate this risk. In the present study, urine metabolomics of the ACR-exposed and non-exposed groups to identify potential metabolites was carried out using ultra high performance liquid chromatography coupled with quadrupole time of flight mass spectrometry. Serum biochemical indexes of the exposed and non-exposed groups were also determined. Principal component analysis showed a differential separation between exposed group and non-exposed group and a total of 7 metabolites were identified in positive and negative ionization modes; Area under curve of anthranilic acid, β-guanidinopropionic acid and mesobilirubinogen were 0.980, 0.843 and 0.801 respectively and these metabolites showed high sensitivity and specificity. The 13 biochemical indexes were divided into three classes based on physiological functions. Only biomarkers of dysregulated liver

his study identifies important related metabolic changes in the bodies of workers after long-term occupational exposure to low concentration ACR and suggests new biomarkers of nervous system injury caused by ACR.

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function including alanine aminotransferase, aspartic transaminase, total bilirubin, direct bilirubin and triglyceride were significantly higher in the exposed group than in the non-exposed group. This study identifies important related metabolic changes in the bodies of workers after long-term occupational exposure to low concentration ACR and suggests new biomarkers of nervous system injury caused by ACR. The study also provides a sound basis for exploring the biochemical mechanisms and metabolic pathways of nervous system toxicity caused by ACR.

Authors: Wang SY, Han D, Yu CP, Zhou XR, Xin R, Wang R, Ma WW, Wang C, Wu YH

FullSource:Archives of biochemistry and biophysics. 2020 Mar 15;681:108279. doi: 10.1016/j.abb.2020.108279. Epub 2020 Jan 23.

Zinc acetate lozenges for the treatment of the common cold: a randomised controlled trial.

2020-02-23

OBJECTIVE:

To examine a commercially available zinc acetate lozenge for treating the common cold.

DESIGN:

Randomised, double-blinded, placebo-controlled trial.

SETTING:

Working population in Finland.

PARTICIPANTS:

We included men and women aged ≥18 years who usually had ≥1 cold per winter. Exclusions were pregnancy, lactation, chronic runny nose or chronic cough.

INTERVENTION:

We randomised 253 participants to receive a package of lozenges to be taken if they caught the common cold. Of the 253 participants, 88 contracted the common cold and 87 were included in our primary analysis. Zinc acetate lozenges contained 13 mg elemental zinc and placebo lozenges contained sucrose octa-acetate to camouflage the taste of zinc. Instruction to use was six times per day for the maximum of 5 days.

PRIMARY OUTCOME:

Rate of recovery from the common cold analysed by Cox regression.

RESULTS:

There was no difference in the recovery rate between zinc and placebo participants during the 10-day follow-up (rate ratio for zinc vs placebo=0.68, 95% CI 0.42 to 1.08; p=0.10). The recovery rate for the two groups was similar during the 5-day intervention, but for 2 days after

In the zinc group, 37% did not report adverse effects, the corresponding proportion being 69% in the placebo group.

the end of zinc/placebo use, the zinc participants recovered significantly slower compared with the placebo participants (p=0.003). In the zinc group, 37% did not report adverse effects, the corresponding proportion being 69% in the placebo group.
CONCLUSIONS:
A commercially available zinc acetate lozenge was not effective in treating the common cold when instructed to be used for 5 days after the first symptoms. Taste has been a common problem in previous zinc lozenge trials, but a third of zinc participants did not complain of any adverse effects. More research is needed to evaluate the characteristics of zinc lozenges that may be clinically efficacious before zinc lozenges can be widely promoted for common cold treatment.
TRIAL REGISTRATION NUMBER:
NCT03309995.
Authors: Hemilä H, Haukka J, Alho M, Vahtera J, Kiyimäki M
Full Source:BMJ Open. 2020 Jan 23;10(1):e031662. doi: 10.1136/bmjopen-2019-031662.

Molecular mechanisms of posaconazole- and itraconazole-induced pseudohyperaldosteronism and assessment of other systemically used azole antifungals.

2020-02-23
Recent reports described cases of severe hypertension and hypokalemia accompanied by low renin and aldosterone levels during antifungal therapy with posaconazole and itraconazole. These conditions represent characteristics of secondary endocrine hypertension caused by mineralocorticoid excess. Different mechanisms can cause mineralocorticoid excess, including inhibition of the adrenal steroidogenic enzymes CYP17A1 and CYP11B1, inhibition of the peripheral cortisol oxidizing enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) or direct activation of the mineralocorticoid receptor (MR). Compared to previous experiments revealing a threefold more potent inhibition of 11β-HSD2 by itraconazole than with posaconazole, the current study found sevenfold stronger CYP11B1 inhibition by posaconazole over itraconazole. Both compounds most potently inhibited CYP11B2. The major pharmacologically active itraconazole metabolite hydroxyitraconazole (OHI) resembled the effects of itraconazole but was considerably less active. Molecular modeling calculations assessed the binding of posaconazole, itraconazole and OHI to 11β-HSD2 and the relevant CYP enzymes, and predicted important interactions not formed by the other systemically used azole antifungals, thus providing

Therapeutic drug monitoring and introduction of upper plasma target levels may help preventing the occurrence of drug-induced hypertension and hypokalemia.

an initial explanation for the observed inhibitory activities. Together with available clinical observations, the presented data suggest that itraconazole primarily causes pseudohyperaldosteronism through cortisol-induced MR activation due to 11β-HSD2 inhibition, and posaconazole by CYP11B1 inhibition and accumulation of the mineralocorticoids 11-deoxycorticosterone and 11-deoxycortisol because of hypothalamus-pituitary-adrenal axis (HPA) feedback activation. Therapeutic drug monitoring and introduction of upper plasma target levels may help preventing the occurrence of drug-induced hypertension and hypokalemia. Furthermore, the systemically used azole antifungals voriconazole, isavuconazole and fluconazole did not affect any of the mineralocorticoid excess targets, offering alternative therapeutic options.
AuthorsBeck KR, Telisman L, van Koppen CJ, Thompson GR 3rd, Odermatt A
Full Source: The Journal of steroid biochemistry and molecular biology. 2020 Jan 23;199:105605. doi: 10.1016/j.jsbmb.2020.105605. [Epub ahead of print]

OCCUPATIONAL

Refined reference doses and new procedures for phthalate mixture risk assessment focused on male developmental toxicity.

2019-12-23

New procedures for phthalate mixture risk assessments (MRAs) focused on male developmental toxicity (anti-androgenicity) are overdue. Previous efforts suffer from several shortcomings: There is a lack of consistency in terms of the phthalates entered into the assessments, and in the choice of tolerable intakes. Many of these values do not reflect new evidence about low dose male developmental effects. Nearly all previous mixture risk assessments have focused solely on phthalates, with no regard for exposures to other chemicals that also induce male developmental toxicity, leading to underestimations of risks. Here, we address these weaknesses and inconsistencies by proposing criteria for the selection of phthalates for MRA based on structure-activity relationships. We suggest new reference doses for phthalates for use in MRA, as follows: DBP 6.7 μg/kg/d, DIBP 100 μg/kg/d, BBP 10 μg/kg/d, DEHP 10 μg/kg/d, DINP 59 μg/kg/d. We conclude that the fixation on the Hazard Index (HI) = 1 as signalling acceptable combined phthalate exposures is misguided as it ignores co-exposure to other anti-androgenic chemicals that also contribute to male developmental risks. Until more comprehensive

There is a lack of consistency in terms of the phthalates entered into the assessments, and in the choice of tolerable intakes.

assessments of phthalates in combination with other anti-androgens become feasible, we propose the use of a HI of 0.1-0.2 as a benchmark for interpreting phthalate mixture risk assessments.
Authors: Kortenkamp A, Koch HM
Full Source: International Journal of Hygiene and Environmental Health. 2020 Mar;224:113428. doi: 10.1016/j.ijheh.2019.113428. Epub 2019 Dec 23.

International landscape of limits and recommendations for occupational exposure to engineered nanomaterials.

2020-01-22
The increasing concern of possible adverse effects on human health derived from occupational engineered nanomaterials (ENMs) exposure is an issue addressed by entities related to provide guidelines and/or protocols for ENMs regulation. Here we analysed 17 entities from America, Europe and Asia, and some of these entities provide limits of exposure extrapolated from the non-nanosized counterparts of ENMs. The international landscape shows that recommendations are mostly made for metal oxide based ENMs and tonnage is one of the main criteria for ENMs registration, however, sub-nanometric ENMs are emerging and perhaps a novel category of ENMs will appear soon. We identify that besides the lack of epidemiological evidence of ENMs toxicity in humans and difficulties in analysing the toxicological data derived from experimental models, the lack of information on airborne concentrations of ENMs in occupational settings is an important limitation to improve the experimental designs. The development of regulations related to ENMs exposure would lead to provide safer work places for ENMs production without delaying the nanotechnology progress but will also help to protect the environment by taking opportune and correct measures for nanowaste, considering that this could be a great environmental problem in the coming future.
Authors: Rodríguez-Ilbarra C, Déciga-Alcaraz A, Ispanixtlahuatl-Meráz O, Medina-Reyes EI, Delgado-Buenrostro NL, Chirino YI
Full Source:Toxicology Letters. 2020 Apr 1;322:111-119. doi: 10.1016/j.toxlet.2020.01.016. Epub 2020 Jan 22.

Here we analysed 17 entities from America, Europe and Asia, and some of these entities provide limits of exposure extrapolated from the non-nanosized counterparts of ENMs.

Characterization of bone aluminum, a potential biomarker of cumulative exposure, within an occupational population from Zunyi, China.

2020-01-14
OBJECTIVES:
Aluminum (Al) is a neurotoxicant; however, efforts to understand Al toxicity are limited by the lack of a quantitative biomarker of cumulative exposure. Bone Al measurements may address this need. Here, we

describe and compare non-invasive bone Al measurements with fingernail Al and Al cumulative exposure indices (CEIs).
METHODS:
We completed a cross-sectional study of 43 factory workers in Zunyi, China. Bone Al measurements were taken with a compact in-vivo neutron activation analysis system (IVNAA). Fingernail samples were analyzed using inductively coupled plasma mass spectrometry. CEIs, based on self-reported work history and prior literature, were calculated for the prior 5, 10, 15, 20 years and lifetime work history. Linear regressions adjusted for age and education compared fingernail Al and Al CEIs with bone Al.
RESULTS:
Median (interquartile range (IQR)) Al measurements were: 15 μg/g dry bone (IQR = 28) for bone Al; 34.9 μg/g (43.3) for fingernail; and 24 (20) for lifetime CEI. In adjusted regression models, an increase in 15-year CEI was significantly associated with increased bone Al (β = 0.91, 95% confidence interval (CI): 0.16, 1.66). Associations of bone Al with 10- and 20-year CEI were approaching statistical significance (β = 0.98, 95% CI: -0.14, 2.1; β = 0.59, 95% CI: -0.01, 1.18, respectively). Other models were not statistically significant.
CONCLUSIONS:
Bone Al was significantly associated with 15-year Al CEI, but not other Al CEIs or fingernail Al. Bone Al may be a useful measure of cumulative, rather than short-term, Al exposure. Additional refinement of this method is ongoing.
Authors: Hasan Z, Rolle-McFarland D, Liu Y, Zhou J, Mostafaei F, Li Y, Fan Q, Zhou Y, Zheng W, Nie LH, Wells EM
Full Source: Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS). 2020 Jan 14;59:126469. doi: 10.1016/j.jtemb.2020.126469. [Epub ahead of print]

Occupational and dietary differences in hydroxylated and methoxylated PBDEs and metals in plasma from Puget Sound, Washington, USA region volunteers.

2020-01-07
Electronic waste (E-waste) recycling is a rapidly growing occupation in the USA with the potential for elevated exposure to flame retardants and metals associated with electronic devices. We previously measured polybrominateddiphenyl ethers (PBDEs) in plasma from E-waste workers and found them similar to non-E-waste workers. This study focused on structurally related PBDE derivatives, the hydroxylated (OH-PBDEs) and methoxylated (MeO-PBDEs) forms along with metals known to occur in

Humans can metabolize PBDEs and some MeO-PBDEs into OH-PBDEs, which is a concern due to greater health risks associated with OH-PBDEs.

E-waste. Humans can metabolize PBDEs and some MeO-PBDEs into OH-PBDEs, which is a concern due to greater health risks associated with OH-PBDEs. We measured 32 different OH-PBDEs and MeO-PBDEs in plasma samples provided by 113 volunteers living in the greater Puget Sound region of Washington State, USA. We measured 14 metals in a subset of 10 E-waste and 10 non-E-waste volunteers. Volunteers were selected based on occupational and dietary habits: work outdoors and consume above average amounts of seafood (outdoor), electronic waste recycling (E-waste) or non-specific indoor occupations (indoor). A two-week food consumption diary was obtained from each volunteer prior to blood sampling. OH-PBDEs were detected in all volunteers varying between 0.27 and 102 ng/g/g-lipid. The MeO-PBDEs were detected in most, but not all volunteers varying between n.d. - 60.4 ng/g/g-lipid. E-waste recyclers had OH-PBDE and MeO-PBDE plasma levels that were similar to the indoor group. The outdoor group had significantly higher levels of MeO-PBDEs, but not OH-PBDEs. Comparison of plasma concentrations of BDE-47 with its known hydroxylated metabolites suggested OH-PBDE levels were likely determined by biotransformation and at least two subpopulations identified differing in their apparent rates of OH-PBDE formation. The metals analysis indicated no significant differences between E-waste workers and non-E-waste workers. Our results indicate E-waste workers do not have elevated plasma levels of these contaminants relative to non-E-waste workers.

Authors: Schultz IR, Kuo LJ, Cullinan V, Cade S

Full Source: The Science of the total environment. 2020 Jan 7;714:136566. doi: 10.1016/j.scitotenv.2020.136566. [Epub ahead of print]

Chloropicrin is toxic via all routes of exposure but the main route of systemic exposure is inhalation of the ambient air.

Chloropicrin-induced toxicity in the respiratory system

2020-01-23

Chloropicrin is a volatile and reactive chemical that has been utilized as a warfare agent and a pesticide to fumigate soil against insects, fungi and nematodes. It poses a health risk to humans and animals if inhaled. The main source of chloropicrin exposure is occupational and occurs during its manufacture, transport and fumigation. Chloropicrin is toxic via all routes of exposure but the main route of systemic exposure is inhalation of the ambient air. Thus, the toxicity mainly affects the respiratory system. After a low level exposure, the first sign is irritation of the upper respiratory tract and eyes. Irritation is mediated by the sensory nerve fibers, which coordinate further activation of various protective reflexes. Chloropicrin-induced irritation is generally reversible but can alter airway responsiveness to other inhalation toxicants. Severe exposures cause

injuries in the respiratory tract, inflammation, and even life-threatening edema. Much of the chloropicrin-caused symptoms and toxicity in the respiratory system displays similarities with those evoked by chlorine, which is also a breakdown product of chloropicrin. This review summarizes the latest information on chloropicrin with emphasis on the toxicity in the respiratory system. The data indicates that oxidative stress, modification of macromolecules, mutations, dysfunctions of cell organelles and cell death are involved in acute chloropicrin-induced toxicity in the respiratory system.

Authors: Pesonen M, Vähäkangas K

Full Source: Toxicology Letters. 2020 May 1;323:10-18. doi: 10.1016/j.toxlet.2020.01.022. Epub 2020 Jan 23.

Effects of diet on skin sensitization by nickel, poison ivy, and sesquiterpene lactones.

2020-01023

Skin contact or exposure to sensitizers often occurs as a consequence of occupational exposures (e.g. poison ivy in forestry), wearing jewelry (e.g. nickel), or use of cosmetics (e.g. fragrances). However, many of the known skin sensitizers or their chemical variants are also consumed orally through foods or other sources. Since oral exposure to antigenic substances can lead to tolerance, consumption of sensitizers may impact the development and potency of skin sensitization, especially if the sensitizer is consumed early in life, prior to the first skin contact. To address this issue, we have reviewed human clinical and epidemiological literature relevant to this subject and evaluated whether early oral exposures to relevant sensitizers, or their chemical variants, are associated with reduced prevalence of skin sensitization to three main allergic sensitizers - nickel, urushiols of poison ivy, and sesquiterpene lactones of chrysanthemum and other plants.

However, many of the known skin sensitizers or their chemical variants are also consumed orally through foods or other sources.

Authors: An N, Pourzal S, Luccioli, Vukmanović S

Full Source: Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association. 2020 Jan 23;137:111137. doi: 10.1016/j.fct.2020.111137. [Epub ahead of print]