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CHEMICAL EFFECTS

Key Opportunities to Replace, Reduce and Refine Regulatory Fish Acute Toxicity Tests

2020-07-18

Fish acute toxicity tests are conducted as part of regulatory hazard identification and risk assessment packages for industrial chemicals and plant protection products. The aim of these tests is to determine an LC50 endpoint - that is, the concentration which would be lethal to 50% of the animals treated. These tests are therefore associated with suffering in the test animals, and OECD Test Guideline 203 (fish, acute toxicity) studies are the most widely conducted regulatory vertebrate ecotoxicology tests for prospective chemical safety assessment. There is great scope to apply the 3Rs principles - the reduction, refinement and replacement of animals - in this area of testing. An expert ecotoxicology working group, led by the UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), including members from government, academia and industry, reviewed global fish acute test data requirements for the major chemical sectors. This article highlights ongoing initiatives and provides an overview of the key challenges and opportunities associated with replacing, reducing and/or refining fish acute toxicity studies - without compromising environmental protection. This article is protected by copyright. All rights reserved.

Authors: Natalie Burden, Rachel Benstead, Kate Benyon, Mark Clook, Christopher Green, John Handley, Neil Harper, Samuel K Maynard, Chris Mead, Audrey Pearson, Kathryn Ryder, Dave Sheahan, Roger van Egmond, James R Wheeler, Thomas H Hutchinson

Full Source: Environmental toxicology and chemistry 2020 Jul 18. doi: 10.1002/etc.4824.

A Preliminary Report on the Largest Ongoing Outbreak of Lead Toxicity in Iran

2020-07-16

No countrywide data exists on the patients' characteristics of lead exposure in Iran. We aimed to evaluate the demographic characteristics and blood lead level (BLL) of these patients in the country scale during five consecutive years, including the epidemic outbreak year (2016). Between 2014 and 2018, records of all patients who had referred to two reference laboratories in Tehran, Iran, to check BLL were evaluated. Of 58,642 patients, 48,589 were male. Mean age was 44.9 ± 20.7 years. Males had

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higher BLLs and were significantly older. Median BLL was $16 \mu\text{g}/\text{dL}$ (0.3 to $263 \mu\text{g}/\text{dL}$). Median BLL was significantly higher in 45- to 60-year-old patients. The highest median BLL was reported in May 2016 confirming our records about the peak of the epidemic. Although the frequency of high BLL declined after 2016, it never returned to the measures before that. Considering the ongoing high prevalence of increased BLLs after 2016 and similar environmental and occupational exposures as before, lead-contaminated opium still seems to persist in the Iranian opium black market. Substitution of this lead-contaminated opium by Opioid Maintenance Therapy (OMT)-prescribed opium tincture is recommended. Authors: Nasim Zamani, Omid Mehrpour, Hossein Hassanian-Moghaddam, Maryam Jalali, Alireza Amirabadizadeh, Saeed Samie, Shahram Sabeti, Ali-Asghar Kolahi
Full Source: Scientific reports 2020 Jul 16;10(1):11797. doi: 10.1038/s41598-020-64859-8.

Interactions of sulfuric acid with common atmospheric bases and organic acids: Thermodynamics and implications to new particle formation

2020-09

Interactions of the three common atmospheric bases, dimethylamine ((CH_3) $_2\text{NH}$), methylamine (CH_3NH_2), ammonia (NH_3), all considered to be efficient stabilizers of binary clusters in the Earth's atmosphere, with H_2SO_4 , the key atmospheric precursor, and 14 common atmospheric organic acids (COAs) (formic, acetic, oxalic, malonic, succinic, glutaric acid, adipic, benzoic, phenylacetic, pyruvic, maleic acid, malic, tartaric and pinonic acids) have been studied using the density functional theory (DFT) and composite high-accuracy G3MP2 method. The thermodynamic stability of mixed (COA)(H_2SO_4), (COA)(B1), (COA)(B2) and (COA)(B3) dimers and (COA)(H_2SO_4)(B1), (COA)(H_2SO_4)(B2) and (COA)(H_2SO_4)(B3) trimers, where B1, B2 and B3 refer to (CH_3) $_2\text{NH}$, CH_3NH_2 and NH_3 , respectively, have been investigated and their impacts on the thermodynamic stability of clusters containing H_2SO_4 have been studied. Our investigation shows that interactions of H_2SO_4 with COA, (CH_3) $_2\text{NH}$, CH_3NH_2 and NH_3 lead to the formation of more stable mixed dimers and trimers than (H_2SO_4) $_2$ and (H_2SO_4) $_2$ (base), respectively, and emphasize the importance of common organic species for early stages of atmospheric nucleation. We also show that although amines are generally confirmed to be more active than NH_3 as stabilizers of binary clusters, in some cases mixed trimers containing NH_3 are more stable thermodynamically than those containing CH_3NH_2 . This study indicates

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an important role of COA, which coexist and interact with that H₂SO₄ and common atmospheric bases in the Earth atmosphere, in formation of stable pre-nucleation clusters and suggests that the impacts of COA on new particle formation (NPF) should be studied in further details.

Authors: Yunfeng Li, Haijie Zhang, Qingzhu Zhang, Yisheng Xu, Alexey B Nadykto

Full Source: Journal of environmental sciences (China) 2020 Sep;95:130-140. doi: 10.1016/j.jes.2020.03.033.

ENVIRONMENTAL RESEARCH

The first environmental assessment of hexa(methoxymethyl)melamine and co-occurring cyclic amines in Australian waterways

2020-07-08

Hexa(methoxymethyl)melamine (HMMM) is commonly used as a cross-linking agent in coatings and as a vulcaniser in tyre production to increase the durability of tyres. Early reports of elevated aquatic concentrations of HMMM and a range of co-occurring cyclic amines have been linked to toxicity and mortality events of aquatic organisms. There are currently only few studies reporting environmental concentrations of HMMM and the co-occurring cyclic amines, and this study reports the first environmental assessment in Australian surface waters. Archive passive water samples from 40 rivers, creeks and lakes in South East Queensland, Australia, and covering five years of biannual sampling, were analysed to determine spatial and temporal trends. Concentrations of HMMM and cyclic amines in Australian surface waters (<5-46 and <MDL-280 ng/L respectively) were towards the low end of concentrations reported in surface water in North America/Europe. While previous studies have indicated that HMMM can be used as an indicator chemical of tyre wear particle inputs from stormwater runoff to a water system, the variable spatial and temporal trends at these sites indicates there are a range of different sources, and more research is needed into these chemicals to understand their occurrence in the environment.

Authors: Cassandra Rauert, Sarit L Kaserzon, Cameron Veal, Ruby Y Yeh, Jochen F Mueller, Kevin V Thomas

Full Source: The Science of the total environment 2020 Jul 8;743:140834. doi: 10.1016/j.scitotenv.2020.140834.

Hexa(methoxymethyl) melamine (HMMM) is commonly used as a cross-linking agent in coatings and as a vulcaniser in tyre production to increase the durability of tyres.

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Leveraging the Comparative Toxicogenomics Database to fill in knowledge gaps for environmental health: a test case for air pollution-induced cardiovascular disease

2020-07-14

Environmental health studies relate how exposures (e.g., chemicals) affect human health and disease; however, in most cases, the molecular and biological mechanisms connecting an exposure with a disease remain unknown. To help fill in these knowledge gaps, we sought to leverage content from the public Comparative Toxicogenomics Database (CTD) to identify potential intermediary steps. In a proof-of-concept study, we systematically compute the genes, molecular mechanisms, and biological events for the environmental health association linking air pollution toxicants with two cardiovascular diseases (myocardial infarction and hypertension) as a test case. Our approach integrates five types of curated interactions in CTD to build sets of "CGPD-tetramers", computationally constructed information blocks relating a Chemical-Gene interaction with a Phenotype and Disease. This bioinformatics strategy generates 653 CGPD-tetramers for air pollution-associated myocardial infarction (involving 5 pollutants, 58 genes, and 117 phenotypes) and 701 CGPD-tetramers for air pollution-associated hypertension (involving 3 pollutants, 96 genes, and 142 phenotypes). Collectively, we identify 19 genes and 96 phenotypes shared between these two air pollutant-induced outcomes, and suggest important roles for oxidative stress, inflammation, immune responses, cell death, and circulatory system processes. Moreover, CGPD-tetramers can be assembled into extensive chemical-induced disease pathways involving multiple gene products and sequential biological events, and many of these computed intermediary steps are validated in the literature. Our method does not require a priori knowledge of the toxicant, interacting gene, or biological system, and can be used to analyze any environmental chemical-induced disease curated within the public CTD framework.

Authors: Allan Peter Davis, Thomas C Wieggers, Cynthia J Grondin, Robin J Johnson, Daniela Sciaky, Jolene Wieggers, Carolyn J Mattingly

Full Source: Toxicological sciences : an official journal of the Society of Toxicology 2020 Jul 14;kfaa113. doi: 10.1093/toxsci/kfaa113.

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OCCUPATIONAL

Biomonitoring of occupational exposure to phthalates: A systematic review

2020-07-10

Introduction: Phthalates, a group of ubiquitous industrial chemicals, have been widely used in occupational settings, mainly as plasticizers in a variety of applications. Occupational exposure to different phthalates has been studied in several occupational settings using human biomonitoring (HBM).

Aim: To provide a comprehensive review of the available literature on occupational exposure to phthalates assessed using HBM and to determine future data needs on the topic as part of the HBM4EU project.

Methods: A systematic search was carried out in the databases of Pubmed, Scopus, and Web of Science for articles published between 2000 and September 4, 2019 using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A total of 22 studies on the occupational HBM of phthalates was considered suitable for review.

Results and discussion: Among the reviewed studies, 19 (86%) focused on DEHP, an old phthalate that is now subject to authorization and planned to be restricted in the EU. Concentrations of MEHHP, one of its metabolites, varied up to 13-fold between studies and across sectors when comparing extreme geometric means, ranging from 11.6 (similar to the general populations) to 151 µg/g creatinine. Only 2 studies focused on newer phthalates such as DiNP and DPHP. Concerning the geographical distribution, 10 studies were performed in Europe (including 6 in Slovakia), 8 in Asia, and 4 in North America, but this distribution is not a good reflection of phthalate production and usage levels worldwide. Most HBM studies were performed in the context of PVC product manufacturing. Future studies should focus on: i) a more uniform approach to sampling timing to facilitate comparisons between studies; ii) newer phthalates; and iii) old phthalates in waste management or recycling.

Conclusion: Our findings highlight the lack of recent occupational HBM studies on both old and new phthalate exposure in European countries and the need for a harmonized approach. Considering the important policy actions taken in Europe regarding phthalates, it seems relevant to

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evaluate the impact of these actions on exposure levels and health risks for workers.

Authors: Nadine Fréry, Tiina Santonen, Simo P Porras, Aleksandra Fucic, Veruscka Leso, Radia Bousoumah, Radu Corneliu Duca, Mounia El Yamani, Marike Kolossa-Gehring, Sophie Ndaw, Susana Viegas, Ivo Iavicoli
Full Source: International journal of hygiene and environmental health 2020 Jul 10;229:113548. doi: 10.1016/j.ijheh.2020.113548.

Prescription opioid use and associated factors among US construction workers

2020-07-16

Background: Construction workers are among the segments of the US population that were hit hardest by the opioid prescription and overdose deaths in the past decades. Factors that underlie opioid use in construction workers have been compartmentalized and isolated in existing studies of opioid use and opioid overdose, but they ignore the overall context of their use. This study examines prescription opioid use and its association with a variety of occupational and nonoccupational factors in construction workers in the United States. Methods: Data from the 2011-2017 Medical Expenditure Panel Survey (n = 7994) were analyzed. The prevalence of prescribed opioid use and the association with occupational and nonoccupational characteristics among construction workers were examined in four multiple logistic regression models.

Results: The odds of prescription opioid use for workers with occupational injuries was more than triple that of their noninjured counterparts when demographics and occupational factors were controlled (odds ratio = 3.38, 95% confidence interval: 2.38-4.81). Odds of prescription opioid use were higher in older construction workers, workers who were white, non-Hispanic, working part-time, and in poorer health, while Hispanic workers and those without health insurance were much less likely to report prescription opioid use.

Conclusions: Prescription opioid use among construction workers encompasses both occupational and nonoccupational factors. As an insight into opioid use among construction workers becomes clearer, effectively responding to the opioid crisis remains a challenge.

Authors: Xiuwen S Dong, Raina D Brooks, Chris T Cain
Full Source: American journal of industrial medicine 2020 Jul 16. doi: 10.1002/ajim.23158.

Background: Construction workers are among the segments of the US population that were hit hardest by the opioid prescription and overdose deaths in the past decades.

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ANCA vasculitis and IgA nephropathy linked to silica exposure

2020-07-17

There is a recognized association between silica exposure and Antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV); however, no clear association between silica exposure and Immunoglobulin A (IgA) nephropathy. We describe the case of a 26-year-old male stonemason who presents with hilar lymphadenopathy, haematuria and acute kidney injury related to silica exposure, AAV and IgA nephropathy. He was asymptomatic on presentation; urinalysis revealed glomerular haematuria (>1000 red blood cells/L) and proteinuria (protein-to-creatinine ratio 84 mg/mmol). ANCA anti-myeloperoxidase serology was strongly positive. Mediastinal lymph node biopsy revealed multiple necrotizing granulomas with silica inclusions, and renal biopsy demonstrated crescentic glomerulonephritis and mesangial IgA staining. The patient was treated with cyclophosphamide and high-dose prednisolone with subsequent improvement in renal function. To our knowledge, this is the first report of both ANCA vasculitis and IgA nephropathy in the setting of silica exposure. This case highlights the relevance of occupational exposures in renal disease, and the immunostimulatory effect of silica.

Authors: N Rao, A Bendall, M Lanteri

Full Source: Occupational medicine (Oxford, England) 2020 Jul 17;kqaa122. doi: 10.1093/occmed/kqaa122.

PHARMACEUTICAL/TOXICOLOGY**Social Media Message Designs to Educate Adolescents About E-Cigarettes**

2020-07-09

Purpose: E-cigarette use is increasing among adolescents, despite potential harms. Social media messages are a promising way to educate youth about e-cigarettes, yet little is known about what message topics and formats will have beneficial impacts for message reception, reach, e-cigarette knowledge, and beliefs about harms.

Methods: A national convenience sample of adolescents (n = 928, aged 15-18 years) in high school was recruited for an online experiment. In October 2019, participants were randomized to view one of three social media formats (visual based, quiz, and text only) or a no-message control. Participants in format conditions viewed six unique topics in a random

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order. Outcomes were e-cigarette knowledge and beliefs. Message reactions and sharing preferences were also assessed among youth who saw social media messages. Results: Social media messages led to greater knowledge (Cohen's $f = .19$; $p < .001$) and beliefs ($f = .16$; $p < .001$) about harms of e-cigarettes compared with the control, regardless of format. Almost four in five adolescents (79%) reported they would share the social media messages, most likely in person (49%) and with friends (52%). Message topics for missing out because of lung damage, having uncontrolled moods, and ingesting specific harmful chemicals elicited higher intended message reactions.

Conclusions: Social media messages can educate about e-cigarette harms. Social media campaigns are a promising e-cigarette education strategy to reach youth, directly and potentially through peer-to-peer sharing.

Authors: Allison J Lazard

Full Source: The Journal of adolescent health: official publication of the Society for Adolescent Medicine 2020 Jul 9;S1054-139X(20)30280-9. doi: 10.1016/j.jadohealth.2020.05.030.

Effect of valproic acid on overall survival in patients with high-grade gliomas undergoing temozolomide: A nationwide population-based cohort study in Taiwan

2020-07-10

High-grade gliomas (HGGs) are a rapidly progressive and highly recurrent group of primary brain tumors. Despite aggressive surgical resection with chemoradiotherapy, prognoses remained poor. Valproic acid (VPA), a histone deacetylase inhibitor has shown the potential to inhibit glioma cell growth in vitro through several diverse mechanisms. However clinical studies regarding the effect of VPA on HGGs are limited. This study aimed to investigate whether using VPA in patients with HGGs under temozolomide (TMZ) would lead to a better overall survival (OS). We used the Taiwan National Health Insurance Research database to conduct this population-based cohort study. A total of 2379 patients with HGGs under TMZ treatment were included and were further classified into VPA (n = 1212, VPA ≥ 84 defined daily dose [DDD]) and non-VPA (n = 1167, VPA < 84 DDD) groups. Each patient was followed from 1998 to 2013 or until death. A Cox proportional hazard regression was performed to evaluate the effect of VPA and OS. The VPA group had a longer mean OS time compared with the non-VPA group (OS: 50.3 ± 41.0 vs 42.0 ± 37.2 months, $P < .001$). In patients between 18 and 40 years old, the difference is most significant (OS: 70.5 ± 48.7 vs 55.1 ± 46.0 , $P = .001$). The adjusted hazard ratio is 0.81 [95% confidence interval, 0.72-0.91] for the

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VPA group relative to the non-VPA group.VPA at over 84 DDD improved OS in HGGs TMZ treatment.

Authors: Yu-Jen Kuo, Yao-Hsu Yang, I-Yun Lee, Pau-Chung Chen, Jen-Tsung Yang, Ting-Chung Wang, Martin Hsiu-Chu Lin, Wei-Hsun Yang, Chun-Yu Cheng, Kuo-Tai Chen, Wei-Chao Huang, Ming-Hsueh Lee

Full Source: *Medicine* 2020 Jul 10;99(28):e21147. doi: 10.1097/MD.00000000000021147.