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CHEMICAL EFFECTS

Effect of Carbon Monoxide Poisoning on Epilepsy Development: A Nationwide Population-Based Cohort Study

2023-02-14

Study objective: Carbon monoxide (CO) poisoning causes central nervous system toxicity resulting in delayed neurologic sequelae. This study aims to evaluate the risk of epilepsy in patients with a history of CO intoxication. **Methods:** We conducted a retrospective population-based cohort study using the Taiwan National Health Insurance Research Database and enrolled patients with and without CO poisoning matched for age, sex, and index year in a 1:5 ratio, between 2000 and 2010. Multivariable survival models were used to assess the risk of epilepsy. The primary outcome was newly developed epilepsy after the index date. All patients were followed until a new diagnosis of epilepsy, death, or December 31, 2013. Stratification analyses by age and sex were also conducted.

Results: This study included 8,264 patients with CO poisoning and 41,320 without. Patients with a history of CO poisoning were strongly associated with subsequent epilepsy (adjusted hazard ratio [HR] 8.40; 95% confidence interval [CI], 6.48 to 10.88). In the age-stratified analysis, intoxicated patients aged 20 to 39 years had the highest HR (adjusted HR 11.06; 95% CI, 7.17 to 17.08). In the sex-stratified analysis, adjusted HRs for male and female patients were 8.00 (95% CI, 5.86 to 10.92) and 9.53 (95% CI, 5.95 to 15.26), respectively.

Conclusion: Patients with CO poisoning were associated with an increased risk of developing epilepsy compared with those without CO poisoning. This association was more prominent in the young population.

Authors: Yu-Hsiang Meng, Ming-Shun Hsieh, Yu-Chi Chi, Chorng-Kuang How, Pau-Chung Chen, Chia-Ming Chang

Full Source: Annals of emergency medicine 2023 Feb 14;S0196-0644(22)01315-4. doi: 10.1016/j.annemergmed.2022.11.021.

In vitro and in vivo acute toxicity of an artificial butter flavoring

2023-02-15

Flavorings used in cookies, electronic cigarettes, popcorn, and breads contain approximately 30 chemical compounds, which makes it difficult to determine and correlate signs and symptoms of acute, subacute or chronic toxicity. The aim of this study was to characterize a butter flavoring

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chemically and subsequently examine the in vitro and in vivo toxicological profile using cellular techniques, invertebrates, and lab mammals. For the first time, the ethyl butanoate was found as the main compound of a butter flavoring (97.75%) and 24 h-toxicity assay employing *Artemia salina* larvae revealed a linear effect and LC50 value of 14.7 (13.7-15.7) mg/ml (R2 = 0.9448). Previous reports about higher oral doses of ethyl butanoate were not found. Observational screening with doses between 150-1000 mg/kg by gavage displayed increased amount of defecation, palpebral ptosis, and grip strength reduction, predominantly at higher doses. The flavoring also produced clinical signs of toxicity and diazepam-like behavioral changes in mice, including loss of motor coordination, muscle relaxation, increase of locomotor activity and intestinal motility, and induction of diarrhea, with deaths occurring after 48 h exposure. This substance fits into category 3 of the Globally Harmonized System. Data demonstrated that butter flavoring altered the emotional state in Swiss mice and disrupted intestinal motility, which may be a result of neurochemical changes or direct lesions in the central/peripheral nervous systems.

Authors: Nárcia Mariana Fonseca Nunes, Jurandy do Nascimento Silva, Micaely Lorrana Pereira Conceição, Joaquim Soares da Costa Júnior, Edymilais da Silva Sousa, Maria das Dores Alves de Oliveira, Antonia Maria das Graças Lopes Citó, Dalton Dittz, Ana Paula Peron, Paulo Michel Pinheiro Ferreira

Full Source: Journal of toxicology and environmental health. Part A 2023 Feb 15;1-17. doi: 10.1080/15287394.2023.2172502.

Nickel induces hepatotoxicity by mitochondrial biogenesis, mitochondrial dynamics, and mitophagy dysfunction

2023-02-16

Nickel (Ni) is an important and widely hazardous chemical industrial waste. Excessive Ni exposure could cause multi-organs toxicity in human and animals. Liver is the major target organ of Ni accumulation and toxicity, however, the precise mechanism is still unclear. In this study, nickel chloride (NiCl₂)-treatment induced hepatic histopathological changes in the mice, and, transmission electron microscopy results showed mitochondrial swollen and deformed of hepatocyte. Next, the mitochondrial damages including mitochondrial biogenesis, mitochondrial dynamics, and mitophagy were measured after NiCl₂ administration. The results showed that NiCl₂ suppressed mitochondrial biogenesis by decreasing PGC-1 α , TFAM, and NRF1 protein and mRNA expression levels. Meanwhile, the proteins involved in mitochondrial

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fusion were reduced by NiCl₂, such as Mfn1 and Mfn2, however, mitochondrial fission proteins Drip1 and Fis1 were significantly increased. The up-regulation of mitochondrial p62 and LC3II expression indicated that NiCl₂ increased mitophagy in the liver. Moreover, the receptor-mediated mitophagy and ubiquitin (Ub)-dependent mitophagy were detected. NiCl₂ promoted PINK1 accumulation and Parkin recruitment on mitochondria. And, the receptor proteins of mitophagy Bnip3 and FUNDC1 were increased in the NiCl₂-treated mice liver. Overall, these results show that NiCl₂ could induce mitochondria damage in the liver of mice, and, dysfunction of mitochondrial biogenesis, mitochondrial dynamics and mitophagy involved in the molecular mechanism of NiCl₂-induced hepatotoxicity.

Authors: Hongrui Guo, Ling Wei, Yihan Wang, Hengmin Cui, Huidan Deng, Yanqiu Zhu, Junliang Deng, Yi Geng, Ping Ouyang, Weiming Lai, Zongjun Du, Xueqin Ni, Heng Yin, Jing Fang, Zhicai Zuo
Full Source: Environmental toxicology 2023 Feb 16. doi: 10.1002/tox.23758.

ENVIRONMENTAL RESEARCH

Early childhood exposure to environmental phenols and parabens, phthalates, organophosphate pesticides, and trace elements in association with attention deficit hyperactivity disorder (ADHD) symptoms in the CHARGE study

2023-02-10

Background A growing body of literature investigated childhood exposure to environmental chemicals in association with attention deficit hyperactivity disorder (ADHD) symptoms, but limited studies considered urinary mixtures of multiple chemical classes. This study examined associations of concurrent exposure to non-persistent chemicals with ADHD symptoms in children diagnosed with autism spectrum disorder (ASD), developmental delay, and typical development. Methods A total of 574 children aged 2-5 years from the Childhood Autism Risks from Genetics and Environment (CHARGE) case-control study was administered the Aberrant Behavior Checklist (ABC). This study focused on the Hyperactivity subscale and its two subdomains (hyperactivity/impulsivity, inattention). Sixty-two chemicals from four classes (phenols/parabens, phthalates, organophosphate pesticides, trace elements) were quantified in child urine samples, and 43 chemicals detected in > 70% samples were used in statistical analyses. Weighted quantile sum regression

Background A growing body of literature investigated childhood exposure to environmental chemicals in association with attention deficit hyperactivity disorder (ADHD) symptoms, but limited studies considered urinary mixtures of multiple chemical classes.

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for negative binomial outcomes with repeated holdout validation was performed to investigate covariate-adjusted associations between mixtures and ABC scores in 574 children. The mixture analyses were further restricted to 232 children with ASD. Results Phthalate metabolite mixtures, weighted for mono-n-butylphthalate (MNBP), mono-2-heptyl phthalate, and mono-carboxy isononyl phthalate, were associated with the Hyperactivity subscale (mean incidence rate ratio [mIRR] = 1.11; 2.5th, 97.5th percentile: 1.00, 1.23), especially the hyperactivity/impulsivity subdomain (mIRR = 1.14; 2.5th, 97.5th percentile: 1.06, 1.26). These associations remained similar after restricting to children with ASD. The inattention subdomain was associated with a phenols/parabens mixture, weighted for several parabens and bisphenols (mIRR = 1.13; 2.5th, 97.5th percentile: 1.00, 1.28) and a total mixture, weighted for 3,4-dihydroxy benzoic acid, MNBP, and mono-(2-ethyl-5-carboxypentyl) phthalate (mIRR = 1.11; 2.5th, 97.5th percentile: 1.01, 1.25) only among children with ASD. Conclusions Concurrent exposure to phthalate mixtures was associated with hyperactivity in early childhood. Though causal inference cannot be made based on our cross-sectional findings, this study warrants further research on mixtures of larger number of chemicals from multiple classes in association with ADHD-related behaviors in young children.

Authors: Jiwon Oh, Kyoungmi Kim, Kurunthachalam Kannan, Patrick J Parsons, Agnieszka Mlodnicka, Rebecca J Schmidt, Julie B Schweitzer, Irva Hertz-Picciotto, Deborah H Bennett
Full Source: Research square 2023 Feb 10;rs.3.rs-2565914. doi: 10.21203/rs.3.rs-2565914/v1.

Ecotoxicity and resistance genes induction changing of antibiotic tetracycline degradation products dominated by differential free radicals

2023-02-14

Studying the ecological risks of antibiotics and their degradation products is of great importance to water environment security and advanced oxidation processes (AOPs) development. This work studied the changes and internal influencing mechanisms of ecotoxicity and the capacity for inducing antibiotic resistance genes (ARGs) shown by the tetracycline (TC) degradation products generated in AOPs with differential free radicals. Under the action of superoxide radicals and singlet oxygen in the ozone system, and sulfate and hydroxyl radicals in the thermally activated potassium persulfate system, TC exhibited differential degradation pathways and resulted in the differential growth inhibition trends on the determined strains. Microcosm experiments combined with

Studying the ecological risks of antibiotics and their degradation products is of great importance to water environment security and advanced oxidation processes (AOPs) development.

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metagenomics were also performed to analyze the remarkable changes in the TC resistance genes *tetA* (60), *tetT*, and *otr(B)* induced by the degradation products and ARG hosts in the natural water environment. Microcosm experiments exhibited that the microbial community in actual water have changed significantly with the addition of TC and degradation intermediates. Furthermore, the richness of genes related to oxidative stress was investigated to discuss the effect on reactive oxygen species production and SOS response caused by TC and its intermediates.

Authors: Heshan Zheng, Yitong Ji, Shuo Li, Wei Li, Jun Ma, Junfeng Niu
Full Source: Environmental research 2023 Feb 14;115427. doi: 10.1016/j.envres.2023.115427.

PHARMACEUTICAL/TOXICOLOGY

Acute and Chronic Toxicity of Uncured Resin Feedstocks for Vat Photopolymerization 3D Printing to a Cladoceran (*Ceriodaphnia Dubia*)

2023-02-16

The accessibility and popularity of additive manufacturing (AM) has increased over the past decade. Environmental hazard assessment and safety data sheets for 3D printer feedstocks has lagged technology development. Vat photopolymerization may have unique risks relative to other AM technologies due to mishandling of uncured monomers/ oligomer feedstocks and its decreasing cost enabling uninformed residential use. The acute and chronic toxicity of six uncured resins to *Ceriodaphnia dubia* was explored. Two-day acute toxicity (LC50) ranged from 2.6 to 33 mg/L and inhibition concentrations (IC25) values for reproduction ranged from 0.33 to 16 mg/L. Cleaning and waste management procedures recommended in user guides could be the most hazardous handling scenario as use of isopropyl alcohol increases miscibility and thus the fate, transport and bioavailability of the uncured resins. Residential users may often be poorly informed about potential toxicity and the need for a plan for use, handling, and waste management of uncured resins.

Authors: Mark Ballentine, Alan Kennedy, Nicolas Melby, Anthony Bednar, Robert Moser, Lee C Moores, Erik M Alberts, Charles H Laber, Rebecca A Crouch

Full Source: Bulletin of environmental contamination and toxicology 2023 Feb 16;110(3):56. doi: 10.1007/s00128-023-03698-5.

The accessibility and popularity of additive manufacturing (AM) has increased over the past decade.

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Toxicity and Estrogenicity of Bisphenol TMC in *Oryzias melastigma* via In Vivo and In Silico Studies

2023-02-16

Bisphenol 4-[1-(4-hydroxyphenyl)-3,3,5-trimethylcyclohexyl] phenol (BPTMC), as a substitute for bisphenol A, has been detected in environments. However, the ecotoxicological data of BPTMC are extremely scarce. Here, the lethality, developmental toxicity, locomotor behavior, and estrogenic activity of BPTMC at different concentrations (0.25-2000 µg/L) in marine medaka (*Oryzias melastigma*) embryos were examined. In addition, the in silico binding potentials of *O. melastigma* estrogen receptors (omEsrs) with BPTMC were assessed by docking study. Low-concentration BPTMC exposure (including an environmentally relevant concentration, 0.25 µg/L) resulted in stimulating effects, including hatching rate, heart rate, malformation rate, and swimming velocity. However, elevated concentrations of BPTMC led to an inflammatory response, changed heart rate and swimming velocity in the embryos and larvae. In the meantime, BPTMC (including 0.25 µg/L) altered the concentrations of estrogen receptor, vitellogenin, and endogenous 17 β-estradiol as well as the transcriptional levels of estrogen-responsive genes in the embryos or/and larvae. Furthermore, elaborate tertiary structures of omEsrs were built by ab initio modeling, and BPTMC exerted potent binding potential with three omEsrs with -47.23, -49.23, and -50.30 kJ/mol for Esr1, Esr2a, and Esr2b, respectively. This work suggests that BPTMC has potent toxicity and estrogenic effects in *O. melastigma*.

Authors: Xiao-Pei Li, Shu-Qing Qiu, Guo-Yong Huang, Dong-Qiao Lei, Chen-Si Wang, Lingtian Xie, Guang-Guo Ying

Full Source: Environmental science & technology 2023 Feb 16. doi: 10.1021/acs.est.2c08009.

Bisphenol 4-[1-(4-hydroxyphenyl)-3,3,5-trimethylcyclohexyl] phenol (BPTMC), as a substitute for bisphenol A, has been detected in environments.

The impact of prolonged, maternal iodine exposure in early gestation on neonatal thyroid function

2023-01-31

Context: Hysterosalpingography (HSG) using oil-soluble contrast medium (OSCM) improves pregnancy rates but results in severe and persistent iodine excess, potentially impacting the fetus and neonate. Objective: To determine the incidence of thyroid dysfunction in newborns conceived within six months of OSCM HSG. Design: Offspring study of a prospective cohort of women who underwent OSCM HSG. Setting: Auckland region, New Zealand (2020-2022).

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Participants: Offspring from the SELFI (Safety and Efficacy of Lipiodol in Fertility Investigations) study cohort (n=57).

Measurements: All newborns had a dried blood spot card for TSH measurement 48 hours after birth as part of New Zealand's Newborn Metabolic Screening Programme. Forty-one neonates also had a heel prick serum sample at one week to measure thyroid-stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3). Maternal urine iodine concentration (UIC) and TSH in the six months after OSCM HSG were retrieved from the SELFI study for analyses.

Primary outcome: Incidence of hypothyroidism in the neonatal period.

Results: There was no evidence of primary hypothyroidism on newborn screening (TSH 2-10 mIU/L). All neonates tested at one week had normal serum TSH, FT4, and FT3 levels. However, increasing maternal peak UIC levels during pregnancy were associated with lower TSH levels (p= 0.006), although also associated with lower FT4 levels (p=0.032).

Conclusions: While pre-conceptional OSCM HSG in women did not result in neonatal hypothyroidism, gestational iodine excess was associated with a paradoxical lowering of neonatal TSH levels despite lower FT4 levels. These changes likely reflect alterations in deiodinase activity in the fetal hypothalamic-pituitary axis from iodine excess.

Trial registration: <https://anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12620000738921>, identifier 12620000738921.

Authors: Divya M Mathews, Jane M Peart, Robert G Sim, Susannah O'Sullivan, José G B Derraik, Natasha L Heather, Dianne Webster, Neil P Johnson, Paul L Hofman

Full Source: Frontiers in endocrinology 2023 Jan 31;14:1080330. doi: 10.3389/fendo.2023.1080330.

OCCUPATIONAL

Risk perception of automotive fuel poisoning among gas station attendants

2023-02-03

Introduction: Everyday, gas station attendants are exposed to numerous toxic substances found in fuels. Benzene stands out among these toxic chemical agents; depending on its concentration, it can cause mucosal irritation or even pulmonary edema. A considerable number of gas station attendants is aware of the risks associated with benzene poisoning, but they are not aware of the risks associated with other automotive pollutants.

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Objectives: To evaluate and understand the risk perception of automotive fuel poisoning among gas station attendants in the Sorocaba region, state of São Paulo.

Methods: Sixty gas station attendants were evaluated in the Sorocaba region. Data were collected between October 2019 and September 2020 using a semi-structured, individual, closed-ended questionnaire whose questions identified the participants' perception and aimed to analyze: the general profile of the studied population; practices for handling fuels and knowledge on their toxic effects, use and instructions of personal protective equipment, symptoms possibly associated with fuel exposure, the participants' perception of poisoning risks, and their participation in occupational medicine programs.

Results: The obtained results demonstrated that most gas station attendants wore at least basic personal protective equipment, and some of them reported symptoms linked with benzene exposure. Still, a considerable number of employers does not provide adequate training to gas station attendants, which is possibly associated with inadequate use of personal protective equipment.

Conclusions: Our data showed indications of non-compliance by gas station attendants as to the use of personal protective equipment at the workplace, and by employers as to the provision of adequate training.

Authors: Larissa Guerino Ferla, Gustavo Henrique Oliveira da-Rocha, Rômulo Tadeu Dias de-Oliveira, Éric Diego Barioni

Full Source: Revista brasileira de medicina do trabalho : publicacao oficial da Associacao Nacional de Medicina do Trabalho-ANAMT 2023 Feb 3;20(3):422-429. doi: 10.47626/1679-4435-2022-745.

Occupational health risk assessment of airborne formaldehyde in medical laboratories

2023-02-16

The professional use of formaldehyde is a major occupational health concern in medical laboratory operations. Quantification of various risks associated with chronic exposure to formaldehyde may help in understanding the related hazards. This study designed to assess the health risks associated with inhalation exposure to formaldehyde involving biological, cancer, and non-cancer risks in medical laboratories. This study was performed in the hospital laboratories at Semnan Medical Sciences University. Risk assessment was performed in pathology, bacteriology, hematology, biochemistry, and serology laboratories with 30 employees, using formaldehyde in their daily routine operations. We determined area and personal exposures to airborne contaminant,

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applied standard air sampling, and analytical method recommended by National Institute of Occupational Safety and Health (NIOSH). We addressed formaldehyde-specific hazard by estimating peak blood level, life cancer risk, and the hazard quotient of non-cancer risks, adapted from Environmental Protection Agency (EPA) assessment method. The airborne formaldehyde concentrations in the laboratory personal samples ranged 0.0156-0.5940 ppm (mean = 0.195 ppm, SD = 0.048) and area exposure ranged 0.0285-1.0810 ppm (mean = 0.462 ppm, SD = 0.087). Based on workplace exposure, peak blood levels of formaldehyde were estimated at minimum 0.0026 mg/l to maximum 0.152 mg/l (mean = 0.015 mg/l, SD = 0.016). The mean cancer risk levels in terms of area and personal exposures were estimated respectively at $3.93 \times 10^{-8} \mu\text{g}/\text{m}^3$ and $1.84 \times 10^{-4} \mu\text{g}/\text{m}^3$, and for the non-cancer risk levels of the same exposures measured respectively at $0.03 \mu\text{g}/\text{m}^3$ and $0.07 \mu\text{g}/\text{m}^3$. Formaldehyde levels were significantly higher among laboratory employees, especially bacteriology workers. Exposure and risk could be minimized by strengthening control measures including the use of management controls, engineering controls, and respiratory protection equipment to reduce exposure levels of all workers to less than the allowed exposure limits and improve indoor air quality in the workplace.

Authors: Marzieh Belji Kangarlou, Farin Fatemi, Alireza Dehdashti, Hasan Irvani, Elahe Saleh

Full Source: Environmental science and pollution research international 2023 Feb 16. doi: 10.1007/s11356-023-25523-6.