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CHEMICAL EFFECTS

Benzalkonium chloride accumulates and causes toxicity in the heart and pancreas following the repeated inhalation exposures

2025-11-29

Benzalkonium chloride (BKC) is used as a disinfectant and preservative in aerosolized formulations, including various household cleaning products. Although primary organ toxicity of BKC has been reported, secondary organ toxicity after inhalation exposure remains unclear. This study evaluated the biodistribution of radiolabeled [14C] BKC using quantitative whole-body autoradiography in rats. Autoradiography after a single intranasal administration revealed significant accumulation and prolonged retention of radioactivity in the heart and pancreas, suggesting potential secondary organ toxicity following inhalation. To assess potential toxic effects without confounding pulmonary inflammation, rats were administered repeated intratracheal instillations (10 times, 3-day intervals) at non-inflammatory doses of 50 and 100 μg/rat. Despite the absence of pulmonary toxicity, BKC accumulation in the heart caused inflammation in the pericardium and myocardium, accompanied by transcriptomic alterations linked to mitochondrial dysfunction, reactive oxygen species (ROS) generation, inflammation, and cell death. Additionally, pancreas tissues exhibited histopathological changes, including acinar cell vacuolization, and gene expression changes associated with ROS generation, inflammation, and disrupted glucose regulation. These findings suggest that repeated inhalation exposure to BKC can damage the heart and pancreas at pulmonary non-toxic and occupationally relevant doses due to accumulation in these secondary organs, warranting further research to clarify hazards and mechanisms.

Authors: Gyuri Kim, Jiyoung Jeong, Jung Eun Park, Soyeon Jeon, Jae-Jun Kim, Se-Hwan Choi, Jaebaek Jang, Mi Hye Kwon, Min-Seok Kim, Iljung Lee, Tae Hwan Shin, Dong Hyun Kim, Jongho Jeon, Wan-Seob Cho

Full Source: The Science of the total environment 2025 Nov 29:1009:181067. doi: 10.1016/j.scitotenv.2025.181067.

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Unsymmetrical Dimethylhydrazine Induces Dose-Dependent Liver Toxicity in Rats via Oxidative Stress and PI3K/Akt Pathway-Mediated Apoptosis

2025-11-28

Unsymmetrical dimethylhydrazine (UDMH), a hypergolic propellant widely used in aerospace, is classified as a Group 2B carcinogen. Although UDMH induces dose-dependent hepatotoxicity, the underlying mechanisms remain unclear. This study tested the hypothesis that PI3K/Akt-mediated apoptosis drives UDMH-induced subacute liver injury. Male Sprague-Dawley rats were exposed to filtered air (control), 141 ± 10 ppm (low-dose), or 282 ± 10 ppm (high-dose) UDMH via inhalation (1 h/d, 5 d/wk) for 4 weeks. UDMH exposure caused mild weight loss and elevated serum ALT, ALP, and TBA while reducing ALB, indicating hepatic dysfunction. It also induced oxidative stress, evidenced by decreased T-SOD, GSH, and CAT activities, increased MDA levels, and upregulated proinflammatory cytokines (IL-1β, IL-6, TNF-α). Histology revealed dose-dependent inflammatory cell infiltration and hepatic sinusoidal hemorrhage with severe cytoplasmic disruption; TUNEL staining confirmed increased hepatocyte apoptosis. RNA-seq identified 1,700 DEGs enriched in PI3K-Akt and apoptosis pathways. Western blotting confirmed dose-dependent inhibition of PI3K/Akt signaling (reduced p-PI3K/PI3K and p-Akt/Akt ratios) and apoptosis activation (elevated Bax/Bcl-2 and cleaved caspase-3/caspase-3 ratios). Notably, oxidative stress preceded PI3K/Akt suppression, suggesting redox imbalance triggers PI3K/Akt-dependent hepatocyte death. These findings establish PI3K/Akt-mediated apoptosis as a core mechanism of UDMH hepatotoxicity, providing a rationale for targeting this pathway to protect aerospace workers.

Authors: Jiawei Zheng, Luting Wu, Xueming Duan, Wei Ding, Jiayou Zhou, Shuai Zhou, Donghui Wu, Hongguo Li

Full Source: Chemico-biological interactions 2025 Nov 28:111852. doi: 10.1016/j.cbi.2025.111852.

A bioreporter-toxicity-characteristic-leaching-procedure (Bio-TCLP) test battery approach for risk assessment and Cr-remediation performance optimization

2025-11-28

Hexavalent chromium [Cr(VI)] is a highly toxic metal, and its extensive use in industry has led to widespread soil contamination. Biochar is a cost-effective and practical amendment for Cr stabilisation, with remediation performance typically assessed using conventional chemical methods

such as the toxicity characteristic leaching procedure (TCLP). However, reliance solely on chemical concentration data may be inadequate for comprehensive risk assessment. There is a growing need for integrated approaches that combine chemical and toxicological evaluations. In this study, we developed a novel test battery approach, termed Bio-TCLP, by coupling whole-cell bioreporter assays with the TCLP to concurrently evaluate Cr leaching potential and associated toxicity. Although remediation using nanoscale zerovalent iron (nZVI) and biochar effectively reduced Cr(VI) levels as determined by TCLP, the Bio-TCLP results revealed residual leachate toxicity, primarily attributed to reactive oxygen species (ROS). To enhance the efficacy of remediation, an Eucalyptus-derived biochar functionalised with nZVI (EBC-nZVI) was synthesised. This composite achieved over 80% Cr(VI) reduction and, importantly, EBC-NZVI significantly reduced measurable ecotoxicity to below detection limits in the Bio-TCLP assay. This study introduces and validates the Bio-TCLP test battery approach as a dual-function tool for evaluating both the chemical and biological dimensions of remediation performance, supporting more robust risk assessment frameworks for contaminated site management.

Authors: Naifu Jin, Qinwen Liu, Jiasuan Song, Ying Hou, Aizhong Ding, Dayi Zhang

Full Source: Bioresource technology 2025 Nov 28:133740. doi: 10.1016/j.biortech.2025.133740.

ENVIRONMENTAL RESEARCH

Association among persistent chemical pollutants and infectious encephalitis: a mixture exposure and mediation approach

2025-11-28

Background: Most overlook the harmful effects on diseases, particularly the chronic neurotoxicity, which remains undetermined. This study aims to determine the impact of major environmental factors on infectious encephalitis.

Methods: Our study investigated the correlation between persistent chemical pollutants and reports and mortality cases of infectious encephalitis (Epidemic cerebrospinal meningitis and Encephalitis B). First, the quantile-based g computation (qgcomp) statistical method was used to analyze the correlation of different chemical pollutants. Bayesian Kernel Machine Regression-Causal Mediation Analysis (BKMR-CMA) method was applied to explore the mediating effect of greenhouse gases between

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persistent chemical pollution mixtures and incidence and mortality of infectious encephalitis. Finally, the Lasso regression method was used to assess the sensitivity of different age groups of encephalitis patients to the risks of different chemical pollutants.

Results: For epidemic cerebrospinal meningitis report cases, N2O mediates at the 10% and 90% levels, and PCB and OC exhibit a positive risk effect at all levels. For death cases, N2O mediates at the 10% and 90% levels, and the direct effect risk of the controlled chemical pollution mixture shows a downward trend, with PCB and NMVOC exhibiting a positive risk effect at all levels. For encephalitis B reports and death cases, N2O mediates at the 10% and 90% levels, and the direct effect risk of the controlled chemical pollution mixture shows a trend of first decreasing and then increasing, with CH4 and HCB exhibiting a positive risk effect at all levels. The mediating effect of N2O is concentrated in encephalitis B reports and deaths, where the control direct effects (CDE) of the CH4, N2O, and HCB chemical pollutant model were assessed at three different quantiles. The CDEs at the 10%, 50%, and 75% quantiles were 757.37 (95% CI: 85.36, 1580.16), 872.86 (95% CI: 215.66, 1706.86), and 894.98 (95% CI: 209.22, 1726.33), respectively. The death effects were 31.31 (95% CI: -0.05, 66.40), 36.76 (95% CI: 8.62, 71.13), and 38.06 (95% CI: 8.46, 75.09).

Conclusions: We found that most persistent chemical pollutants in the air increase the risk of neurotoxicity-related morbidity and mortality. Among them, epidemic cerebrospinal meningitis is primarily driven by PCB and OC, while encephalitis B is mainly driven by CH4 and HCB. The greenhouse gas N2O may play a mediating role between chemical pollutant exposure and the outcomes of infectious encephalitis. In the future, identifying the effects of chemical mixtures can better support the causal relationship between air pollution and neurotoxicity.

Authors: Guolong Qu, Jianqiang Han, Zhenyao Song, Weiming Hou

Full Source: BMC public health 2025 Nov 28. doi: 10.1186/s12889-025-25768-5.

Environmental pollutant-induced cholinergic disruption: Advances and perspectives in mechanistic insights, target heterogeneity, and neurotoxic synergy

2025-11-29

The cholinergic system serves as a central regulatory network for neurotransmission and behavioral control, and its complex signaling architecture renders it highly vulnerable to mixed environmental pollutants. In real-world scenarios, pollutants typically exist as complex mixtures whose synergistic or antagonistic interactions increase toxicity

uncertainty, thereby challenging the traditional single-pollutant, single-target paradigm in mixture risk prediction. Integrating evidence across pollutant categories to uncover shared mechanistic principles is therefore essential for building a predictive assessment framework. Through quantitative interactome analysis of twenty pollutant categories, we identify two unifying principles of cholinergic disruption: mechanistic convergence and target heterogeneity. Pollutant effects converge on a limited set of shared pathways, primarily acetylcholinesterase (AChE) inhibition and acetylcholine receptor (AChR) modulation, while molecular targets differ in sensitivity, forming an AChE and nicotinic AChRs (nAChRs) core attack module. We further propose a dual-axis model of damage facilitation and regulatory remodeling, delineating the transition from acute target-specific perturbations to chronic regulatory dysfunction. The model establishes chemical structure as a key determinant through a three-tier cascade encompassing molecular initiating events, distributional behavior, and metabolic fate. This framework supports a tiered risk-assessment strategy that integrates qualitative, quantitative, and computational approaches. By linking molecular perturbations to ecological outcomes, we establish an exposure-target-outcome paradigm that captures multilayered pollutant impacts. Finally, we identify key bottlenecks in predictive modeling, cross-species extrapolation, and regulatory translation, and propose a translational roadmap integrating multi-omics biomarkers, advanced in vitro models, and artificial intelligence to advance environmental neurotoxicology toward a mechanism-driven predictive science.

Authors: Wei Li, Ke Gao, Liping Lu

Full Source: Ecotoxicology and environmental safety 2025 Nov 29:308:119470. doi: 10.1016/j.ecoenv.2025.119470.

Comparing activated carbon and graphene-based electrodes using electrosorption process to quantify environmental impact associated with thorium extraction via LCA framework

2025-11-29

Thorium extraction from radioactive waste via various methods, including solvent extraction, ion exchange, adsorption, and electrosorption, raises significant concerns regarding radiological risks, human health, emissions, and other environmental impacts. To date, previous research estimated an optimal thorium recovery efficiency of 92% using electrosorption from a rare earth facility, though without a life cycle assessment (LCA) paradigm. To the best of our knowledge, this article quantified the

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environmental impact and emissions lifecycle of thorium extraction via the electrosorption process, employing activated carbon electrodes (ACE) and graphene-based electrodes (GBE) within a sustainable LCA framework. In this context, the inventory data for LCA were compiled from Ecoinvent database 3, sourcing input including raw material extraction, energy consumption, and chemical compounds. The comparative outcomes of midpoint analysis indicated that for each 1 kg of thorium extracted, the ACE system showed substantially higher environmental impacts than GBE, especially regarding human toxicity, freshwater ecotoxicity, and marine ecotoxicity, signifying a heightened release of toxins detrimental to ecosystems and human health. Also, the comparing results of endpoint indicators revealed that ACE showed a high impact over GBE in human health (0.0003-0.0001 DALY), ecosystems (7.14E-07-1.87E-07 species·yr), and resources (7.549-2.921 USD 2013), probably due to differences in chemical usage and emissions release during processing. In terms of output effectiveness and adverse environmental impacts, the GBE technique is more effective in removing thorium compared to ACE for the sustainable management of radioactive waste.

Authors: Naseem Akhtar, Aznan Fazli Ismail, Marlia M Hanafiah, Syazwani Binti Mohd Fadzil

Full Source: Scientific reports 2025 Nov 29. doi: 10.1038/s41598-025-28011-8.

PHARMACEUTICAL/TOXICOLOGY

Bisphenol A triggers adipocyte dysfunction, thereby fostering triple-negative breast cancer aggressiveness

2025-11-27

Bisphenol A (BPA) is an organic compound widely used in the production of polycarbonate plastics and epoxy resins. As a pervasive environmental pollutant, BPA accumulates in adipose tissue (AT) due to its lipophilic properties. AT, an endocrine organ central to homeostasis, constitutes the main component of breast stroma and plays a pivotal role in the microenvironment of breast cancer, including triple-negative breast cancer (TNBC). This study investigated how BPA disrupts adipocyte differentiation and metabolism, and the subsequent effects on the crosstalk between adipocytes and TNBC cells. We induced adipogenic differentiation of preadipocytes in the presence of BPA and evaluated alterations in differentiation and cytokine secretion. TNBC cells were cultured in homotypic and heterotypic organoids, exposing them to BPA either directly or indirectly, through a conditioned medium of BPA-treated

adipocytes. BPA exposure altered adipocyte differentiation, reducing lipid accumulation and perturbing cytokines release, leading to the upregulation of molecules involved in cell migration and invasiveness. TNBC cells exposed to conditioned medium of BPA-treated adipocytes exhibited enhanced growth, migration and invasiveness, whereas direct BPA treatment did not induce significant changes. These indirect effects were, at least in part, mediated by SDF1α and GAS1. Moreover, TNBC organoids showed increased infiltrative capacity when co-cultured with BPA-conditioned adipocytes. These findings highlight the profound impact of environmental pollution on cancer progression. BPA perturbates adipose differentiation, creating a dysfunctional adipocyte that fosters cancer growth and invasiveness in TNBC. This study underscores the impact of environmental pollutants on tumour progression by revealing the importance of BPA perturbation on tissue homeostasis and how this could promote cancer.

Authors: Anna Citarella, Tanja Milena Autilio, Zein Mersini Besharat, Elena Vicentini, Federica Barbagallo, Elena Splendiani, Annamaria Di Fiore, Mary Anna Venneri, Enrico De Smaele, Giuseppina Catanzaro, Laura Masuelli, Roberto Bei, Alessandra Fabi, Stefania Mardente, Antonio Angeloni, Silvia Migliaccio, Agnese Po, Elisabetta Ferretti

Full Source: Environmental research 2025 Nov 27:123446. doi: 10.1016/j.envres.2025.123446.

Aflatoxin B1-induced lipid disturbance and neuroinflammation contribute to Alzheimer's disease-like neuropathology in C57BL/6J mice

2025-11-29

Aflatoxin B1 (AFB1) is a ubiquitous foodborne mycotoxin that has been associated with cognitive decline. In this study, we investigated the neuropathology linked to Alzheimer's disease (AD) caused by AFB1 and revealed the underlying mechanism. Here, C57BL/6 J mice received AFB1 (1.5 mg/L in drinking water) for 8 weeks. Behavioral tests, including Morris water maze and Y-maze, were conducted alongside hippocampal histology and immunostaining to detect cognitive deficits and hippocampal neuronal impairment. Non-targeted lipidomics was also employed to dissect alterations in the hippocampal lipid profile. Furthermore, dysregulation of the lipid-driven inflammatory response was confirmed by gene and protein assays for lipid metabolism and inflammatory signaling, as well as serum cytokine measurements. Results showed that AFB1 impaired spatial learning and memory, caused hippocampal neuronal loss and increased App and phosphorylated

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Tau. Non-targeted lipidomics revealed that the AFB1 exposure led to derangements in glycerophospholipid metabolism and increased the abundance of pro-inflammatory phosphatidylcholine (PC) species. Concurrently, the Tlr4/NF-κB cascade contributed to the enhanced systemic and hippocampal pro-inflammatory cytokine responses. Taken together, these results indicate that exposure to a low dose of AFB1 results in an increase in pro-inflammatory PC species and hippocampal neuroinflammation via the Tlr4/NF-κB axis and hence contribute to the development of AD-like neuropathology. This highlights the therapeutic significance of targeting dysregulated lipid metabolism to counteract AFB1-induced neurotoxicity in relation to AD.

Authors: Jinxian Lin, Jiayi Li, Zhengwei Liang, Haiyan Yu, Sicheng Liu, Qixue Zheng, Jinping Yu, Zhulin Du, Kun Luo, Xionghua Yang, Lingling Yang, Ping Deng, Huifeng Pi, Zhengping Yu, Zhou Zhou, Wei Yuan, Huihui Hong

Full Source: Ecotoxicology and environmental safety 2025 Nov 29:308:119495. doi: 10.1016/j.ecoenv.2025.119495.

OCCUPATIONAL

Low-dose radiation exposure and health outcomes among healthcare workers: a multi-center prospective cohort study

2025-11-28

Background: The long-term effects of chronic low-dose radiation exposure remain a subject of debate, with studies suggesting a range of outcomes from negligible to significant health impacts.

Methods: This multi-center cohort study followed 210 newly hired healthcare workers in radiation-related occupations for 9 years, from January 2015 to December 2023. Health effects were evaluated using Repeated Measures Analysis of Variance (rMANOVA). Significant interactions were explored using Bonferroni's post hoc analysis and Bayesian methods. Repeated-measures regression models and Restricted Cubic Splines (RCS) models were employed to further assess the statistical significance and strength of evidence. Sensitivity analyses were performed employing Generalized Estimating Equations (GEE) to ensure robustness of the results.

Results: The per-protocol set included 111 subjects after accounting for exclusions and losses to follow-up. The rMANOVA models identified subtle but statistically significant differences across multiple follow-up intervals for various health indices. Parameters with Bayes factors (BF10) greater than 100, indicating extremely strong evidence for the alternative hypothesis, included RBC, MCV, MCH, MCHC, PH, SG, TP, ALB, GLB, and

A/G. Per 1-mSv increment in instantaneous Hp(10), MCV decreased by 5.96 fL (95%CI -8.92 to -3.00, P < 0.001), MCH by 2.31 pg (95%CI -3.54 to -1.08, P < 0.001), and urine PH by 1.02 units (95%CI -1.65 to -0.40, P = 0.001). Conversely, each additional 1 mSv of cumulative Hp(10) was associated with an increase of 8.22 fL in MCV (95%CI 6.54-9.91, P < 0.001) and 2.37 pg in MCH (95%CI 1.67-3.07, P < 0.001), but also with reductions in hemoglobin (-3.48 g/L, 95%CI -6.36 to -0.59, P = 0.018), plateletcrit (-0.022%, 95%CI -0.037 to -0.008, P = 0.002), large-platelet ratio (-8.40%, 95%CI -14.35 to -0.25, P = 0.006), total protein (-2.10 g/L, 95%CI -3.67 to -0.52, P = 0.009), and globulin (-1.56 g/L, 95%CI -2.80 to -0.31, P = 0.014), together with a rise in the albumin/globulin ratio (0.123, 95%CI 0.01-0.23, P = 0.031). RCS models after adjusting for age, gender and profession revealed statistically significant dose-response relationships between Ln-transformed Hp(10) and the health indices of RBC, MCHC, and A/G.
Conclusions: This pioneering longitudinal cohort study in western China demonstrates that chronic low-dose radiation exposure among healthcare workers can induce subtle yet significant health effects, underscoring the necessity of adhering to the ALARA principle for radiation exposure management.

Authors: Xiaobin Liu, Qian Su, Jing Zhang, Yan Chen, Fei Li, Caixia Xie, Li He, Shiyu Liu, Yu Lv

Full Source: Journal of health, population, and nutrition 2025 Nov 28;44(1):414. doi: 10.1186/s41043-025-01133-5.

Association between prenatal phthalate exposure and preschoolers' blood pressure: Mediating role of DNA methylation in hypertension-related genes

2025-11-27

Background: Emerging evidence links prenatal phthalate (PAE) exposure to offspring cardiovascular risks, yet mechanisms underlying early-life hypertension remain elusive. Epigenetic regulation may represent a critical pathway connecting environmental exposures to developmental origins of cardiovascular disease.
Objective: To investigate whether DNA methylation of hypertension-related genes mediates the association between gestational PAEs exposure and elevated blood pressure in preschoolers.
Methods: In this prospective cohort of 198 mother-preschooler pairs (preschoolers aged 3-7 years), we quantified eight PAE metabolites (mPAEs) in third-trimester maternal urine. Preschoolers' blood pressure (BP) was measured clinically, with hypertension defined per the 2017 American Academy of Pediatrics guidelines. We assessed methylation

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in cardiovascular-related genes using targeted bisulfite sequencing. Generalized linear models (GLMs) examined associations between prenatal PAE exposure, DNA methylation levels, and BP z-scores. Mediation analysis evaluated whether DNA methylation mediated the effect of prenatal PAEs on SBP/DBP z-scores. Mediation analysis evaluated whether weighted methylation risk scores (wMRS) mediated the effect of prenatal PAEs on SBP/DBP z-scores.
Result: The wMRS of Endothelin-converting Enzyme 1 (ECE1) significantly mediated the associations of maternal urinary monomethyl phthalate (MMP), monoethyl phthalate (MEP), and mono(2-ethylhexyl) phthalate (MECPP) with increased systolic blood pressure (SBP) z-scores in preschoolers. Methylation at a specific site in the ECE1 gene (ECE1_position2) also significantly mediated the associations of prenatal MMP, MEP, and MECPP with increased systolic blood pressure z-scores. Positive associations were observed between MEP and MECPP with elevated SBP/DBP z-scores (β=0.11-0.24, all P<0.05). MMP, MEP, and MECPP were associated with methylation levels in ECE1 and the epithelial sodium channel gamma subunit (SCNN1G) genes, which in turn were linked to BP changes.
Conclusions: Our findings suggest that prenatal phthalate exposure programs later cardiovascular risk through an epigenetic pathway, highlighting ECE1 as a potential biomarker for early-life hypertension prevention.

Authors: Wei Wu, Zihao Wang, Wenwen Yang, Xiaoyuan Feng, Yifan Yang, Mengfei Xu, Beini Li, Ping Wu, Zhongqiang Cao

Full Source: Environmental pollution (Barking, Essex: 1987) 2025 Nov 27:127450. doi: 10.1016/j.envpol.2025.127450.