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CHEMICAL EFFECTS

sPLA2-IIA inhibitor Tricyclic Dipyrido Diazepinone derivative 6 f suppresses poultry organic dust-induced pulmonary inflammation by downregulating ERK1/2-cPLA2 pathway

2025-12-13

Poultry farm workers are highly susceptible to developing lung inflammatory diseases (asthma, COPD, ARDS, and ALI) due to prolonged exposure to organic dust and other airborne irritants in confined poultry facilities. Secretory phospholipase A2 (sPLA2-IIA) is a vital proinflammatory enzyme play an important role in the production of inflammatory mediators. Hence, this study examined the regulatory role of secretory phospholipase A2 enzyme in poultry dust induced lung inflammation in in vitro and in vivo models. Lung epithelial A549 cells and BALB/c mice treated with poultry dust increased the sPLA2-IIA mRNA expression and stimulated the induction of inflammatory symptoms. Inhibition of sPLA2 enzyme activity by Tricyclic Dipyrido Diazepinone derivative 6 f (sPLA2 inhibitor) markedly ameliorated ODE-induced lung histopathological conditions, decreased lung edema, cellular infiltration, and protein secretion. Further, downregulated activation of cPLA2 via decreasing phosphorylation of ERK1/2 and p38. Suppressing cPLA2 signalling cascade significantly reduced the production of inflammatory cytokines (IL-6, IL-8, and TNF-α) and chemokines (MIP-1, MCP, and RANTES). Consequently, the activation of COX-2 and the production of prostaglandin E2 and thromboxane B2 were significantly decreased. Conclusively, these findings indicated that sPLA2-IIA could potentially serve as a novel therapeutic target for treating lung inflammation in disease conditions.

Authors: Deepadarshan Urs, Abdul Rahman, H S Shuba, N D Satyanarayan, Rajkumar S Meti, K K Dharmappa

Full Source: Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 2025 Dec 13:194:118869. doi: 10.1016/j.biopha.2025.118869.

Copper Nanoparticles Atomized into Zerovalent Copper Single Atoms at Water/Mineral Interfaces Mediated by ortho-Phenolic Hydroxyl of Dissolved Organic Matter

2025-12-13

The interaction of copper nanoparticles (CuNPs) from anthropogenic and natural sources in the environment with dissolved organic matter (DOM) governs their occurrence, fate, and transportation. Here, we report

Poultry farm workers are highly susceptible to developing lung inflammatory diseases (asthma, COPD, ARDS, and ALI) due to prolonged exposure to organic dust and other airborne irritants in confined poultry facilities.

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that DOM can mediate CuNP transformation into atomically dispersed zerovalent copper single atoms (Cu0-SAs) at water/mineral interfaces. The mechanism proposes that the ortho-phenolic hydroxyl of DOM likely forms the five-membered ring structure with copper atoms on the CuNP surface, inducing inner-sphere electron transfer to weaken Cu-Cu bonds and enabling the liberation of Cu0-SAs and stabilization via Cu-O bonds on natural mineral surfaces, which diverges fundamentally from the conventional dissolution process. Cu0-SAs represent a paradoxical species that exhibit both relatively high environmental toxicity and stability, combining enhanced bactericidal activity, decreased copper ion leaching compared with parent CuNPs, and resistance to aggregation under reducing conditions. This study unveils an unreported CuNP transformation process in the environment, demonstrating Cu0-SAs as an emerging yet significant copper species. Our findings should be helpful for better understanding the fate, migration, and toxicity of copper in the ecosystem by identifying atomic-level copper intermediates.

Authors: Haibin Li, Yina Guan, Chunguang Liu, Site Han, Yating Zhang, Lingshuai Kong, Jinhua Zhan

Full Source: Environmental science & technology 2025 Dec 13. doi: 10.1021/acs.est.5c15342.

ENVIRONMENTAL RESEARCH

The association of environmental toxicants exposure with cardiovascular disease risk: A comprehensive analysis from population to molecular mechanism

2025-12-12

Background: Prior studies on toxicants and CVD focused on limited compounds, restricting their relevance to real-world exposure scenarios, a comprehensive assessment multiple toxicants is therefore warranted.
Methods: An exposome-wide association study (ExWAS) was conducted using 61 toxicants in 10 categories among 3577 participants from the 2013-2016 NHANES. Weighted quantile sum (WQS) regression and Bayesian kernel machine regression (BKMR) were applied to identify dominant contributors. Mediation analysis and network toxicology were used to explore the mediating roles of the systemic inflammatory response index (SIRI) and phenotypic age acceleration.
Results: ExWAS identified 29 toxicants from eight chemical families positively associated with CVD risk. WQS regression revealed that mixed exposures to toxicant family of nicotine metabolites (aOR = 1.45, 95 %

Background: Prior studies on toxicants and CVD focused on limited compounds, restricting their relevance to real-world exposure scenarios, a comprehensive assessment multiple toxicants is therefore warranted.

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CI: 1.18-1.78), metals (aOR = 2.16, 95 % CI: 1.35-3.45), polycyclic aromatic hydrocarbons (PAHs) (aOR = 1.34, 95 % CI: 1.07-1.69), perchlorate/nitrate/thiocyanate (aOR = 1.26, 95 % CI: 1.03-1.53), and volatile organic compound metabolites (VOCs) (aOR = 1.33, 95 % CI: 1.03-1.73) were significantly associated with CVD risk, and BKMR results indicated that metals showed the highest posterior inclusion probability (1.000), followed by PAHs (0.655) and VOCs (0.591). Mediation analysis revealed that SIRI and phenotypic age acceleration significantly mediated the associations of 21 and 18 toxicants with CVD, respectively. Network toxicology analysis demonstrated that toxicants were enriched in multiple inflammaging-related pathways.
Conclusion: When multiple toxicants are considered simultaneously, the metals, PAHs, and VOCs families contribute most substantially to CVD risk, and inflammaging emerged as mediator of the associations.
Authors: Hua Fang, Guan-Hua Fang, Dan-Jing Chen, Hua-Jing Chang, Ming-Huan Yang, He Zhang, Yi-Jun Jiang, Yong-Feng Cai, Zhi-Jian Hu, Xian-E Peng
Full Source: Ecotoxicology and environmental safety 2025 Dec 12:309:119562. doi: 10.1016/j.ecoenv.2025.119562.

Seasonal dynamics of groundwater pollution and health risks in municipal solid waste-affected urban settlements of Bengaluru, Kolkata and Durgapur, India

2025-12-14

Groundwater contamination is a concern for drinking and domestic supply across India.

Groundwater contamination is a concern for drinking and domestic supply across India. Escalating volumes of municipal solid waste (MSW) generation, and unsystematic dumping with the rapid urbanization process, enhance these concerns. This study investigates three MSW-affected groundwater systems in diverse climatic regions to elucidate contaminant transport and associated health risks. Objectives include seasonal pollutant analysis, groundwater pollution index (PIG) assessments, and non-carcinogenic health risk evaluations. Three location targets are Kolkata, Durgapur, and Bangalore, which represent urban settlements from Humid to Dry climates. Findings reveal significant pollution levels near Kolkata's Dhapa dumpsite, with approximately 70% of groundwater classified as low pollution risk (PIG > 1 to 1.5). In Bengaluru, nitrate contamination (HQNitrate > 1) poses health risks for 20%, 37.5%, and 66.7% of adults during pre-monsoon, monsoon, and post-monsoon periods, respectively. Similarly, Kolkata's dumpsite exposes 87.5%, 80%, and 62.5% of adults to health risks across corresponding seasons. Nitrate contamination poses health risks to 100% of the children's population near

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Kolkata's dumpsite, irrespective of season. Whereas HITotal for the Nitrate, Fluoride and heavy metals combinedly showing all the samples from the three studied cities having potential for human health risk spatially and temporally. Additionally, heavy metal pollution index (HPI) exceeds the thresholds in all samples across the seasons suggest critical pollution levels in Kolkata. This information is vital for effective groundwater management to protect human health, ensure water quality, and quantify potential hydrological contaminants, especially in regions near MSW dumpsites where the demand for groundwater is high.
Authors: Utpal Majee, Prosenjit Ghosh, Gabriel M Filippelli
Full Source: Environmental geochemistry and health 2025 Dec 14;48(1):47. doi: 10.1007/s10653-025-02928-5.

Identification and assessment of urban groundwater pollution based on Monte Carlo health risk modeling and self-organizing map (SOM)

2025-12-10

With the acceleration of urbanization, groundwater quality is severely threatened, posing health risks to public health and the environment.

With the acceleration of urbanization, groundwater quality is severely threatened, posing health risks to public health and the environment. In reality, the highly heterogeneous geological background and hydrochemical relationships not only increase the difficulty in identifying pollution, but also pose significant challenges in groundwater risk prevention and control. Taking Guangzhou, a megacity in the bustling Pearl River Delta, as the research object, this study leverages the ability of machine learning to mine complex data and the advantage of Monte Carlo simulation in quantifying random uncertainties to deeply analyze the driving factors, pollution sources, and potential health risks of urban groundwater chemistry. Through the SOM model, a cluster analysis was conducted on 107 groundwater samples, resulting in the classification of 5 distinct water chemical groups with significant characteristics (Clusters I - V). Among them, human activities (domestic pollution) have a significant impact on groundwater chemistry mainly in Cluster I (a total contribution of 52.9 %). Manganese (Mn) and nitrate (NO3-) pose non-carcinogenic risks, with the highest risks observed for Mn in Cluster II and NO3- in Cluster III. Monte Carlo simulation indicates that the overall health risk in the region is low, with only 1.3 % of children potentially exposed to high HI conditions. This study provides valuable insights for the precision

prevention, control, and risk management of complex groundwater pollution in cities such as those in the Pearl River Delta.
Authors: Di Kang, Qizhi Hu, Hailong Qin, Hao Chen, Xiaoyu Xu, Xianming Xie, Xiang Ren, Xinyuan Zhang, Bingbing Cao, Chih-Huang Weng, Kai Liu, Na Liu
Full Source: Journal of contaminant hydrology 2025 Dec 10:277:104807. doi: 10.1016/j.jconhyd.2025.104807.

PHARMACEUTICAL/TOXICOLOGY

Silver Nanoparticles Synthesized From Aloe vera Extract Have Lower Toxicity Than Chemically Synthesized Forms on Hepatic, Renal, Oxidative/Antioxidative Profiles, and Histopathological Damage in Male Mice

2025-12-12
Nanoparticles (NPs) are widely studied due to their unique properties and diverse applications. Among them, silver nanoparticles (AgNPs) are commonly used in paints, plastics, ceramics, and magnetic products. However, concerns over their potential toxicity have led to increased interest in safer, environmentally friendly synthesis methods. This study evaluates the toxicological effects of green-synthesized AgNPs using Aloe vera extract compared to chemically synthesized AgNPs on vital organs (liver, kidney, spleen, and testis) in male mice. Twenty-eight healthy adult male mice were randomly divided into four equal groups. Group I (control) received 0.9% NaCl; Group II received Aloe vera extract (5 mg/kg); Group III received chemically synthesized AgNPs; and Group IV received green-synthesized AgNPs with Aloe vera. Blood samples were analyzed for biochemical parameters, including glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), urea, and creatinine. Tissue samples were examined for oxidative stress markers such as total oxidative stress (TOS) and total antioxidant capacity (TAC) and underwent histological and histochemical analysis. Results showed that the AgNPs and AgNPs (Aloe vera) groups exhibited significant increases in TOS, GOT, GPT, urea, and creatinine, with a concurrent reduction in TAC. However, only the chemically synthesized AgNPs group displayed marked histological damage in the liver, kidney, and testis, manifested as necrosis, inflammation, collagen deposition, and cellular degeneration. These changes were absent in the green-synthesized AgNPs group. It can be concluded that AgNPs synthesized using Aloe vera exhibit fewer harmful

Nanoparticles (NPs) are widely studied due to their unique properties and diverse applications.

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health effects compared to those synthesized chemically, making green synthesis a safer and more reliable method.
Authors: Eatemad A Awadalla, Souad H M Bekheet, Yahia A Amin, Samia A Gbr, Zeinab Ebrahim, Amna H M Nour
Full Source: Environmental toxicology 2025 Dec 12. doi: 10.1002/tox.70010.

Preliminary insights into methylation patterns in Agent Orange exposed thyroid cancers: a pilot study

2025-12-11
During the Vietnam War, US military personnel were widely exposed to a tactical defoliant called Agent Orange, contaminated with a toxic endocrine-disrupting chemical, 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (TCDD). Vietnam-era US Veterans exposed to Agent Orange display increased risk of thyroid cancer, yet the molecular mechanisms behind this risk remain largely unexplored. As aberrant DNA methylation is a hallmark of cancer development, we conducted a retrospective case-case study of Vietnam-era US Veterans to investigate differential DNA methylation profiles of Agent Orange exposed thyroid cancers compared to unexposed thyroid cancers. This exploratory study included 44 Veterans with differentiated thyroid cancer, treated at two Veterans Affairs (VA) medical centers (1990-2020): 23 Agent Orange exposed cases, identified through VA benefits/ medical record review, and 21 unexposed cases. We profiled genome-wide tumor DNA methylation with the Infinium Methylation EPICv2 array. We used linear regression models to compare methylation in the exposed compared to unexposed group. Models were adjusted for age, VA location, and cell type proportions. Differentially methylated CpGs were used for gene set enrichment analyses. Agent Orange exposure was associated with differential methylation at 309 CpGs (nominal p-value < 0.001) in thyroid tumors from exposed compared to those from the unexposed group. However, we did not detect significant CpGs after adjusting for multiple comparisons. Some of the top associations included CpGs located to cancer-related genes (i.e. CELF2, OTX2, SSR1, and EBF1). Gene set enrichment analysis revealed enrichment of hedgehog signaling and anti-folate resistance pathways. In this exploratory analysis, we identified differentially methylated loci linked to thyroid cancer in Agent Orange exposed Veterans. Further research is necessary to replicate our findings in a larger cohort including Agent Orange

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exposure determination through biomarker assessment, and to elucidate mechanisms behind these associations in in vitro exposure models.
Authors: Bushra Amreen, Corina Lesseur, Hachem Sadikki, Shira R Saul, Sofia Kazi, Angela M Leung, Elise Y Nguyen, Mathilda Monaghan, Emanuela Taioli, Eric M Genden, Jia Chen, Maaike van Gerwen
Full Source: Environmental pollution (Barking, Essex : 1987) 2025 Dec 11:127475. doi: 10.1016/j.envpol.2025.127475.

OCCUPATIONAL

Association of co-exposure to EDCs in early pregnancy with threatened abortion: The mediation effect of progesterone

2025-12-11
Endocrine-disrupting chemicals (EDCs) are ubiquitous environmental pollutants linked to adverse pregnancy outcomes, but their combined effects on threatened abortion (TA) remain unclear. Progesterone (P4) plays a critical role in maintaining pregnancy, yet its potential modifying effect on EDC-associated TA is underexplored. This study aimed to investigate the association between patterns of EDC co-exposure and TA, and to evaluate the potential mediating effect of P4. A prospective cohort study was conducted among 1,122 pregnant women in China. Urine concentrations of 24 EDCs (including bisphenols, parabens, per- and polyfluoroalkyl substances, and organophosphate flame retardants) were measured, and serum P4 levels were obtained from clinical records. Generalized linear regression model (GLM), LASSO, Bayesian kernel machine regression (BKMR), and quantile g-computation (QGC) were used to assess individual and mixture effects. Mediation analysis was performed to examined the role of P4 in EDC-TA associations. BPB (OR = 1.18, 95 % CI: 1.03, 1.37), BPP (OR = 1.15, 95 % CI: 1.01, 1.30), and BuP (OR = 1.09, 95 % CI: 1.01, 1.17) were positively associated with TA, while DPHP showed a negative association (OR = 0.91, 95 % CI: 0.83, 0.99). Reduced P4 levels significantly increased TA risk (OR = 0.92, 95 % CI: 0.91, 0.94). Mediation analysis revealed that decreased P4 level mediated BPB's harmful effect on TA. Age-stratified analyses showed stronger effedcts of BPP in women ≤ 29 years and BPB effects in those ≥ 30 years. BKMR indicated dose-dependent TA risk elevation at higher mixture exposures (≥ 35th percentile). In conclusion, early-pregnancy co-exposure to specific EDCs increases TA risk, with decreased P4 level mediated BPB's harmful effect on TA. Age modifies

Endocrine-disrupting chemicals (EDCs) are ubiquitous environmental pollutants linked to adverse pregnancy outcomes, but their combined effects on threatened abortion (TA) remain unclear.

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susceptibility, highlighting the need for targeted interventions in high-risk subgroups.
Authors: Ting-Ting Jiang, Dong-Yang Zhang, Zi-Yi Liu, Zi-Shun Lu, Lu-Ming Yan, Shu Sun, Ji-An Xie, Min Zhu, Zhi-Hua Zhang, Yu-Hui Wan, Hua Wang, Jia-Hu Hao, Chao Zhang
Full Source: Environment international 2025 Dec 11:207:110001. doi: 10.1016/j.envint.2025.110001.

Water consumption contributes to maternal PFAS exposure: From source to metabolic perturbations

2025-12-10
Per- and polyfluoroalkyl substances (PFAS) are widespread persistent pollutants and pose a risk to human health. However, the transfer efficiencies (TEs) of PFAS from source water into maternal serum, and its metabolic pathways linking PFAS exposure and human disease are remain unclear. Here, we present an integrative study combining multi-water and serum PFAS analysis, lipidomics, and machine learning to decipher TEs and PFAS-metabolism interactions. Analyzing 30 PFAS across source water (N = 18), tap water (N = 18), water during drinking water treatment process (DWTP, N = 12), and serum of pregnant women alongside 297 lipid species, we developed a SHAP (Shapley Additive Explanations) framework to quantify PFAS origins and serum-specific lipid responses. We found PFAS were prevalent in source water samples, with PFBA, PFPeA, 6:2 FTS, PFOA, and PFOS being predominant chemicals. In addition, DWTP may not be effective in removing PFAS, with most of target chemicals tested exhibiting removal below 50 %. Moreover, source water outperforms tap water in predicting maternal serum PFAS concentrations, suggesting source water contamination reflects maternal exposure more directly. Machine learning further showed that maternal serum lipid metabolism was influenced by PFAS, such as HFPO-DA and N-MeFOSAA mainly disrupted glycerphospholipid homeostasis (e.g., PC and LPC), highlighting risks to maternal metabolism. Our findings pioneer AI-driven tracing of PFAS transfer dynamics and lipidomic disruptions, warranting a comprehensive strategy beyond drinking water to handle water PFAS contamination.
Authors: Wei Chang, Yong-Wei Xiong, Jian Sun, Lan-Lan Wu, Shen-Dong Xu, Qi Lu, Zhi Yuan, Yi-Fan Hu, Cheng Chen, Kai-Yong Liu, Hua-Long Zhu, De-Xiang Xu, Yichao Huang, Dao-Zhen Chen, Lin Tao, Hua Wang
Full Source: Environment international 2025 Dec 10:207:109996. doi: 10.1016/j.envint.2025.109996.

Per- and polyfluoroalkyl substances (PFAS) are widespread persistent pollutants and pose a risk to human health.

Arsenic exposure, arsenic metabolism, and plasma lipidome in relation to type 2 diabetes and glycemic traits: a lipidome-wide association study

2025-12-11

Introduction: Both arsenic exposure and lipid metabolism disturbances are implicated in type 2 diabetes (T2D), whereas arsenic-associated lipidomic alterations and their contributions to T2D remain unclear.

Objectives: To map the plasma lipidomic profiles of incident T2D, glycemic traits, and arsenic exposure/metabolism, and to assess the mediating roles of lipids in arsenic-related diabetogenesis.

Methods: A nested case-control study of 92 incident T2D cases and 184 controls was conducted within an urban adult-based prospective cohort. Plasma lipidome and urinary arsenic species (As3+, As5+, MMA, DMA, and AsB) were measured. Orthogonal partial least squares-discriminant analysis, t-test, and conditional logistic regression were applied to identify T2D-associated lipids, while partial least squares regression, t-test, and linear regression were conducted to identify glycemic traits- and arsenic-associated lipids. Mediation analyses quantified lipid-mediated effects.

Results: Several arsenic exposure indicators (tAs, iAs, As3+, As5+, and DMA) were associated with increased T2D incidence (odds ratios [ORs]: 1.37-1.76), whereas metabolism indices (MMA% and primary methylation index [PMI]) showed protective associations with T2D (ORs: 0.59-0.61) and improved glucose homeostasis. We identified 163 T2D-associated lipids, characterized by increased triacylglycerols (TGs) and diacylglycerols (DGs) but reduced lysophosphatidylcholines, sphingomyelins (SMs), and hexosylceramides. Most TGs, DGs, and ceramides (Cers) were positively associated with fasting plasma insulin and HOMA-IR. Arsenic exposure was associated with higher TGs but lower DGs, Cers, and SMs. Efficient arsenic metabolism (higher DMA% and secondary methylation index [SMI]) was positively associated with most lipids, whereas MMA% and iAs% were inversely associated. Mediation analyses revealed 19 (mainly TGs/DGs), 16 (mainly SMs/phosphocholines), and 35 (mainly TGs/Cers) lipids that partially mediated arsenic exposure-T2D, arsenic metabolism-T2D, and arsenic metabolism-insulin resistance associations, respectively, with mediation proportions of 11.4%-54.7%.

Conclusion: Arsenic exposure and metabolism are associated with distinct lipidomic profiles that may precede T2D onset. Specific lipids partially mediated arsenic-related diabetogenic effects, providing candidate biomarkers and intervention targets.

Authors: Yongfang Zhang, Jiahao Song, Shuhui Wan, Zhiying Huo, Qing Liu, Le Hong, Yani Xiong, Feifei Wang, Ming Zhang, Gaoyin Xiong, Pengfei Chen, Ruiyi Liang, Yanjun Guo, Bin Wang, Weihong Chen

Full Source: Journal of advanced research 2025 Dec 11:S2090-1232(25)00999-3. doi: 10.1016/j.jare.2025.12.009.

Introduction: Both arsenic exposure and lipid metabolism disturbances are implicated in type 2 diabetes (T2D), whereas arsenic-associated lipidomic alterations and their contributions to T2D remain unclear.
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