CHEMWATCH

Bulletin Board

Contents

SEP. 06, 2024

(click on page numbers for links)

CONTACT US

subscribers@chemwatch.net
tel +61 3 9572 4700
fax +61 3 9572 4777

1227 Glen Huntly Rd
Glen Huntly
Victoria 3163 Australia

CHEMICAL EFFECTS

Contrasting effects of iron oxides on soil organic carbon accumulation in paddy and upland fields under long-term fertilization

2024-08-29

Active iron oxides, especially poorly crystalline forms, benefit soil organic carbon (SOC) accumulation via directly bounding and indirectly promoting aggregation. However, it remains unclear on the impacts of active iron oxides on SOC accumulation in paddy and upland soils under long-term fertilization regimes. Here, we attempted to clarify the underlying mechanisms of amorphous (FeO) and organically complexed (FeP) iron oxides mediating SOC accumulation in paddy and upland soils based on two long-term fertilization experiments (both including no fertilization [CK]; chemical nitrogen, phosphorus and potassium [NPK] and NPK plus manure [NPKM] treatments). Results showed that compared to upland soil, Fe-bound organic carbon (Fe-bound OC) content in paddy soil, occupying 21-30% of SOC, was 77% higher on average, due to larger amounts of FeO (+31%) and FeP (+224%). The FeO and FeP were positively related to mean weight diameter (MWD) of soil aggregates across paddy and upland soils. Compared to NPK treatment, NPKM treatment strongly increased FeO (+41%), FeP (+60%) and associated Fe-bound OC (+19%) in paddy soil, and increased FeO (+17%) and FeP (+25%) while decreasing Fe-bound OC (-9%) in upland soil. These combined findings indicated the importance of poorly crystalline iron oxides facilitating Fe-bound OC formation and its contribution to SOC accumulation in paddy soil rather than upland soil. Moreover, long-term manure amendment could enhance SOC accumulation by increasing Fe-bound OC and aggregation stability in paddy soil and enhancing physical protection in upland soil, largely attributed to increased poorly crystalline iron oxides. Overall, these results highlight the potential mechanisms through which active iron oxides regulate SOC accumulation and guide fertilization management in paddy and upland soils.

Active iron oxides, especially poorly crystalline forms, benefit soil organic carbon (SOC) accumulation via directly bounding and indirectly promoting aggregation.

Authors: Dong Wu, Lei Wu, Kailou Liu, Jianying Shang, Wenju Zhang
Full Source: Journal of environmental management 2024 Aug 29:369:122286. doi: 10.1016/j.jenvman.2024.122286.

CHEMWATCH
Bulletin Board
Technical
SEP. 06, 2024

Persistent endocrine-disrupting chemicals and incident uterine leiomyomata: A mixtures analysis

2024-08-30

Background: Uterine leiomyomata (UL; fibroids) are hormone-dependent neoplasms that can cause significant gynecologic morbidity. Studies have documented associations between concentrations of persistent endocrine-disrupting chemicals (EDCs) and UL incidence; however, few have assessed the effects of EDC mixtures on UL.

Methods: In the Study of Environment, Lifestyle, and Fibroids, a prospective cohort study, participants attended study visits at baseline and approximately every 20 months for up to 10 years; at each visit, they completed questionnaires, provided blood samples, and underwent standardized ultrasound examinations. In baseline plasma samples (n = 1155), we quantified concentrations of polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), and organochlorine pesticides using high-resolution mass spectrometry. We selected nine EDCs detected in >60 % of samples (4 PCBs, 4 PBDEs, and 2,2-bis(4-chlorophenyl)-1,1-dichloroethene (p,p'-DDE)) and conducted probit Bayesian kernel machine regression with hierarchical variable selection to estimate effects of the EDC mixture and individual EDCs on UL incidence, adjusting for potential confounders.

Results: During 10 years of follow-up, 32 % of participants developed ultrasound-detected UL. The EDC mixture was not appreciably associated with the probit of UL (β comparing all EDCs at their 75th vs. 50th percentile:= - 0.01, 95 % credible interval [CrI]: -0.11, 0.10). However, individual EDC concentrations were associated with UL in opposing directions: PCB138/158 was positively associated with UL (β for 25th-to-75th-percentile increase when all other chemicals were set to their 50th percentile = 0.18, 95 % CrI: -0.09, 0.44), whereas PBDE99 and p,p'-DDE were inversely associated with UL (β = -0.06, 95 % CrI: -0.21, 0.10 and β = -0.12, 95 % CrI: -0.34, 0.10, respectively). There was little evidence of interaction between EDCs.

Conclusion: In this prospective ultrasound study, a mixture of persistent EDCs was not appreciably associated with incident UL during 10 years of follow-up, but individual EDCs were associated with UL in opposite directions.

Background: Uterine leiomyomata (UL; fibroids) are hormone-dependent neoplasms that can cause significant gynecologic morbidity.

Authors: Amelia K Wesselink, Birgit Claus Henn, Victoria Fruh, Ruth J Geller, Chad M Coleman, Samantha Schildroth, Andreas Sjodin, Traci N Bethea, Nyia L Noel, Donna D Baird, Ganesa Wegienka, Lauren A Wise
Full Source: The Science of the total environment 2024 Aug 30:951:175871. doi: 10.1016/j.scitotenv.2024.175871.

Extracellular vesicles-derived long noncoding RNAs participated in benzene hematotoxicity by mediating apoptosis and autophagy

2024-08-28

Benzene is a common contaminant in the workplace and wider environment, which induces hematotoxicity. Our previous study has implicated that lncRNAs mediated apoptosis and autophagy induced by benzene. Nevertheless, the roles of extracellular vesicle(EVs)-derived lncRNAs in benzene toxicity are unknown. However, the role of EVs and EVs-derived lncRNAs in benzene-induced toxicity remains unclear. In this research, we explored the function of EVs and EVs-derived lncRNAs in cell-cell communication through benzene-induced apoptosis and autophagy. Our findings demonstrated that EVs derived from 1,4-BQ-treated cells treated cells and coculture with 1,4-BQ-treated cells enhanced apoptosis and autophagy via regulating the pathways of PI3K-AKT-mTOR and chaperone-mediated autophagy. Treating with GW4869 in 1,4-BQ-treated cells significantly inhibited EV secretion, which reduced apoptosis and autophagy. Furthermore, we identified a set of differentially expressed autophagy- and apoptosis-related lncRNAs using EVs-derived lncRNA sequencing. Among them, 8 candidate lncRNAs were upregulated in EVs derived from 1,4-BQ-treated cells, as determined by lncRNA sequencing and qRT-PCR. Importantly, these lncRNAs were also increased in the serum EVs of benzene-exposed workers. 1,4-BQ-treated cells released EVs that transfer differentially expressed lncRNAs, thereby inducing apoptosis and autophagy in the recipient cells. The above results support the hypothesis that EVs-derived lncRNAs participate in intercellular communication during benzene-induced hematotoxicity and function as potential biomarkers for risk assessment of benzene-exposed workers.

Authors: Yujiao Chen, Jingyu Wang, Wei Zhang, Xiaoli Guo, Jing Ren, Lei Zhang, Ai Gao

Full Source: Toxicology and applied pharmacology 2024 Aug 28:491:117076. doi: 10.1016/j.taap.2024.117076.

Benzene is a common contaminant in the workplace and wider environment, which induces hematotoxicity.

ENVIRONMENTAL RESEARCH

Photodegradation Processes and Weathering Products of Microfibers in Aquatic Environments

2024-08-31

Microplastics, particularly microfibers (MFs), pose a significant threat to the environment. Despite their widespread presence, the photochemical reactivity, weathering products, and environmental fate of MFs remain poorly understood. To address this knowledge gap, photodegradation experiments were conducted on three prevalent MFs: polyester (POL), nylon (NYL), and acrylic (ACR), to elucidate their degradation pathways, changes in surface morphology and polymer structure, and chemical and colloidal characterization of weathering products during photochemical degradation of MFs. The results showed that concentrations of dissolved organic carbon, chromophoric dissolved organic matter (DOM), and fluorescent components consistently increased during weathering, exhibiting a continuous release of DOM. Scanning electron microscopy and Raman spectroscopy revealed changes in the surface morphology and polymer spectra of the MFs. During the weathering experiments, DOM aromaticity (SUVA254) decreased, while spectral slope increased, indicating concurrent DOM release and degradation of aromatic components. The released DOM or nanoplastics were negatively charged with sizes between 128 and 374 nm. The production rate constants of DOM or the photochemical reactivity of MFs followed the order ACR > NYL ≥ POL, consistent with their differences in chemical structures. These findings provide an improved understanding of the photochemical reactivity, degradation pathways, weathering products, and environmental fate of microfibers in the environment.

Authors: Shimaa M Kteeba, Laodong Guo

Full Source: Environmental science & technology 2024 Aug 31. doi: 10.1021/acs.est.4c03667.

The influence of environmental factors related to Juvenile Dermatomyositis (JDM), its course and refractoriness to treatment

2024-08-30

Objective: To evaluate the influence of environmental factors and prematurity relating to juvenile dermatomyositis (JDM), its course and refractoriness to treatment.

Methods: A case-control study with 35 patients followed up at a tertiary hospital and 124 healthy controls, all residents of São Paulo. Patients were classified according to monocyclic, polycyclic or chronic disease courses and refractoriness to treatment. The daily concentrations of pollutants (inhalable particulate matter-PM10, sulfur dioxide-SO2, nitrogen dioxide-NO2, ozone-O3 and carbon monoxide-CO) were provided by the Environmental Company of São Paulo. Data from the population were obtained through a questionnaire.

Objective: To evaluate the influence of environmental factors and prematurity relating to juvenile dermatomyositis (JDM), its course and refractoriness to treatment.

.

Copyright Chemwatch 2024 ©

Results: Fifteen patients had monocyclic courses, and 19 polycyclic/chronic courses. Eighteen patients were refractory to treatment. Maternal occupational exposure to inhalable agents (OR = 17.88; IC 95% 2.15-148.16, p = 0.01) and exposure to O3 in the fifth year of life (third tertile > 86.28µg/m3; OR = 6.53, IC95% 1.60-26.77, p = 0.01) were risk factors for JDM in the multivariate logistic regression model. The presence of a factory/quarry at a distance farther than 200 meters from daycare/school (OR = 0.22; IC 95% 0.06-0.77; p = 0.02) was a protective factor in the same analysis. Prematurity, exposure to air pollutants/cigarette smoke/sources of inhalable pollutants in the mother's places of residence and work during the gestational period were not associated with JDM. Prematurity, maternal exposure to occupational pollutants during pregnancy as well as patient's exposure to ground-level pollutants up to the fifth year of life were not associated with disease course and treatment refractoriness.
Conclusion: Risk factors for JDM were maternal occupational exposure and exposure to O3 in the fifth year of life.

Authors: Clarissa C M Valões, Tamima M Arabi, Alfésio L F Braga, Lúcia M A Campos, Nádia E Aikawa, Kátia T Kozu, Clovis A Silva, Sylvia C L Farhat, Adriana M Elias
Full Source: Advances in rheumatology (London, England) 2024 Aug 30;64(1):64. doi: 10.1186/s42358-024-00408-5.

PHARMACEUTICAL/TOXICOLOGY

Eganelisib combined with immune checkpoint inhibitor therapy and chemotherapy in frontline metastatic triple-negative breast cancer triggers macrophage reprogramming, immune activation and extracellular matrix reorganization in the tumor microenvironment

2024-08-30

Background: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer with a poor prognosis particularly in the metastatic setting. Treatments with anti-programmed cell death protein-1/programmed death-ligand 1 (PD-L1) immune checkpoint inhibitors (ICI) in combination with chemotherapies have demonstrated promising clinical benefit in metastatic TNBC (mTNBC) but there is still an unmet need, particularly for patients with PD-L1 negative tumors. Mechanisms of resistance to ICIs in mTNBC include the presence of immunosuppressive tumor-associated macrophages (TAMs) in the tumor microenvironment (TME). Eganelisib is a potent and selective, small molecule PI3K-γ inhibitor

Background: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer with a poor prognosis particularly in the metastatic setting.

CHEMWATCH
Bulletin Board
Technical
SEP. 06, 2024

that was shown in preclinical studies to reshape the TME by reducing myeloid cell recruitment to tumors and reprogramming TAMs from an immune-suppressive to an immune-activating phenotype and enhancing activity of ICIs. These studies provided rationale for the clinical evaluation of eganelisib in combination with the anti-PD-L1 atezolizumab and nab-paclitaxel in firstline mTNBC in the phase 2 clinical trial MAcrophage Reprogramming in Immuno-Oncology-3 (MARIO-3, NCT03961698). We present here for the first time, in-depth translational analyses from the MARIO-3 study and supplemental data from eganelisib monotherapy Ph1/b study in solid tumors (MARIO-1, NCT02637531).
Methods: Paired pre-treatment and post-treatment tumor biopsies were analyzed for immunophenotyping by multiplex immunofluorescence (n=11), spatial transcriptomics using GeoMx digital spatial profiling (n=12), and PD-L1 immunohistochemistry, (n=18). Peripheral blood samples were analyzed using flow cytometry and multiplex cytokine analysis.
Results: Results from paired tumor biopsies from MARIO-3 revealed gene signatures of TAM reprogramming, immune activation and extracellular matrix (ECM) reorganization. Analysis of PD-L1 negative tumors revealed elevated ECM gene signatures at baseline that decreased after treatment. Gene signatures of immune activation were observed regardless of baseline PD-L1 status and occurred in patients having longer progression-free survival. Peripheral blood analyses revealed systemic immune activation.
Conclusions: This is the first report of translational analyses including paired tumor biopsies from a phase 2 clinical study of the first-in-class PI3K-γ inhibitor eganelisib in combination with atezolizumab and nab-paclitaxel in frontline mTNBC. These results support the mechanism of action of eganelisib as a TAM-reprogramming immunotherapy and support the rationale for combining eganelisib with ICI and chemotherapy in indications with TAM-driven resistance to ICI.

Authors: Brenda C O'Connell, Charley Hubbard, Nora Zizlsperger, Donna Fitzgerald, Jeffrey L Kutok, Judith Varner, Robert Ilaria Jr, Melody A Cobleigh, Dejan Juric, Kate H R Tkaczuk, Anthony Elias, Arielle Lee, Shaker Dakhil, Erika Hamilton, Hatem Soliman, Stephane Peluso
Full Source: Journal for immunotherapy of cancer 2024 Aug 30;12(8):e009160. doi: 10.1136/jitc-2024-009160.

A Phase I Trial of Alpelisib Combined With Capecitabine in Patients With HER2-Negative Metastatic Breast Cancer

2024-08-08

Background: Alpelisib is an oral α-specific class I PI3K inhibitor approved in combination with fulvestrant for the treatment of PIK3CA-mutated hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) metastatic breast cancer. The tolerability of this drug with the oral chemotherapy capecitabine is unknown.
Patients and methods: This phase I trial evaluated the dose-limiting toxicities (DLTs) and maximum tolerated dose (MTD) of alpelisib (250 mg or 300 mg daily for 3-weeks) with capecitabine (1000 mg/m2 twice daily for 2-weeks followed by a 1-week rest period) in patients with metastatic HER2-negative breast cancer, regardless of PIK3CA mutation status.
Results: Eighteen patients were treated with alpelisib-capecitabine. Half of the patients had HR+ breast cancer, and 16 had prior systemic therapy for metastatic disease. The MTD of alpelisib was 250 mg daily in combination with capecitabine 1000 mg/m2 twice daily. DLTs included hyperglycemia, QTc prolongation, fatigue, and chest pain. The most common grade 3 adverse event (AE) was hyperglycemia (28%). No grade 4 AEs were observed. Three patients discontinued therapy due to an AE. One-third of patients required dose reduction of both alpelisib and capecitabine. Four patients experienced a partial response and 8 patients experienced stable disease. The median progression-free survival was 9.7 months (95% CI 2.8-13.5 months) and median overall survival was 18.2 months (95% CI 7.2-35.2 months). Twelve patients had PIK3CA mutation testing completed, of these 2 had known or likely deleterious PIK3CA mutation.
Conclusion: This study provides safety data for an oral combination therapy of alpelisib-capecitabine and defines tolerable doses for further study.

Authors: Danielle M File, Yara Abdou, Jeremy Force, Dominic T Moore, Carey K Anders, Katherine Reeder-Hayes, Lisa A Carey, Hyman B Muss, Charles M Perou, P Kelly Marcom, E Claire Dees

Full Source: Clinical breast cancer 2024 Aug 8:S1526-8209(24)00213-1. doi: 10.1016/j.clbc.2024.08.001.

Background: Alpelisib is an oral α-specific class I PI3K inhibitor approved in combination with fulvestrant for the treatment of PIK3CA-mutated hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) metastatic breast cancer.

CHEMWATCH
Bulletin Board
Technical
SEP. 06, 2024

The toxic effect of 2,6-di-tert-butylphenol on embryonic development in zebrafish (Danio rerio): Decreased survival rate, morphological abnormality, and abnormal vascular development

2024-08-29

2,6-di-tert-butylphenol (2,6-DTBP) has been used extensively in plastics, rubber and polymer phenolic antioxidants. It is discharged into the aquatic environment through industrial waste. However, the toxicity assessment of 2,6-DTBP is insufficient. Here, zebrafish embryos were used as an animal model to investigate the toxicological effects of 2,6-DTBP. The results showed that 2,6-DTBP induced mitochondrial dysfunction and reactive oxygen species accumulation, which caused apoptosis, and further led to developmental toxicity of zebrafish embryos, such as delayed incubation, reduced survival rate, and increased malformation rate and heart rate. 2,6-DTBP can also cause morphological changes in the zebrafish endothelial cell (zEC) nucleus, inhibit zEC migration, trigger abnormal angiogenesis and zEC sprouting angiogenesis, and ultimately affect vascular development. In addition, 2,6-DTBP interfered with the endogenous antioxidant system, causing changes in activities of superoxide dismutase, catalase, and glutathione S-transferase and contents of malondialdehyde and glutathione. Transcriptome sequencing showed that 2,6-DTBP altered the mRNA levels of genes associated with vascular development, oxidative stress, apoptosis, extracellular matrix components and receptors. Integrative biomarker response assessment found that 12 μM 2,6-DTBP had the highest toxicity. These results indicated that 2,6-DTBP induced apoptosis through oxidative stress, leading to toxicity of zebrafish embryo development. This study contributes to understanding the effects of environmental 2,6-DTBP exposure on early development of aquatic organisms and draws public attention to the health risks posed by chemicals in aquatic organisms.

Authors: Juan Liu, Huiyun Wang, Mingyang Lu, Yuan Tian, Tingzhang Hu

Full Source: Environmental research 2024 Aug 29;262(Pt 1):119881. doi: 10.1016/j.envres.2024.119881.

2,6-di-tert-butylphenol (2,6-DTBP) has been used extensively in plastics, rubber and polymer phenolic antioxidants.

OCCUPATIONAL

Workplace Exposures Vary Across Neighborhoods in the US: Implications on Social Vulnerability and Racial/Ethnic Health Disparities

2024-08-30

Ignoring workplace exposures that occur beyond the local residential context in place-based risk indices like the CDC's Social Vulnerability Index (SVI) likely misclassifies community exposure by under-counting risks and obscuring true drivers of racial/ethnic health disparities. To investigate this hypothesis, we developed several place-based indicators of occupational exposure and examined their relationships with race/ethnicity, SVI, and health inequities. We used publicly available job exposure matrices and employment estimates from the United States (US) Census to create and map six indicators of occupational hazards for every census tract in the US. We characterized census tracts with high workplace-low SVI scores. We used natural cubic splines to examine tract level associations between the percentage of racial/ethnic minorities (individuals who are not non-Hispanic White) and the occupational indicators. Lastly, we stratified each census tract into high/low occupational noise, chemical pollutant, and disease/infection exposure to examine racial/ethnic health disparities to diabetes, asthma, and high blood pressure, respectively, as a consequence of occupational exposure inequities. Our results show that racial/ethnic minority communities, particularly those that are also low-income, experience a disproportionate burden of workplace exposures that may be contributing to racial/ethnic health disparities. When composite risk measures, such as SVI, are calculated using only information from the local residential neighborhood, they may systematically under-count occupational risks experienced by the most vulnerable communities. There is a need to consider the role of occupational justice on nationwide, racial/ethnic health disparities.

Authors: Abas Shkembi, Jon Zelner, Sung Kyun Park, Richard Neitzel

Full Source: Journal of racial and ethnic health disparities 2024 Aug 30. doi: 10.1007/s40615-024-02143-5.

Occupational agents-mediated asthma: From the perspective of autophagy

2024-08-29

Occupational asthma (OA) is a common occupational pulmonary disease that is frequently underdiagnosed and underreported. The complexity

Ignoring workplace exposures that occur beyond the local residential context in place-based risk indices like the CDC's Social Vulnerability Index (SVI) likely misclassifies community exposure by under-counting risks and obscuring true drivers of racial/ethnic health disparities.

CHEMWATCH
Bulletin Board
Technical
SEP. 06, 2024

of diagnosing and treating OA creates a significant social and economic burden, making it an important public health issue. In addition to avoiding allergens, patients with OA require pharmacotherapy; however, new therapeutic targets and strategies need further investigation. Autophagy may be a promising intervention target, but there is a lack of relevant studies summarizing the role of autophagy in OA. In this review consolidates the current understanding of OA, detailing principal and novel agents responsible for its onset. Additionally, we summarize the mechanisms of autophagy in HMW and LMW agents induced OA, revealing that occupational allergens can induce autophagy disorders in lung epithelial cells, smooth muscle cells, and dendritic cells, ultimately leading to OA through involving inflammatory responses, oxidative stress, and cell death. Finally, we discuss the prospects of targeting autophagy as an effective strategy for managing OA and even steroid-resistant asthma, encompassing autophagy interventions focused on organoids, organ-on-a-chip systems, nanomaterials vehicle, and nanobubbles; developing combined exposure models, and the role of non-classical autophagy in occupational asthma. In briefly, this review summarizes the role of autophagy in occupational asthma, offers a theoretical foundation for OA interventions based on autophagy, and identifies directions and challenges for future research.

Authors: Xiu He, Dengxiang Yao, Xiaoli Yuan, Jiaqi Ban, Yuxuan Gou, Mingdan You

Full Source: The Science of the total environment 2024 Aug 29:175880. doi: 10.1016/j.scitotenv.2024.175880.