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PHARMACEUTICAL/TOXICOLOGY

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CHEMICAL EFFECTS

Highly sensitive response to the toxicity of environmental chemicals in transparent casper zebrafish

2024-07-18

The response sensitivity to toxic substances is the most concerned performance of animal model in chemical risk assessment. Casper (mitfaw2/w2;mpv17a9/a9), a transparent zebrafish mutant, is a useful in vivo model for toxicological assessment. However, the ability of casper to respond to the toxicity of exogenous chemicals is unknown. In this study, zebrafish embryos were exposed to five environmental chemicals, chlorpyrifos, lindane, α-endosulfan, bisphenol A, tetrabromobisphenol A (TBBPA), and an antiepileptic drug valproic acid. The half-lethal concentration (LC50) values of these chemicals in casper embryos were 62-87 % of that in the wild-type. After TBBPA exposure, the occurrence of developmental defects in the posterior blood island of casper embryos was increased by 67-77 % in relative to the wild-type, and the halfmaximal effective concentration (EC50) in casper was 73 % of that in the wild type. Moreover, the casper genetic background significantly increased the hyperlocomotion caused by chlorpyrifos and lindane exposure compared with the wild type. These results demonstrated that casper had greater susceptibility to toxicity than wild-type zebrafish in acute toxicity, developmental toxicity and neurobehavioral toxicity assessments. Our data will inform future toxicological studies in casper and accelerate the development of efficient approaches and strategies for toxicity assessment via the use of casper.

Authors: Yingjun Xu, Yiming Han, Li Liu, Shanshan Han, Shibiao Zou, Bo Cheng, Fengbang Wang, Xunwei Xie, Yong Liang, Maoyong Song, Shaochen Pang

Full Source: The Science of the total environment 2024 Jul 18:174865. doi: 10.1016/j.scitotenv.2024.174865.

Microplastic-derived dissolved organic matter: Generation, characterization, and environmental behaviors

2024-07-18

Microplastics (MPs) represent a substantial and emerging class of pollutants distributed widely in various environments, sparking growing concerns about their environmental impact. In environmental systems, dissolved organic matter (DOM) is crucial in shaping the physical, chemical, and biological processes of pollutants while significantly

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contributing to the global carbon budget. Recent findings have revealed that microplastic-derived dissolved organic matter (MP-DOM) constitutes approximately 10 % of the DOM present on the ocean surface, drawing considerable attention. Hence, this study's primary objective is to explore, the generation, characterization, and environmental behaviors of MP-DOM. The formation and characteristics of MP-DOM are profoundly influenced by leaching conditions and types of MPs. This review delves into the mechanisms of the generation of MP-DOM and provides an overview of a wide array of analytical techniques, including ultravioletvisible (UV-Vis) spectroscopy, fluorescence spectroscopy, Fourier transform infrared spectroscopy (FTIR), and mass spectroscopy, used to assess the MP-DOM characteristics. Furthermore, this review investigates the environmental behaviors of MP-DOM, including its impacts on organisms, photochemical processes, the formation of disinfection by-products (DBPs), adsorption behavior, and its interaction with natural DOM. Finally, the review outlines research challenges, perspectives for future MP-DOM research, and the associated environmental implications.

Authors: Xigui Liu, Liping Fang, Jorge L Gardea-Torresdey, Xiaoxia Zhou, Bing Yan

Full Source: The Science of the total environment 2024 Jul 18:948:174811. doi: 10.1016/j.scitotenv.2024.174811.

Novel herbicide flusulfinam: absolute configuration, enantioseparation, enantioselective bioactivity, toxicity and degradation in paddy soils

2024-06-21

Background: Flusulfinam, a novel chiral herbicide, effectively controls Echinochloa crusgalli and Digitaria sanguinalis in paddy fields, indicating significant potential for practical agricultural applications. However, limited information is available on flusulfinam from a chiral perspective. A comprehensive evaluation of the enantiomeric levels of flusulfinam was performed.

Results: Two enantiomers, R-(+)- and S-(-)-flusulfinam, were separately eluted using a Chiralcel OX-RH column. The bioactivity of R-flusulfinam against the two was 1.4-3.1 fold that of Rac-flusulfinam against two weed species. R-flusulfinam toxicity to Danio rerio larvae and Selenastrum capricornutumwere was 0.8- and 3.0-fold higher than Rac-flusulfinam, respectively. Degradation experiments were conducted using soil samples from four Chinese provinces. The findings indicated that S-flusulfinam (half-life T1/2 = 40.8 days) exhibits preferential degradation than R-flusulfinam (T1/2 = 46.2-57.8 days) in the soils of three provinces. Under

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anaerobic conditions, soil from Anhui exhibited preferential degradation of R-flusulfinam (T1/2 = 46.2 days) over S-flusulfinam (T1/2 = 63 days). Furthermore, two hydrolysis products of flusulfinam (M299 and M100) are proposed for the first time.

Conclusion: The enantioselective bioactivity, toxicity and degradation of flusulfinam were investigated. Our findings indicate that R-flusulfinam is an extremely effective and low-toxicity enantiomer for the tested species. The soil degradation test indicated that the degradation of flusulfinam was accelerated by higher organic matter content and lower soil pH. Furthermore, microbial communities may play a crucial role in driving the enantioselective degradation processes. This study lays the groundwork for the systematic evaluation of flusulfinam from an enantiomeric perspective. © 2024 Society of Chemical Industry.

Authors: Shiling Liu, Xiaoli Li, Junqi Zhu, Liying Liang, Heng Zhang, Ying Liao, Jiaheng Li, Lei Lian, Huihua Tan, Feng Zhao Full Source: Pest management science 2024 Jun 21. doi: 10.1002/ps.8251.

ENVIRONMENTAL RESEARCH

Air pollution generated in an industrial region: effect on the cardiovascular health of humans and damage caused to a plant species, Piper gaudichaudianum (Piperaceae), used for biomonitoring

2024-07-18

Atmospheric pollution due to anthropogenic activities is a complex mixture of gasses and particulate matter (PM) that is currently one of the main causes of premature death in the world. Similarly, it is also capable of directly interfering with plant species by reducing their photosynthetic capacity and growth and killing cells. This work is about an observational study conducted in a region with two industries: a mine and an automobile parts manufacturer. Mining rocks is a source of PM in the air like that caused by other industrial activities. Twenty-five people that work or live in the industrial region cited (area A) and 25 people that live further away (area B) were selected to evaluate their vital signs and conduct a transthoracic echocardiogram. Leaves of Piper gaudichaudianum (Piperaceae), a native plant species, were also collected in both areas and evaluated in a laboratory. The PM accumulated on the leaves was evaluated using scanning electron microscopy (SEM) and inductively coupled plasma-optical emission spectrometry (ICP-OES). A statistical difference (P < 0.05) was verified for the levels of systolic blood pressure

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(SBP), diastolic blood pressure (DBP), and left ventricular mass index by echocardiography; the values were greater in people in area A. For the plant analysis, there was a statistical difference for all characters evaluated, chlorophyll levels, fresh mass, dry mass and leaf area were reduced, and thickness was greater in area A (P < 0.001). The PM analysis revealed a predominance of silicon, iron, and aluminum chemical elements. The present study suggests that particulate matter pollution is harmful to both humans and the flora.

Authors: Ana Carenina Gheller Schaidhauer, Fábio Voigt da Costa, João Carlos Ferreira de Melo-Júnior

Full Source: Environmental pollution (Barking, Essex: 1987) 2024 Jul 18:124584. doi: 10.1016/j.envpol.2024.124584.

Understanding and addressing microplastic pollution: Impacts, mitigation, and future perspectives

2024-07-17

Improper disposal of household and industrial waste into water bodies has transformed them into de facto dumping grounds. Plastic debris, weathered on beaches degrades into micro-particles and releases chemical additives that enter the water. Microplastic contamination is documented globally in both marine and freshwater environments, posing a significant threat to aquatic ecosystems. The small size of these particles makes them susceptible to ingestion by low trophic fauna, a trend expected to escalate. Ingestion leads to adverse effects like intestinal blockages, alterations in lipid metabolism, histopathological changes in the intestine, contributing to the extinction of vulnerable species and disrupting ecosystem balance. Notably, microplastics (MPs) can act as carriers for pathogens, potentially causing impaired reproductive activity, decreased immunity, and cancer in various organisms. Studies have identified seven principal sources of MPs, including synthetic textiles (35%) and tire abrasion (28%), highlighting the significant human contribution to this pollution. This review covers various aspects of microplastic pollution, including sources, extraction methods, and its profound impact on ecosystems. Additionally, it explores preventive measures, aiming to guide researchers in selecting techniques and inspiring further investigation

Improper disposal of household and industrial waste into water bodies has transformed them into de facto dumping grounds.



into the far-reaching impacts of microplastic pollution, fostering effective solutions for this environmental challenge.

Authors: Rajesh Debnath, Gora Shiva Prasad, Adnan Amin, Monisa M Malik, Ishtiyaq Ahmad, Adnan Abubakr, Simanku Borah, Mohd Ashraf Rather, Federica Impellitteri, Ifra Tabassum, Giuseppe Piccione, Caterina Faggio Full Source: Journal of contaminant hydrology 2024 Jul 17:266:104399. doi: 10.1016/j.jconhyd.2024.104399.

Tracking fine particles in urban and rural environments using honey bees as biosamplers in Mexico

2024-07-18

This work explores the efficiency of honey bees (Apis mellifera) as biosamplers of metal pollution. To understand this, we selected two cities with different urbanization (a medium-sized city and a megacity), and we collected urban dust and honey bees captured during flight. We sampled two villages and a university campus as control areas. The metal content in dust was analyzed by inductively coupled plasma mass spectrometry (ICP-MS). Atomic Force Microscopy (AFM) and Scanning electron microscopy (SEM) were used to investigate the shape and size distribution of the particles, and to characterize the semiquantitative chemical composition of particles adhered to honey bee's wings. Principal Component Analysis (PCA) shows a distinctive urban dust geochemical signature for each city, with component 1 defining V-Cr-Ni-Tl-Pt-Pb-Sb as characteristic of Mexico City and Ce-As-Zr for dust from Hermosillo. Particle count using SEM indicates that 69% and 63.4% of the resuspended dust from Hermosillo and Mexico City, respectively, corresponds to PM2.5. Instead, the particle count measured on the honey bee wings from Hermosillo and Mexico City is mainly PM2.5, 91.4% and 88.9%, respectively. The wings from honey bees collected in the villages and the university campus show much lower particle amounts. AFM-histograms confirmed that the particles identified in Mexico City have even smaller sizes (between 60 and 480 nm) than those in Hermosillo (between 400 and 1400 nm). Particles enriched in As, Zr, and Ce mixed with geogenic elements such as Si, Ca, Mg, K, and Na dominate honey bee' wings collected in Hermosillo. In contrast, those particles collected from Mexico City contain V, Cr, Ni, Tl, Pt, Pb, and Sb. Such results agree with the urban dust data. This work shows that honey

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bees are suitable biosamplers for the characterization of fine dust fractions by microscopy techniques and reflect the urban pollution of the sites.

Authors: Diana Meza-Figueroa, Francisco Berrellez-Reyes, Benedetto Schiavo, Ofelia Morton-Bermea, Belem Gonzalez-Grijalva, Claudio Inguaggiato, Erika Silva-Campa

Full Source: Chemosphere 2024 Jul 18:142881. doi: 10.1016/j. chemosphere.2024.142881.

PHARMACEUTICAL/TOXICOLOGY

Perfluorooctanesulfonic acid (PFOS) induced cancer related DNA methylation alterations in human breast cells: A whole genome methylome study

2024-07-18

DNA methylation plays a pivotal role in cancer. The ubiquitous contaminant perfluorooctanesulfonic acid (PFOS) has been epidemiologically associated with breast cancer, and can induce proliferation and malignant transformation of normal human breast epithelial cells (MCF-10A), but the information about its effect on DNA methylation is sparse. The aim of this study was to characterize the whole-genome methylome effects of a PFOS in our breast cell model and compare the findings with previously demonstrated DNA methylation alterations in breast tumor tissues. The DNA methylation profile was assessed at single CpG resolution in MCF-10A cells treated with 1 µM PFOS for 72 h by using Enzymatic Methyl sequencing (EM-seq). We found 12,591 differentially methylated CpG-sites and 13,360 differentially methylated 100 bp tiles in the PFOS exposed breast cells. These differentially methylated regions (DMRs) overlapped with 2406 genes of which 494 were long non-coding RNA and 1841 protein coding genes. We identified 339 affected genes that have been shown to display altered DNA methylation in breast cancer tissue and several other genes related to cancer development. This includes hypermethylation of GACAT3, DELEC1, CASC2, LCIIAR, MUC16, SYNE1 and hypomethylation of TTN and KMT2C. DMRs were also found in estrogen receptor genes (ESR1, ESR2, ESRRG, ESRRB, GREB1) and estrogen responsive genes (GPER1, EEIG1, RERG). The gene ontology analysis revealed pathways related to cancer phenotypes such as cell adhesion and growth. These findings improve the understanding of PFOS's potential role in breast cancer and illustrate the value of whole-genome methylome analysis in uncovering mechanisms

DNA methylation plays a pivotal role in cancer.



of chemical effects, identifying biomarker candidates, and strengthening epidemiological associations, potentially impacting risk assessment.

Authors: Paula Pierozan, Andrey Höglund, Eleftheria Theodoropoulou, Oskar Karlsson

Full Source: The Science of the total environment 2024 Jul 18:174864. doi: 10.1016/j.scitotenv.2024.174864.

Drug metabolism of ciprofloxacin, ivacaftor, and raloxifene by Pseudomonas aeruginosa cytochrome P450 CYP107S1

2024-07-18

Drug metabolism is one of the main processes governing the pharmacokinetics and toxicity of drugs via their chemical biotransformation and elimination. In humans, the liver, enriched with cytochrome P450 (CYP) enzymes, plays a major metabolic and detoxification role. The gut microbiome and its complex community of microorganisms can also contribute to some extent to drug metabolism. However, during an infection when pathogenic microorganisms invade the host, our knowledge of the impact on drug metabolism by this pathobiome remains limited. The intrinsic resistance mechanisms and rapid metabolic adaptation to new environments often allow the human bacterial pathogens to persist, despite the many antibiotic therapies available. Here, we demonstrate that a bacterial CYP enzyme, CYP107S1, from Pseudomonas aeruginosa, a predominant bacterial pathogen in cystic fibrosis (CF) patients, can metabolize multiple drugs from different classes. CYP107S1 demonstrated high substrate promiscuity and allosteric properties much like human hepatic CYP3A4. Our findings demonstrated binding and metabolism by the recombinant CYP107S1 of fluoroquinolone antibiotics (ciprofloxacin and fleroxacin), a CF transmembrane conductance regulator potentiator (ivacaftor), and a SERM antimicrobial adjuvant (raloxifene). Our in vitro metabolism data were further corroborated by molecular docking of each drug to the heme active site using a CYP107S1 homology model. Our findings raise the potential for microbial pathogens modulating drug concentrations locally at the site of infection, if not systemically, via CYP-mediated biotransformation reactions. To our knowledge, this is the first report of a CYP enzyme from a known bacterial pathogen that is capable of metabolizing clinically utilized drugs.

Authors: Sylvie E Kandel, Brian C Tooker, Jed N Lampe Full Source: The Journal of biological chemistry 2024 Jul 18:107594. doi: 10.1016/j.jbc.2024.107594. Drug metabolism is one of the main processes governing the pharmacokinetics and toxicity of drugs via their chemical biotransformation and elimination.

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Actinium-225 as an example for monitoring of internal exposure of occupational intakes of radionuclides in face of new nuclear-medical applications for short-lived alpha emitting particles

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2024-07-20

Monitoring of internal exposure to short-lived alpha-emitting radionuclides such as actinium-225 (225Ac), which are becoming increasingly important in nuclear medicine, plays an important role in the radiation protection of occupationally exposed persons. After having tested gamma spectrometry, liquid scintillation counting and alpha spectrometry for monitoring of internal exposure, the focus of the present study was on solid phase extraction of 225Ac from urine in combination with alpha spectrometry. The development of the method was based on recent findings from the literature on this topic. The method was used in a pilot phase to monitor internal exposure of four workers who were directly or indirectly involved in the manufacture and/or use of 225Ac. The monitoring protocol allowed a relatively short 24-hour urine sample analysis with excellent recovery of the internal standard, but it did not allow for a detection limit of less than 1 mBq nor a sufficient yield of 225Ac. Based on these results it is concluded that an in vitro excretion analysis alone is not appropriate for monitoring internal exposure to 225Ac. Instead, different radiation monitoring techniques have to be combined to ensure the radiation protection of employees.

Authors: Sven Hartmann, Kerstin Taubner, Tobias Vogt, Oliver Meisenberg, Uwe-Karsten Schkade, Christian Steyer, Marian Meckel, Christian Kesenheimer

Full Source: Radiation and environmental biophysics 2024 Jul 20. doi: 10.1007/s00411-024-01081-4.

A cross-sectional comparison of gut metagenomes between dairy workers and community controls

2024-07-20

Background: As a nexus of routine antibiotic use and zoonotic pathogen presence, the livestock farming environment is a potential hotspot for the emergence of zoonotic diseases and antibiotic resistant bacteria. Livestock can further facilitate disease transmission by serving as intermediary hosts for pathogens before a spillover event. In light of this, we aimed to characterize the microbiomes and resistomes of dairy workers, whose

Monitoring of internal exposure to short-lived alpha-emitting radionuclides such as actinium-225 (225Ac), which are becoming increasingly important in nuclear medicine, plays an important role in the radiation protection of occupationally exposed persons.

exposure to the livestock farming environment places them at risk for facilitating community transmission of antibiotic resistant genes and emerging zoonotic diseases.

Results: Using shotgun sequencing, we investigated differences in the taxonomy, diversity and gene presence of 10 dairy farm workers and 6 community controls' gut metagenomes, contextualizing these samples with additional publicly available gut metagenomes. We found no significant differences in the prevalence of resistance genes, virulence factors, or taxonomic composition between the two groups. The lack of statistical significance may be attributed, in part, to the limited sample size of our study or the potential similarities in exposures between the dairy workers and community controls. We did, however, observe patterns warranting further investigation including greater abundance of tetracycline resistance genes and prevalence of cephamycin resistance genes as well as lower average gene diversity (even after accounting for differential sequencing depth) in dairy workers' metagenomes. We also found evidence of commensal organism association with tetracycline resistance genes in both groups (including Faecalibacterium prausnitzii, Ligilactobacillus animalis, and Simiaoa sunii).

Conclusions: This study highlights the utility of shotgun metagenomics in examining the microbiomes and resistomes of livestock workers, focusing on a cohort of dairy workers in the United States. While our study revealed no statistically significant differences between groups in taxonomy, diversity and gene presence, we observed patterns in antibiotic resistance gene abundance and prevalence that align with findings from previous studies of livestock workers in China and Europe. Our results lay the groundwork for future research involving larger cohorts of dairy and non-dairy workers to better understand the impact of occupational exposure to livestock farming on the microbiomes and resistomes of workers.

Authors: Pauline Trinh, Sarah Teichman, Marilyn C Roberts, Peter M Rabinowitz, Amy D Willis

Full Source: BMC genomics 2024 Jul 20;25(1):708. doi: 10.1186/s12864-024-10562-1.