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CHEMICAL EFFECTS

High-throughput screening of estrogen receptor activity for personalized mixtures of persistent organic pollutants detected in blood of Swedish adults

2025-11-20

Toxicological studies of single chemicals overlook the real-world complexity of human exposure, where multiple compounds may interact to disrupt biological processes such as endocrine signaling. Moreover, the chemical exposome, the sum of an individual's chemical burden, varies markedly between people, yet its biological implications remain unclear. To address this gap, we reconstructed individualized human chemical exposomes to assess their effects on estrogen receptor (ER) activity. Sixteen exposomes comprising 24 persistent organic pollutant (POP) were derived from blood profiles of participants in the Swedish Västerbotten Intervention Programme. Using automated, non-contact acoustic liquid dispensing, we reconstructed 14 personalized mixtures (PMs) reflecting individual blood compositions and two formulated mixtures (FM) representing the cohort's median and maximum population exposure levels. ER activity was assessed in VM7Luc4E2 cells using a high-throughput 384-well adaption of the OECD No. 455 assay at 1×, 10× and 100× blood concentrations. While most individual POPs showed no or weak ER activity, three mixtures induced ER agonism. The PM-high, corresponding to the individual with the highest total POP levels, and the FM-Median activated the ER at 100×, while the FM-Maximum induced activation at 10× and 100×. Removing β-HCH and trans-nonachlor from the active mixtures abolished or reduced ER activity. Co-treatment with physiological estradiol levels increased ER responses in six mixtures, PM#1 (1× and 10×), PM#4 (100×), PM#8 (10×), PM#9 (100×), PM#10 (1×) and the FM-Median (1×), indicating potentiation of endogenous hormonal signaling. Overall, this study reveals endocrine activity in real-world POP mixtures and advances high-throughput screening as a scalable approach for individualized exposome-based health risk evaluation.

Authors: Luã Reis, Denise Strand, Andrey Höglund, Bo Lundgren, Ingvar A Bergdahl, Jonathan W Martin, Oskar Karlsson

Full Source: Environmental research 2025 Nov 20:123388. doi: 10.1016/j.envres.2025.123388.

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What do people need to know about endocrine disrupting chemicals and health? A mental models approach using focus groups of community-engaged research teams and a national survey

2025-11-22

Background: Endocrine disrupting chemicals (EDCs), which interfere with the body's natural hormones, are ubiquitous in everyday environments and consumer products. Nearly everyone is routinely exposed, and growing evidence links them to adverse health outcomes including cancers, impaired fertility, metabolic disorders, and neurodevelopmental effects. Major medical and scientific groups recommend exposure reduction. To make informed decisions about individual- and societal-level exposures to EDCs, people need relevant knowledge. Knowledge is one component of environmental health literacy, a multidimensional concept supporting readiness to protect health from environmental risks. This study sought to develop expert consensus about communications targets for EDCs and to learn how public knowledge matches these targets.

Methods: We convened focus groups with community-engaged research teams (n = 38) to define targets for public understanding. We coded transcripts, mapped causal pathways influencing EDC exposures and health outcomes using a mental models approach, and identified communication priorities. We then fielded a quantitative online survey among adults living in the U.S. (n = 504) to compare their knowledge with the mental model. We computed response frequencies and used multiple regression to evaluate associations between a knowledge index and participant characteristics.

Results: Focus group participants highlighted that people need to know that EDCs affect nearly all systems in the human body and that scientific evidence supports limiting exposure. They emphasized that policy controls can be more effective than personal action at reducing exposure, and that current U.S. chemicals regulations are not protective. Survey respondents were generally aware that EDCs can affect fertility, cancer, and child brain development (84-90%, n = 426-452), and they had some understanding of exposure pathways (58-86%, n = 295-435). However, most participants had large knowledge gaps about U.S. chemicals regulation and wrongly believed that chemicals must be safety-tested before being used in products (82%, n = 414), that product ingredients must be disclosed (73%, n = 368), and that restricted chemicals cannot be replaced by similar substitutes (63%, n = 317).

Conclusions: U.S. adults typically understood that EDCs affect health. However, incomplete information about how people get exposed to EDCs and misconceptions about U.S. chemicals regulations limit appropriate actions. These knowledge gaps are targets for future communications about EDCs and harmful chemicals more broadly.
Authors: Katherine E Boronow, Julia Green Brody
Full Source: BMC public health 2025 Nov 22. doi: 10.1186/s12889-025-25561-4.

Interpretable machine learning framework for predicting pesticide phytotoxicity in wastewater reuse: Integrating molecular, quantum, and experimental descriptors

2025-11-20
Pesticides are essential for crop protection, but their potential toxicity poses significant environmental and health risks. Although numerous toxicological studies have been conducted, accurately predicting pesticide phytotoxicity remains challenging due to the complex interactions between molecular properties and environmental factors. Current predictive models, such as quantitative structure-activity relationship (QSAR) approaches, often rely predominantly on molecular descriptors, neglecting the influence of contextual environmental conditions.
This study addresses this gap by developing an explainable machine learning (ML) framework for predicting pesticide phytotoxicity (EC50) that integrates molecular descriptors, quantum chemical descriptors (QCDs), and experimental conditions. This integration of intrinsic chemical properties and contextual environmental factors not only enhanced predictive accuracy but also provided crucial model interpretability, moving beyond traditional black-box approaches. Using a carefully curated dataset from seed germination and growth inhibition assays across diverse plant species and media types, XGBoost demonstrated superior performance, achieving an R2 of 0.69 and RMSE of 0.80 in 10-fold cross-validation, and an R2 of 0.75 and RMSE of 0.81 in external validation. Model interpretability was explored using Shapley Additive Explanations (SHAP), partial dependence plots (PDPs), and two-dimensional PDPs, revealing that exposure duration, log Koc, and water solubility were key determinants of phytotoxicity. Local SHAP analysis confirmed the mechanistic consistency of our model with established toxicological principles, showing how contextual exposure factors modulate compound-specific toxicity outcomes. Overall, this study demonstrates that interpretable ML models can enhance ecotoxicological assessments by combining predictive accuracy with mechanistic insights, offering

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a valuable tool for environmental monitoring, sustainable pesticide regulation, and agricultural wastewater reuse.
Authors: Aubin Siewetcheu Toukak, Wenjie Gao, Xianglin Chang, Ning Li, Guanyi Chen
Full Source: Environmental research 2025 Nov 20:289:123389. doi: 10.1016/j.envres.2025.123389.

ENVIRONMENTAL RESEARCH

Current Insights into the Impact of Plastic-derived Pollutants (Phthalates), Microplastics, and Nanoplastics on Hypothalamic Phenotype and Molecular Pathways: A Scoping Review

2025-11-19
Plastic is a ubiquitous material worldwide, and its derivatives - such as phthalates as Endocrine-Disrupting Chemicals (EDCs) derived from plastics and Microplastics (MPs) and Nanoplastics (NPs) as plastics waste - have raised increasing concern due to their potential adverse effects on human health, particularly on the neuroendocrine system and hypothalamic regulatory pathways. This critical scoping review integrates experimental and theoretical evidence on the metabolic impacts of chemical additives (phthalates) and micro and nanometric plastic waste (MNPs), emphasizing hypothalamic alterations and their systemic consequences. The eligibility criteria were to select articles that specifically traced the correlation between exposure to phthalates or MPs/NPs on the hypothalamic structure or molecular aspects, from studies present in PubMed using the mapping method by Nanoplastics and hypothalamus, Microplastics and hypothalamus, and Phthalates and hypothalamus. Plastic-derived EDCs have been shown to impair energy homeostasis, eating behavior, reproduction, and neurodevelopment. Both gestational and chronic exposures promote hypothalamic inflammation and disrupt key metabolic pathways by altering the sensitivity of hormone receptors, axis pathways, reproductive parameters, and biological development. Evidence also highlights sex-specific differences in hypothalamic responses and the role of EDCs in inducing epigenetic changes with potential transgenerational transmission. Despite these advances, significant gaps remain, particularly regarding studies directly targeting the hypothalamus and its nuclei. Elucidating the neurotoxic mechanisms of plastics and their derivatives is

essential to guide public health strategies and regulatory policies aimed at mitigating exposure risks.
Authors: Matheus Naia Fioretto, Victória Cristina Pinha, Carolina Beatriz Pinheiro Basso, Patrick Vieira de Souza, Natália Magosso, Mirella Franco Moreira, Vanessa Aguiar Rocha, Luis Antonio Justulin, Wellerson Rodrigo Scarano
Full Source: Environmental pollution (Barking, Essex: 1987) 2025 Nov 19:127413. doi: 10.1016/j.envpol.2025.127413.

Sources, health risks, environmental implications, and management strategies of microplastics with a focus on landfill leachate

2025-11-21
Plastic waste is one of the most common types of waste found in municipal solid waste (MSW), that ends up in landfills. Various physical, chemical, and biological processes can transform plastic waste into microplastics (MPs), which are the plastic particles less than 5 mm in size. MPs have unveiled significant threats to human health and the environment. Since landfill leachate is a notable source of both primary and secondary MPs, this paper addresses the existing knowledge gap by reviewing studies on MP detection in landfill leachates from domestic and international sources. The review covers the abundance, characteristics (such as polymer type, size, color, and shape), also the health and environmental risks associated with MPs. It also discusses the effectiveness of current leachate treatment plants in removing these particles. Furthermore, the implications of nanoplastics (NPs), their detection, and the challenges faced by existing treatment processes are examined. While most studies focus on MP detection and removal, there is a pressing need for further research on NPs and their fate in landfill leachate effluent, which is eventually discharged into aquatic environments. Management strategies for MPs in landfill leachate are compared across different treatment technologies. Additionally, some critical topics and future perspectives are proposed to better understand the real-world effects of MPs in human health-related risk assessments and toxicological thresholds.
Authors: Mehrdad Safaei, Parnia Bashardoust, Babak Kakavandi, Emad Dehghanifard, Suresh Sagadevan, Rasool Pelalak
Full Source: Journal of environmental management 2025 Nov 21:396:127966. doi: 10.1016/j.jenvman.2025.127966.

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PHARMACEUTICAL/TOXICOLOGY

Exposure to diesel particulates induces an immunosuppressive microenvironment that promotes the progression of lung cancer

2025-11-21
A comprehensive understanding of the mechanisms by which air pollutant exposure drives cancer progression remains incomplete. Particulate matter has been shown to induce genotoxicity and mutagenesis through oxidative stress both in vivo and in vitro. However, its impact on the pulmonary immune microenvironment and its role in modulating anti-tumour immune responses remains poorly characterized. Here, we report that chronic exposure to diesel exhaust particles (DEPs), a major component of PM2.5, induces an immunosuppressive lung microenvironment that promotes tumour progression in a KRAS-driven lung adenocarcinoma model (KrasLSL-G12D/+-Trp53lox/lox or KP mice). This environment is characterized by the emergence of PMN-MDSC (CD14pos PMNs) that exhibit NET formation and an immunosuppressive gene expression and functional profile. Additionally, we observed increased infiltration of regulatory T cells (Tregs), and upregulation of exhaustion/activation and immunosuppressive markers on T cells, factors that likely contribute to the increased tumour burden and enhanced tumour cell proliferation seen in DEP-exposed KP mice. Our study reveals how chronic DEP exposure reshapes the lung microenvironment in ways that may impair the ability to mount effective anti-tumour immune responses. These findings highlight the need for stronger public and occupational health policies aimed at reducing air pollution and its associated disease burden.
Authors: Marie-Laure Delhez, Maëlle Bosmans, Lucia Rodriguez Rodriguez, Alison Gillard, Silvia Blacher, Arnaud Blomme, Pierre Close, Bénédicte Machiels, Marie-Julie Nokin, Didier Cataldo
Full Source: Neoplasia (New York, N.Y.) 2025 Nov 21:71:101255. doi: 10.1016/j.neo.2025.101255.

Fiber length and shape-dependent differences in hepatic nanomaterial localization in mice following pulmonary exposure

2025-11-22
Background: Inhaled nanomaterials can translocate from the lungs into systemic circulation and reach the liver, which is the main secondary

organ for nanomaterial uptake, potentially causing adverse effects. Understanding how inhaled nanomaterials localize within liver tissue is important for understanding their clearance mechanisms and potential toxicity. Previous in vivo studies have primarily focused on spherical particles, highlighting the need for studies on fiber-shaped nanomaterials.
Methods: This study examines the hepatic distribution of five fiber-shaped nanomaterials (three multiwalled carbon nanotubes, gallium phosphide nanowires, and short TiO_2 nanotubes) compared to spherical TiO_2 nanoparticles. Liver samples were collected at 1, 3, 6, and 12 months after pulmonary exposure using a single intratracheal (IT) instillation in mice. Paraffin-embedded liver sections were stained with Hematoxylin and Eosin (H&E), and analyzed using enhanced darkfield microscopy. The localization of the nanomaterials within sections was categorized into four categories: hepatocyte, non-parenchymal cell, sinusoid/vessel, and another placement. Localization was further validated using cell-specific immunohistochemical staining. Furthermore, morphological changes were assessed in liver sections and 1 year post-exposure from mice following pulmonary exposure to eleven different MWCNTs.
Results: The hepatic localization of six different nanomaterials were assessed, with more than 10,000 fibers or particles manually counted across all samples. There were significant differences in the localization of long and thick fibers as compared to spherical nanoparticles and short and thin fibers, at all assessed post-exposure time points. Long and thick fiber-shaped nanomaterials were more frequently localized within the liver parenchyma compared to spherical particles and the short TiO2 tubes, which were more frequently found in non-parenchymal cells. Histological analysis revealed that short, thin, and entangled MWCNTs caused minor tissue alterations, including inflammatory cell infiltration and mild connective tissue hyperplasia in portal zones, whereas long and thick MWCNTs did not induce morphological changes.
Conclusion: These findings demonstrate that the intrahepatic localization of nanomaterials is strongly influenced by fiber shape and dimensions.

Authors: Mathilde Sundberg, Trine Berthing, Pernille Høgh Danielsen, Alicja Mortensen, Józef Szarek, Christelle N Prinz, Pernille Tveden-Nyborg, Ulla Vogel

Full Source: Particle and fibre toxicology 2025 Nov 22. doi: 10.1186/s12989-025-00652-7.

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Low-dose occupational ionising radiation exposure and gastrointestinal cancer mortality among US radiologic technologists, 1983-2021

2025-11-23

Objectives: We evaluated the relationship between cumulative occupational ionising radiation exposure and gastrointestinal cancer mortality in a cohort of US radiologic technologists (USRT).
Methods: Among 106 072 USRT cohort participants who were cancer-free at completion of the baseline questionnaire (1983-1998, representing completion of the first (1983-1989) or second questionnaire (1994-1998) as baseline), protracted low- to moderate-dose occupational ionising radiation exposure was evaluated in relation to gastrointestinal cancer mortality over the follow-up period (through 2021). Poisson regression was used to calculate linear excess relative rates (ERR) of gastrointestinal cancer mortality per 100 mGy colon-absorbed dose (mean=15 mGy; range 0-754 mGy), lagged 10 years, adjusting the baseline mortality rate for attained age, sex, birth cohort, race and other potential confounders (alcohol consumption, smoking, body mass index, non-steroidal anti-inflammatory drug (NSAID) use).
Results: Over follow-up (mean=31.4 years), 570 pancreatic, 504 colon, 171 liver, 131 oesophageal, 106 stomach and 73 rectal cancer deaths were identified. In the full cohort, no significant dose-response relationships were observed for pancreatic, colon, liver, oesophageal or rectal cancer mortality. A non-significant positive association for stomach cancer mortality was observed in a model minimally adjusted for attained age, sex and birth cohort; however, this association was attenuated after additionally adjusting for race and NSAID use (ERR/100mGy=1.56; 95% CI <0 to 159). Evidence for effect modification for stomach cancer mortality was observed by birth year (P-interaction=0.002) and year first worked (0.004), although based on small number of deaths, most positive associations within categories were not statistically significant.
Conclusions: In this nationwide cohort of radiologic technologists, cumulative occupational ionising radiation exposure was not clearly associated with mortality from specific gastrointestinal cancers. Studies with cancer incidence follow-up and pooled analyses of ionising radiation-

exposed populations may provide more comprehensive and robust dose-response estimates for specific gastrointestinal cancers.
Authors: Jim Z Mai, Raquel Velazquez-Kronen, Martha S Linet, Jo L Freudenheim, Jean Wactawski-Wende, Taeeun Kwon, Choonsik Lee, Dale L Preston, Bruce H Alexander, Elizabeth K Cahoon, Cari M Kitahara
Full Source: Occupational and environmental medicine 2025 Nov 23:oemed-2025-110223. doi: 10.1136/oemed-2025-110223.

OCCUPATIONAL

Oxidative stress, inflammation and the metabolic EpOME are associated with occupational exposure to isoflurane

2025-11-20
This study assessed the occupational exposure to the waste anesthetic gas (WAG) isoflurane in veterinarians focusing on oxidative stress and inflammatory markers in addition to metabolomic profiling. This was a case-control study with matched individuals related to dosimeter data for WAG. Systemic oxidative stress markers (malondialdehyde, 8-iso-prostaglandin F2α and carbonylated proteins) were screened, as well as carbonylated protein degradation products and 8-hydroxydeoxyguanosine in urine. Cholesterol and fractions were also assessed. Antioxidant enzymes were evaluated in washed red blood cells, while antioxidant capacity was evaluated in plasma. Primary and oxidative DNA damage were assessed using comet assays. Inflammatory markers were detected via flow cytometry. Untargeted metabolomics were evaluated in plasma by flow infusion electrospray ionization high-resolution mass spectrometry (FIE-MS). Dosimeter data indicated high-level of WAG exposure by veterinarians which was associated with elevated lipid and protein oxidations as well as DNA damage (primary lesions and oxidized pyrimidines). The antioxidant response showed reduced superoxide dismutase and elevated glutathione peroxidase activities. Inflammatory profiling revealed higher levels of IL-8, IL-12p70, IL-17A, IL-18, and IL-23 in the exposed group. Metabolomic analysis revealed a distinct metabolite signature in exposed individuals with perturbations in lipid (linoleic, alpha-linolenic, and arachidonic acid pathways), glutathione metabolism and ubiquinone, aligning with the observed oxidative and inflammatory profiles. In addition, we targeted an epoxyoctadecenoic acid (EpOME) with an area under the curve value of 1.0 that was related to anesthetic occupational exposure. These integrative findings demonstrate that high-level of occupational exposure to the WAG isoflurane is associated with systemic biological disruptions involving oxidative stress, inflammation, and lipid metabolic dysregulation.
Authors: Mariane Aparecida P Silva, Tony F Grassi, Luis A J Mur, Nur Aimi A Zainurin, Manfred Beckmann, Hendrew Jesus B C de Souza, Maria Vitória Destro, Debora C Damasceno, Camila R Corrêa, Marjorie A Golim, Renata Ferrari, João Paulo C Marcondes, Leandro G Braz, Mariana G Braz
Full Source: Free radical biology & medicine 2025 Nov 20: S0891-5849(25)01374-7. doi: 10.1016/j.freeradbiomed.2025.11.029.

Caudate nucleus atrophy as a neuroimaging feature of mild cognitive impairment induced by occupational aluminum exposure

2025-11-22
Occupational aluminum (Al) exposure is linked to mild cognitive impairment (MCI), yet its neuroanatomical mechanisms remain unclear. We investigated gray matter volume (GMV) alterations specifically associated with Al-induced MCI. This study enrolled 86 participants: 30 Al-exposed MCI (Al-MCI), 26 Al-exposed cognitively normal (Al-HC), and 30 non-exposed controls (Non-Al-HC). Structural MRI quantified whole-brain GMV. Plasma Al concentrations, Montreal Cognitive Assessment (MoCA), the Rey Auditory Verbal Learning Test (AVLT), and the Trail Making Test (TMT) were assessed in Al-exposed individuals. Intergroup GMV differences were analyzed via ANCOVA. Partial correlations and mediation analyses explored cognition-GMV relationships. We found that Al-MCI and Al-HC showed comparable plasma Al concentrations (42.74 ± 26.00 vs. 32.52 ± 30.86 μg/L, $p = 0.184$). A graded pattern of bilateral caudate nucleus (CAU) atrophy was observed: most severe atrophy in the Al-MCI group, intermediate atrophy in the Al-HC group, and the largest volumes in the Non-Al-HC group ($p < 0.05$ for all pairwise comparisons). In Al-exposed individuals, left CAU volume correlated positively with abstraction ($r = 0.294$, $p = 0.028$), language ($r = 0.321$, $p = 0.016$), and AVLT-immediate recall ($r = 0.289$, $p = 0.030$). Right CAU volume correlated negatively with TMT-A error responses ($r=-0.306$, $p = 0.022$). In conclusions, CAU atrophy was significantly associated with cognitive decline and may represent a specific neuroimaging feature of occupational Al-induced MCI.
Authors: Yangyang Li, Feifei Zhang, Bo Liu, Xiaochun Wang, Huaxing Meng, Qiao Niu, Hui Zhang, Yan Tan
Full Source: Scientific reports 2025 Nov 22. doi: 10.1038/s41598-025-29829-y.