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ENVIRONMENTAL RESEARCH

Synergetic effects of novel aromatic brominated and chlorinated disinfection by-products on *Vibrio qinghaiensis* sp.-Q67

2019-05-27

Aromatic halogenated chemicals are an unregulated class of by-products (DBPs) generated from disinfection processes in the water environment. Information on the toxicological interactions, such as antagonism and synergism, present in DBP mixtures remains limited. This study aimed to determine the toxicological effects of aromatic halogenated DBP mixtures on the freshwater bacterium *Vibrio qinghaiensis* sp.-Q67. The acute toxicities of seven DBPs and their binary mixtures toward *V. qinghaiensis* sp.-Q67 were determined through microplate toxicity analysis. The toxicities of single DBPs were ranked as follows: 2,5-dibromohydroquinone > 2,4-dibromophenol > 4-bromo-2-chlorophenol \approx 2,6-dibromo-4-nitrophenol > 2,6-dichloro-4-nitrophenol > 2-bromo-4-chlorophenol > 4-bromophenol. The percentages of synergism (experimental values higher than the predicted concentration addition) on the levels of 50%, 20%, and 10% effective concentrations reached 61%, 41%, and 31%, respectively. These results indicated that the probability of synergism decreased as concentration levels decreased. The synergetic effects of the compounds were dependent on concentration levels and concentration ratios. The proposed quantitative structure-activity relationship model can be used to predict the interactive toxicities exerted by 105 binary DBP mixture rays of 21 DBP mixture systems.

Authors: Chen YH, Qin LT, Mo LY, Zhao DN, Zeng HH, Liang YP.

Full Source: Environmental Pollution. 2019 Apr 14; 250:375-385. doi: 10.1016/j.envpol.2019.04.009. [Epub ahead of print]

This study aimed to determine the toxicological effects of aromatic halogenated DBP mixtures on the freshwater bacterium *Vibrio qinghaiensis* sp.-Q67.

Marine natural products as source of new drugs: a patent review (2015-2018)

2019-05-27

Natural products from plants, animals, microbes, and minerals have long been a traditional source for the treatment of human diseases. In the past decades, research on natural products for the pharmaceutical industry had declined due to numerous challenges. However, the recent developments in analytical technology, spectroscopy, and high-throughput screening have tremendously revived natural product drug discovery, including contribution from marine-based drugs. The marine environment is

a unique resource enclosing a massive biological diversity, which if genuinely explored might potentially lead to breakthrough therapies. A growing number of compounds from marine sources are entering clinical trials and thus, the impact of this field on the pharmaceutical industry is increasing. This review summarises the progress in the field of marine natural products as therapeutic agents based on an analysis of the patents published in the period January 2015 through June 2018. Marine organisms are excellent producers of natural chemicals with diverse structures and pharmacological activities. Cumulative increase in the number of patents published in the last few years clearly justifies the importance of these chemicals as sources of new therapeutic agents and this study. Despite the critical supply challenges, marine-derived actives are being explored as sources for anticancer, antimicrobial, antiviral and anti-inflammatory drugs and treatments for several other conditions.

Authors: Shinde P, Banerjee P, Mandhare A.

Full Source: Expert Opinion on Therapeutic Patents. 2019 Apr;29(4):283-309. doi: 10.1080/13543776.2019.1598972. Epub 2019 Apr 3.

Recent advances in the biocontrol of *Xanthomonas* spp

2019-05-27

Bacterial diseases caused by members of the genus *Xanthomonas* affect agricultural crops of great importance in the world. At least 350 different plant diseases are caused by species of *Xanthomonas*. Important crops, such as: rice, citrus, cassava, tomato, sugar cane, passionfruit and brassicas are severely affected by bacteria of this genus. Due to its rapid propagation, handling difficulties, problems with chemical control and severity of the losses of the affected plantations *Xanthomonas* is a difficult obstacle for agriculture around the world. In addition, chemical control of some of these diseases is carried out using copper-based chemicals, which causes a negative impact on health and the environment. A more sustainable alternative to combat these diseases is the control of *Xanthomonas* by microorganisms directly or indirectly through the use of its secondary metabolites involved in biocontrol. This review is a report concerning the recent advances in the search for microorganisms for the biocontrol of several *Xanthomonas* that are important for the world economy.

Authors: Marin VR, Ferrarezi JH, Vieira G, Sass DC.

Full Source: World Journal of Microbiology and Biotechnology. 2019 Apr 22;35(5):72. doi: 10.1007/s11274-019-2646-5.

This review is a report concerning the recent advances in the search for microorganisms for the biocontrol of several *Xanthomonas* that are important for the world economy.

Volatiles from Different Instars of Honeybee Worker Larvae and Their Food

2019-05-27

(E)- β -Ocimene was the only volatile chemical found to be emitted by whole, live worker larvae of *Apis mellifera* L. when sampling in the vapor phase. In addition to (E)- β -ocimene, there is evidence for the existence of other volatiles, but the changes in their composition and contents remain unknown during larval development, as are their differences from larvae to larval food. In the present study, the authors investigated volatile components of worker larvae and larval food using solid phase dynamic extraction (SPDE) coupled with gas chromatography-mass spectrometry (GC-MS). Nine compounds were identified with certainty and six tentatively, including terpenoids, aldehydes, hydrocarbons, an ester and a ketone. The contents of volatiles in the second-instar worker larvae differ greatly from those in larvae of other stages. This is mainly attributable to terpenoids, which resulted in the second-instar worker larvae having significantly higher amounts of overall volatiles. Larval food contained significantly higher amounts of aldehydes and hydrocarbons than the corresponding larvae from the fourth to fifth-instar. The authors discovered that volatiles in worker larvae and their food that were never reported before; we also determined the content changes of these volatiles during larval development.

Authors: Zhang H, Hou C, Dai P, Liu Y, Wu Y, Pang Y, Diao Q.

Full Source: *Insects*. 2019 Apr 25;10(4). pii: E118. doi: 10.3390/insects10040118.

Antibiotics in corals of the South China Sea: Occurrence, distribution, bioaccumulation, and considerable role of coral mucus

2019-05-27

Manmade antibiotics are emerging organic pollutants widely detected in the marine environment. In this study, 14 out of 19 target antibiotics were detected in corals collected from coastal and offshore regions in the South China Sea. The average total antibiotic concentrations (Σ 19ABs) in the two regions were similar: 28 ng/g for coastal corals and 31 ng/g for offshore corals, based on dry tissue weight (dw). Fluoroquinolones (FQs) were predominant antibiotics in the coastal corals (mean Σ FQs: 18 ng/g dw), while sulfonamides (SAs) predominated in the offshore corals (mean Σ SAs: 23 ng/g dw). However, corals living in coastal regions tend to excrete more mucus than corals in offshore habitat. The authors found 53% by average

In the present study, the authors investigated volatile components of worker larvae and larval food using solid phase dynamic extraction (SPDE) coupled with gas chromatography-mass spectrometry (GC-MS).

of Σ 19ABs in the mucus of the coastal corals; while in offshore corals, most antibiotics (88% by average) were accumulated in the tissues. In addition, the tissue-mucus mass distribution differs among individual antibiotics. Sulfonamides were mainly accumulated in tissues while fluoroquinolones were present mainly in mucus. The results of this study suggest that mucus played an important role in the bioaccumulation of antibiotics by corals. It may resist the bioaccumulation of antibiotics by coral tissue, especially for the coastal corals. Additionally, corals were compared with other marine biotas in the study area and found to be more bioaccumulative towards antibiotics.

Authors: Zhang R, Yu K, Li A, Wang Y, Huang X.

Full Source: Environmental Pollution. 2019 Jul; 250:503-510. doi: 10.1016/j.envpol.2019.04.036. Epub 2019 Apr 13.

MEDICAL RESEARCH

Biosafety evaluation of Janus Fe₃O₄-TiO₂ nanoparticles in Sprague Dawley rats after intravenous injection

2019-05-27

Newly synthesised Janus-structured Fe₃O₄-TiO₂ nanoparticles (NPs) appear to be a promising candidate for the diagnosis and therapy of cancer. Although the toxicity of individual Fe₃O₄ or TiO₂ NPs has been studied extensively, the toxicity of Janus Fe₃O₄-TiO₂ NPs is not clear. In this study, the biosafety of both Janus Fe₃O₄-TiO₂ NPs (20-25 nm) and the maternal material TiO₂ NPs (7-10 nm) were evaluated in Sprague Dawley rats after one intravenous injection into the tail vein. Healthy rats were randomly divided into one control group and six experimental groups. Thirty days after treatment, rats were killed, then blood and tissue samples were collected for haematological, biochemical, element-content, histopathological, and Western blot analysis. The results show that only a slight Ti element accumulation in the heart, spleen, and liver could be found in the Janus Fe₃O₄-TiO₂ NP groups ($P > 0.05$ compared with control). However, significant Ti element accumulation in the spleen, lungs, and liver was found in the TiO₂ NP-treated rats. Both Fe₃O₄-TiO₂ NPs and TiO₂ NPs could induce certain histopathological abnormalities. Western blot analysis showed that both NPs could induce certain apoptotic or inflammatory-related molecular protein upregulation in rat livers. A certain degree of alterations in liver function and electrolyte and lipid parameters was also observed in rats treated with both materials. However, compared to Janus structure Fe₃O₄-TiO₂ NP-treated groups, TiO₂ NPs at 30 mg/kg showed more severe adverse effects. The authors concluded that the

In this study, the biosafety of both Janus Fe₃O₄-TiO₂ NPs (20-25 nm) and the maternal material TiO₂ NPs (7-10 nm) were evaluated in Sprague Dawley rats

results showed that under a low dose (5 mg/kg), both NP types had no significant toxicity in rats. Janus NPs certainly seem less toxic than TiO₂ NPs in rats at 30 mg/kg. To ensure safe use of these newly developed Janus NPs in cancer diagnosis and therapy, further animal studies are needed to evaluate long-term bioeffects.

Authors: Su H, Song X, Li J, Iqbal MZ, Kenston SSF, Li Z, Wu A, Ding M, Zhao J.

Full Source: International Journal of Nanomedicine. 2018 Oct 31; 13:6987-7001. doi: 10.2147/IJN.S167851. eCollection 2018.

Complement regulatory protein CD59a plays a protective role in immune liver injury of trichloroethylene-sensitized BALB/c mice

2019-05-27

Trichloroethylene (TCE) is a major occupational and environmental chemical compound which causes occupational dermatitis medicamentosa-like of TCE with severe liver damage. Previous studies showed that complement activation was a newly recognised mechanism for TCE-induced liver damage. The objective of this study was to explore the role of the key complement regulatory protein, CD59a, in TCE-induced immune liver injury. The authors firstly evaluated the changes of CD59a expression in liver tissue and then investigated if the changes were associated with membrane attack complex (MAC) formation, nuclear factor kappa B (NF- κ B) activation and liver damage in BALB/c mice model of TCE-induced skin sensitisation in the absence or presence of soluble recombinant rat CD59-Cys. The results showed that low expression of CD59a accompanied by MAC deposition in the liver of TCE-sensitized BALB/c mice, which was consistent in time. In addition, activation of NF- κ B pathway, upregulation of inflammatory cytokine and liver damage also occurred. Additional experiment showed that recombinant rat sCD59-Cys alleviated inflammation and liver damage in TCE-sensitized BALB/c mice. Moreover, recombinant rat sCD59-Cys reduced MAC formation and inhibited NF- κ B activation measured by P-I κ B α and nuclear NF- κ B p65 in the liver of TCE-sensitized BALB/c mice. In conclusion, recombinant rat sCD59-Cys plays a protective role in immune liver injury of TCE-sensitized BALB/c mice.

Authors: Wang X, Yu Y, Xie HB, Shen T, Zhu QX.

Full Source: Ecotoxicology & Environmental Safety. 2019 Jan 24; 172:105-113. doi: 10.1016/j.ecoenv.2019.01.049. [Epub ahead of print]

The objective of this study was to explore the role of the key complement regulatory protein, CD59a, in TCE-induced immune liver injury.

Bradykinin contributes to immune liver injury via B2R receptor-mediated pathways in trichloroethylene sensitized mice: A role in Kupffer cell activation

2019-05-27

Previously it has been shown that trichloroethylene (TCE) induced occupational medicamentosa-like dermatitis due to TCE (OMLDT) with immune liver injury, and kallikrein-kinin system (KKS) activation as a probably mechanism underlying the immune damage. Bradykinin (BK) is an important active component of KKS system function, but the specific role of BK in the immune liver injury has never been examined. The present study aimed to explore the important role of BK and mechanisms of action in immune liver injury induced by TCE. TCE sensitisation significantly increased the expression of BK receptor (B2R) in the liver. Compared to blank and vehicle control group, TCE sensitization positive mice developed exacerbated liver injury evidenced by elevated AST, ALT levels and hepatocyte damage. TCE sensitisation also stimulated MAPK and STAT3 activation in liver tissue. B2R antagonist HOE140 ameliorated these changes. Kupffer cells (KCs) of the liver were also activated following TCE sensitization; both CD68+ KCs and CD16/CD32+ M1 type KCs were increased in TCE positive group. Further experiments isolated the KCs from the liver in each group and showed that TCE sensitisation resulted activation of MAPK signal pathway which in turn caused release of the pro-inflammatory cytokines, IL-1 β , IL-6, TNF- α , in KCs; the antagonist HOE140 again decreased these changes in KCs. These results uncover a novel role of BK and B2R cross-talk in KCs activation in TCE sensitised mice, mediated by pro-inflammatory cytokine release via MAPK and STAT3 activation, contributing to the immune liver injury.

Authors: Zhang J, Li N, Yang L, Xie H, Yang Y, Wang H, Wu C, Shen T, Zhu Q.

Full Source: Toxicology. 2019 Jan 24; 415:37-48. doi: 10.1016/j.

tox.2019.01.015. [Epub ahead of print]

The present study aimed to explore the important role of bradykinin and mechanisms of action in immune liver injury induced by TCE.

Benzene metabolite hydroquinone promotes DNA homologous recombination repair via the NF- κ B pathway

2019-05-27

Benzene, a widespread environmental pollutant, induces DNA double-strand breaks (DSBs) and DNA repair, which may further lead to oncogenic mutations, chromosomal rearrangements and leukemogenesis. However, the molecular mechanisms underlying benzene-induced DNA repair and carcinogenesis remain unclear. The human osteosarcoma cell line (U2OS/DR-GFP), which carries a GFP-based homologous recombination

(HR) repair reporter, was treated with hydroquinone, one of the major benzene metabolites, to identify the potential effects of benzene on DSB HR repair. RNA-sequencing was further employed to identify the potential key pathway that contributed to benzene-initiated HR repair. We found that treatment with hydroquinone induced a significant increase in HR. NF- κ B pathway, which plays a critical role in carcinogenesis in multiple tumours, was significantly activated in cells recovered from hydroquinone treatment. Furthermore, the upregulation of NF- κ B by hydroquinone was also found in human hematopoietic stem and progenitor cells. Notably, the inhibition of NF- κ B activity by small molecule inhibitors (QNZ and JSH-23) significantly reduced the frequency of hydroquinone-initiated HR (-1.36- and -1.77-fold, respectively, $P < 0.01$). The results demonstrate an important role of NF- κ B activity in promoting HR repair induced by hydroquinone. These findings shed light on the underlying mechanisms involved in benzene-induced genomic instability and leukemogenesis and may contribute to the larger exploration of the influence of other environmental pollutants on carcinogenesis.

Authors: Yang X, Lu Y, He F, Hou F, Xing C, Xu P, Wang QF.

Full Source: Carcinogenesis. 2019 Feb 16. pii: bgy157. doi: 10.1093/carcin/bgy157. [Epub ahead of print]

Exposure to MPA-capped CdTe quantum dots causes reproductive toxicity effects by affecting oogenesis in nematode *Caenorhabditis elegans*

2019-05-27

Quantum dots (QDs), considered as a type of excellent semiconductor nanomaterial, are widely employed and have a number of important applications. However, QDs have the potential to produce adverse effects and toxicity with the underlying molecular mechanisms not well understood. In this study, *Caenorhabditis elegans* was used for in vivo toxicity assessment to detect the reproductive toxicity of CdTe QDs. The authors found that exposure to CdTe QDs particles (≥ 50 mg/L) resulted in a defect in reproductive capacity, dysfunctional proliferation and differentiation, as well as an imbalance in oogenesis by reducing the number of cells in pachytene and diakinesis. Further, we identified a SPO-11 and PCH-2 mediated toxic mechanism and a GLP-1/Notch mediated protective mechanism in response to CdTe QDs particles (≥ 50 mg/L). Taken together, these results demonstrate the potential adverse impact of

In this study, *Caenorhabditis elegans* was used for in vivo toxicity assessment to detect the reproductive toxicity of CdTe QDs.

CdTe QDs (≥ 50 mg/L) exposure on oogenesis and provide valuable data and guidelines for evaluation of QD biocompatibility.

Authors: Qu M, Qiu Y, Lv R, Yue Y, Liu R, Yang F, Wang D, Li Y.

Full Source: *Ecotoxicology & Environmental Safety*. 2019 May 30; 173:54-62. doi: 10.1016/j.ecoenv.2019.02.018. Epub 2019 Feb 12.

OCCUPATIONAL RESEARCH

Maternal circadian disruption is associated with variation in placental DNA methylation

2019-05-27

Circadian disruption is a common environmental and occupational exposure with public health consequences, but not much is known about whether circadian disruption affects in utero development. This study investigated whether maternal circadian disruption, using night shift work as a proxy, is associated with variations in DNA methylation patterns of placental tissue in an epigenome-wide association study (EWAS) of night shift work. The authors compared cytosine-guanosine dinucleotide (CpG) specific methylation genome-wide of placental tissue (measured with the Illumina 450K array) from participants ($n = 237$) in the Rhode Island Child Health Study (RICHS) who did ($n = 53$) and did not ($n = 184$) report working the night shift, using robust linear modelling and adjusting for maternal age, pre-pregnancy smoking, infant sex, maternal adversity, and putative cell mixture. Statistical analyses were adjusted for multiple comparisons and results presented with Bonferroni or Benjamini and Hochberg (BH) adjustment for false discovery rate. Night shift work was associated with differential methylation in placental tissue, including CpG sites in the genes NAV1, SMPD1, TAPBP, CLEC16A, DIP2C, FAM172A, and PLEKHG6 (Bonferroni-adjusted $p < 0.05$). CpG sites within NAV1, MXRA8, GABRG1, PRDM16, WNT5A, and FOXG1 exhibited the most hypomethylation, while CpG sites within TDO2, ADAMTSL3, DLX2, and SERPINA1 exhibited the most hypermethylation (BH $q < 0.10$). Functional analysis indicated GO-terms associated with cell-cell adhesion and enriched GWAS results for psoriasis. Night shift work was associated with differential methylation of the placenta, which may have implications for foetal health and development. This is the first study to examine the epigenetic impacts of night shift exposure, as a proxy for circadian disruption, on placental methylation in humans, and, while results should

This study investigated whether maternal circadian disruption, using night shift work as a proxy, is associated with variations in DNA methylation patterns of placental tissue in an epigenome-wide association study (EWAS) of night shift work.

be interpreted with caution, suggests circadian disruption may have epigenetic impacts.

Authors: Clarkson-Townsend DA, Everson TM, Deysenroth MA, Burt AA, Hermetz KE, Hao K, Chen J, Marsit CJ.

Full Source: PLoS One. 2019 Apr 26;14(4):e0215745. doi: 10.1371/journal.pone.0215745. eCollection 2019.

Biochemical study on occupational inhalation of benzene vapours in petrol station

2019-05-27

Fuel station workers are most susceptible to benzene inhalation toxicity. Samples were collected twice, at beginning of the study and 6 months later from 40 fuel station workers from different Egyptian governorates and 10 control healthy volunteers. Fuel station workers were sub divided into four groups according to years working in the station. All of them are exposed to benzene vapours and exhausts during their duties, their work shifts were 8 hrs./day. Results indicated that; benzene vapours exposure induced significant increasing in serum Lead and Cadmium and Myeloperoxidase (MPO) enzyme activity levels. This goes with marked immunologic changes presented by decreases in immunoglobulins; IgA and IgG, along with increases in levels of IgM and IgE. Also, Malondialdehyde (MDA) levels were significantly increased. Meanwhile, reduction in some other biochemical parameters including; Copper, Zinc and Iron micronutrients, as well as; Superoxide Dismutase (SOD), Catalase (CAT) enzyme levels and Glutathione (GSH) content. Hence, the study inferred that prolonged benzene inhalation can lead to biochemical and immune disorders, probably through potentiating oxidative stress and inflammation pathways.

Authors: Abdel Maksoud HA, Elharrif MG, Mahfouz MK, Omnia MA, Abdullah MH, Eltabey ME.

Full Source: Respiratory Medicine Case Reports. 2019 Apr 8; 27:100836. doi: 10.1016/j.rmcr.2019.100836. eCollection 2019.

Fuel station workers are most susceptible to benzene inhalation toxicity.

Occupational Radiation Protection Aspects of Alkaline Leach Uranium in Situ Recovery (ISR) Facilities in the United States

2019-05-27

In situ recovery or in situ leach (ISR/ISL) uranium facilities, also referred to in the past as "uranium solution mining" have operated since the late 1960s in the US and in recent years have accounted for over 70%

of US production and, internationally, approximately half of worldwide uranium supplies. Note that throughout this paper, the uranium in situ recovery process, also known as in situ leach, will be abbreviated as "ISR." This study presents a summary of the occupational radiation protection aspects of typical ISR processes being employed in the United States today that have traditionally used alkaline-based uranium recovery solutions known as lixivants. The study describes the health physics and associated monitoring programs necessary to adequately measure and control radiological doses to workers based on the radiological character of these processes. Although many radiological characteristics are similar to that of conventional mills, conventional-type tailings as such are not generated. However, liquid and solid by-product materials may be generated and impounded, which can result in sources of occupational exposure. Some special monitoring considerations are required due to the manner in which Rn gas is involved in the process. The major aspects of the health physics and radiation protection programs that have been developed at these facilities over many years are discussed and listed in the Conclusion section of the paper.

Author: Brown SH.

Full Source: Health Physics. 2019 Apr 23. doi: 10.1097/HP.0000000000001062. [Epub ahead of print]

Effects of oxidative stress on blood pressure and electrocardiogram findings in workers with occupational exposure to lead

2019-05-27

In this study, the authors observed the correlation between the oxidative stress index and cardiovascular system damage in a population with lead exposure. Two populations (144 manufacturing workers and 94 administrators) from a lead-acid battery manufacturer in Shandong Province in China were recruited. The blood lead level, oxidative stress index, blood pressure, electrocardiogram findings, and their correlations were analysed in both groups. The blood lead level was significantly higher in manufacturing workers than administrators (254.34 vs. 65.32 $\mu\text{g/L}$, respectively). The differences in the oxidative stress index, serum total superoxide dismutase (T-SOD) concentration, and malondialdehyde (MDA) concentration between the two populations were statistically significant. The rates of abnormal blood pressure and electrocardiogram findings were significantly higher in manufacturing workers than administrators. Workers with middle- and high-dose lead exposure had lower T-SOD and higher MDA concentrations than those with low-dose lead exposure.

In this study, the authors observed the correlation between the oxidative stress index and cardiovascular system damage in a population with lead exposure.

Significant correlations were found between the blood lead level and the MDA concentration, systolic pressure, diastolic pressure, and electrocardiogram findings. Linear multiple regression analysis showed that T-SOD was negatively associated with blood lead, electrocardiogram findings, and MDA. Lead exposure can lead to oxidative stress, increased blood pressure, and abnormal electrocardiogram findings and may impact cardiovascular diseases through oxidative stress.

Authors: Qu W, Du GL, Feng B, Shao H.

Full Source: Journal of International Medical Research. 2019 Apr 21:300060519842446. doi: 10.1177/0300060519842446. [Epub ahead of print]

Animal production, insecticide use and self-reported symptoms and diagnoses of COPD, including chronic bronchitis, in the Agricultural Health Study

2019-05-27

Occupational exposure to animal production is associated with chronic bronchitis symptoms; however, few studies consider associations with chronic obstructive pulmonary disease (COPD). In the present study, the authors estimated associations between animal production activities and prevalence of self-reported COPD among farmers in the Agricultural Health Study. During a 2005-2010 interview, farmers self-reported information about: their operations (i.e., size, type, number of animals, insecticide use), respiratory symptoms, and COPD diagnoses (i.e., COPD, chronic bronchitis, emphysema). Operations were classified as small or medium/large based on regulatory definitions. Farmers were classified as having a COPD diagnosis, chronic bronchitis symptoms (cough and phlegm for ≥ 3 months during 2 consecutive years), or both. Polytomous logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI). Of 22,491 participating farmers (median age: 59 years), 922 (4%) reported a COPD diagnosis only, 254 (1%) reported a diagnosis and symptoms, and 962 (4%) reported symptoms only. Compared to raising no commercial animals, raising animals on a medium/large operation was positively associated with chronic bronchitis symptoms with (OR: 1.59; 95% CI: 1.16, 2.18) and without a diagnosis (OR: 1.69; 95% CI: 1.42, 2.01). Ever use of multiple organophosphates, carbaryl, lindane, and permethrin were positively associated with chronic bronchitis symptoms. Animal production work, including insecticide use, was positively associated with chronic bronchitis symptoms; but not consistently with COPD diagnosis alone. These results support the need for further investigation into the role of animal production-related exposures

Occupational exposure to animal production is associated with chronic bronchitis symptoms; however, few studies consider associations with chronic obstructive pulmonary disease (COPD).

Technical

CHEMWATCH

in the aetiology of COPD and better respiratory protection for agricultural workers.

Authors: Rinsky JL, Richardson DB, Kreiss K, Nylander-French L, Beane Freeman LE, London SJ, Henneberger PK, Hoppin JA.

Full Source: Environment International. 2019 Jun; 127:764-772. doi: 10.1016/j.envint.2019.02.049. Epub 2019 Apr 25.

PUBLIC HEALTH RESEARCH

Non-Hodgkin lymphoma risk and organophosphate and carbamate insecticide use in the north American pooled project

2019-05-27

Organophosphates and carbamates have been among the most commonly used insecticides, with both agricultural and residential uses. Previous studies have suggested associations of non-Hodgkin lymphoma (NHL) with some of these chemicals; however, many studies have been limited in their ability to evaluate associations with lymphoma subtypes. In the present study, the authors evaluated the use of eleven organophosphate and two carbamate insecticides in association with NHL in the North American Pooled Project, which includes data from case-control studies in the United States and Canada (1690 cases/5131 controls). Unconditional logistic regression adjusting for potential confounders was used, including use of other pesticides, to estimate odds ratios (OR) and 95% confidence intervals (CI) for associations between these chemicals and NHL overall, and NHL subtypes, i.e., follicular (FL), diffuse large B-cell (DLBCL), small lymphocytic lymphoma (SLL) and others. Ever use of malathion was associated with increased risk of NHL overall (OR = 1.43; 95% CI: 1.14-1.81) compared with never users. Categories using tertiles of duration (<4 yrs., 4-12 yrs., and >12 yrs) also showed a significant exposure-response for increasing years of use of malathion and risk of NHL (OR<4vsUnex = 1.33 (0.88, 2.03), OR4-12vsUnex = 1.42 (1.02, 1.96), OR>12vsUnex = 1.55 (1.05, 2.28, p-trend < 0.01)). In addition, malathion use was statistically significantly associated with FL (OR = 1.58; 95% CI: 1.11-2.27) and DLBCL (OR = 1.61; 95% CI: 1.16-2.22) while there were no apparent associations with SLL or other subtypes, the p-value for heterogeneity across subtypes, however, was not significant. These results support previous studies suggesting an association between insecticide

In the present study, the authors evaluated the use of eleven organophosphate and two carbamate insecticides in association with NHL in the North American Pooled Project

use and NHL overall, and provide new information on associations with NHL subtypes.

Authors: Koutros S, Harris SA, Spinelli JJ, Blair A, McLaughlin JR, Zahm SH, Kim S, Albert PS, Kachuri L, Pahwa M, Cantor KP, Weisenburger DD, Pahwa P, Pardo LA, Dosman JA, Demers PA, Beane Freeman LE.

Full Source: Environment International. 2019 Mar 27; 127:199-205. doi: 10.1016/j.envint.2019.03.018. [Epub ahead of print]

Peak Exposures in Epidemiologic Studies and Cancer Risks: Considerations for Regulatory Risk Assessment

2019-05-27

The authors review approaches for characterising “peak” exposures in epidemiologic studies and methods for incorporating peak exposure metrics in dose-response assessments that contribute to risk assessment. The focus was on potential etiologic relations between environmental chemical exposures and cancer risks. The epidemiologic literature on environmental chemicals classified as carcinogens in which cancer risks were described in relation to “peak” exposures were searched. These articles were evaluated to identify some of the challenges associated with defining and describing cancer risks in relation to peak exposures. We found that definitions of peak exposure varied considerably across studies. Of nine chemical agents included in our review of peak exposure, six had epidemiologic data used by the U.S. Environmental Protection Agency (US EPA) in dose-response assessments to derive inhalation unit risk values. These were benzene, formaldehyde, styrene, trichloroethylene, acrylonitrile, and ethylene oxide. All derived unit risks relied on cumulative exposure for dose-response estimation and none, to our knowledge, considered peak exposure metrics. This is not surprising, given the historical linear no-threshold default model (generally based on cumulative exposure) used in regulatory risk assessments. With newly proposed US EPA rule language, fuller consideration of alternative exposure and dose-response metrics will be supported. “Peak” exposure has not been consistently defined and rarely has been evaluated in epidemiologic studies of cancer risks. The authors recommend developing uniform definitions of “peak” exposure to facilitate fuller evaluation of dose response for environmental chemicals and cancer risks, especially where mechanistic understanding indicates that the dose response is unlikely linear and that short-term high-intensity exposures increase risk.

Authors: Checkoway H, Lees PSJ, Dell LD, Gentry PR, Mundt KA.

Full Source: Risk Analysis. 2019 Mar 29. doi: 10.1111/risa.13294. [Epub ahead of print]

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Elucidating Conserved Transcriptional Networks Underlying Pesticide Exposure and Parkinson's Disease: A Focus on Chemicals of Epidemiological Relevance

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While a number of genetic mutations are associated with Parkinson's disease (PD), it is also widely acknowledged that the environment plays a significant role in the aetiology of neurodegenerative diseases. Epidemiological evidence suggests that occupational exposure to pesticides (e.g., dieldrin, paraquat, rotenone, maneb, and ziram) is associated with a higher risk of developing PD in susceptible populations. Within dopaminergic neurons, environmental chemicals can have an array of adverse effects resulting in cell death, such as aberrant redox cycling and oxidative damage, mitochondrial dysfunction, unfolded protein response, ubiquitin-proteome system dysfunction, neuroinflammation, and metabolic disruption. More recently, our understanding of how pesticides affect cells of the central nervous system has been strengthened by computational biology. New insight has been gained about transcriptional and proteomic networks, and the metabolic pathways perturbed by pesticides. These networks and cell signalling pathways constitute potential therapeutic targets for intervention to slow or mitigate neurodegenerative diseases. Here we review the epidemiological evidence that supports a role for specific pesticides in the aetiology of PD and identify molecular profiles amongst these pesticides that may contribute to the disease. Using the Comparative Toxicogenomics Database, these transcripts were compared to those regulated by the PD-associated neurotoxicant MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine). While many transcripts are already established as those related to PD (alpha-synuclein, caspases, leucine rich repeat kinase 2, and parkin2), lesser studied targets have emerged as "pesticide/PD-associated transcripts" [e.g., phosphatidylinositol glycan anchor biosynthesis class C (Pigc), allograft inflammatory factor 1 (Aif1), TIMP metallopeptidase inhibitor 3, and DNA damage inducible transcript 4]. The authors also compared pesticide-regulated genes to a recent meta-analysis of genome-wide association studies in PD which revealed new genetic mutant alleles; the pesticides under review regulated the expression of many of these genes (e.g., ELOVL fatty acid elongase 7, ATPase H⁺ transporting V0 subunit a1, and bridging integrator 3). The significance is that these proteins may contribute to pesticide-related increases in PD risk. This review collates information on transcriptome

This review collates information on transcriptome responses to Parkinson's Disease-associated pesticides to develop a mechanistic framework for quantifying PD risk with exposures.

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Authors: Cao F, Souders li CL, Perez-Rodriguez V, Martyniuk CJ.

Full Source: *Frontiers in Genetics*. 2019 Jan 25; 9:701. doi: 10.3389/fgene.2018.00701. eCollection 2018.

Low-cost photoionisation sensors as detectors in GC × GC systems designed for ambient VOC measurements

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Conventional volatile organic compound (VOC) monitoring based on thermal desorption - gas chromatography-mass spectrometry (TD-GC-MS) or gas chromatography-flame ionisation detector (TD-GC-FID) is relatively cumbersome and expensive. In this study commercial off the shelf low-cost and low-power photo-ionisation detector (PID) sensors are used as simple detectors in VOC analysis systems based on GC, including a miniaturised GC × GC device with portable, low-cost, and low-energy-consumption features. PID sensors produce a voltage signal positively proportional to VOC concentration, which when incorporated into a TD-GC system gave limit of detection of 0.02 ppbV for isoprene. To test PID performance in real-world applications, PID sensors were deployed as (i) a second alternative detector in a GC-Quadruple Time Of Flight Mass spectrometry (GC-Q-TOF-MS), and (ii) the main detector in a compact two-dimensional gas chromatograph (GC × GC). PID sensors with 10.6 eV and 11.7 eV lamps were used to measure eight toxic chemicals including organic sulfide and organic phosphonates via GC; two species were ionised by a 10.6 eV lamp and four species by the 11.7 eV lamp. Commercially available low-cost PIDs designed for standalone could be straightforwardly and effectively re-used as detectors in compact GC × GC systems, in this work showing excellent VOC sensitivity, fast response and low operational demands compared to comparable field instruments based on GC-FID or MS.

Authors: Pang X, Nan H, Zhong J, Ye D, Shaw MD, Lewis AC.

Full Source: *Science of the Total Environment*. 2019 May 10; 664:771-779. doi: 10.1016/j.scitotenv.2019.01.348. Epub 2019 Feb 5.

Early lead exposure and pubertal development in a Mexico City population

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Previous studies have examined the association between blood lead levels and pubertal timing in adolescent girls; however, the evidence

In this study commercial off the shelf low-cost and low-power photo-ionisation detector (PID) sensors are used as simple detectors in VOC analysis systems based on GC

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is lacking on the role of lead exposure during sensitive developmental periods on sexual maturation. This study examined the association of prenatal and early childhood lead exposure with pubertal stages among 264 boys and 283 girls aged 9.8-18.0 years in Mexico City. The authors measured maternal bone lead (a proxy for cumulative foetal exposure to lead from maternal bone stores mobilized during pregnancy) at 1 month postpartum. Blood lead was measured annually from 1 to 4 years. Pubertal stage was assessed by a paediatrician. The authors examined the association between lead and pubertal stages of breast, pubic hair and genitalia using ordinal regression. Age at menarche was evaluated using Cox proportional-hazard models. Multivariate models showed that maternal patella lead and early childhood blood lead were inversely associated with breast growth (patella OR = 0.72, 95% CI: 0.51-1.00; blood OR = 0.70, 95% CI: 0.53-0.93) in girls. Girls with maternal patella lead in the 3rd tertile and child blood lead in the 2nd tertile had a later age at menarche compared with girls in the 1st tertile (patella HR = 0.60, 95% CI: 0.41-0.88; blood HR = 0.65, 95% CI 0.46-0.91). Additionally, early childhood blood lead was negatively associated with pubic hair growth (OR = 0.68, 95% CI: 0.51-0.90) in girls. No associations were found in boys. The authors concluded that the data suggest that higher prenatal and early childhood exposure to lead may be associated with delayed pubertal development in girls but not boys. The findings are consistent with previous analyses and reinforce the reproductive effects of lead for girls.

Authors: Liu Y, Téllez-Rojo MM, Sánchez BN, Zhang Z, Afeiche MC, Mercado-García A, Hu H, Meeker JD, Peterson KE.

Full Source: Environment International. 2019 Apr; 125:445-451. doi: 10.1016/j.envint.2019.02.021. Epub 2019 Feb 11.