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CHEMWATCH

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### ENVIRONMENTAL RESEARCH

#### Co-exposure to ketoconazole alters effects of bisphenol A in *Danio rerio* and H295R cells

2019-08-26

Chemicals are present in combination in ambient water; however, toxicities of their mixtures are not well understood. This study investigated the effects of ketoconazole (KCZ) on the responses induced by bisphenol A (BPA) in zebrafish and in human adrenocarcinoma (H295R) cells. After exposure to BPA alone or mixed with KCZ for 21 d, egg production, relative tissue weights, sex hormone levels, cytochrome P450 (CYP)3a activity, and transcriptions of genes related to CYP metabolism, vitellogenesis, and steroidogenesis were determined in zebrafish. Male fish were more sensitive to the adverse effects of BPA than females, and the presence of KCZ potentiated the BPA-induced estrogenic responses in the male and anti-oestrogenic responses in the female fish. In male zebrafish exposed to BPA, a significant reduction in egg number and relative gonad weight, an increase in 17 $\beta$ -oestradiol (E2) to testosterone (T) ratio, and an upregulation of *vtg*, *era*, and *cyp19a* genes were observed. Under KCZ, BPA exposure resulted in a significant downregulation of *cyp3a65* and *pxr* genes and an increase in estrogenic responses in males. In female fish, anti-oestrogenic effects, such as a decrease in E2 concentration, were observed following the combined exposure. These results indicate that KCZ could increase the toxicity of the chemicals that depend on the given CYP metabolism for their elimination or other crucial functions such as steroidogenesis. Co-exposure to BPA and KCZ in H295R cells also increased E2 and decreased T production. Release and presence of this azole compound warrant caution, because it could modify adverse effects of BPA.

Authors: Ji K, Seo J, Kho Y, Choi K.

Full Source: *Chemosphere*. 2019 Jul 20; 237:124414. doi: 10.1016/j.chemosphere.2019.124414. [Epub ahead of print]

This study investigated the effects of ketoconazole (KCZ) on the responses induced by bisphenol A (BPA) in zebrafish and in human adrenocarcinoma (H295R) cells.

#### Telomere dynamic in humans and animals: Review and perspectives in environmental toxicology

2019-08-26

Telomeres (TLs) play major roles in stabilising the genome and are usually shortened with ageing. The maintenance of TLs is ensured by two mechanisms involving telomerase (TA) enzyme and alternative lengthening telomeres (ALT). TL shortening and/or TA inhibition have been

related to health effects on organisms (leading to reduced reproductive lifespan and survival), suggesting that they could be key processes in toxicity mechanisms (at molecular and cellular levels) and relevant as an early warning of exposure and effect of chemicals on human health and animal population dynamics. Consequently, a critical analysis of knowledge about relationships between TL dynamic and environmental pollution is essential to highlight the relevance of TL measurement in environmental toxicology. The first objective of this review is to provide a survey on the basic knowledge about TL structure, roles, maintenance mechanisms and causes of shortening in both vertebrates (including humans) and invertebrates. Overall, TL length decreases with ageing but some unexpected exceptions are reported (e.g., in species with different lifespans, such as the nematode *Caenorhabditis elegans* or the crustacean *Homarus americanus*). Inconsistent results reported in various biological groups or even between species of the same genus (e.g., the microcrustacean *Daphnia* sp.) indicate that the relation usually proposed between TL shortening and a decrease in TA activity cannot be generalised and depends on the species, stage of development or lifespan. Although the scientific literature provides evidence of the effect of ageing on TL shortening, much less information on the relationships between shortening, maintenance of TLs, influence of other endogenous and environmental drivers, including exposure to chemical pollutants, is available, especially in invertebrates. The second objective of this review is to connect knowledge on TL dynamic and exposure to contaminants. Most of the studies published on humans rely on correlative epidemiological approaches and few *in vitro* experiments. They have shown TL attrition when exposed to contaminants, such as polycyclic aromatic hydrocarbons (PAH), polychlorinated biphenyls (PCB), pesticides and metallic elements (ME). In other vertebrates, the studies we found deals mainly with birds and, overall, report a disturbance of TL dynamic consecutively to exposure to chemicals, including metals and organic compounds. In invertebrates, no data are available and the potential of TL dynamic in environmental risk assessment remains to be explored. On the basis of the main gaps identified some research perspectives (e.g., impact of endogenous and environmental drivers, dose response effects, link between TL length, TA activity, longevity and ageing) are proposed to better understand the potential of TL and TA measurements in humans and animals in environmental toxicology.

Authors: Louzon M, Coeurdassier M, Gimbert F(1), Pauget B, de Vaufléury A.

Full Source: Environment International. 2019 Jul 25; 131:105025. doi: 10.1016/j.envint.2019.105025. [Epub ahead of print]

### Identification of moracin N in mulberry leaf and evaluation of antioxidant activity

2019-08-26

Mulberry leaf is a newly accepted vegetable for daily diet. It tastes good and has multiple health benefits, including antioxidant and anti-inflammatory activities. However, the chemicals responsible for these health benefits remain unveiled. Prenylated phenolics are characteristic bioactive compounds in mulberry leaf, which are recognised as good antioxidants. In this study, moracin N was purified from mulberry leaf. It showed better antioxidant activities than resveratrol. The EC<sub>50</sub> value of cellular antioxidant activity was 24.92  $\mu\text{M}$ , and the IC<sub>50</sub> value against DPPH radical was 40.00  $\mu\text{M}$ . The prenyl group rendered the molecule more membrane affinity which improved the bioavailability. The furan ring was critical for the antioxidant behaviour. The cell viability test revealed that moracin N had a good safety. These results pointed out that moracin N contributed to the antioxidant activity of mulberry leaf.

Authors: Tu J, Shi D, Wen L, Jiang Y, Zhao Y, Yang J, Liu H, Liu G, Yang B.  
Full Source: Food Chemistry & Toxicology. 2019 Jul 29; 132:110730. doi: 10.1016/j.fct.2019.110730. [Epub ahead of print]

### The dataset for antifeedant activity of eugenol derived compounds against red palm weevil (*Rhynchophorus ferrugineus*, Olivier) larvae

2019-08-26

*Rhynchophorus ferrugineus* or red palm weevil (RPW) is a destructive insect pest of major cultivated palms such as coconut, date and oil palm. One of the control management of RPW is trunk injection using monocrotophos or methamidophos, but these chemicals are found to affect ecosystems and human health. Thus, in the present study, the authors aimed to determine a bio-pesticide to replace these synthetic chemicals. The antifeedant activity of three eugenol-based compounds were tested as potential control agent against RPW larvae in vitro condition for two weeks. All these compounds show significant effect as feeding deterrent agent on 4th instar larvae, while WN16 (4-allyl-2-methoxy-1-(4-trifluoromethyl-benzyloxy)-benzene) shows the highest feeding deterrent index (FDI = 64.42%). Here the data regarding the

In the present study, the authors aimed to determine a bio-pesticide to replace these synthetic chemicals.

biological aspect on treated RPW larvae as well as antifeedant activity index of these eugenol derived compounds is presented.

Authors: Yan TK, Asari A, Abdullah S, Ismail M, Azmi WA.

Full Source: Data Brief. 2019 Jul 8; 25:104227. doi: 10.1016/j.dib.2019.104227. eCollection 2019 Aug.

### Green kiwifruit extracts protect motor neurons from death in a spinal muscular atrophy model in *Caenorhabditis elegans*

2019-08-26

Kiwifruit is considered a functional food and a good source of nutraceuticals. Among the possible beneficial effects of kiwifruit species, a neuroprotective activity exerted in rats with learning and memory impairment induced by exposure to different chemicals was reported. In this study, the authors sought to investigate the neuroprotective activities of kiwifruit toward spinal muscular atrophy (SMA). To this purpose, the authors have used a recently developed *Caenorhabditis elegans* SMA model, displaying an age-dependent degeneration of motor neurons detected as locomotory defects, disappearance of fluorescent markers, and apoptotic death of targeted neurons. Although an anti-nematode activity is reported for kiwifruit, it has been verified that neither green (*Actinidia deliciosa*, cultivar Hayward) nor gold (*Actinidia chinensis*, cultivar Hort 16A) kiwifruit extracts cause detectable effects on wild-type *C. elegans* growth and life cycle. Conversely, green kiwifruit extracts have a clear effect on the *C. elegans* SMA model by partially rescuing the degeneration and death of motor neurons and the locomotion impairment. The gold species does not show the same effect. The components responsible for the neuroprotection are macromolecules with a molecular weight higher than 3 kDa, present in the green and not in the yellow kiwifruit. In conclusion, this is the first study reporting a protective activity of green kiwifruit toward motor neurons. In addition, it has been demonstrated that *C. elegans* is an animal model suitable to study the biological activities contained in kiwifruit. Therefore, this model can be exploited for future investigations aimed at identifying kiwifruit molecules with potential applications in the field of human health.

Authors: Mazzarella N, Giangrieco I, Visone S, Santonicola P, Achenbach J, Zampi G, Tamburrini M, Di Schiavi E, Ciardiello MA.

Full Source: Food Science & Nutrition. 2019 Jun 17;7(7):2327-2335. doi: 10.1002/fsn3.1078. eCollection 2019 Jul.

### MEDICAL RESEARCH

#### Modelling the binding of diverse ligands within the Ah receptor ligand binding domain

2019-08-26

The Ah receptor (AhR) is a ligand-dependent transcription factor belonging to the basic helix-loop-helix Per-Arnt-Sim (bHLH-PAS) superfamily. Binding to and activation of the AhR by a variety of chemicals results in the induction of expression of diverse genes and production of a broad spectrum of biological and toxic effects. The AhR also plays important roles in several physiological responses, which has led it to become a novel target for the development of therapeutic drugs. Differences in the interactions of various ligands within the AhR ligand binding domain (LBD) may contribute to differential modulation of AhR functionality. In the present study, the authors combined computational and experimental analyses to investigate the binding modes of a group of chemicals representative of major classes of AhR ligands. On the basis of a novel computational approach for molecular docking to the homology model of the AhR LBD that includes the receptor flexibility, specific residues within the AhR binding cavity were predicted to play a critical role in binding of three distinct groups of chemicals. The prediction was validated by site-directed mutagenesis and evaluation of the relative ligand binding affinities for the mutant AhRs. These results provide an avenue for understanding ligand modulation of the AhR functionality and for rational drug design.

Authors: Giani Tagliabue S, Faber SC, Motta S, Denison MS, Bonati L.

Full Source: Science Reports. 2019 Jul 23;9(1):10693. doi: 10.1038/s41598-019-47138-z.

In the present study, the authors combined computational and experimental analyses to investigate the binding modes of a group of chemicals representative of major classes of AhR ligands.

#### Characterisation of rat glutathione transferases in olfactory epithelium and mucus

2019-08-26

The olfactory epithelium is continuously exposed to exogenous chemicals, including odorants. During the past decade, the enzymes surrounding the olfactory receptors have been shown to make an important contribution to the process of olfaction. Mammalian xenobiotic metabolising enzymes, such as cytochrome P450, esterases and glutathione transferases (GSTs), have been shown to participate in odorant clearance from the olfactory receptor environment, consequently contributing to the maintenance of sensitivity toward odorants. GSTs have previously been shown to be

involved in numerous physiological processes, including detoxification, steroid hormone biosynthesis, and amino acid catabolism. These enzymes ensure either the capture or the glutathione conjugation of a large number of ligands. Using a multi-technique approach (proteomic, immunocytochemistry and activity assays), the results indicate that GSTs play an important role in the rat olfactory process. First, proteomic analysis demonstrated the presence of different putative odorant metabolising enzymes, including different GSTs, in the rat nasal mucus. Second, GST expression was investigated in situ in rat olfactory tissues using immunohistochemical methods. Third, the activity of the main GST (GSTM2) odorant was studied with in vitro experiments. Recombinant GSTM2 was used to screen a set of odorants and characterise the nature of its interaction with the odorants. These results support a significant role of GSTs in the modulation of odorant availability for receptors in the peripheral olfactory process.

Authors: Heydel JM, Menetrier F, Belloir C, Canon F, Faure P, Lirussi F, Chavanne E, Saliou JM, Artur Y, Canivenc-Lavier MC, Briand L, Neiers F.  
Full Source: PLoS One. 2019 Jul 24;14(7):e0220259. doi: 10.1371/journal.pone.0220259. eCollection 2019.

### sAOP: Linking chemical stressors to Adverse Outcomes Pathway Networks

2019-08-26

Adverse outcome pathway (AOP) is a toxicological concept proposed to provide a mechanistic representation of biological perturbation over different layers of biological organization. Although AOPs are by definition chemical-agnostic, many chemical stressors can putatively interfere with one or several AOPs and such information would be relevant for regulatory decision-making. With the recent development of AOPs networks aiming to facilitate the identification of interactions among AOPs, the authors developed a stressor-AOP network (sAOP). Using the "cytotoxicity burst" (CTB) approach, bioactive compounds from the ToxCast data were mapped to a list of AOPs reported in AOP-Wiki database. With this analysis, a variety of relevant connections between chemicals and AOP components can be identified suggesting multiple effects not observed in the simplified "one-biological perturbation to one-adverse outcome" model. The results may assist in the prioritisation of chemicals to assess

Adverse outcome pathway (AOP) is a toxicological concept proposed to provide a mechanistic representation of biological perturbation over different layers of biological organization.

risk-based evaluations in the context of human health. sAOP is available at <http://saop.cpr.ku.dk>.

Authors: Aguayo-Orozco A, Audouze K, Siggaard T, Barouki R, Brunak S, Taboureau O.

Full Source: Bioinformatics. 2019 Jul 22. pii: btz570. doi: 10.1093/bioinformatics/btz570. [Epub ahead of print]

### Toxicogenomic analyses of the effects of BDE-47/209, TBBPA/S and TCBPA on early neural development with a human embryonic stem cell in vitro differentiation system

2019-08-26

Flame retardants are detected in the environment worldwide, and thus pose great risks to human health. The potential effects of these chemicals on the development of the central nervous system, have recently raised public concern. In this study, to explore the toxicity of these chemicals during the early developmental stages of the human central nervous system, the authors induced human embryonic stem cells to differentiate into neural ectoderm in the presence of five halogenated flame retardants, BDE-47, BDE-209, TBBPA, TBBPS and TCBPA, individually or in combination. A set of neural development-related biological processes that responded to these chemicals were identified, by analysing the whole transcriptional changes. The authors confirmed the RNA-seq results by qRT-PCR and found that transcription factors crucial for neural development, such as ZIC1, ZIC3, HES3, IGFBP3 and DLX5, were dysregulated by those chemicals. In addition, the five flame retardants might also influence axon growth/guidance and neuron transmission-related processes, by dysregulating genes including CNTN2, SLIT1, LRRC4C, RELN, CBLN1, CHRNB4 and GDF7. Furthermore, the chemical treatments seemed to interfere with the WNT and AHR signalling pathways. Overall, the current findings revealed that BDE-209 had similar toxicity as BDE-47, whereas TBBPS and TCBPA might not be safe alternatives to TBBPA. Interestingly, no obvious synergistic effects were observed when the authors mixed those five flame retardants together.

Authors: Liang S, Liang S, Yin N, Hu B, Faiola F.

Full Source: Toxicology & Applied Pharmacology. 2019 Jul 18; 379:114685. doi: 10.1016/j.taap.2019.114685. [Epub ahead of print]

In this study, to explore the toxicity of these chemicals during the early developmental stages of the human central nervous system, the authors induced human embryonic stem cells to differentiate into neural ectoderm in the presence of five halogenated flame retardants, BDE-47, BDE-209, TBBPA, TBBPS and TCBPA, individually or in combination.

### Identification of potential endocrine disrupting chemicals using gene expression biomarkers

2019-08-26

Recent technological advances have moved the field of toxicogenomics from reliance on microarray platforms to high-throughput transcriptomic (HTTr) technologies that measure global gene expression. Gene expression biomarkers are emerging as useful tools for interpreting gene expression profiles to identify perturbations of targets of xenobiotic chemicals including those that act as endocrine disrupting chemicals (EDCs). Gene expression biomarkers are lists of similarly-regulated genes identified in global gene expression comparisons of cells or tissues 1) exposed to known agonists or antagonists of the transcription factor (TF) and 2) after expression of the TF itself is knocked down/knocked out or overexpressed. Oestrogen receptor  $\alpha$  (ER $\alpha$ ) and androgen receptor (AR) biomarkers have been shown to be very accurate at identifying both agonists (94-97%) and antagonists (93-98%) in microarray data derived from human breast or prostate cancer cell lines. Importantly, the biomarkers have been shown to accurately replicate the results of computational models that predict ER $\alpha$  or AR modulation using multiple ToxCast HT screening assays. An integrated screening strategy using sets of biomarkers that simultaneously predict various EDC targets in relevant cell lines should simplify chemical screening without sacrificing accuracy. The biomarker predictions can be put into the context of the adverse outcome pathway framework to help prioritize chemicals with the greatest risk of potential adverse outcomes in the endocrine systems of animals and people.

Authors: Corton JC, Kleinstreuer NC, Judson RS.

Full Source: Toxicology & Applied Pharmacology. 2019 Jul 17:114683. doi: 10.1016/j.taap.2019.114683. [Epub ahead of print]

### OCCUPATIONAL RESEARCH

#### Setting up a collaborative European human biological monitoring study on occupational exposure to hexavalent chromium

2019-08-26

The EU human biomonitoring initiative, HBM4EU, aims to co-ordinate and advance human biomonitoring (HBM) across Europe. Within its remit, the project is gathering new, policy relevant, EU-wide data on occupational exposure to relevant priority chemicals and developing new approaches for occupational biomonitoring. In this study, the hexavalent chromium

The aim is to collect new data on current occupational exposure to Cr(VI) in Europe and to test new methods for Cr biomonitoring, specifically the analysis of Cr(VI) in exhaled breath condensate (EBC) and Cr in red blood cells (RBC) in addition to traditional urinary total Cr analyses.

[Cr(VI)] study design is presented as the first example of this HBM4EU approach. This study involves eight European countries and plans to recruit 400 workers performing Cr(VI) surface treatment e.g. electroplating or stainless- steel welding activities. The aim is to collect new data on current occupational exposure to Cr(VI) in Europe and to test new methods for Cr biomonitoring, specifically the analysis of Cr(VI) in exhaled breath condensate (EBC) and Cr in red blood cells (RBC) in addition to traditional urinary total Cr analyses. Furthermore, exposure data will be complemented with early biological effects data, including genetic and epigenetic effects. Personal air samples and wipe samples are collected in parallel to help informing the biomonitoring results. We present standard operational procedures (SOPs) to support the harmonised methodologies for the collection of occupational hygiene and HBM samples in different countries.

Authors: Santonen T, Alimonti A, Bocca B, Duca RC, Galea KS, Godderis L, Göen T, Gomes B, Hanser O, Iavicoli I, Janasik B, Jones K, Kiilunen M, Koch HM, Leese E, Leso V, Louro H, Ndaw S, Porras SP, Robert A, Ruggieri F, Scheepers PTJ, Silva MJ, Viegas S, Wasowicz W, Castano A, Sepai O.

Full Source: Environmental Research. 2019 Jul 10; 177:108583. doi: 10.1016/j.envres.2019.108583. [Epub ahead of print]

### An atypical *Bacillus anthracis* infection in a bull-A potential occupational health hazard

2019-08-26

*Bacillus anthracis* infecting cattle is usually identified based on the typical symptom: sudden death. *Bacillus anthracis* causing atypical symptoms may remain undiagnosed and represent a potential occupational health hazard for, that is veterinarians and producers, butchers and tanners. In the year 2004, one case of sudden death in a dairy farm in southern Finland was diagnosed as bovine anthrax. Four years later 2008, an atypical case of anthrax was diagnosed in the same holding. The bull was taken to the Production Animal Hospital of the Faculty of Veterinary Medicine, University of Helsinki because of fever, loss of appetite and a symmetrically swollen scrotal sac. Penicillin treatment cured the fever but not the swollen scrotum. Before the intended therapeutic castration, a punctuate consisting of 10 ml fluid collected into a syringe from the scrotal sac was cultivated on blood agar at 37°C. After 24 hr, an almost pure culture of a completely non-haemolytic *Bacillus cereus*-like bacteria was obtained. The strain was identified as *B. anthracis* using Ba-specific primers by the Finnish Food Safety Authority (RUOKAVIRASTO). After the diagnosis, the bull was euthanised and destroyed, the personnel were treated with

prophylactic antibiotics and the clinic was disinfected. In this particular case, treatment with water, Virkon S and lime seemed to be effective to eliminate endospores and vegetative cells since no relapses of anthrax have occurred in 10 years. This case is the last reported anthrax case in Finland.

Authors: Friman M, Kakko L, Constantin C, Simojoki H, Andersson MA, Nagy S, Salonen H, Andersson M.

Full Source: Reproduction in Domestic Animals. 2019 Jul 26. doi: 10.1111/rda.13532. [Epub ahead of print]

### Dermatitis among workers in Ontario: results from the Occupational Disease Surveillance System

2019-08-26

Dermatitis is the most common occupational skin disease, and further evidence is needed regarding preventable risk factors. The Occupational Disease Surveillance System (ODSS) derived from administrative data was used to investigate dermatitis risk among industry and occupation groups in Ontario. ODSS cohort members were identified from Workplace Safety and Insurance Board (WSIB) accepted lost time claims. A case was defined as having  $\geq 2$  dermatitis physician billing claims during a 12-month period within 3 years of cohort entry. A 3-year look-back period prior to cohort entry was used to exclude prevalent cases without a WSIB claim. Workers were followed for 3 years or until dermatitis diagnosis, age 65 years, emigration, death or end of follow-up (31 December 2016), whichever occurred first. Age-adjusted and sex-adjusted Cox proportional hazard models estimated HRs and 95% CIs. The risk of dermatitis was explored using a job exposure matrix that identifies exposure to asthmagens, many of which also cause contact dermatitis. Among 597 401 workers, 23 843 cases of new-onset dermatitis were identified. Expected elevated risks were observed among several groups including furniture and fixture industries, food and beverage preparation and chemicals, petroleum, rubber, plastic and related materials processing occupations and workers exposed to metal working fluids and organic solvents. Decreased risk was observed among farmers, nurses and construction industries, and occupations exposed to latex and indoor cleaning products. ODSS can contribute to occupational dermatitis surveillance in Ontario by

The Occupational Disease Surveillance System (ODSS) derived from administrative data was used to investigate dermatitis risk among industry and occupation groups in Ontario.

identifying occupational groups at risk of dermatitis that can then be prioritised for prevention activities.

Authors: Shakik S, Arrandale V, Holness DL, MacLeod JS, McLeod CB, Peter A, Demers PA.

Full Source: Occupational & Environmental Medicine. 2019 Jul 18. pii: oemed-2018-105667. doi: 10.1136/oemed-2018-105667. [Epub ahead of print]

### Urinary parabens in adults from South China: Implications for human exposure and health risks

2019-08-26

Parabens are a kind of preservatives widely used in cosmetic and personal care products and ubiquitously detected in the environment. However, little is known on human exposure to these chemicals. In this study, the authors mainly investigated the urinary parabens in adults from South China to evaluate the cumulative risk of paraben exposure. A total of 562 urine samples were collected from adult workers for the determination of methyl paraben (MeP), ethyl paraben (EtP), propyl paraben (PrP), butyl paraben, and benzyl parabens. High detection frequencies ( $\geq 98\%$ ) were observed for MeP, EtP, and PrP with median concentrations of 8.88, 5.11, and 1.44  $\mu\text{g/L}$ , respectively. Urinary parabens were 4.5-46.2 fold higher in urine of females than those in males. Urinary MeP was associated with alcohol drinking and a history of tumour, while urinary PrP was negatively associated with education levels of the subjects. There were not significant associations between urinary concentrations of parabens and body mass index, which indicated that obesity was not associated with paraben exposure. Also, parabens did not correlate with human dietary habits. Although the total estimated daily intake (TEDI) of the major compound MeP and EtP in adult workers was lower than the acceptable daily intake (ADI), the TEDI of PrP exceed the ADI for a very few subjects, especially for females and low-educated ones, suggesting potential health risks.

Authors: Yu Y, Li W, Lu S, Wu S, Wang F, Tse LA, Kang L, Ma S.

Full Source: Ecotoxicology & Environmental Safety. 2019 Oct 30; 182:109419. doi: 10.1016/j.ecoenv.2019.109419. Epub 2019 Jul 10.

In this study, the authors mainly investigated the urinary parabens in adults from South China to evaluate the cumulative risk of paraben exposure.

### Characterising Occupational Health Risks and Chemical Exposures Among Asian Nail Salon Workers on the East Coast of the United States

2019-08-26

The products used in nail care services contain toxic chemicals. This study aimed to characterise occupational health risk factors and chemical exposures among Asian nail salon workers on the East Coast of the U.S. for informing the development of more effective, culturally appropriate interventions. The authors conducted a community-based participatory research (CBPR) study to characterise occupational health risks. A face-to-face, self-reported survey was performed, and personal exposure to volatile organic compounds (VOCs) was evaluated. Three VOCs, acetone, methyl methacrylate (MMA), and toluene, were measured using 3M 3500 organic vapor monitors. Data on 112 workers with 100 personal chemical exposure measurements was collected from 25 nail salons. Self-reported health problems that emerged or worsened after participants started working in the nail salon industry included headaches (8%); light-headedness (9.8%); and irritation to the nose, eyes, throat, and skin (21.2%). Approximately 70% of participants reported that they had been pregnant, 11.7% of whom had at least one miscarriage. The mean concentrations of acetone, MMA, and toluene were 18.51 parts per million (ppm), 39.45 ppm, and 0.09 ppm, respectively. Mean concentrations of acetone and MMA measured from salons in New York City were significantly lower than those measured in Philadelphia and southern New Jersey. CBPR proved to be as an efficient approach for recruiting hard-to-reach Asian immigrant nail salon workers. Adverse health symptoms and problems associated with providing nail salon services were identified in these workers. Further studies are needed to better understand the long-term health effects of chronic chemical exposures in nail salon environments.

Authors: Ma GX, Wei Z, Husni R, Do P, Zhou K, Rhee J, Tan Y, Navder K, Yeh MC.

Full Source: Journal of Community Health. 2019 Jul 11. doi: 10.1007/s10900-019-00702-0. [Epub ahead of print]

The authors aimed to examine maternal urinary BPA and BPS levels longitudinally measured across pregnancy in relation to gestational age and PTB.

### PUBLIC HEALTH RESEARCH

#### Bisphenol A and bisphenol S exposures during pregnancy and gestational age – A longitudinal study in China

2019-08-26

Bisphenol A (BPA) and its substitute bisphenol S (BPS) are endocrine-disrupting chemicals and metabolised rapidly in human body. BPA exposure in late pregnancy has been suggested to be associated with preterm birth (PTB), but the associations of trimester BPA and BPS exposures with gestational age have been rarely studied. The authors aimed to examine maternal urinary BPA and BPS levels longitudinally measured across pregnancy in relation to gestational age and PTB. A prenatal cohort study was conducted between 2014 and 2015 in Wuhan, China. Maternal urinary BPA and BPS concentrations were measured in a complete series of urine samples collected in the 1st, 2nd and 3rd trimesters from 850 pregnant women and corrected by specific gravity. In comparison with the lowest tertile of maternal urinary BPA, higher levels of averaged BPA concentration across pregnancy was associated with a 1.97-day decrease in gestation (95% CI: 3.25, -0.68) and an adjusted odds ratio of 3.19 (95% CI: 1.00, 10.45) for PTB. Higher BPA concentrations in three trimesters were also negatively associated with gestational age and positively correlated with PTB. In contrast, only a positive association of third-trimester BPS with gestational age was found, but the significant association disappeared in the adjusted models. Both maternal trimester and averaged BPA exposure across pregnancy were significantly associated with shortened gestation and increased risk of PTB. However, the results showed little evidence of a relationship between BPS and PTB. Authors: Huang S, Li J, Xu S, Zhao H, Li Y, Zhou Y, Fang J, Liao J, Cai Z, Xia W. Full Source: *Chemosphere*. 2019 Jul 22; 237:124426. doi: 10.1016/j.chemosphere.2019.124426. [Epub ahead of print]

The objective of the current study was to examine the potential modifying effect of stressful life events and their subjective impact on associations between prenatal phthalates and anogenital distance.

#### Do stressful life events during pregnancy modify associations between phthalates and anogenital distance in newborns?

2019-08-26

Anogenital distance (AGD) has been used as a marker of foetal androgen action to identify endocrine disrupting chemicals. A US study (TIDES) has reported that the association between some phthalates and reduced AGD in males was only apparent in sons of mothers reporting no stressful life events (SLEs) during pregnancy. The objective of the current study was to

examine the potential modifying effect of SLEs and their subjective impact on associations between prenatal phthalates and AGD. First trimester urines from the MIREC Study were analysed for phthalate metabolites and AGD was measured in neonates. Post-delivery, the women answered questions on SLEs during the pregnancy. Women reporting 1 or more SLEs during pregnancy were considered a “higher stressor” group, whereas women reporting no SLEs or who reported a SLE that was perceived as not at all stressful were considered a “lower stressor” group. Multivariable linear regression models were fit stratified by stressor group. Maternal stressor, AGD and phthalates results were available for 153 females and 147 males. A summary measure of androgen-disrupting phthalates ( $\Sigma$  AD) was associated with significantly longer AGDs in females from the higher stressor group. These effect sizes were increased when the perceived impact was restricted to moderately or very much stressful. In males, all phthalates were associated with longer anopenile distance (APD), regardless of stressor group; however, higher  $\Sigma$  AD was associated with significantly longer APD in the lower stressor group. In contrast to the TIDES study, the authors did not observe shorter AGDs in male infants prenatally exposed to di-(2-ethylhexyl) phthalates, regardless of maternal stressor level. In conclusion, we were unable to replicate the findings of the TIDES study, but did find some evidence that prenatal SLEs may modify associations between phthalates and female AGD. Further research with other populations and measures of prenatal stress may shed more light on whether prenatal stress is an important effect modifier of associations between phthalates (or other chemicals) and anogenital distance.

Authors: Arbuckle TE, MacPherson S, Barrett E, Muckle G, Séguin JR, Foster WG, Sathyanarayana S, Dodds L, Fisher M, Agarwal A, Monnier P, Walker M, Fraser WD.

Full Source: Environmental Research. 2019 Jul 19; 177:108593. doi: 10.1016/j.envres.2019.108593. [Epub ahead of print]

### Application of new statistical distribution approaches for environmental mixture risk assessment: A case study

2019-08-26

There is growing evidence that single substances present below their individual thresholds of effect may still contribute to combined effects. In component-based mixture risk assessment (MRA), the risks can be addressed using information on the mixture components. This is, however, often hampered by limited availability of ecotoxicity data. Here, the possible use of ecotoxicological threshold concentrations of no concern (i.e. 5th percentile of statistical distribution of ecotoxicological values)

In component-based mixture risk assessment (MRA), the risks can be addressed using information on the mixture components.

is investigated to fill data gaps in MRA. For chemicals without available aquatic toxicity data, ecotoxicological threshold concentrations of no concern have been derived from Predicted No Effect Concentration (PNEC) distributions and from chemical toxicity distributions, using the EnviroTox tool, with and without considering the chemical mode of action. For exposure, chemical monitoring data from European rivers have been used to illustrate four realistic co-exposure scenarios. Based on those monitoring data and available ecotoxicity data or threshold concentrations when no data were available, Risk Quotients for individual chemicals were calculated, to then derive a mixture Risk Quotient (RQmix). A risk was identified in two of the four scenarios. Threshold concentrations contribute from 24 to 95% of the whole RQmix; thus, they have a large impact on the predicted mixture risk. Therefore, they could only be used for data gap filling for a limited number of chemicals in the mixture. The use of mode of action information to derive more specific threshold values could be a helpful refinement in some cases.

Authors: Kienzler A, Bopp S, Halder M, Embry M, Worth A.

Full Source: Science of the Total Environment. 2019 Jul 21; 693:133510. doi: 10.1016/j.scitotenv.2019.07.316. [Epub ahead of print]

### Oxidative Stress Markers, Trace Elements and Endocrine Disrupting Chemicals in Children with Hashimoto's Thyroiditis

2019-08-26

In this study, the authors aimed to investigate whether bisphenol A (BPA) and di(2-ethylhexyl) phthalate (DEHP) exposure has any association with Hashimoto's thyroiditis (HT) and its biomarkers and to determine whether oxidative stress biomarkers and trace element levels showed any alterations in children with HT. The authors found that superoxide dismutase and glutathione peroxidase activities are lower in HT group from control (24% and 46% respectively,  $p < 0,05$ ). Zinc levels were significantly lower in HT group vs. control. In addition, the levels of mono(2-ethylhexyl) phthalate (MEHP) which is the primary metabolite for DEHP, were markedly higher in HT group compared to control ( $p < 0.05$ ). A negative correlation was observed between urinary BPA levels and ft4. In children with HT, oxidant/antioxidant balance is changed and these differences may be related by EDC exposure, the importance of which should be elucidated with further studies.

Authors: Sur U, Erkekoglu P, Bulus AD, Andiran N, Kocer-Gumusel B.

Full Source: Toxicology Mechanisms and Methods. 2019 Jul 29:1-30. doi: 10.1080/15376516.2019.1646367. [Epub ahead of print]

In this study, the authors aimed to investigate whether bisphenol A (BPA) and di(2-ethylhexyl) phthalate (DEHP) exposure has any association with Hashimoto's thyroiditis (HT) and its biomarkers and to determine whether oxidative stress biomarkers and trace element levels showed any alterations in children with HT.

### Chemical characterisation and bioactivity of phenolics from Tieguanyin oolong tea

2019-08-26

Phenolics are the main bioactive components in tea and greatly contribute to human health. Three phenolic-enriched extracts, the ethyl acetate fraction (TEF), n-butanol fraction (TBF), and water fraction (TWF), were obtained from Tieguanyin oolong tea, which is considered a typical type of semi-fermented tea. The chemicals in the extracts and their antioxidant activity and cytotoxicity against 4T1 breast cancer cells were investigated in the present work. TEF was found to have the highest contents of phenolics, flavonoids, procyanidins, sugars, and catechin monomers. Meanwhile, TEF exhibited the strongest antioxidant capacity, which may be due to its abundant bioactive compounds, as validated by Pearson correlation and hierarchical clustering analysis. Furthermore, TEF showed greater inhibition of the growth of 4T1 murine breast cancer cells than TBF and TWF. Fermentation during the processing of oolong tea causes many alterations in polyphenols, leading to different bioactivities. In the present work, three phenolic-enriched extracts, the ethyl acetate fraction (TEF), n-butanol fraction (TBF), and water fraction (TWF), were obtained from Tieguanyin oolong tea. Further tests showed that TEF and TBF from Tieguanyin oolong tea possessed remarkable antioxidant activity and inhibitory potential inhibition of the growth of 4T1 murine breast cancer cells in vitro due to their main bioactive compounds, including phenolics and flavonoids. Thus, the phenolic-enriched extracts from Tieguanyin tea are expected to have a potential application in the food and pharmaceutical industries after further study.

Authors: Wang Y, Kong D, Gao Y, Ying L, Huang Q, Xu P.

Full Source: Journal of Food Biochemistry. 2019 Jul;43(7):e12894. doi: 10.1111/jfbc.12894. Epub 2019 May 15.