

Bulletin Board

Contents

OCT. 16, 2020

[click on page numbers for links]

CHEMICAL EFFECTS

An inadvertent issue of human retina exposure to endocrine disrupting chemicals: A safety assessment.....	3
Are Persistent Organic Pollutants Linked to Lipid Abnormalities, Atherosclerosis and Cardiovascular Disease? A Review.....	3
Agrochemicals in freshwater systems and their potential as endocrine disrupting chemicals: A South African context.....	4

ENVIRONMENTAL RESEARCH

Pre- and Post-harvest Factors Affecting Glucosinolate Content in Broccoli	5
Plasma titanium level is positively associated with metabolic syndrome: A survey in China's heavy metal polluted regions.....	6

OCCUPATIONAL

Occupational Exposure to Electric Shocks and Extremely Low-Frequency Magnetic Fields and Motor Neurone Disease.....	7
Self-reported disease symptoms of stone quarry workers exposed to silica dust in Ghana.....	7
Quantitative microbial risk assessment and sensitivity analysis for workers exposed to pathogenic bacterial bioaerosols under various aeration modes in two wastewater treatment plants.....	8

PHARMACEUTICAL/TOXICOLOGY

Cetuximab produced from a goat mammary gland expression system is equally efficacious as innovator cetuximab in animal cancer models.....	9
Histone methylation status of H3K4me3 and H3K9me3 under methionine restriction is unstable in methionine-addicted cancer cells, but stable in normal cells.....	10

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Bulletin Board

Technical

OCT. 16, 2020

CHEMICAL EFFECTS

An inadvertent issue of human retina exposure to endocrine disrupting chemicals: A safety assessment

2020-09-30

Endocrine disrupting chemicals (EDCs) are a group of chemical compounds that present a considerable public health problem due to their pervasiveness and associations with chronic diseases. EDCs can interrupt the endocrine system and interfere with hormone homeostasis, leading to abnormalities in human physiology. Much attention has been focused on the adverse effects EDCs have on the reproductive system, neurogenesis, neuroendocrine system, and thyroid dysfunction. The eye is usually directly exposed to the surrounding environment; however, the influences of EDCs on the eye have received comparatively little attention. Ocular diseases, such as ocular surface diseases and retinal diseases, have been implicated in hormone deficiency or excess. Epidemiologic studies have shown that EDC exposure not only causes ocular surface disorders, such as dry eye, but also associates with visual deficits and retinopathy. EDCs can pass through the human blood-retinal barrier and enter the neural retina, and can then accumulate in the retina. The retina is an embryologic extension of the central nervous system, and is extremely sensitive and vulnerable to EDCs that could be passed across the placenta during critical periods of retinal development. Subtle alterations in the retinal development process usually result in profound immediate, long-term, and delayed effects late in life. This review, based on extensive literature survey, briefly summarizes the current knowledge about the impact of representative manufactured EDCs on retinal toxicity, including retinal structure alterations and dysfunction. We also highlight the potential mechanism of action of EDCs on the retina, and the predictive retinal models of EDC exposure.

Authors: Minghui Li, Tian Yang, Lixiong Gao, Haiwei Xu

Full Source: Chemosphere 2020 Sep 30;264(Pt 1):128484. doi: 10.1016/j.chemosphere.2020.128484.

Are Persistent Organic Pollutants Linked to Lipid Abnormalities, Atherosclerosis and Cardiovascular Disease? A Review

2020-09

The term persistent organic pollutants (POPs) denotes chemicals with known or suspected adverse health effects in animals or humans and with chemical properties that make them accumulate in the

Bulletin Board

Technical

OCT. 16, 2020

environment, including animals or humans. Lipid-soluble POPs, like dioxins, polychlorinated biphenyls (PCBs) and organochlorine pesticides are transported by lipoproteins and accumulate in adipose tissue. High levels of these compounds in the circulation have been associated with elevated cholesterol and triglycerides in cross-sectional studies and with an increase in mainly low-density lipoprotein cholesterol in a longitudinal study. Also, non-lipid-soluble POPs, such as perfluoroalkyl substances (PFASs) compounds have been associated with increased total cholesterol levels. Carotid artery atherosclerosis has been related to elevated levels of mainly highly chlorinated PCBs and to highly fluorinated PFASs, but in this case only in women. Both cross-sectional and prospective studies have shown dioxins, PCBs, as well as PFASs to be linked to cardiovascular disease (CVD) and mortality. In conclusion, as highlighted in this review, several lines of evidence support the view that POPs of different chemical classes could be linked to lipid abnormalities, carotid atherosclerosis and overt CVD like myocardial infarction and stroke.

Authors: P Monica Lind, Lars Lind

Full Source: Journal of lipid and atherosclerosis 2020 Sep;9(3):334-348. doi: 10.12997/jla.2020.9.3.334.

Agrochemicals in freshwater systems and their potential as endocrine disrupting chemicals: A South African context

2020-09-24

South Africa is the largest agrochemical user in sub-Saharan Africa, with over 3000 registered pesticide products. Although they reduce crop losses, these chemicals reach non-target aquatic environments via leaching, spray drift or run-off. In this review, attention is paid to legacy and current-use pesticides reported in literature for the freshwater environment of South Africa and to the extent these are linked to endocrine disruption. Although banned, residues of many legacy organochlorine pesticides (endosulfan and dichlorodiphenyltrichloroethane (DDT)) are still detected in South African watercourses and wildlife. Several current-use pesticides (triazine herbicides, glyphosate-based herbicides, 2,4-dichlorophenoxyacetic acid (2,4-D) and chlorpyrifos) have also been reported. Agrochemicals can interfere with normal hormone function of non-target organism leading to various endocrine disrupting (ED) effects: intersex, reduced spermatogenesis, asymmetric urogenital papillae, testicular lesions and infertile eggs. Although studies investigating the occurrence of agrochemicals and/or ED effects in freshwater aquatic environments in South Africa have increased, few studies determined both

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Bulletin Board

Technical

OCT. 16, 2020

the levels of agricultural pesticides present and associated ED effects. The majority of studies conducted are either laboratory-based employing in vitro or in vivo bioassays to determine ED effects of agrochemicals or studies that investigate environmental concentrations of pesticides. However, a combined approach of bioassays and chemical screening will provide a more comprehensive overview of agrochemical pollution of water systems in South Africa and the risks associated with long-term chronic exposure.

Authors: Ilzé Horak, Suranie Horn, Rialet Pieters

Full Source: Environmental pollution (Barking, Essex : 1987) 2020 Sep 24;268(Pt A):115718. doi: 10.1016/j.envpol.2020.115718.

ENVIRONMENTAL RESEARCH

Pre- and Post-harvest Factors Affecting Glucosinolate Content in Broccoli

2020-09-10

Owing to several presumed health-promoting biological activities, increased attention is being given to natural plant chemicals, especially those frequently entering the human diet. Glucosinolates (GLs) are the main bioactive compounds found in broccoli (*Brassica oleracea* L. var. *italica* Plenck). Their regular dietary assumption has been correlated with reduced risk of various types of neoplasms (lung, colon, pancreatic, breast, bladder, and prostate cancers), some degenerative diseases, such as Alzheimer's, and decreased incidence of cardiovascular pathologies. GL's synthesis pathway and regulation mechanism have been elucidated mainly in *Arabidopsis*. However, nearly 56 putative genes have been identified as involved in the *B. oleracea* GL pathway. It is widely recognized that there are several pre-harvest (genotype, growing environment, cultural practices, ripening stage, etc.) and post-harvest (harvesting, post-harvest treatments, packaging, storage, etc.) factors that affect GL synthesis, profiles, and levels in broccoli. Understanding how these factors act and interact in driving GL accumulation in the edible parts is essential for developing new broccoli cultivars with improved health-promoting bioactivity. In this regard, any systematic and comprehensive review outlining the effects of pre- and post-harvest factors on the accumulation of GLs in broccoli is not yet available. Thus, the goal of this paper is to fill this gap by giving a synoptic overview of the most relevant and recent literature. The existence of substantial cultivar-to-cultivar variation in GL content in response to pre-harvest factors and post-harvest manipulations has been highlighted and discussed. The paper also stresses the need for adapting particular

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Bulletin Board

Technical

OCT. 16, 2020

pre- and post-harvest procedures for each particular genotype in order to maintain nutritious, fresh-like quality throughout the broccoli value chain.

Authors: Riadh Ilahy, Imen Tlili, Zoltán Pék, Anna Montefusco, Mohammed Wasim Siddiqui, Fozia Homa, Chafik Hdider, Thouraya R'Him, Helyes Lajos, Marcello Salvatore Lenucci

Full Source: Frontiers in nutrition 2020 Sep 10;7:147. doi: 10.3389/fnut.2020.00147.

Plasma titanium level is positively associated with metabolic syndrome: A survey in China's heavy metal polluted regions

2020-10-07

Objective: Several heavy metals have been reported to be associated with metabolic syndrome (MetS) in general population, while effects of multiple metals exposure on MetS in residents living in heavy metal polluted regions have not been investigated. We aimed to assess the association of 23 metal levels and MetS among population living in China's heavy metal polluted regions.

Methods: From August 2016 to July 2017, a total of 2109 eligible participants were consecutively enrolled in our study in Hunan province, China. The levels of plasma and urine metals were measured by inductively coupled plasma mass spectrometer (ICP-MS). MetS was defined by the criteria of the International Diabetes Federation. Multivariable regression models were applied to analysis the potential relationship.

Results: In the overall population, crude model showed positive relationship of plasma titanium (Ti) with MetS and negative association of urine vanadium, iron, and selenium with MetS. After adjusted for potential confounders, only plasma Ti was positive associated with MetS (adjusted OR for Q4 versus Q1: 1.46; 95% CI: 1.06-1.99), and this positive correlation was explained by abdominal obesity (OR = 1.84, 95% CI: 1.41-2.39) and high triglycerides (OR = 2.23, 95% CI: 1.68-2.96). Further linear regression analysis revealed significant association of plasma Ti levels with waist circumference ($\beta = 0.0056$, 95% CI: 0.0004-0.0109, $P = 0.036$) and triglycerides ($\beta = 0.0012$, 95% CI: 0.0006-0.0019, $P < 0.001$), respectively.

Conclusion: High plasma Ti level was associated with increased risk of MetS via increasing waist circumference and triglycerides in people under high metal exposure.

Authors: Miao Huang, Jingyuan Chen, Guangyu Yan, Yiping Yang, Dan Luo, Xiang Chen, Meian He, Hong Yuan, Zhijun Huang, Yao Lu

Full Source: Ecotoxicology and environmental safety 2020 Oct 7;208:111435. doi: 10.1016/j.ecoenv.2020.111435.

Objective: Several heavy metals have been reported to be associated with metabolic syndrome (MetS) in general population, while effects of multiple metals exposure on MetS in residents living in heavy metal polluted regions have not been investigated.

Bulletin Board

Technical

OCT. 16, 2020

OCCUPATIONAL

Occupational Exposure to Electric Shocks and Extremely Low-Frequency Magnetic Fields and Motor Neurone Disease

2020-10-09

In a New Zealand population-based case-control study we assessed associations with occupational exposure to electric shocks, extremely low-frequency magnetic fields (ELF-MF) and motor neurone disease using job-exposure matrices to assess exposure. Participants were recruited between 2013 and 2016. Associations with ever/never, duration, and cumulative exposure were assessed using logistic regression adjusted for age, sex, ethnicity, socioeconomic status, education, smoking, alcohol consumption, sports, head or spine injury and solvents, and mutually adjusted for the other exposure. All analyses were repeated stratified by sex. An elevated risk was observed for having ever worked in a job with potential for electric shocks (odds ratio (OR)=1.35, 95% confidence interval (CI): 0.98, 1.86), with the strongest association for the highest level of exposure (OR=2.01, 95%CI: 1.31, 3.09). Analysis by duration suggested a non-linear association: risk was increased for both short-duration (<3 years) (OR= 4.69, 95%CI: 2.25, 9.77) and long-duration in a job with high level of electric shock exposure (>24 years; OR=1.88; 95%CI: 1.05, 3.36), with less pronounced associations for intermediate durations. No association with ELF-MF was found. Our findings provide support for an association between occupational exposure to electric shocks and motor neurone disease but did not show associations with exposure to work-related ELF-MF.

Authors: Grace X Chen, Andrea't Mannetje, Jeroen Douwes, Leonard H Berg, Neil Pearce, Hans Kromhout, Bill Glass, Naomi Brewer, Dave J McLean

Full Source: American journal of epidemiology 2020 Oct 9;kwaa214. doi: 10.1093/aje/kwaa214.

Self-reported disease symptoms of stone quarry workers exposed to silica dust in Ghana

2020-10-05

Background and aims: Understanding the importance of using personal protective equipment (PPE) and the influence of work-post (working distance to main dust source-crusher) in stone quarries is vital for designing tailored interventions in minimizing workers' exposure to silica

Bulletin Board

Technical

OCT. 16, 2020

dust. Nonetheless, studies on silica dust and disease symptoms in Ghana are nascent. This study assessed how work-post and use of required PPE jointly influence exposure to silica dust and disease symptoms in Ghana. Methods: Generalized linear models (complementary log-log regression) were fitted to cross-sectional survey data of 524 stone quarry workers in Ghana to assess the joint effect of work-post and PPE usage on self-reported disease symptoms while controlling for relevant compositional and contextual factors.

Results: Stone quarry workers who work between 1-100 m and beyond 100 m from the crusher with the required PPE were 90% and 87% respectively less likely to report eye irritation compared with their counterparts who work between 1 and 100 m from the crusher without the required PPE. Individuals who work between 1-100 m and beyond 100 m from the crusher with the required PPE were 94% and 95% respectively less likely to report breathing difficulty compared with the reference group. Workers who work between 1-100 m and beyond 100 m from the crusher with the required PPE were 97% and 99% respectively less likely to report coughing compared with the reference group. Workers who work between 1-100 m and beyond 100 m from the crusher with the required PPE were 93% and 97% respectively less likely to report common cold compared with their counterparts who work between 1 and 100 m from the crusher without the required PPE. Conclusion: There are adverse health implications for people who work in silica dust polluted environments, suggesting the need for a national safety and health policy to target them.

Authors: Dzifa Francis Ahadzi, Abdul-Rahaman Afitiri, Bernard Ekumah, Verona Kanatey, Abdullah Afedzi

Full Source: Health science reports 2020 Oct 5;3(4):e189. doi: 10.1002/hsr.2.189.

Quantitative microbial risk assessment and sensitivity analysis for workers exposed to pathogenic bacterial bioaerosols under various aeration modes in two wastewater treatment plants

2020-10-01

Wastewater treatment plants (WWTPs) could emit a large amount of bioaerosols containing pathogenic bacteria. Assessing the health risks of exposure to these bioaerosols by using quantitative microbial risk assessment (QMRA) is important to protect workers in WWTPs. However, the relative impacts of the stochastic input variables on the health risks determined in QMRA remain vague. Hence, this study performed a Monte

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Bulletin Board

Technical

OCT. 16, 2020

Carlo simulation-based QMRA case study for workers exposing to *S. aureus* or *E. coli* bioaerosols and a sensitivity analysis in two WWTPs with various aeration modes. Results showed that when workers equipped without personal protective equipment (PPE) were exposed to *S. aureus* or *E. coli* bioaerosol in the two WWTPs, the annual probability of infection considerably exceeded the U.S. EPA benchmark ($\leq 10E-4$ pppy), and the disease burden did not satisfy the WHO benchmark ($\leq 10E-6$ DALYs pppy) [except exposure to *E. coli* bioaerosol for disease health risk burden]. Nevertheless, the use of PPE effectively reduced the annual infection health risk to an acceptable level and converted the disease health risk burden to a highly acceptable level. Referring to the sensitivity analysis, the contribution of mechanical aeration modes to the variability of the health risks was absolutely dominated in the WWTPs. On the aeration mode that showed high exposure concentration, the three input exposure parameters (exposure time, aerosol ingestion rate, and breathing rate) had a great impact on health risks. The health risks were also prone to being highly influenced by the various choices of the dose-response model and related parameters. Current research systematically delivered new data and a novel perspective on the sensitivity analysis of QMRA. Then, management decisions could be executed by authorities on the basis of the results of this sensitivity analysis to reduce related occupational health risks of workers in WWTPs.

Authors: Yan-Huan Chen, Cheng Yan, Ya-Fei Yang, Jia-Xin Ma

Full Source: The Science of the total environment 2020 Oct 1;755(Pt 2):142615. doi: 10.1016/j.scitotenv.2020.142615.

PHARMACEUTICAL/TOXICOLOGY

Cetuximab produced from a goat mammary gland expression system is equally efficacious as innovator cetuximab in animal cancer models

2020-09-22

There is increasing demand for improved production and purification systems for biosimilar or biobetter humanised monoclonal antibodies and animal production systems offer one such possible option. Cetuximab, also known as 'Erbix', is a humanised monoclonal antibody widely used in cancer therapy. We have previously reported on a genetically engineered goat system to produce cetuximab (gCetuximab) in milk. Herein we report that gCetuximab has similar bioactivity and pharmacokinetic properties compared with the commercial product produced in mammalian cell

Bulletin Board

Technical

OCT. 16, 2020

culture. In particular both forms have very similar efficacy in a HT29 colorectal cancer xenograft model alone or when conjugated to the toxin MMAE. This also demonstrates that the gCetuximab will be a viable vehicle for antibody drug conjugate based therapies. Taken together, this shows that the goat milk monoclonal antibody production system is an effective way of producing a biosimilar form of cetuximab.

Authors: Qian Wang, William Gavin, Nicholas Masiello, Khanh B Tran, Götz Laible, Peter R Shepherd

Full Source: Biotechnology reports (Amsterdam, Netherlands) 2020 Sep 22;28:e00533. doi: 10.1016/j.btre.2020.e00533.

Histone methylation status of H3K4me3 and H3K9me3 under methionine restriction is unstable in methionine-addicted cancer cells, but stable in normal cells

2020-10-02

Methionine addiction is a fundamental and general hallmark of cancer. Methionine addiction prevents cancer cells, but not normal cells from proliferation under methionine restriction (MR). Previous studies reported that MR altered the histone methylation levels in methionine-addicted cancer cells. However, no study has yet compared the status of histone methylation status, under MR, between cancer cells and normal cells. In the present study, we compared the histone methylation status between cancer cells and normal fibroblasts of H3K4me3 and H3K9me3, using recombinant methioninase (rMETase) to effect MR. Human lung and colon cancer cell lines and human normal foreskin fibroblasts were cultured in control medium or medium with rMETase. The viability of foreskin fibroblasts was approximately 10 times more resistant to rMETase than the cancer cells in vitro. Proliferation only of the cancer cells ceased under MR. The histone methylation status of H3K4me3 and H3K9me3 under MR was evaluated by immunoblotting. The levels of the H3K4me3 and H3K9me3 were strongly decreased by MR in the cancer cells. In contrast, the levels of H3K4me3 and H3K9me3 were not altered by MR in normal fibroblasts. The present results suggest that histone methylation status of H3K4me3 and H3K9me3 under MR was unstable in cancer cells but stable in normal cells and the instability of histone methylation status under MR may determine the high methionine dependency of cancer cells to survive and proliferate.

Authors: Jun Yamamoto, Qinghong Han, Sachiko Inubushi, Norihiko Sugisawa, Kazuyuki Hamada, Hiroto Nishino, Kentaro Miyake, Takafumi

Methionine addiction is a fundamental and general hallmark of cancer.

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Bulletin Board

Technical

OCT. 16, 2020

Kumamoto, Ryusei Matsuyama, Michael Bouvet, Itaru Endo, Robert M Hoffman

Full Source: Biochemical and biophysical research communications 2020

Oct 2;S0006-291X(20)31861-1. doi: 10.1016/j.bbrc.2020.09.108.