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Food Safety Briefs

Risk Assessment

Risk-Based Chemical Ranking and Generating a Prioritized Human Exposome Database

Zhao F, Li L, Chen Y, Huang Y, Keerthisinghe TP, Chow A, et al. *Environ Health Perspect*. 2021 Apr;129(4):47014. doi: 10.1289/EHP7722. **Article link**.

Significance: Creating an exposome database composed of thousands of chemicals can guide biomonitoring in human health investigations and more rapidly aid in setting priorities in environmental management.

Background: Due to the ubiquitous use of chemicals in modern society, humans are increasingly exposed to thousands of chemicals that contribute to a major portion of the human exposome. Should a comprehensive and risk-based human exposome database be created, it would be conducive to the rapid progress of human exposomics research. In addition, once a xenobiotic is biotransformed with distinct half-lives upon exposure, monitoring the parent compounds alone may not reflect the actual human exposure. To address these questions, a comprehensive and risk-prioritized human exposome database is needed. **Objectives:** Our objective was to set up a comprehensive risk-prioritized human exposome database including physicochemical properties as well as risk prediction and develop a graphical user interface (GUI) that has the ability to conduct searches for content associated with chemicals in our database. **Methods:** We built a comprehensive risk-prioritized human exposome database by text mining and database fusion. Subsequently, chemicals were prioritized by integrating exposure level obtained from the Systematic Empirical Evaluation of Models with toxicity data predicted by the Toxicity Estimation Software Tool and the Toxicological Priority Index calculated from the ToxCast database. The biotransformation half-lives (HLBsHLBs) of all the chemicals were assessed using the Iterative Fragment Selection approach and biotransformation products were predicted using the previously developed BioTransformer machine-learning method. **Results:** We compiled a human exposome database of >20,000>20,000 chemicals, prioritized 13,441 chemicals based on probabilistic hazard quotient and 7,770 chemicals based on risk index, and provided a predicted biotransformation metabolite database of >95,000>95,000 metabolites. In addition, a user-interactive Java software (Oracle)-based search GUI was generated to enable open access to this new resource. **Discussion:** Our database can be used to guide chemical management and enhance scientific understanding to rapidly and effectively prioritize chemicals for comprehensive biomonitoring in epidemiological investigations.

Expert Elicitation to Estimate the Feed Safety Impact of Criteria Included in the Canadian Food Inspection Agency Risk Assessment Model for Feed Mills

Lachapelle V, Racicot M, Comeau G, Rhouma M, Leroux A, Noubissie OW, et al. *J Food Prot*. 2021 Apr 1;84(4): 611-627. doi: 10.4315/JFP-20-371. **Article link**.

Significance: A validated Establishment-Based Risk Assessment for livestock feed mills will guide Canadian developers of an algorithm for government oversight.

The Canadian Food Inspection Agency is developing an Establishment-based Risk Assessment (ERA) model for commercial and on-farm mills involved in the manufacture, storage, packaging, labeling, or distribution of livestock feed (ERA-Feed Mill model). This model will help inform the allocation of inspection resources on the basis of feed safety risk, including animal health and food safety risk. In a previous study, 34 risk factors, grouped into inherent, mitigation, and compliance clusters, along with assessment criteria were selected. The objective of this current study was to estimate the relative risk (RR) of the 203 assessment criteria on the basis of the impact on feed safety to design an ERA-Feed Mill model algorithm. Furthermore, the intent of this study was to

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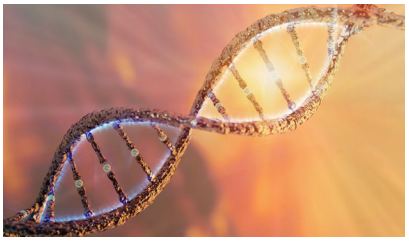
assess the maximum increase or decrease of risk obtained when multiple criteria belonging to a same cluster were identified in a specific feed mill. To do so, a two-round face-to-face expert elicitation was conducted with 28 Canadian feed experts. Results showed no significant association between respondent profiles (years of experience and work sector) and estimated RR. Uniformity of answers between experts improved between rounds. Criteria having the highest increase in risk (median RR ≥ 4) included the presence of materials prohibited to be fed to ruminants in a facility that produces ruminant feed, the presence of multiple livestock species on-site, and historical noncompliances related to the inspection of the feed mill's process control and end-product control programs. Risk mitigation criteria having the highest impact on decreasing the risk were the implementation of feed safety certifications, the use of dedicated manufacturing lines (prohibited materials or medications), and having a hazard sampling plan in place for finished feed. The median RR assigned to each criterion and cluster will be used to build an algorithm of the Canadian Food Inspection Agency's ERA-Feed Mill model.

Foodborne Pathogens

Sensitive Detection of Foodborne Pathogens Based on CRISPR-Cas13a

Gao S, Liu J, Li Z, Ma Y, Wang J. *J Food Sci*. 2021 Apr 30. doi: 10.1111/1750-3841.15745. **Article link.**

Significance: A new PCF detection method can identify *Salmonella* sensitively and specifically, providing a new tool for the detection of pathogens in food.



Salmonella, being one of the most widespread foodborne pathogens, is a compulsory test item required by national food safety standard of China and many other countries. More sensitive and specific *Salmonella* detection method is still needed since traditional methods are time consuming and highly dependent on enormous manpower and material resources. In this research, a bacteria detection method based on CRISPR-Cas13a system (where CRISPR is Clustered Regularly Interspaced Short Palindromic Repeats) was proposed. The target DNA was amplified by PCR and transcribed into RNA by T7 transcriptase, which can activate the RNase activity of the Cas13a protein. The self-folding quenched fluorescent probe can be cleaved by the activated Cas13a protein to generate fluorescent signal. We named this method as PCF detection (PCR-CRISPR-Fluorescence based nucleic acid detection). In this study, PCF detection showed excellent sensitivity, which can detect *Salmonella* genomic DNA with a minimum of 101 aM or 10° CFU/ml *Salmonella* bacteria in 2 hr. It also showed good specificity with no cross-reaction with other common foodborne bacteria. PRACTICAL APPLICATION: The PCF detection method proposed in this article can detect *Salmonella* sensitively and specifically, providing a novel strategy for the detection of foodborne pathogens in food and has great application potential in other microbial detection fields.

Mycotoxins

g-C_3N_4/Fe_3O_4 Nanocomposites as Adsorbents Analyzed by UPLC-MS/MS for Highly Sensitive Simultaneous Determination of 27 Mycotoxins in Maize: Aiming at Increasing Purification Efficiency and Reducing Time

Ma S, Pan LG, You T, Wang K. *J Agric Food Chem*. 2021 Apr 28;69(16):4874-4882. doi: 10.1021/acs.jafc.1c00141. **Article link.**

Significance: An effective new method has been developed to evaluate mycotoxins in maize specimens.

According to known studies, numerous mycotoxins have been found simultaneously in foods and have a certain expansion toxicity, so the simultaneous detection of multiple mycotoxins is absolutely critical. In this article, multifunctional magnetic g-C_3N_4/Fe_3O_4 nanocomposites have been fabricated to employ as modified QuEChERS adsorbents. In addition, they were also used in conjunction with ultrahigh-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS), an accurate quantitative approach, to analyze 27 mycotoxins in maize. The improved method not only has a powerful adsorption effect on the complex matrix by g- C_3N_4/Fe_3O_4 but also enables magnetic separation from the sample solution. Experiments proved that this method can exhibit good linearity under the appropriate and optimal external environment (r2 ≥ 0.9954), high sensitivity (the threshold of detection limit is 0.0004-0.6226 μg kg-1, and the threshold of quantification limit is 0.0014-2.0753 μg kg-1), adequate recoveries (77.81-115.21%), and excellent repeatability (with a threshold of intraday precision of 1.5-10.8% and interday precision in the range of 2.9-12.5%). In practice this method has been used to evaluate a variety of mycotoxins in maize specimens, and certain actual outcomes have been achieved.

Reduction of T-2 and HT-2 Mycotoxins by Atmospheric Cold Plasma and Its Impact on Quality Changes and Germination of Wheat Grains

Iqdiam BM, Feizollahi E, Arif MF, Jeganathan B, Vasanthan T, Thilakarathna MS, et al. *J Food Sci*. 2021 Apr;86(4): 1354-1371. doi: 10.1111/1750-3841.15658. **Article link**.

Significance: With further development and scale-up, new ACP technology has the potential to promote significant mycotoxin degradation in grains.

Wheat (Triticum aestivum) is susceptible to mycotoxin contamination, which can result in significant health risks and economic losses. This research examined the ability of air atmospheric cold plasma (air-ACP) treatment to reduce pure and spiked T-2 and HT-2 mycotoxins' concentration on wheat grains. This study also evaluated the effect of ACP treatment using different gases on wheat grain germination parameters. The T-2 and HT-2 mycotoxin solutions applied on round cover-glass were placed on microscopy slides and wheat grains (0.5 g) were individually spiked with T-2 and HT-2 on their surfaces. Samples were then dried at room temperature (~24 °C) and treated by air-ACP for 1 to 10 min. Ten minutes of air-ACP treatment significantly reduced pure T-2 and HT-2 concentrations by 63.63% and 51.5%, respectively. For mycotoxin spiked on wheat grains, 10 min air-ACP treatment significantly decreased T-2 and HT-2 concentrations up to 79.8% and 70.4%, respectively. No significant change in the measured quality and color parameters was observed in the ACP-treated samples. Wheat grain germination parameters were not significantly different, when treated with ACP using different gases. Air-ACP treatment and ACP treatment using 80% nitrogen + 20% oxygen improved the germination of wheat grains by 10% and 6%, respectively. This study demonstrated that ACP is an innovative technology with the potential to improve the safety of wheat grains by reducing T-2/HT-2 mycotoxins with an additional advantage of improving their germination. **Practical Application:** Atmospheric cold plasma (ACP) technology has a huge potential to degrade mycotoxins in food grains. This study evaluated the efficacy of ACP to reduce two major mycotoxins (T-2 and HT-2 toxins) in wheat grains. The results of this study will help to develop and scale-up the ACP technology for mycotoxin degradation in grains.

Food Packaging

Superhydrophobic and Antioxidative Film Based on Edible Materials for Food Packaging

Zhang S, Li M, Wang R, Chang L, Ju H, Lin W, et al. *Langmuir*. 2021 Apr 27;37(16):5066-5072. doi: 10.1021/acs.langmuir.1c00637. **Article link**.

Significance: A novel edible multifunctional film constructed from chitosan, tea polyphenol and carnauba wax material integrates superhydrophobicity and antioxidant ability and has the potential to be applied as a functional packaging material.

Significant wastage of the food deterioration in the food preserving process and residual liquid in a container has become a major concern for scientists and the whole society. In this study, an edible multifunctional film integrated superhydrophobicity and antioxidant ability is constructed by chitosan, tea polyphenol, carnauba wax material that is food and drug administration (FDA)-approved for food packaging. The formed edible packaging materials that exhibit great antioxidant property and extremely low water-absorbing quality, was thus proven to display excellent fresh beef preservation effect during storage of 14 days. Importantly, the formed edible multifunctional interface was also demonstrated to perform excellent superhydrophobicity due to the carnauba wax and exhibited large contact angles for various liquid foods, which could effectively reduce the liquid residue. Moreover, the formed edible multifunctional packaging materials showed good thermostability and biocompatibility, which has the potential to be applied as a functional packaging material.

Chemical Contaminants

Chemical Mixture Calculator - A Novel Tool for Mixture Risk Assessment

Boberg J, Bredsdorff L, Petersen A, Löbl N, Jensen BH, Vinggaard AM, et al. *Food Chem Toxicol*. 2021 Apr 3;152: 112167. doi: 10.1016/j.fct.2021.112167. **Article link**.

Significance: A Chemical Mixture Calculator analyzes cumulative risk impacts on biological systems as illustrated by a case example of phthalate compounds.

Humans are continuously exposed to complex chemical mixtures from foods and the environment. Experimental models in vivo and in vitro have increased our knowledge on how we can predict mixture effects. To accommodate a need for tools for efficient mixture risk assessment across different chemical classes and exposure sources, we have developed fit-for-purpose

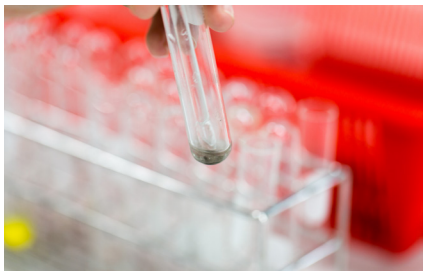
criteria for grouping of chemicals and a web-based tool for mixture risk assessment. The Chemical Mixture Calculator (available at www.chemicalmixturecalculator.dk) can be used for mixture risk assessment or identification of main drivers of risk. The underlying database includes hazard and exposure estimates for more than 200 chemicals in foods and environment. We present a range of cumulative assessment groups for effects on haematological system, kidney, liver, nervous system, developmental and reproductive system, and thyroid. These cumulative assessment groups are useful for grouping of chemicals at several levels of refinement depending on the question addressed. We present a mixture risk assessment case for phthalates, evaluated with and without contributions from other chemicals with similar effects. This case study shows the usefulness of the tool as a starting point for mixture risk assessment by the risk assessor and emphasizes that solid scientific insight regarding underlying assumptions and uncertainties is crucial for result interpretation.

Heavy Metals

Cadmium Causes Hepatopathy by Changing the Status of DNA Methylation in the Metabolic Pathway

Ren C, Ren L, Yan J, Bai Z, Zhang L, Zhang H, et al. *Toxicol Lett*. 2021 Apr 1;340:101-113. doi: 10.1016/j.toxlet.2020.12.009. **Article link.**

Significance: Human liver metabolism changes after cadmium poisoning, which suggests DNA demethylation in metabolic pathways, as illustrated in an animal study.



Toxicity caused by the heavy metal Cadmium leads to liver diseases; this finding has generated interest among researchers. We detected DNA methylation using Whole Genome Bisulfite Sequencing (WGBS) to study the relationship between Cadmium exposure and liver damage. Forty-eight Sprague-Dawley rats were randomly divided into six groups, and given normal saline or 2.5, 5, 10, 20, and 40 mg/kg body weight per day $CdCl_2$ by gavage. Twelve weeks later, their liver tissues were collected for pathological examination and DNA extraction. Increased exposure to Cadmium led to a reduction in the amount of weight gain as well as pathological degeneration and necrosis of liver cells of the rats. Using WGBS, we found that DNA methylation changes in the high-dose exposure group were more remarkable, and most of the changes occurred in the gene promoter region. GO enrichment analysis showed that the genes were enriched in the biological process of «response to stimulus.» KEGG analysis revealed that metabolic pathways, like MAPK, PI3K-Akt and cAMP, had the largest number of enriched genes. Using Integrative Genomics Viewer (IGV), the demethylation of F2rl3 after Cadmium poisoning was established. This finding may explain why there are changes in liver metabolism after Cadmium poisoning.

Caffeine

Natural Products Targeting into Cancer Hallmarks: An Update on Caffeine, Theobromine, and (+)-Catechin

Cadoná FC, Dantas RF, de Mello GH, Silva-Jr FP. *Crit Rev Food Sci Nutr*. 2021 Apr 23:1-20. doi: 10.1080/10408398.2021.1913091. **Article link.**

Significance: This review provides the updated state of research on the anticancer activity of caffeine, theobromine and (+)-catechin with a focus on causal antitumor mechanisms of action.

Natural products have been studied to reveal new therapies against human dysfunctions since they present several medicinal properties. Caffeine, theobromine and (+)-catechin are remarkable natural agents in the class of methylxanthines and flavonoids. These bioactive molecules have several biological activities, for instance, antioxidant, anti-inflammatory, and antitumor capacity. In this sense, studies focusing on these molecules have been performed to discover new treatments against diseases, such as cancer. Cancer is a serious public health problem worldwide responsible for more than 70% of all deaths globally. Industrialized products associated with a sedentary lifestyle and a diet low in antioxidants are related to neoplasms development. Unfortunately, many types of cancers are extremely aggressive and untreatable since, in many cases, they are resistant to chemotherapy. Therefore, revealing new strategies to block cancer growth is one of the biggest challenges to science. In this context, despite the known anticancer actions of caffeine, theobromine and (+)-catechin, it is still essential to elucidate the causal antitumor mechanism of these molecules by analyzing the dysfunctional cancer pathways associated with the hallmarks of cancer. Hence, this review aims to describe the anticancer activity of caffeine, theobromine, and (+)-catechin against the different hallmarks and enabling characteristics of cancer.

Allergens

Multidimensional Study of the Oral Microbiome, Metabolite, and Immunologic Environment in Peanut Allergy

Ho HE, Chun Y, Jeong S, Jumreornvong O, Sicherer SH, Bunyavanich S. *J Allergy Clin Immunol*. 2021 Apr 2: S0091-6749(21)00550-9. doi: 10.1016/j.jaci.2021.03.028. **Article link.**

Significance: The oral environment is the site of interest to examine host-microbiome dynamics in food allergy, particularly with peanuts.

Background: The oral mucosa is the initial interface between food antigens, microbiota, and mucosal immunity, yet, little is known about oral host-environment dynamics in food allergy. **Objective:** Our aim was to determine oral microbial, metabolic, and immunologic profiles associated with peanut allergy. **Methods:** We recruited 105 subjects (56 with peanut allergy and 49 healthy subjects) for salivary microbiome profiling using 16S ribosomal RNA sequencing, short-chain fatty acid (SCFA) metabolite assays using liquid chromatography/mass spectrometry, and measurement of oral secreted cytokines using multiplex assays. Analyses within and across data types were performed. **Results:** The oral microbiome of individuals with peanut allergy was characterized by reduced species in the orders Lactobacillales, Bacteroidales (*Prevotella* spp), and Bacillales, and increased Neisseriales spp. The distinct oral microbiome of subjects with peanut allergy was accompanied by significant reductions in oral SCFA levels, including acetate, butyrate, and propionate, and significant elevation of IL-4 secretion. Decreased abundances of oral *Prevotella* spp and *Veillonella* spp in subjects with peanut allergy were significantly correlated with reduced oral SCFA levels (false discovery rate < 0.05), and increased oral *Neisseria* spp was correlated with lower oral SCFA levels (false discovery rate < 0.05). Additionally, oral *Prevotella* spp abundances were correlated with decreased local secretion of TH2-stimulating epithelial factors (IL-33 and thymic stromal lymphopoietin) and TH2 cytokines (IL-4, IL-5, and IL-13), whereas oral *Neisseria* spp abundance was positively associated with a TH2-skewed oral immune milieu. **Conclusion:** Our novel multidimensional analysis of the oral environment revealed distinct microbial and metabolic profiles associated with mucosal immune disturbances in peanut allergy. Our findings highlight the oral environment as an anatomic site of interest to examine host-microbiome dynamics in food allergy.