Food Safety Briefs

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Risk Assessment

Cancer Weight of Evidence for Three Lower Acrylates: Conclusions and Recommendations from an Expert Panel

C R Kirman, P J Boogaard, J S Bus, V L Dellarco, L R DePass, B R Stern, S M Hays. *Regul Toxicol Pharmacol*. 2023 Aug;143:105469. doi: 10.1016/j.yrtph.2023.105469. Article link

Significance: A panel of experts, using the cancer weight of evidence (WOE), determined that methyl acrylate, ethyl acrylate and 2-ethylhexyl acrylate are not likely to be carcinogenic to humans.

An international panel of experts was engaged to assess the cancer weight of evidence (WOE) for three lower acrylates: methyl acrylate, ethyl acrylate, and 2-ethylhexyl acrylate. The review was structured as a three-round, modified Delphi format, a systematic process for collecting independent and deliberative input from panel members, and it included procedural elements to reduce bias and groupthink. Based upon the available science, the panel concluded: (1) The MOA for point of contact tumors observed in rodent cancer bioassays that is best supported by available data involves increased cell replication by cytotoxicity and regenerative proliferation; (2) The WOE supports a cancer classification of "Not likely to be carcinogenic to humans" a conclusion that is more in line with an IARC classification of Group 3 rather than Group 2 B; (3) Quantitative cancer potency values based on rodent tumor data are not required for these chemicals; and (4) Human health risk assessment for these chemicals should instead rely on non-cancer, precursor endpoints observed at the point of contact (e.g., hyperplasia). The degree of consensus (consensus scores of 0.84-0.91 out of a maximum score of 1) and degree of confidence (7.7-8.7 out of a maximum score of 10) in the WOE conclusions is considered high.

Foodborne Pathogens

Environmental Monitoring of Food Manufacturing Facilities for *Listeria*: A Case Study

Yukako Shimojima, Yuji Kanai, Takatoshi Moriyama, Sayoko Arakawa, Yumi Tamura, Yumiko Okada, Yukio Morita. *J Food Prot*. 2023 Aug 24;100149. doi: 10.1016/j.jfp.2023.100149. Article link

Significance: Environmental monitoring programs effectively revealed the presence of *Listeria* in three food production facilities and allowed remedial measures to be undertaken.

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Environmental monitoring programs (EMPs) for food production facilities are useful for verifying general sanitation controls and recommended as verification measures to ensure that the Hazard Analysis Critical Control Point plan is working effectively. In this study, EMPs for *Listeria* were conducted at three food production facilities to assess the efficacy of sanitation control and establish effective sanitation control methods. In Facility A, *L. monocytogenes* was detected in the clean area although in Zone 3, nonfood-contact surfaces. To prevent contamination from dirty areas, the cleaning practices in the preparation room were investigated. Normal cleaning combined with disinfection with carbonated hypochlorite water (chlorine concentration, 150 ppm) proved effective. At Facility B, a salad product and its ingredients (pastrami and salami) were positive for *L. monocytogenes* serotype 3b. The bacterial count was <10/g in all samples. However, when inoculated with *L. monocytogenes* isolates, growth of approximately 2 log cfu/g was observed on pastrami after 48 h of incubation at 10°C. The ingredients were commercially purchased blocks that were sliced in a slicer at Facility B and used as salad toppings. Because both unopened blocks were negative for *L. monocytogenes*, contamination of the slicer was suspected. Sampling of the slicer revealed that contamination by *L. monocytogenes* serotype 3b was more extensive after use than before use. Therefore, the slicer was disassembled, cleaned, and disinfected thoroughly. In Facility C, *L. monocytogenes* serotype 4b (4e) was detected in all the dirty, semi-clean, and clean areas. The strain was also isolated from the wheels of a smoking cart transported across the zones. Therefore, efforts were made to frequently clean and disinfect the cart. EMPs revealed the presence of *Listeria* in each facility and allowed remedial measures to be undertaken. Continued monitoring and Plan-Do-Check-Act cycles were considered desirable.

Foodborne Illness

Foodborne Botulism, Canada, 2006-2021

Richard A Harris, Christine Tchao, Natalie Prystajecky, Kelly Weedmark, Yassen Tcholakov, Manon Lefebvre, John W Austin. *Emerg Infect Dis*. 2023 Sep;29(9):1730-1737. doi: 10.3201/eid2909.230409. Article link

Significance: Botulism cases in Canada from 2006-2021 involved 55 outbreaks and often led to hospitalizations and the need for special care, highlighting the need for increased clinician awareness for improved diagnosis of patients.

During 2006-2021, Canada had 55 laboratory-confirmed outbreaks of foodborne botulism, involving 67 cases. The mean annual incidence was 0.01 case/100,000 population. Foodborne botulism in Indigenous communities accounted for 46% of all cases, which is down from 85% of all cases during 1990-2005. Among all cases, 52% were caused by botulinum neurotoxin type E, but types A (24%), B (16%), F (3%), and AB (1%) also occurred; 3% were caused by undetermined serotypes. Four outbreaks resulted from commercial products, including a 2006 international outbreak caused by carrot juice. Hospital data indicated that 78% of patients were transferred to special care units and 70% required mechanical ventilation; 7 deaths were reported. Botulinum neurotoxin type A was associated with much longer hospital stays and more time spent in special care than types B or E. Foodborne botulism often is misdiagnosed. Increased clinician awareness can improve diagnosis, which can aid epidemiologic investigations and patient treatment.

Mycotoxins

Endophytic Fungus Reshapes Spikelet Microbiome to Reduce Mycotoxin Produced by *Fusarium proliferatum* through Altering Rice Metabolites

Qiang Zhu, Yan-Jun Fei, Yi-Bo Wu, De-Lin Luo, Man Chen, Kai Sun, Wei Zhang, et. al. *J Agric Food Chem*. 2023 Aug 2;71(30):11350-11364. doi: 10.1021/acs.jafc.3c02616. Article link

Significance: This study found that B3 significantly reduced the abundance of pathogens and enriched resistant microbes *Pseudomonas* and *Proteobacteria* in the spikelet microbial community.

Rice spikelet rot disease (RSRD) caused by *Fusarium proliferatum* seriously reduces rice yield and produces mycotoxins that threaten human health. The root symbiotic endophytic fungus *Phomopsis liquidambaris* reduces RSRD incidence and fumonisins accumulation in grain by 21.5 and 9.3%, respectively, while the mechanism of disease resistance remains largely elusive. Here, we found that B3 significantly reduced the abundance of pathogen from 79.91 to 2.84% and considerably enriched resistant microbes *Pseudomonas* and *Proteobacteria* in the spikelet microbial community. Further study revealed that B3 altered the metabolites of spikelets, especially hordenine and l-aspartic acid, which played a key role

in reshaping the microbiome and supporting the growth of the functional core microbe *Pseudomonas*, and inhibited the pathogen growth and mycotoxin production. This study provided a feasibility of regulating the function of aboveground microbial communities by manipulating plant subsurface tissues to control disease and mycotoxin pollutants in agricultural production.

Heavy Metals

An Updated Systematic Review and Dose-Response Meta-Analysis on the Relation between Exposure to Arsenic and Risk of Type 2 Diabetes

Nader Rahimi Kakavandi, Taraneh Mousavi, Tayebeh Asadi, Ayda Moradi, Mahta Esmaeili, Ahmad Habibian Sezavar, Shekoufeh Nikfar, et. al. *Toxicol Lett*. 2023 Aug 1;384:115-127. doi: 10.1016/j.toxlet.2023.08.001. Article link

Significance: A dose-response meta-analysis found a correlation between arsenic exposure and the risk of Type 2 Diabetes.

Arsenic is among the most critical environmental toxicants associated with many human disorders. However, its effect on type 2 diabetes mellitus (T2DM) is contradictory. This systematic review and dose-response meta-analysis aim to update information on the association between arsenic exposure and the risk of T2DM. The sample type (drinking water, urine, blood, and nails) conducted the subgroup analysis. Evaluation of the high vs. low arsenic concentrations showed a significant association between drinking water arsenic (OR: 1.58, 95% CI: 1.20-2.08) and urinary arsenic (OR: 1.37, 95% CI: 1.24-1.51) with the risk of T2DM. The linear dose-response meta-analysis showed that each 1 µg/L increase in levels of drinking water arsenic (OR: 1.01, 95% CI: 1.00-1.01) and urinary arsenic (OR: 1.01, 95% CI: 1.00-1.02) was associated with a 1% increased risk of T2DM. The non-linear dose-response analysis indicated that arsenic in urine was associated with the risk of T2DM (Pnon-linearity<0.001). However, this effect was not statistically significant for arsenic in drinking water (Pnon-linearity=0.941). Our findings suggest that blood arsenic was not significantly linked to the increased risk of T2DM in high vs. low (OR: 1.21, 95% CI: 0.85-1.71), linear (OR: 1.04, 95% CI: 0.99-1.09), and non-linear (Pnon-linearity=0.365) analysis. Also, nail arsenic was not associated with the risk of T2DM in this meta-analysis (OR: 1.33, 95% CI: 0.69-2.59). This updated dose-response meta-analysis indicated that arsenic exposure was significantly correlated with the risk of T2DM.

Food Packaging

Suitability of Material Recovery Facility-Recovered Post-Consumer Polypropylene Applications in Extrusion Blow Molded Bottle Food Packaging

Ignacio MC, Tumu KN, Munshi M, Vorst KL, Curtzwiler GW. *Polymers,* Aug.19, 2023, 15(16), 3471; ddoi.org/10.3390/polym15163471. Article link

Significance: A new study provides critical information on the use of recycling facility-recovered post-consumer material in food packaging applications without compromising performance integrity.

This work was supported by IAFNS Food Packaging Safety and Sustainability Committee.

Polypropylene (PP) is one of the most abundant plastics used due to its low price, moldability, temperature and chemical resistance, and outstanding mechanical properties. Consequently, waste from plastic materials is anticipated to rapidly increase with continually increasing demand. When addressing the global problem of solid waste generation, post-consumer recycled materials are encouraged for use in new consumer and industrial products. As a result, the demand is projected to grow in the next several years. In this study, material recovery facility (MRF)-recovered post-consumer PP was utilized to determine its suitability for extrusion blow molded bottle food packaging. PP was sorted and removed from mixed-polymer MRF-recovered bales, ground, trommel-washed, then washed following the Association of Plastics Recyclers' protocols. The washed Post-Consumer Recycled-PP flake was pelletized then manually blended with virgin PP resin at 25%, 50%, 75, and 100% PCR-PP concentrations and fed into the extrusion blow molding (EBM) machine. The EBM bottles were then tested for physical performance and regulatory compliance (limits of TPCH: 100 µg/g). The results showed an increased crystallization temperature but no practical difference in crystallinity as a function of PCR-PP concentrations. Barrier properties (oxygen and water vapor) remained relatively constant except for 100% MRF-recovered PCR-PP, which was higher for both gas types. Stiffness significantly improved in bottles with PCR-PP (p-value < 0.05). In addition, a wider range of N/IAS was detected in PCR-PP due to plastic additives, food additives, and degradation byproducts. Lastly, targeted phthalates did not exceed the limits of TPCH, and trace levels of BPA were detected in the MRF PCR-PP. Furthermore, the study's results provide critical information on the use of MRF recovered in food packaging applications without compromising performance integrity.

Chemical Contaminants

Machine Learning for Predicting Chemical Migration from Food Packaging Materials to Foods

Shan-Shan Wang, Pinpin Lin, Chia-Chi Wang, Ying-Chi Lin, Chun-Wei Tung. *Food Chem Toxicol*. 2023 Aug;178:113942. doi: 10.1016/j.fct.2023.113942. Article link

Significance: Nonlinear machine learning can be utilized to accelerate the migration potential assessments for food contact chemicals.

Food contact chemicals (FCCs) can migrate from packaging materials to food posing an issue of exposure to FCCs of toxicity concern. Compared to costly experiments, computational methods can be utilized to assess the migration potentials for various migration scenarios for further experimental investigation that can potentially accelerate the migration assessment. This study developed a nonlinear machine learning method utilizing chemical properties, material type, food type and temperature to predict chemical migration from package to food. Nine nonlinear algorithms were evaluated for their prediction performance. The ensemble model leveraging multiple algorithms provides state-of-the-art performance that is much better than previous linear regression models. The developed prediction models were subsequently applied to profile the migration potential of FCCs of high toxicity concern. The models are expected to be useful for accelerating the assessment of migration of FCCs from package to foods.

Caffeine

Nutrients Mediate Caffeine Inhibition of *Escherichia coli*

Megan N McConnell, Corien Bakermans. *Environ Microbiol Rep*. 2023 Oct;15(5):422-425. doi: 10.1111/1758-2229.13165. Article link

Significance: A significant negative correlation was observed between caffeine concentration and *E. coli* growth rate under all conditions, suggesting that caffeine can act as an antimicrobial agent when ingested.

The consumption of coffee and other caffeinated drinks is increasingly popular across the globe. In the United States, 90% of adults consume at least one caffeinated beverage a day. While caffeine consumption of up to 400 mg/d is not generally associated with negative effects on human health, the impact of caffeine on the gut microbiome and individual gut microbiota remains unclear. We examined the effect of caffeine on the growth rate of *Escherichia coli*, a bacterium commonly found in the human gut, when grown aerobically or anaerobically in nutrient-rich or minimal medium. A significant negative correlation was observed between caffeine concentration and growth rate under all conditions, suggesting that caffeine can act as an antimicrobial agent when ingested. Caffeine reduced growth rates significantly more in nutrient-poor, but not in anoxic, conditions. Given the highly variable nutrient and oxygen conditions of the gut, these results suggest a need to further explore caffeine's inhibitory effects on the gut microbiome and its relation to human health.

Food Allergens

Delayed Gut Microbiota Maturation in the First Year of Life is a Hallmark of Pediatric Allergic Disease

Courtney Hoskinson, Darlene L Y Dai, Kate L Del Bel, Allan B Becker, Theo J Moraes, Piushkumar J Mandhane, B Brett Finlay, et. al. *Nat Commun*. 2023 Aug 29;14(1):4785. doi: 10.1038/s41467-023-40336-4. Article link

Significance: This study finds a core set of functional and metabolic imbalances in the gut to be a significant mediator between microbiota maturation at age 1 year and allergic diagnoses at age 5 years.

Allergic diseases affect millions of people worldwide. An increase in their prevalence has been associated with alterations in the gut microbiome, i.e., the microorganisms and their genes within the gastrointestinal tract. Maturation of the infant immune system and gut microbiota occur in parallel; thus, the conformation of the microbiome may determine if tolerant immune programming arises within the infant. Here we show, using deeply phenotyped participants in the CHILD birth cohort (n = 1115), that there are early-life influences and microbiome features which are uniformly associated with four distinct allergic diagnoses at 5 years: atopic dermatitis (AD, n = 367), asthma (As, n = 165), food allergy (FA, n = 136), and allergic rhinitis (AR, n = 187). In a subset with shotgun metagenomic and metabolomic profiling (n = 589), we discover that

impaired 1-year microbiota maturation may be universal to pediatric allergies (AD p = 0.000014; As p = 0.0073; FA p = 0.00083; and AR p = 0.0021). Extending this, we find a core set of functional and metabolic imbalances associated with four distinct allergic diagnoses at 5 years: atopic dermatitis (AD, n = 367), asthma (As, n = 165), food allergy (FA, n = 136), and allergic rhinitis (AR, n = 187). In a subset with shotgun metagenomic and metabolomic profiling (n = 589), we discover that impaired 1-year microbiota maturation may be universal to pediatric allergies (AD p = 0.000014; As p = 0.0073; FA p = 0.00083; and AR p = 0.0021). Extending this, we find a core set of functional and metabolic imbalances characterized by compromised mucous integrity, elevated oxidative activity, decreased secondary fermentation, and elevated trace amines, to be a significant mediator between microbiota maturation at age 1 year and allergic diagnoses at age 5 years (βindirect = -2.28; p = 0.0020). Microbiota maturation thus provides a focal point to identify deviations from normative development to predict and prevent allergic disease.

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