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Food Safety Briefs

Risk Assessment

Integration of Evidence to Evaluate the Potential for Neurobehavioral Effects Following Exposure to USFDA-Approved Food Colors

Gentry R, Greene T, Chappell G, Lea I, Borghoff S, Yang C, et al. *Food Chem Toxicol*. 2021 May;151:112097. doi: 10.1016/j.fct.2021.112097. **Article link**

Significance: Three streams of evidence are combined to support risk assessments of neurobehavioral endpoints of FDA-approved food dyes but like other authorities, the study concludes that other health effects are more appropriate for estimating ADIs.

California's Office of Environmental Health Hazard Assessment was tasked with conducting risk assessments for United States Food and Drug Administration-approved food dyes relative to neurobehavioral concerns. The purpose of this assessment was to evaluate the evidence for neurodevelopment effects based on three streams of evidence: 1) studies identified by OEHHA for consideration in a quantitative risk assessment; 2) studies relevant to understanding mechanisms of neurobehavioral effects; 3) an in silico assessment of the bioavailability of USFDA-approved food dyes. The results indicate a lack of adequate or consistent evidence of neurological effects, supported by a lack of bioavailability and brain penetration predicted by the in silico assessment. Further, the mechanistic evidence supports a lack of activity from in vitro neurotransmitter assays, and a lack of evidence to support molecular initiating events or key events in adverse outcome pathways associated with neurodevelopmental effects, supporting a lack of biological plausibility for neurobehavioral effects following food exposures to colors. These conclusions are consistent with other authoritative bodies, such as JECFA and EFSA, that have determined (i) other effects are more appropriate for estimating acceptable daily intakes and (ii) evidence from the neurobehavioral studies lack the strength to be relied upon for quantitative risk assessment.

Foodborne Pathogens

Review: Trends in Point-of-Care Diagnosis for *Escherichia coli* O157:H7 in Food and Water

Rani A, Ravindran VB, Surapaneni A, Mantri N, Ball AS. *Int J Food Microbiol*. 2021 Jul 2;349:109233. doi: 10.1016/j.ijfoodmicro.2021.109233. **Article link**

Significance: Early diagnosis is the best preventive strategy to minimize *E. coli*-related infections. To support this, less-burdensome but ASSURED detection methods are needed in laboratories and in the field.

Escherichia coli O157:H7, a Shiga-producing *E. coli* is a major pathogenic *E. coli* strain which since the early 1980s has become a crucial food and water-borne pathogen. Several management strategies can be applied to control the spread of infection; however early diagnosis represents the optimum preventive strategy to minimize the infection. Therefore, it is crucial to detect this pathogen in a fast and efficient manner in order to reduce the morbidity and mortality. Currently used gold standard tests rely on culture and pre-enrichment of *E. coli* O157:H7 from the contaminated source; they are time consuming and laborious. Molecular methods such as polymerase chain reaction are sensitive; however, they require expensive instrumentation. Therefore, there is a requirement for Accurate, Sensitive, Specific, User friendly, Rapid, Equipment free and Deliverable (ASSURED) detection methods for use in the laboratory and in the field. Emerging technologies such as isothermal amplification methods, biosensors, surface enhanced Raman Spectroscopy, paper-based diagnostics and smartphone-based digital methods are recognized as new approaches in the field of *E. coli* O157:H7 diagnostics and are discussed in this review. Mobile PCR and CRISPR-Cas diagnostic platforms have been identified as new tools in *E. coli*

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O157:H7 POC diagnostics with the potential for implementation by industry. This review describes advances and progress in the field of *E. coli* O157:H7 diagnosis in the context of food and water industry. The focus is on emerging high throughput point-of-care (POC) *E. coli* O157:H7 diagnostics and the requirement for the transformation to service routine diagnostics in the food and water industry.

Foodborne Illness

Foods Implicated in U.S. Outbreaks Differ from the Types Most Commonly Consumed

Richardson LC, Cole D, Hoekstra RM, Rajasingham A, Johnson SD, Bruce BB. *Food Prot*. 2021 May 1;84(5):869-875. doi: 10.4315/JFP-20-293. **Article link**

Significance: Comparing the frequency of food categories commonly consumed in the U.S. to those implicated in foodborne illness outbreaks provides insights into foods that are over- or under- represented in outbreaks relative to their consumption frequency.

Foodborne disease outbreak investigations identify foods responsible for illnesses. However, it is not known the degree to which foods implicated in outbreaks reflect the distribution of food consumption in the U.S. population or the risk associated with their consumption. We compared the distribution of 24 categories of foods implicated in outbreaks with the distribution of foods consumed by the U.S. population. Beef, chicken, eggs, fish, herbs, mollusks, pork, sprouts, seeded vegetables, and turkey were implicated in outbreaks significantly more often than expected based on the frequency of their consumption by the general population, suggesting a higher risk of contamination or mishandling from foods in these categories than from foods in other categories. In contrast, pasteurized dairy, fruits, grains and beans, oils and sugars, and root and underground vegetables were less frequently implicated in outbreaks than their frequency of consumption by the general population, suggesting a lower health risk associated with these food categories.

Mycotoxins

Multidimensional Analysis of the Epigenetic Alterations in Toxicities Induced by Mycotoxins

Zhu L, Yuhan J, Huang K, He X, Liang Z, Xu W. *Food Chem Toxicol*. 2021 May 4;153:112251. doi: 10.1016/j.fct.2021.112251. **Article link**

Significance: This review sheds light on the epigenetic alterations induced by the non-genotoxic effects of mycotoxins, which still pose risks to all types of food and feed.

Mycotoxins contaminate all types of food and feed, threatening human and animal health through food chain accumulation, producing various toxic effects. Increasing attention is being focused on the molecular mechanism of mycotoxin-induced toxicity in all kinds of in vivo and in vitro models. Epigenetic alterations, including DNA methylation, non-coding RNAs (ncRNAs), and protein post-translational modifications (PTMs), were identified as being involved in various types of mycotoxin-induced toxicity. In this review, the emphasis was on summarizing the epigenetic alterations induced by mycotoxin, including aflatoxin B1 (AFB1), ochratoxin A (OTA), zearalenone (ZEA), fumonisin B1 (FB1), and deoxynivalenol (DON). This review summarized and analyzed the roles of DNA methylation, ncRNAs, and protein PTMs after mycotoxin exposure based on recently published papers. Moreover, the main research methods and their deficiencies were determined, while some remedial suggestions are proposed. In summary, this review helps to understand better the epigenetic alterations induced by the non-genotoxic effects of mycotoxin.

Food Packaging

Development of Quaternary Nanocomposites Made Up of Cassava Starch, Cocoa Butter, Lemongrass Essential Oil Nanoemulsion, and Brewery Spent Grain Fibers

Mendes JF, Norcino LB, Martins HH, Manrich A, Otoni CG, Carvalho EEN, et al. *J Food Sci*. 2021 May;86(5):1979-1996. doi: 10.1111/1750-3841.15689. **Article link**

Significance: Quaternary nanocomposites were produced in a pilot-scale lamination unit with good properties for packaging. The development relates to sustainability as it is both biodegradable and based on plant biomass and is also produced via a clean, high-yield process.

We report on production of novel quaternary nanocomposite films based on thermoplastic starch (TPS, 8% w/v) derived from cassava, cocoa butter (CB, 30% wt.%), and lemongrass essential oil (LEO, 1:1) nanoemulsions reinforced with different concentrations of brewery spent grain (BSG, 5 or 10 wt.%) fibers, by continuous casting. The chemical composition,

the morphological, thermal, mechanical properties, film barrier, biodegradability in the vegetable compound, in addition to the application in chocolates, have been widely studied. The addition of CB, LEO, and BSG caused relevant changes in the starch-based films, such as increased extensibility (from 2.4-BSG5 to 9.4%-BSG10) and improved barrier to moisture (2.9 and 2.4 g.mm.kPa-1 .h-1 .m-2). Contrastingly, the thermal stability of the starch film was slightly decreased. The biodegradability of the herein developed quaternary nanocomposite films was the same as that of TPS films, eliminating concerns on the supplementation with active ingredients that are expected to have some biocidal effect. Despite checking antimicrobial activity only by contact under the biocomposites, chocolates packed with the films were well accepted by consumers, especially the samples of white chocolate stored in the BSG5 biocomposite. Overall, this new approach towards quaternary active, biodegradable films produced in a pilot-scale lamination unit was successful in either improving or at least maintaining the essential properties of TPS-based films for food packaging applications, while providing them with unique features and functionalities. **Practical Application:** This contribution relates to new approach toward quaternary films produced in a pilot-scale lamination unit. It relates to sustainability as it is both biodegradable and based on plant biomass, as well as produced via a clean, through high-yield process. The four components of the edible films we developed provide it with good in properties performance, as both a passive barrier (i.e. purely physical), and active, related to the sensory attributes of food, essential to be applied in food packaging. The valorization of a BSG also adds to the relevance of our contribution within the circular bioeconomy framework.

Chemical Contaminants

Bioavailability Evaluation of Perchlorate in Different Foods In Vivo: Comparison with In Vitro Assays and Implications for Human Health Risk Assessment

Liu X, Zhang H, Tian Y, Fang M, Xu L, Wang Q, et al. *J Agric Food Chem*. 2021 May 5;69(17):5189-5197. doi: 10.1021/acs.jafc.1c00539. **Article link**

Significance: Moisture, fiber and fat in foods affected perchlorate bioavailability in both living and test models. Food matrices affect perchlorate bioavailability and further research could enhance perchlorate dietary exposure risk assessments.

Perchlorate in various foods continuously arouses public health concern. Bioavailability is a critical parameter to better estimate perchlorate exposure from diets. In this study, perchlorate bioavailability in five foods was determined in an in vivo mouse model and compared with in vitro bioaccessibility/bioavailability. The estimated in vivo perchlorate bioavailability for different foods ranged from 18.01 ± 4.53% to 45.60 ± 7.11%, with the order lettuce > pork > rice > milk powder > soybean. Moisture, fiber, and fat in foods were identified as critical factors affecting perchlorate bioavailability (correlation r = 0.71, 0.52, and -0.67, respectively). Linear regression analysis revealed that the in vitro perchlorate bioavailability determined using the Caco-2 cell model has the potential to estimate the in vivo perchlorate bioavailability in foods (R2 = 0.67, slope = 1.33, and y intercept = 4.99). These findings provide insights into the effects of the food matrices on perchlorate bioavailability and could contribute to decrease the uncertainty regarding perchlorate dietary exposure risk assessment.

Heavy Metals

Derivation of Biomonitoring Equivalents for Aluminium for the Interpretation of Population-Level Biomonitoring Data

Poddalgoda D, Hays SM, Kirman C, Chander N, Nong A. *Regul Toxicol Pharmacol*. 2021 Jun;122:104913. doi: 10.1016/j.yrtph.2021.104913. **Article link**

Significance: Deriving blood biomonitoring equivalents for aluminium may help interpret population-level biomonitoring data by contributing to screening and prioritizing substances for human health risk assessment and management.

Aluminium is widely used in many consumer products, however the primary source of aluminium exposure to the Canadian general population is through food. Aluminium can cause neurotoxicity and reproductive toxicity at elevated exposure levels. Health-based exposure guidance values have been established for oral exposure to aluminium, including a Minimal Risk Level (MRL) by the Agency for Toxic Substances and Disease Registry (ATSDR), a Provincial Tolerable Weekly Intake (PTWI) by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and a Tolerable Weekly Intake (TWI) by the European Food Safety Authority (EFSA). Aluminium concentration in blood and urine can be used as a tool for exposure characterization in a population. A pharmacokinetic (PK) model was developed based on human dosing data to derive blood Biomonitoring Equivalents (BEs), whereas a mass balance approach was used to derive urine BEs for the above guidance values. The BEs for blood for daily intake consistent with the MRL, PTWI and TWI were 18, 16 and 8 µg/L, respectively. BEs for urine for the same guidance values were 137, 123 and 57 µg/L, respectively. The derived BEs may be

useful in interpreting population-level biomonitoring data in a health risk context and thereby screening and prioritizing substances for human health risk assessment and risk management.

Caffeine

Energy Drinks and Their Adverse Health Effects: A Systematic Review and Meta-Analysis

Nadeem IM, Shanmugaraj A, Sakha S, Horner NS, Ayeni OR, Khan M. *Sports Health*. 2021 May-Jun;13(3): 265-277. doi: 10.1177/1941738120949181. **Article link**

Significance: This systematic review found that insomnia, stress and depression were the three most reported negative health effects associated with excess energy drink consumption in 32 studies. While caffeine is commonly found in energy drinks, caffeine was not specifically evaluated in this study.

Context: Energy drinks are the fastest growing product in the beverage industry. However, there is concern regarding potential for adverse effects with use. **Objective:** To evaluate the reported adverse effects of energy drink consumption. **Data sources:** The electronic databases MEDLINE, EMBASE, and PubMed were searched for relevant studies from inception to November 2019, and pertinent data were abstracted. **Study selection:** Only clinical studies reporting adverse events after energy drink consumption were included. **Study design:** Systematic review. **Level of evidence:** Level 4. **Data extraction:** Data regarding sample size characteristics, energy drink characteristics, comparators, and all adverse events were extracted in duplicate and recorded. **Results:** A total of 32 studies and 96,549 individuals were included. Frequently reported adverse events in the pediatric population were insomnia (35.4%), stress (35.4%), and depressive mood (23.1%). Frequently reported adverse events in the adult population were insomnia (24.7%), jitteriness/restlessness/shaking hands (29.8%), and gastrointestinal upset (21.6%). Alcohol mixed with energy drinks significantly reduced the likelihood of sedation effects but increased the likelihood of stimulatory effects. Energy drink consumption significantly increased the odds of insomnia (OR, 5.02; 95% CI, 1.72-14.63) and jitteriness/activeness (OR, 3.52; 95% CI, 1.28-9.67) compared with the control group. **Conclusion:** The authors recommend that individuals avoid frequent energy drink consumption (5-7 energy drinks/week) and avoid co-consumption with alcohol; increased regulatory standards should be placed in the sale of energy drinks, particularly with regard to the pediatric population.

Allergens

Bayesian Hierarchical Evaluation of Dose-Response for Peanut Allergy in Clinical Trial Screening

Haber LT, Reichard JF, Henning AK, Dawson P, Chinthrajah RS, Sindher SB, et al. *Food Chem Toxicol*. 2021 May;151:112125. doi: 10.1016/j.fct.2021.112125. **Article link**

Significance: Dose-response data on peanut protein exposures to allergic individuals could lay the groundwork for risk-based food labeling guidelines to help consumers manage food allergies.

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Risk-based labeling based on the minimal eliciting doses (EDs) in sensitized populations is a potential replacement for precautionary allergen labeling of food allergens. We estimated the dose-response distribution for peanut allergen using data from double-blind placebo-controlled food challenges (DBPCFCs) conducted in the US at multiple sites, testing a population believed to be similar to the general U.S. food allergic population. Our final (placebo-adjusted) dataset included 548 challenges of 481 subjects. Bayesian hierarchical analysis facilitated model fitting, and accounted for variability associated with various levels of data organization. The data are best described using a complex hierarchical structure that accounts for inter-individual variability and variability across study locations or substudies. Bayesian model averaging could simultaneously consider the fit of multiple models, but the Weibull model dominated so strongly that model averaging was not needed. The ED01 and ED05 (and 95% credible intervals) are 0.052 (0.021, 0.13) and 0.49 (0.22, 0.97) mg peanut protein, respectively. Accounting for challenges with severe reactions at the LOAEL, by using the dose prior to the LOAEL as the new LOAEL, the ED01 drops to 0.029 (0.014, 0.074) mg peanut protein. Our results could aid in establishing improved food labeling guidelines in the management of food allergies.

Recent Advances in Alleviating Food Allergenicity through Fermentation

Pi X, Yang Y, Sun Y, Cui Q, Wan Y, Fu G, et al. *Crit Rev Food Sci Nutr*. 2021 May 6:1-14. doi: 10.1080/10408398.2021.1913093. **Article link**

Significance: Fermentation is re-emerging as a novel approach through convergence of technologies such as mixing strain fermentation with heat, pulsed light and/or ultrasonication. Such an approach reduces the allergenicity of various foods, yet one is still able to preserve product taste and nutritional content.

The increasing prevalence of food allergies is a significant challenge to global food health and safety. Various strategies have been deployed to decrease the allergenicity of food for preventing and reducing related disorders. Compared to other methods, fermentation has unique advantages in reducing the allergenicity of food and may represent a new trend in preventing food-induced allergies. This review introduces the characteristics of allergens in various foods, including shellfish, soy, peanut, milk, tree nut, egg, wheat, and fish. The mechanism and pathological symptoms of allergic reactions are then summarized. Furthermore, the advantages of fermentation for reducing the allergenicity of these foods and preventing allergies are evaluated. Fermentation is an efficient approach for reducing or eliminating food allergenicity. Simultaneously, it improved the nutritional value and physicochemical properties of food materials. It is conceivable that a combination of mixed strain fermentation with additional processing, such as heat treatment, pulsed light, and ultrasonication, will efficiently reduce the allergenicity of various foods and preserve their unique taste and nutritional components, providing significance for patients with allergies.