Food Safety Briefs

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Risk Assessment

A State-of-the-Science Review of Interactions of Per- and Polyfluoroalkyl Substances (PFAS) with Renal Transporters in Health and Disease: Implications for Population Variability in PFAS Toxicokinetics

Shan Niu, Yuexin Cao, Ruiwen Chen, Megha Bedi, Alison P Sanders, Alan Ducatman, Carla Ng. *Environ Health Perspect*. 2023 Jul;131(7):76002. doi: 10.1289/EHP11885. Article link

Significance: More data are needed on current-use PFAS to study the role of transporters across the PFAS class. Remaining research gaps in transporter expression changes in specific kidney disease states could limit the effectiveness of risk assessment.

Background: Per- and polyfluoroalkyl substances (PFAS) are ubiquitous in the environment and have been shown to cause various adverse health impacts. In animals, sex- and species-specific differences in PFAS elimination half-lives have been linked to the activity of kidney transporters. However, PFAS molecular interactions with kidney transporters are still not fully understood. Moreover, the impact of kidney disease on PFAS elimination remains unclear. **Objectives:** This state-of-the-science review integrated current knowledge to assess how changes in kidney function and transporter expression from health to disease could affect PFAS toxicokinetics and identified priority research gaps that should be addressed to advance knowledge. **Methods:** We searched for studies that measured PFAS uptake by kidney transporters, quantified transporter-level changes associated with kidney disease status, and developed PFAS pharmacokinetic models. We then used two databases to identify untested kidney transporters that have the potential for PFAS transport based on their endogenous substrates. Finally, we used an existing pharmacokinetic model for perfluorooctanoic acid (PFOA) in male rats to explore the influence of transporter expression levels, glomerular filtration rate (GFR), and serum albumin on serum half-lives. **Results:** The literature search identified nine human and eight rat kidney transporters that were previously investigated for their ability to transport PFAS, as well as seven human and three rat transporters that were confirmed to transport specific PFAS. We proposed a candidate list of seven untested kidney transporters with the potential for PFAS transport. Model results indicated PFOA toxicokinetics were more influenced by changes in GFR than in transporter expression. **Discussion:** Studies on additional transporters, particularly efflux transporters, and on more PFAS, especially current-use PFAS, are needed to better cover the role of transporters across the PFAS class. Remaining research gaps in transporter expression changes in specific kidney disease states could limit the effectiveness of risk assessment and prevent identification of vulnerable populations.

Foodborne Pathogens

Sanitizer Type and Contact Time Influence *Salmonella* Reductions in Preharvest Agricultural Water Used on Virginia Farms

Claire M Murphy, Alexis M Hamilton, Kim Waterman, Channah Rock, Donald Schaffner, Laura K Strawn. *J Food Prot*. 2023 Aug;86(8):100110. doi: 10.1016/j.jfp.2023.100110. Article link

Significance: Certain treatment combinations with PAA- and Cl-based sanitizers along with proper contact time were effective at reducing *Salmonella* in preharvest water.

No Environmental Protection Agency (EPA) chemical treatments for preharvest agricultural water are currently labeled to reduce human health pathogens. The goal of this study was to examine the efficacy of peracetic acid- (PAA) and chlorine (Cl)-based sanitizers against *Salmonella* in Virginia irrigation water. Water samples (100 mL) were collected at three time points during the growing season (May, July, September) and inoculated with either the 7-strain EPA/FDA-prescribed cocktail or a 5-strain *Salmonella* produce-borne outbreak cocktail. Experiments were conducted in triplicate for 288 unique

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combinations of time point, residual sanitizer concentration (low: PAA, 6 ppm; Cl, 2-4 ppm or high: PAA, 10 ppm; Cl, 10-12 ppm), water type (pond, river), water temperature (12°C, 32°C), and contact time (1, 5, 10 min). *Salmonella* were enumerated after each treatment combination and reductions were calculated. A log-linear model was used to characterize how treatment combinations influenced *Salmonella* reductions. *Salmonella* reductions by PAA and Cl ranged from 0.0 ± 0.1 to 5.6 ± 1.3 log10 CFU/100 mL and 2.1 ± 0.2 to 7.1 ± 0.2 log10 CFU/100 mL, respectively. Physicochemical parameters significantly varied by untreated water type; however, *Salmonella* reductions did not ($p = 0.14$), likely due to adjusting the sanitizer amounts needed to achieve the target residual concentrations regardless of source water quality. Significant differences ($p < 0.05$) in *Salmonella* reductions were observed for treatment combinations, with sanitizer (Cl > PAA) and contact time (10 > 5 > 1 min) having the greatest effects. The log-linear model also revealed that outbreak strains were more treatment-resistant. Results demonstrate that certain treatment combinations with PAA- and Cl-based sanitizers were effective at reducing *Salmonella* populations in preharvest agricultural water. Awareness and monitoring of water quality parameters are essential for ensuring adequate dosing for the effective treatment of preharvest agricultural water.

Foodborne Illness

Food Safety Incidents in the Red Meat Industry: A Review of Foodborne Disease Outbreaks Linked to the Consumption of Red Meat and its Products, 1991 to 2021

Dein Warmate, Bukola A Onarinde. *Int J Food Microbiol*. 2023 Aug;398:110240. doi: 10.1016/j.ijfoodmicro.2023.110240. Article link

Significance: Implementing food safety management strategies including adequate control measures at all stages of the food supply chain will prevent outbreaks associated with meat and its products.

Red meat is a significant source of human nutrition, and the red meat industry contributes to the economy of nations. Nonetheless, there is a widespread global concern about public health issues posed by severe food safety incidents within the red meat industry. Most of these incidents are associated with foodborne disease outbreaks that impact individual consumers, food businesses and society. This study adopts a systematic search and review approach to identify three decades of published investigation reports of global foodborne disease outbreaks linked with the consumption of red meat and products made from them. The review aims to evaluate the critical features of these outbreak incidents to get insight into their contributing factors and root causes. In particular, this review discusses the transmission setting (origin of pathogenic agents), the food vehicles mostly incriminated, the causative pathogens (bacteria, viruses, and parasites) causing the most illnesses, and the most commonly reported contributing factors to the outbreaks. This information can help researchers and food business operators (FBOs) inform future risk assessment studies and support risk management activities in developing risk-mitigating strategies for the industry. Findings from this study suggest that implementing food safety management strategies which include adequate control measures at all stages of the food chain, from farm to fork, is imperative in preventing outbreak incidents. Of equal importance is the need for enhanced and sustained public education about the risk of foodborne illnesses associated with meat and its products whilst discouraging the consumption of raw meat products, especially by high-risk groups.

Mycotoxins

Deoxynivalenol: Emerging Toxic Mechanisms and Control Strategies, Current and Future Perspectives

Ying Deng, Li You, Xu Wang, Wenda Wu, Kamil Kuca, Qinghua Wu, Wei Wei. *J Agric Food Chem*. 2023 Jul 26;71(29):10901-10915. doi: 10.1021/acs.jafc.3c02020. Article link

Significance: Due to the synergistic toxic effect of DON and other mycotoxins to induce cell growth inhibition, strategies to detect DON and control it biologically are critical.

Deoxynivalenol (DON) is the most frequently present mycotoxin contaminant in food and feed, causing a variety of toxic effects in humans and animals. Currently, a series of mechanisms involved in DON toxicity have been identified. In addition to the activation of oxidative stress and the MAPK signaling pathway, DON can activate hypoxia-inducible factor-1α, which further regulates reactive oxygen species production and cancer cell apoptosis. Noncoding RNA and signaling pathways including Wnt/β-catenin, FOXO, and TLR4/NF-κB also participate in DON toxicity. The intestinal microbiota and the brain-gut axis play a crucial role in DON-induced growth inhibition. In view of the synergistic toxic effect of DON and other mycotoxins, strategies to detect DON and control it biologically and the development of enzymes for the biodegradation of various mycotoxins and their introduction in the market are the current and future research hotspots.

Heavy Metals

Dietary Exposure to Cadmium from Six Common Foods in the United States

Ashish Pokharel, Felicia Wu. *Food Chem Toxicol*. 2023 Aug;178:113873. doi: 10.1016/j.fct.2023.113873. Article link

Significance: The age groups 6-24 months and 24-60 month olds were found to be the most highly exposed to cadmium in this analysis of six foods.

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Recently, the United States (US) Food and Drug Administration (FDA) launched a Closer to Zero Action Plan to assess the risks of and develop action levels for certain heavy metals in food including cadmium (Cd). The problem of foodborne metal contamination has taken on new urgency, thanks in part to a 2021 US Congressional Report detailing high levels of metals found in infant food. Our risk assessment aids this FDA Action Plan by estimating the American population's Cd exposures in food, by age group and consumption patterns of certain high-risk foods; and by determining circumstances in which exposures exceed tolerable daily intakes developed by policymaking groups in the US and worldwide. We found that the age groups 6-24 months and 24-60 month old are the most highly exposed to Cd in common foodstuffs. American infants and young children of these age groups who regularly consumed rice, spinach, oats, barley, potatoes, and wheat had mean Cd exposures exceeding maximum tolerable intake level was set by the Agency for Toxic Substances and Disease Registry (ATSDR). We have identified age groups at highest potential risk, and therefore of interest for developing food safety policies to improve safety of commercial food for children.

Food Packaging

Repair Mechanism and Application of Self-Healing Materials for Food Preservation

Jindi Wang, Qingchao Gao, Fangyuan Zhao, Jian Ju. *Crit Rev Food Sci Nutr*. 2023 Jul 10;1-11. doi: 10.1080/10408398.2023.2232877. Article link

Significance: This article investigates self-healing packing for commercial use including the functionality mechanisms, applications and limitations of this emerging technology.

The traditional packaging concept has reached its limits when it comes to ensuring the quality of food and extending its shelf life. Compared to traditional packaging materials, food packaging with self-healing function is becoming more and more popular. This is because they can automatically repair the damaged area, restore the original properties and prevent the decline of food quality and loss of nutrients. Materials based on various self-healing mechanisms have been developed and used on a laboratory scale in the form of coatings and films for food packaging. However, more efforts are needed for the commercial application of these new self-healing packaging materials. Understanding the self-healing mechanism of these packaging materials is very important for their commercial application. This article first discusses the self-healing mechanism of different packaging materials and compares the self-healing efficiency of self-healing materials under different conditions. Then, the application potential of self-healing coatings and films in the food industry is systematically analyzed. Finally, we give an outlook on the application of self-healing materials in the field of food packaging.

Chemical Contaminants

Covalent Organic Frameworks Assisted for Food Safety Analysis

Ying Huang, Donghui Feng, Xu Li, Wang Li, Jiali Ren, Haiyan Zhong. *Crit Rev Food Sci Nutr*. 2023 Jul 7;1-20. doi: 10.1080/10408398.2023.2230506. Article link.

Significance: Covalent organic frameworks can be designed to assist in the detection of various food contaminants including foodborne pathogens, mycotoxins, pesticides, antibiotics and heavy metals.

Food safety incidents threaten human health and life safety. It is an effective method to prevent and control the occurrence of food safety events by enhancing the rapid and sensitive detection of food contaminants. Emerging porous materials provide

for the development of efficient and stable detection methods. Covalent organic frameworks (COFs) are favored by researchers for their highly ordered pore structure, large specific surface area, and good structural and functional designability. Especially in the sensing field, COFs play the roles of carriers, conductors, quenchers, and reporters, and have broad application prospects. To better understand COFs-based sensing studies, this review briefly introduces the characteristics and different functional roles of COFs in food safety analysis, focusing on the applications of COFs in the detection of various food contaminants (including foodborne pathogens, mycotoxins, pesticides, antibiotics, heavy metals, and others). Finally, the challenges and opportunities for COFs-based sensing are discussed to facilitate further applications and development of COFs in food safety.

Caffeine

Association between Urinary Caffeine and Caffeine Metabolites and Stroke in American Adults: A Cross-Sectional Study from the NHANES, 2009-2014

Jinming Fan, Yajun Yuan, Xiaoting Zhang, Wenhan Li, Wuqin Ma, Wenhao Wang, Jinyan Gu, et. al. *Sci Rep*. 2023 Jul 22;13(1):11855. doi: 10.1038/s41598-023-39126-1. Article link

Significance: This study revealed a negative link between urine paraxanthine levels and the risk of stroke.

This study investigates the potential correlation between urinary caffeine levels and the occurrence of stroke, a serious cerebrovascular disease that can lead to disability or death. The data used in this study was obtained from the National Health and Nutrition Examination Survey conducted between 2009 and 2014. The study analyzed a total of 5,339 individuals, divided into a control group (n = 5,135) and a stroke group (n = 162). The researchers utilized multiple logistic regression and smoothed curve fitting to examine the relationship between urinary caffeine and caffeine metabolites and the incidence of stroke. The study found that higher urinary caffeine levels were associated with a lower risk of stroke in Mexican American participants (odds ratio [OR] = 0.886, 95% confidence interval [CI]: (0.791, 0.993), P = 0.037). After adjusting for certain participant characteristics, it was also found that higher urinary paraxanthine levels were associated with a lower risk of stroke incidence (OR = 0.991, 95% CI (0.984, 0.999), P = 0.027). Meanwhile, the highest urinary paraxanthine levels group had 43.7% fewer strokes than the lowest level group (OR = 0.563, 95% CI (0.341, 0.929), P = 0.025). In this study, we showed a negative link between urine paraxanthine levels and the risk of stroke. Meanwhile, urinary caffeine levels were negatively associated with the incidence of stroke in Mexican Americans, but no correlation in other populations. Our findings may have predictive and diagnostic implications in clinical practice. Further extensive prospective investigations are still needed to validate our conclusions.

Food Allergens

Impact of Using Less Objective Symptoms to Define Tolerated Dose during Food Challenges: A Data-Driven Approach

Paul J Turner, Nandinee Patel, Katharina Blumchen, Stefanie Berkes, Hugh A Sampson, Kirsten Beyer. *J Allergy Clin Immunol*. 2023 Jul;152(1):145-154. doi: 10.1016/j.jaci.2022.12.818. Article link

Significance: Applying a data-driven minor modification in a new set of allergen challenge-stop criteria is simpler to implement and reduces patient discomfort.

Background: Food challenges (FCs) form the basis for assessing efficacy outcomes in interventional studies of food allergy; however, different studies have used a variety of similar but not identical criteria to define a challenge reaction, including subjective (nonobjective) symptoms occurring in a single-organ system as dose limiting. **Objective:** Our aim was to undertake a secondary analysis of 4 interventional studies to assess the impact of using less objective criteria to determine challenge-stop on reaction thresholds and their reproducibility. **Methods:** We analyzed individual participant data, including individual participant data meta-analysis, by using 3 different published challenge-stop criteria: (1) PRACTALL consensus criteria; (2) Consortium for Food Allergy Research version 3 (CoFAR v3) with at least 1 moderate- or severe-grade symptom; or (3) CoFAR v3 with at least 2 mild symptoms occurring in different organ systems. Reproducibility of challenge threshold was also assessed in participants undergoing subsequent repeat FCs. Results: Four studies, with detailed challenge data from a total of 592 participants, were included. Applying CoFAR v3 definitions for dose-limiting

symptoms resulted in an underestimate of reaction thresholds compared with those in PRACTALL ($P < .001$) that is equivalent to almost a single dosing increment when using a semi-log dosing regimen. Reproducibility was also reduced when applying CoFAR v3 ($P < .001$ [n = 223]). Using the least conservative interpretation of CoFAR v3 (≥2 mild symptoms occurring in different systems) resulted in a significant overestimate of 15% when assessing oral immunotherapy efficacy. Applying a data-driven minor modification to CoFAR v3 resulted in a new set of challenge-stop criteria with validity similar to that of PRACTALL but one that is simpler to implement and in which significant gastrointestinal discomfort with observable decreased activity remains a dose-limiting symptom. **Conclusion:** The use of less objective symptoms to define challenge-stop compromises the reproducibility of the FC as a tool to assess efficacy outcomes in interventional studies, and potentially overestimates the efficacy of the intervention tested.

Emerging Science Areas

Emerging topic: Food Safety Innovation

Category: Sustainable Packaging

Development and Characterization of Sustainable-Active-Edible-Bio Based Films from Orange and Pomegranate Peel Waste for Food Packaging: Effects of Particle Size and Acid/Plasticizer Concentrations

Eylem Karakuş, Zehra Ayhan, Guliz Haskaraca. *Food Packaging & Shelf Life.* Vol. 37, June 2023, doi.org/10.1016/j.fpsl.2023.101092. Article link

Significance: Pomegranate and orange peels present options for antioxidant and antimicrobial biopolymer sources for sustainable and active food coatings and packaging.

Sustainable packaging materials especially from food processing waste are of getting interest. The aim of the study was to develop edible bio based films from processing wastes of pomegranate and orange peels. For this purpose, pomegranate and orange peels were dried and processed into flour in different particle sizes. The effects of particle size, concentration of acid and plasticizer on physical and mechanical properties were investigated. Antimicrobial, antioxidant, morphological and thermal properties were further determined for the selected film formulations. Results showed that the particle size significantly affected mechanical properties of the films ($p \leq 0.05$), with improvement of the mechanical properties for the reduced particle size. Pomegranate and orange peel based films showed very high antimicrobial activity against E. coli and S. aureus irrespective of particle sizes. The pomegranate and orange peel based films had homogeneous, smooth, and crack-free surfaces. Pomegranate and orange peel based films showed very similar thermal properties and major thermal degradation was observed between 160 and 300 °C for both type of films irrespective of particle sizes. Pomegranate and orange peels could be good potential as antioxidant and antimicrobial biopolymer sources for sustainable and active food coating/packaging.

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