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Food Safety Briefs

Risk Assessment

Evaluation of Per- and Polyfluoroalkyl Substances (PFAS) *In Vitro* Toxicity Testing for Developmental Neurotoxicity

Kelly E Carstens, Theresa Freudenrich, Kathleen Wallace, Seline Choo, Amy Carpenter, Marci Smeltz, Matthew S Clifton et. al. *Chem Res Toxicol.* 2023 Feb 23. doi: 10.1021/acs.chemrestox.2c00344. **Article link**

Significance: A subset of PFAS have been shown to affect neurodevelopmental processes *in vitro* and suggest focusing future studies of developmental neurotoxicity and PFAS.

Per- and polyfluoroalkyl substances (PFAS) are a diverse set of commercial chemicals widely detected in humans and the environment. However, only a limited number of PFAS are associated with epidemiological or experimental data for hazard identification. To provide developmental neurotoxicity (DNT) hazard information, the work herein employed DNT new approach methods (NAMs) to generate *in vitro* screening data for a set of 160 PFAS. The DNT NAMs battery was comprised of the microelectrode array neuronal network formation assay (NFA) and high-content imaging (HCI) assays to evaluate proliferation, apoptosis, and neurite outgrowth. The majority of PFAS (118/160) were inactive or equivocal in the DNT NAMs, leaving 42 active PFAS that decreased measures of neural network connectivity and neurite length. Analytical quality control indicated 43/118 inactive PFAS samples and 10/42 active PFAS samples were degraded; as such, careful interpretation is required as some negatives may have been due to loss of the parent PFAS, and some actives may have resulted from a mixture of parent and/or degradants of PFAS. PFAS containing a perfluorinated carbon (C) chain length ≥8, a high C:fluorine ratio, or a carboxylic acid moiety were more likely to be bioactive in the DNT NAMs. Of the PFAS positives in DNT NAMs, 85% were also active in other EPA ToxCast assays, whereas 79% of PFAS inactives in the DNT NAMs were active in other assays. These data demonstrate that a subset of PFAS perturb neurodevelopmental processes in vitro and suggest focusing future studies of DNT on PFAS with certain structural feature descriptors.

Foodborne Pathogens

Impact of Food-Relevant Conditions and Food Matrix on the Efficacy of Prenylated Isoflavonoids Glabridin and 6,8-diprenylgenistein as Potential Natural Preservatives against *Listeria monocytogenes*

Alberto Bombelli, Carla Araya-Cloutier, Jean-Paul Vincken, Tjakko Abee, Heidy M W den Besten. *Int J Food Microbiol.* 2023 Feb;390:110109. doi: 10.1016/j.ijfoodmicro.2023.110109. **Article link**

Significance: This study highlights the potential of prenylated isoflavonoids as naturally derived food preservative materials.

T Prenylated isoflavonoids can be extracted from plants of the Leguminosae/Fabaceae family and have shown remarkable antimicrobial activity against Gram-positive food-borne pathogens, such as *Listeria monocytogenes*. Promising candidates from this class of compounds are glabridin and 6,8-diprenylgenistein. This research aimed to investigate the potential of glabridin and 6,8-diprenylgenistein as food preservatives against *L. monocytogenes*. Their antimicrobial activity was tested *in vitro* at various conditions relevant for food application, such as different temperatures (from 10 °C to 37 °C), pH (5 and 7.2), and in the presence or absence of oxygen. The minimum inhibitory concentrations of glabridin and 6,8-diprenylgenistein *in vitro* were between 0.8 and 12.5 μg/mL in all

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tested conditions. Growth inhibitory activities were similar at 10 °C compared to higher temperatures, although bactericidal activities decreased when the temperature decreased. Notably, lower pH (pH 5) increased the growth inhibitory and bactericidal activity of the compounds, especially for 6,8-diprenylgenistein. Furthermore, similar antimicrobial efficacies were shown anaerobically compared to aerobically at the tested conditions. Glabridin showed a more stable inhibitory and bactericidal activity when the temperature decreased compared to 6,8-diprenylgenistein. Therefore, we further determined the antimicrobial efficacy of glabridin against *L. monocytogenes* growth on fresh-cut cantaloupe at 10 °C. In these conditions, concentrations of glabridin of 50, 100 and 250 μg/g significantly reduced the growth of *L. monocytogenes* compared to the control, resulting on average in >1 Log CFU/g difference after 4 days compared to the control. Our results further underscored the importance of considering the food matrix when assessing the activity of novel antimicrobials. Overall, this study highlights the potential of prenylated isoflavonoids as naturally derived food preservatives.

Foodborne Illness

Checklist to Assess Food Safety When Handling Home Enteral Nutrition

Rayane Luizi da Costa, Caroline Opolski Medeiros, Diogo Thimoteo da Cunha, Lize Stangarlin-Fiori. *Nutr Clin Pract*. 2023 Feb 23. doi: 10.1002/ncp.10962. **Article link**

Significance: The FSHEN checklist is relevant, clear, and easy to use. It can help health professionals and individuals to assess and prioritize food safety items.

Background: Identifying food safety risks when handling enteral formulations at home is important to restore and maintain the health of patients. Therefore, this study developed and validated a food safety assessment checklist for handling home enteral nutrition (HEN). **Methods:** This methodological study developed a checklist based on a literature review and interviews with food safety professionals. The content validation, which was conducted by food safety and enteral feeding experts, assessed the relevance, clarity, and simplicity of the checklist using the content validity index of items (CVI-I), categories (CVI-C), and the entire instrument (CVI-EI). Each item was rated as either essential, necessary, or recommended according to the risk in relation to foodborne diseases. **Results:** The Food Safety for Handling Home Enteral Nutrition checklist (FSHEN checklist) that was developed includes 40 items and the following eight categories: physical structure; cleaning of facilities, equipment, furniture, and utensils; pests and waste; water supply; food handlers; ingredients and packaging; handling of enteral formulations; and the bottling and storage of enteral formulations. The CVI-EI was above the recommendation (≥0.93) for the three assessed criteria, as was the CVI-C in terms of clarity (≥0.95), relevance (≥0.98), and simplicity (≥0.84). A total of 52.5% of the items were rated as essential, 32.5% as necessary, and 15% as recommended. **Conclusion**: The FSHEN checklist is relevant, clear, and easy to use. It can help health professionals and individuals working in the field to assess and prioritize items to improve food safety in the management of HEN.

Mycotoxins

Effect of Different Storage Conditions on the Stability and Safety of Almonds

Paula Rodrigues, Arij Jelassi, Elifa Kanoun, Michael Sulyok, Paula Correia, Elsa Ramalhosa, Ermelinda Lopes Pereira. *J Food Sci*. 2023 Feb;88(2):848-859. doi: 10.1111/1750-3841.16453. **Article link**

Significance: Storage of almonds at 60% relative humidity at 25°C is a good storage condition to maintain the stability and safety of nuts in terms of microbial and mycotoxin contaminations.

Almond production in Portugal is of great importance for the economy of their main producing areas. However, the contamination of these nut fruits with fungi and mycotoxins poses a significant risk to food safety and security. This work intended to evaluate the influence of storage conditions on the microbial and mycotoxin stability and safety of almonds throughout long-term storage. Two almond varieties-Lauranne and Guara-were submitted to three different storage conditions, namely, 4°C with noncontrolled relative humidity (RH), 60% RH at 25°C, and 70% RH at 25°C, for a storage period of 9 months. Samples were collected after 0, 3, 6, and 9 months of storage and analyzed for microbial loads (aerobic mesophiles, yeasts, and molds), mold incidence and diversity, and mycotoxin contamination. In total, 26 species were identified belonging to 6 genera: *Aspergillus, Cladosporium, Fusarium, Penicillium, Paecilomyces,* and *Talaromyces*. For the variety Guara, mycotoxins related to *Aspergillus* sect. *Flavi*, such as aflatoxins, averufin, versicolorin C, and norsolorinic acid, were detected only after 9 months of storage at 70% and 60% RH. *Penicillium* mycotoxins, such as quinolactacin A and roquefortine C, were also detected. For the variety Lauranne, *Penicillium* mycotoxins were detected, such as citrinin, quinolactacins A and B, roquefortines C and D, cyclopenin, cyclopenol, penitrem A, viridicatin, and viridicatol. Mycotoxins related to *Aspergillus*, such as aspulvinone E, flavoglaucin, paspalin, asperglaucide, asperphenamate, cyclo(L-Pro-L-Tyr),

and cyclo(L-Pro-L-Val), were also detected. PRACTICAL APPLICATION: The quality of almonds depends on the storage period and the RH and temperature at which they are stored. Storage of almonds at 60% RH at 25°C is a good storage condition to maintain the stability and safety of nuts in terms of microbial and mycotoxin contaminations.

Heavy Metals

Cadmium Exposure and DNA Damage (Genotoxicity): A Systematic Review and Meta-Analysis

Raju Nagaraju, Ravibabu Kalahasthi, Rakesh Balachandar, Bhavani Shankara Bagepally. *Crit Rev Toxicol*. 2023 Feb 21;1-13. doi: 10.1080/10408444.2023.2173557. **Article link**

Significance: Chronic cadmium exposure is associated with DNA damage but more longitudinal studies are required to understand the relationship.

Existing literature suggests an association between chronic cadmium (Cd) exposure and the induction of DNA damage and genotoxicity. However, observations from individual studies are inconsistent and conflicting. Therefore current systematic review aimed to pool evidence from existing literature to synthesize quantitative and qualitative corroboration on the association between markers of genotoxicity and occupational Cd exposed population. Studies that evaluated markers of DNA damage among occupationally Cd-exposed and unexposed workers were selected after a systematic literature search. The DNA damage markers included were chromosomal aberrations (chromosomal, chromatid, sister chromatid exchange), Micronucleus (MN) frequency in mono and binucleated cells (MN with condensed chromatin, lobed nucleus, nuclear buds, mitotic index, nucleoplasmatic bridges, pyknosis, and karyorrhexis), comet assay (tail intensity, tail length, tail moment, and olive tail moment), and oxidative DNA damage (8-hydroxy-deoxyguanosine). Mean differences or standardized mean differences were pooled using a random-effects model. The Cochran-Q test and I2 statistic were used to monitor heterogeneity among included studies. Twenty-nine studies with 3080 occupationally Cd-exposed and 1807 unexposed workers were included in the review. Cd among the exposed group was higher in blood [4.77 µg/L (-4.94-14.48)] and urine samples [standardized mean difference 0.47 (0.10-0.85)] than in the exposed group. The Cd exposure is positively associated with higher levels of DNA damage characterized by increased frequency of MN [7.35 (-0.32-15.02)], sister chromatid exchange [20.30 (4.34-36.26)], chromosomal aberrations, and oxidative DNA damage (comet assay and 8OHdG [0.41 (0.20-0.63)]) compared to the unexposed. However, with considerable between-study heterogeneity. Chronic Cd exposure is associated with augmented DNA damage. However, more extensive longitudinal studies with adequate sample sizes are necessary to assist the current observations and promote comprehension of the Cd's role in inducing DNA damage.

Food Packaging

Wheat Gluten-Based Coatings and Films: Preparation, Properties and Applications

Jingwen Xu, Yonghui Li. *J Food Sci*. 2023 Feb;88(2):582-594. doi: 10.1111/1750-3841.16454. **Article link**

Significance: Antioxidants and antimicrobial agents added to wheat gluten can inhibit microbial growth on foodstuffs, maintain food quality, and extend shelf life. The performance of wheat gluten-based coatings and films can be further improved to expand their packaging applications.

Effective food packaging that can protect foodstuffs from physical, chemical, and biological damage and maintain freshness and quality is essential to the food industry. Wheat gluten shows promise as food packaging materials due to its edibility, biodegradability, wide availability, low cost, film-forming potential, and high resistance to oxygen. The low mechanical properties and poor water permeability of wheat gluten coatings and films limit their wide applications; however, some inferior properties can be improved through various solutions. This work presents a comprehensive review about wheat gluten-based coatings and films, including their formulation, processing methods, properties, functions, and applications. The mechanical and water resistance properties of coatings and films can be reinforced through wheat gluten modification, combinations of different processing methods, and the incorporation of reinforcing macromolecules, antioxidants, and nanofillers. Antioxidants and antimicrobial agents added to wheat gluten can inhibit microbial growth on foodstuffs, maintain food quality, and extend shelf life. Performances of wheat gluten-based coatings and films can be further improved to expand their applications in food packaging. Current research gaps are identified. Future research is needed to examine the optimal formulation and processing of wheat gluten-based coatings and films and their performance.

Chemical Contaminants

Hazard Characterization of Bisphenol A (BPA) based on Rodent Models - Multilevel Meta-Analysis and Dose-Response Analysis for Reproductive Toxicity

Xin Wang, Rajat Nag, Nigel P Brunton, Md Abu Bakar Siddique, Sabine M Harrison, Frank J Monahan, Enda Cummins. *Food Chem Toxicol.* 2023 Feb;172:113574. doi: 10.1016/j.fct.2022.113574. **Article link**

Significance: The potential health risks from BPA exposure are reviewed with regards to reproductive toxicity and other endpoints.

Bisphenol A (BPA) is a widely used synthetic industrial compound frequently detected in food. Dietary exposure to BPA has been recognised as a potential health concern. However, there are uncertainties regarding BPA toxicity. The primary objective of this study was to summarise and analyse multiple toxicity endpoints of adverse reproductive effects caused by BPA exposure in rodent models. Therefore, a multilevel meta-analysis and subsequent dose-response analysis were conducted. Relevant articles published in English between 2012 and 2021 were collected from online databases, viz. Scopus, EmBase, Web of Science, and PubMed. In total, 41 studies were included for statistical analysis. All statistical analyses were performed using open-source RStudio packages. Summary effects indicated the statistical significance of BPA exposure on decreased sperm concentration (Hedges' g: -1.35) and motility (Hedges' g: -1.12) on average, while no significant effects were observed on the absolute and relative weight of male and female reproductive organs. The lowest mean toxicological reference dose values of 0.0011 mg (kg bw)-1 day-1 was proposed for BPA exposure on sperm concentration from the dose-response model. In conclusion, potential health risks from BPA exposure were shown with regards to reproductive toxicity, especially that sperm concentration and sperm motility require further attention.

Probiotic Cultures as a Potential Protective Strategy Against the Toxicity of Environmentally Relevant Chemicals: State-of-the-Art Knowledge

Katarina Baralić, Katarina Živančević, Dragica Bozic, Danijela Đukić-Ćosić. *Food Chem Toxicol.* 2023 Feb;172:113582. doi: 10.1016/j.fct.2022.113582. **Article link**

Significance: Summarizes the state-of-the-art knowledge regarding the potential protective effects of different probiotic strains against environmentally relevant toxic substances (mycotoxins, polycyclic aromatic hydrocarbons, pesticides, etc.).

Environmentally relevant toxic substances may affect human health, provoking numerous harmful effects on central nervous, respiratory, cardiovascular, endocrine and reproductive system, and even cause various types of carcinoma. These substances, to which general population is constantly and simultaneously exposed, enter human body via food and water, but also by inhalation and dermal contact, while accumulating evidence suggests that probiotic cultures are able to efficiently adsorb and/or degrade them. Cell wall of probiotic bacteria/fungi, which contains structures such as exopolysaccharide, teichoic acid, protein and peptidoglycan components, is considered the main place of toxic substances adsorption. Moreover, probiotics are able to induce metabolism and degradation of various toxic substances, making them less toxic and more suitable for elimination. Other probable in vivo protective effects have also been suggested, including decreased intestinal absorption and increased excretion of toxic substances, prevented gut microbial dysbiosis, increase in the intestinal mucus secretion, decreased production of reactive oxygen species, reduction of inflammation, etc. Having all of this in mind, this review aims to summarize the state-of-the-art knowledge regarding the potential protective effects of different probiotic strains against environmentally relevant toxic substances (mycotoxins, polycyclic aromatic hydrocarbons, pesticides, perfluoroalkyl and polyfluoroalkyl substances, phthalates, bisphenol A and toxic metals).

Caffeine

Trends of Caffeine Intake from Food and Beverage among Chinese Adults: 2004-2018

Chen Ye, Xiao Xiao, Haixia Sui, Daoyuan Yang, Ling Yong, Yan Song. *Food Chem Toxicol.* 2023 Mar;173:113629. doi: 10.1016/j.fct.2023.113629. **Article link**

Significance: Traditional tea leaves, coffee and sodas are the main sources of caffeine intake for Chinese adults. Most consume caffeine below the safe level (400 mg/day), but caffeine consumption has grown over the last 14 years.

Caffeine is a kind of psychostimulant that naturally exists in foods. The benefits and risks of caffeine depend on the dose. Moreover, the intake of caffeine from dietary sources in China has seldom been assessed. We calculated the dietary caffeine intake of Chinese adult consumers from 2004 to 2018 and analyzed its consumption trends by using data from

the China Health and Nutrition Survey and the National Food and Beverage Consumption Survey. Caffeine contents in different dietary items were determined by HPLC. Monte Carlo simulations were applied to estimate caffeine intake. Mann-Kendall trend test and linear regression were used to analyze the trend of caffeine consumption. Among 79,173 individuals, 3972 (5%) of the adult Chinese population consumed caffeine between 2004 and 2018. The average caffeine intake was 123 mg/day for male consumers and 116 mg/day for female consumers. The median and P75 caffeine intake raised over the 14 years. Traditional tea leaves, coffee and sodas are the main sources of caffeine intake. Our findings indicate that most Chinese adults consumed caffeine within the safe level (400 mg/day), but the caffeine consumption has shown an increasing trend in recent 14 years.

Food Allergens

Open-Label Study of the Efficacy, Safety and Durability of Peanut Sublingual Immunotherapy in Peanut-Allergic Children

Edwin H Kim, Corinne A Keet, Yamini V Virkud, Stacy Chin, Ping Ye, Anusha Penumarti, Johanna Smeekens, et. al. *J Allergy Clin Immunol.* 2023 Feb 22;S0091-6749(23)00218-X. doi: 10.1016/j.jaci.2023.01.036. **Article link**

Significance: In a prospective study, peanut sublingual immunotherapy was safe and induced clinically significant desensitization in the majority of children lasting more than 17 weeks.

Background: Studies are limited on the efficacy of peanut sublingual immunotherapy (SLIT). The durability of desensitization after SLIT has not been well described. **Objective:** To evaluate the efficacy and safety of 4 mg peanut SLIT and persistence of desensitization after SLIT discontinuation. **Methods:** Challenge proven peanut-allergic 1-11 year old children were treated with open-label 4 mg peanut SLIT for 48 months. Desensitization after peanut SLIT was assessed by 5000 mg double-blind, placebo-controlled food challenge (DBPCFC). A novel randomly assigned avoidance period between 1-17 weeks was followed by a DBPCFC. Skin prick testing (SPT), immunoglobulins, basophil activation testing (BAT), TH1, TH2, and IL-10 cytokines were measured longitudinally. Safety was assessed through patient-reported home diaries. **Results:** Fifty-four participants were enrolled and 47 (87%) completed peanut SLIT and the 48-month DBPCFC per protocol. Mean successfully consumed dose (SCD) during DBPCFC increased from 48 mg to 2723 mg peanut protein after SLIT ($p<0.0001$), with 70% achieving clinically significant desensitization (SCD >800 mg) and 36% full desensitization (SCD = 5000 mg). Modeled median time to loss of clinically significant desensitization was 22 weeks. Peanut SPT; peanut-specific IgE, IgG4, IgG4/IgE ratio; and peanut-stimulated BAT, IL-4, IL-5, IL-13, IFN-gamma, and IL-10 changed significantly compared to baseline with changes seen as early as 6 months. Median rate of reaction per dose was 0.5% with transient oropharyngeal itching most common and no dosing symptoms requiring epinephrine. **Conclusion:** In this open-label, prospective study, peanut SLIT was safe and induced clinically significant desensitization in the majority of children lasting more than 17 weeks after discontinuation of therapy.

Emerging Science Areas

Emerging Areas Food Safety

Category: Exposure Measurement Tool

Geographic and Demographic Variability in Serum PFAS Concentrations for Pregnant Women in the United States

DeLuca, N.M., Thomas, K., Mullikin, A. et al. *J Expo Sci Environ Epidemiol* (2023). doi.org/10.1038/s41370-023-00520-6. **Article link**

Significance: By increasing understanding of maternal and early-life PFAS exposures this study identifies environmental justice considerations and contributes to risk management strategies.

A study using self-reported and location questionnaires to analyze serum PFAS variability in pregnant women in seven US counties, found a correlation between location and all serum PFAS chemicals measured. Additionally, race/ethnicity, income, education level, number of household members, drinking water source, home age, and fast-food consumption were also associated with PFAS levels. Background: While major pathways of human PFAS exposure are thought to be drinking water and diet, other pathways and sources have also been shown to contribute to a person's cumulative exposure. However, the degree of contribution of these other sources to PFAS body burdens is still not well understood and occurrence data for PFAS in consumer products and household materials are sparse. Questionnaire data concordant with biomonitoring may improve understanding of associations between other PFAS exposure pathways and exposure in human populations. Objective: This study aims to better understand maternal and early-life exposures to PFAS from various potential sources and pathways in the context of household and community level characteristics. Methods: PFAS data from the National Children's Study (NCS) Vanguard Data and Sample Archive Access System were

analyzed from serum of 427 pregnant women residing in 7 counties throughout the United States. Location and self-reported questionnaire responses were used to analyze variability in serum concentrations based on demographics, housing characteristics, behaviors, and geography. Spatial mapping analyses incorporated publicly available data to further hypothesize potential sources of exposure in two NCS counties. Results: Location was associated with serum concentrations for all PFAS chemicals measured. Questionnaire responses for race/ethnicity, income, education level, number of household members, drinking water source, home age, and fast-food consumption were associated with PFAS levels. Statistical differences were observed between participants with the same questionnaire responses but in different locations. Spatial mapping analyses suggested that participants' proximity to local point sources can overshadow expected trends with demographic information. Significance: By increasing understanding of maternal and early-life PFAS exposures from various potential sources and pathways, as well as highlighting the importance of proximity to potential sources in identifying vulnerable populations and locations, this work reveals environmental justice considerations and contributes to risk management strategies that maximize public health protection. Impact: This work increases understanding of maternal and early-life PFAS exposures, reveals environmental justice considerations, and contributes to study design and risk management strategies.

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