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Food Safety Briefs

Risk Assessment

A Chemical Interactions and Mixtures in Public Health Risk Assessment: An Analysis of ATSDR's Interaction Profile Database

Przybyla J, McClure PR, Zaccaria KJ, Pohl HR. *Regul Toxicol Pharmacol.* 2021 Aug. doi: 10.1016/j.yrtph.2021.104981. **Article link**

Significance: Using an ATSDR tool to understand the toxicity posed by chemical mixtures resulted in limited ability to make weight-of-evidence conclusions on the direction of chemical interactions.

The Agency for Toxic Substances and Disease Registry (ATSDR) develops interaction profiles using binary weight of evidence (BINWOE) methodology to determine interaction directions of common environmental mixtures. We collected direction of interactions, BINWOE score determination, and BINWOE score confidence rating from 13 interaction profiles along with toxicodynamic and toxicokinetic influences on interaction direction. By doing so, we quantified the 1) direction of interaction and indeterminate evaluations; 2) characterized confidence in the BINWOE determinations; and 3) quantified toxicokinetic/toxicodynamic, and other influences on projected BINWOE interaction directions. Thirty-nine percent (130/336) of the attempts to make a BINWOE were indeterminate due to no interaction data or inadequate or conflicting evidence. Out of remaining BINWOEs, 25% were additive, 9% were greater-than-additive, and 27% were less-than-additive interactions. Fifty-five percent of BINWOEs were explained by toxicokinetic interactions, 12% and 5% were explained by toxicodynamic and other explanations, respectively. High quality mixture toxicology in vivo studies along with mixture in vitro and in silico studies will lead to greater confidence in interaction directions and influences. Limitations for interpretation of the data were also included.

Foodborne Pathogens

Fate of Salmonella and Enterohemorrhagic Escherichia coli on Wheat Grain

Lauer JR, Simsek S, Bergholz T. *J Food Prot*. 4 August 2021. doi.org/10.4315/JFP-21-076. **Article link**

Significance: There were no significant differences in survival amongst four Salmonella strains or amongst six EHEC strains introduced to flour samples, even in low-moisture environments, underscoring food safety concerns given the long shelf life of wheat grain and its products.

Wheat flour has been connected to outbreaks of foodborne illnesses with increased frequency in recent years, specifically, outbreaks involving Salmonella enterica and enterohemorrhagic Escherichia coli (EHEC). However, there is little information regarding the survival of these pathogens on wheat grain during long-term storage in a low-moisture environment. This study aims to evaluate the long-term survival of these enteric pathogens on wheat grain over the course of a year. Hard red spring wheat was inoculated with strains of four serovars of Salmonella enterica (Enteritidis, Agona, Tennessee, and Montevideo) and six serotypes of EHEC (O157:H7, O26:H11, O121:H19, O45:NM, O111:H8, and O103:H2) in triplicate, sealed in Mylar bags to maintain the water activity, and stored at room temperature (22 ± 1°C). The survival of each pathogen was evaluated by plating onto differential media. Viable counts of strains from all four serovars of Salmonella (Enteritidis, Agona, Tennessee, and Montevideo) were detected on wheat grain stored at room temperature (22 ± 1°C) for the duration of the study (52 weeks). Viable counts of strains from EHEC serotypes

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O45:NM, O111:H8, and O26:H11 were only detected for 44 weeks and strains from serotypes O157:H7, O121:H19, and O103:H2 were only detected for 40 weeks until they passed below the limit of detection (2.0 log CFU/g). D -values were found to be significantly different between Salmonella and EHEC (adj. $p \leq 0.05$) with Salmonella D -values ranging from 22.9 ± 2.2 to 25.2 ± 1.0 weeks and EHEC D -values ranging from 11.4 ± 0.6 to 13.1 ± 1.8 weeks.

Antimicrobial Activity of MccJ25(G12Y) Against Gram-Negative Foodborne Pathogens in vitro and in Food Models

Corbalán N, Quiroga M, Masias E, Peralta D. *Int J Food Microbiol.* 16 August 2021. doi: 10.1016/j.ijfoodmicro.2021.109267. **Article link**

Significance: Stability analysis found that MccJ25(G12Y) is capable of remaining active in dairy and beef food matrices for a considerable time during storage at refrigeration temperatures. These results build on other studies on the potential applicability of this microcin as a biopreservative.

The use of bacteriocins is a promising alternative to improve food security through the biocontrol of food pathogens and spoilage microorganisms. Gram-negative produced microcin J25(G12Y), known as (MccJ25(G12Y)) is a variant of the well-studied and characterized antimicrobial peptide, microcin J25 (MccJ25). In the present work, we explored the activity of this microcin against Gram-negative bacteria linked to foodborne diseases. We evaluated the in vitro antimicrobial activity of MccJ25(G12Y) in solid medium against a collection of pathogenic and food-altering strains and studied its activity and stability in meat and dairy food systems. We show that MccJ25(G12Y) exhibited the same in vitro antimicrobial spectrum as its parental microcin (MccJ25) against different Gram-negative foodborne pathogens and spoilage strains. We highlight that low concentrations of MccJ25(G12Y) between 0.45 and 29.4 μM were able to inhibit a substantial number of pathogens, including Salmonella, Escherichia, Shigella and Enterobacter genus. We also demonstrate the antimicrobial effectiveness of the peptide against Escherichia coli O157:H7 NCTC 12900, Enterobacter cloacae CECT 194, and Salmonella enterica CECT 4396 in fish and beef burgers and yogurt. MccJ25(G12Y) was added or not to food matrices inoculated with the foodborne pathogens at 105 CFU/g or mL. Afterward, food products were stored at 4 °C and selective media for the specific enumeration were used to determine the antimicrobial susceptibility of each pathogen to MccJ25(G12Y). The viability of the three pathogens was significantly reduced in the different food biological environments. In yogurt, the peptide decreased E. coli numbers on day 5 by about 4 log 10 CFU/mL as compared to non-treated samples. For S. enterica and E. cloacae no viable cells were detected at the end of the treatment. Adding MccJ25(G12Y) to fish burgers decreased E. cloacae numbers during storage 2 log10 CFU/g on the first day, reaching a difference of about 5 log 10 CFU/g after 10 days compared to non-treated control. Finally, the peptide decreased E. coli O157:H7 numbers on the beef burgers samples during storage on day 10 by about 3 log 10 CFU/g as compared to non-treated samples. The stability analysis demonstrated that MccJ25(G12Y) is capable of remaining active in these food matrices for a considerable time during the storage at refrigeration temperatures. These results reinforce the studies on the potential applicability of this microcin as a biopreservative in the food industry.

Foodborne Illness

Interactions Between Risk Assessors and Risk Managers During Three Major Food Incidents in Europe

Focker M, van den Borne BHP, Fischer M, Schuh E, Mader A, Andersson MG, et. al. *J Food Sci.* 2021 Aug;86(8), p3611-3627. doi: 10.1111/1750-3841.15824. **Article link**

Significance: A review of three food safety controversies – Escherichia coli crisis in 2011 in Germany, the horsemeat scandal in 2013 in Ireland, and the fipronil incident in 2017 in the Netherlands – revealed that scientists and managers' communication processes lacked crisis management protocols.

Risk analysis consists of risk assessment (RA), risk management (RM), and risk communication (RC). In most countries, RA and RM of food safety are separated to achieve a high scientific integrity, and typically occur in sequential order. However, in case of a food safety incident, even though being separate processes, RA and RM are performed simultaneously due to great time pressure and expected high impacts. The aim of this study was to analyze and evaluate the observed interactions between RA and RM processes, during three major food incidents in Europe, and to provide suggestions for possible improvement. Based on the differences observed between the three cases, strengths and weaknesses of each system have been identified. The enterohemorrhagic Escherichia coli (EHEC) crisis in 2011 in Germany, the horsemeat scandal in 2013 in Ireland, and the fipronil incident in 2017 in the Netherlands were used as case studies. Timelines of these incidents and crisis management procedures in place in each of the three countries provided the basis for further analysis. First, results showed that details of the communication processes between RA and RM bodies were frequently lacking in crisis management protocols. Second, RA, RM, and RC processes differed for each incident, due to differences in estimated risk for public health, but also due to differences in the organization within a country. Based on our results, we recommend

that crisis management protocols should contain a section on communication between RA, RM, and on communication between member states in the EU.

Mycotoxins

Hepatotoxicity of Food-Borne Mycotoxins: Molecular Mechanism, Anti-Hepatotoxic Medicines and Target Prediction

Ruan H, Lu Q, Wu J, Qin J, Sui M, Sun X, et. al. *Crit Rev Food Sci Nutr*. 4 August 2021. p1-28. doi: 10.1080/10408398.2021.1960794. **Article link**

Significance: No effective methods have been found to prevent or treat Mycotoxin-Induced Liver Injury (MILI) in clinical and animal husbandry in this review of the molecular mechanisms and potential anti-MILI medicines of six food-borne MILI.

Mycotoxins are metabolites produced by fungi. The widespread contamination of food and feed by mycotoxins is a global food safety problem and a serious threat to people's health. Most food-borne mycotoxins have strong hepatotoxicity. However, no effective methods have been found to prevent or treat Mycotoxin-Induced Liver Injury (MILI) in clinical and animal husbandry. In this paper, the molecular mechanisms and potential anti-MILI medicines of six food-borne MILI are reviewed, and their targets are predicted by network toxicology, which provides a theoretical basis for further study of the toxicity mechanism of MILI and the development of effective strategies to manage MILI-related health problems in the future and accelerate the development of food safety.

Food Packaging

Migration of Substances from Food Contact Plastic Materials into Foodstuff and their Implications for Human Exposure

Shin C, Kim DG, Kim JH, Kim JH, Song MK, Oh KS. *Food Chem Toxicol*. 2021 Aug;154:112373. doi: 10.1016/j.fct.2021.112373. **Article link**

Significance: The dietary exposures of terephthalic acid, acetaldehyde and 1,4-butanediol were assessed using Korean and U.S. government approaches which found that the food contact plastic materials are properly controlled by regulators.

The safety of food contact plastic materials, including PP, PE, PET, PCT, PLA, PBT and cross-linked polyester, was assessed with regard to migrated substances. The migrated concentrations of overall migrants (OMs), terephthalic acid, acetaldehyde, 1,4-butanediol and lead, were determined according to the standards and specifications for utensils, containers and packages in Korea. Food simulants of 4% acetic acid, water and n-heptane were used for the analysis of the substances. The dietary exposures of terephthalic acid, acetaldehyde and 1,4-butanediol were assessed using the dietary concentrations and the food consumption data. As a result, the dietary exposures were considered to be safe comparing to the health-based guidance values. In the case of lead, the margin of exposure (MOE) approach was applied. The MOEs calculated using the UB concentration and mean consumption data were ranged from 3 to 1000, which indicated low concern for health risk. Moreover, in this study, the dietary exposures were estimated by the Korean MFDS and U.S. FDA methods, respectively. As a result, the assessed risks were considered to be low in both cases. Based on the results of current exposure assessments, it could be considered that the food contact plastic materials are properly controlled by the regulatory authorities.

Recent Advances in the Fabrication of pH-sensitive Indicators Films and their Application for Food Quality Evaluation

Luo Q, Hossen A, Sameen DE, Ahmed S, Dai J, Li S, Qin W, Liu Y. *Crit Rev Food Sci Nutr*. 12 August 2021;p1-17. doi:10.1080/10408398.2021.1959296. **Article link**

Significance: Fabrication of colorimetric indicators in smart packaging systems can monitor the freshness or spoilage of perishable foods based on color displays at varying pH values.

Over a few decades, anthocyanin (ACN)-based colorimetric indicators in intelligent packaging systems have been widely used to monitor the freshness or spoilage of perishable food products. Most of the perishable food products are highly susceptible to enzymatic/microbial spoilage and produce several volatile or nonvolatile organic acid and nitrogenous compounds. As a result, the natural pH of fresh foods significantly changes. Fabrication of CAN-based

colorimetric indicators in intelligent packaging systems is an advanced technique that monitors the freshness or spoilage of perishable foods based on the display of color variations at varying pH values. This study focuses on the advancement of pH-sensitive indicators and extraction of colorimetric indicators from commercially available natural sources. Moreover, the fabrication techniques and widespread industrial applications of such indicators have also been discussed. In addition, readers will get information about the color-changing and antioxidant mechanisms of ACN-based indicator films in food packaging.

Chemical Contaminants

Occurrence of Ethyl Carbamate in Foods and Beverages: Review of the Formation Mechanisms, Advances in Analytical Methods, and Mitigation Strategies
Abt E, Incorvati V, Robin LP, Redan B. *J Food Prot*. 4 August 2021. doi: 10.4315/JFP-21-219. **Article link**

Significance: Ethyl carbamate can be found in spirits, breads, soy sauce and wine and more research is needed to refine mitigation strategies and develop methods to rapidly detect EC – a probable human carcinogen – in the food supply.

Ethyl carbamate (EC) is a process contaminant that can be formed as a byproduct during fermentation and processing of foods and beverages. Elevated EC levels are primarily associated with distilled spirits, but this compound has also been found at lower levels in foods and beverages, including breads, soy sauce, and wine. Evidence from animal studies suggests that EC is a probable human carcinogen. Consequently, several governmental institutions have established allowable limits for EC in the food supply. This review will discuss EC formation mechanisms, occurrence of EC in the food supply, and EC dietary exposure assessments. Analytical methods currently used to detect EC, and advances in experimental technologies, such as nanosensors and surface-enhanced Raman spectroscopy (SERS) will also be discussed. Finally, application of mitigation methods to maintain levels of EC under allowable limits will be covered, including distillation practices, enzymatic treatments, and genetic engineering of yeast. Ongoing research in this field is needed to refine mitigation strategies and develop methods to rapidly detect EC in the food supply.

Heavy Metals

Study on the Bioaccessibility and Bioavailability of Cd in Contaminated Rice in vitro and in vivo
Yao L, Wang Y, Deng Z, Wu Q, Fang M, Wu Y, Gong Z. *J Food Sci*. 2021 Aug;86(8):3730-3742. doi: 10.1111/1750-3841.15829. **Article link**

Significance: A study of the bioavailability of cadmium in rice indicates that the oral cavity displayed the lowest bioaccessibility compared with small intestine and the stomach after cooking.

Cadmium (Cd) is a widespread heavy metal pollutant in the environment that damages human health. In this study, the bioaccessibility and bioavailability of Cd in different Cd-contaminated rice (low pollution level cadmium rice (Rice-L, 0.111 mg/kg), medium pollution level cadmium rice (Rice-M, 0.400 mg/kg), and high pollution level cadmium rice (Rice-H, 0.655 mg/kg)) were estimated and determined by an in vitro digestion model Rijksinstituut voor volksgezondheiden milieu (RIVM), Caco-2 cell model, and mouse model. The results indicated that Cd in the oral cavity (15.65-28.28%) displayed the lowest bioaccessibility comparing with small intestine (90.04-94.73%) and the stomach (99.30-100.70%) in vitro after cooking. In addition, the results showed that the bioaccessibility of Cd in CdCl2 , CdCl2 +normal rice (Rice-N), Rice-H, Rice-M, Rice-L group were 99.29%, 92.57%, 90.04%, 94.73%, and 91.11%, respectively; the in vitro bioavailability of Cd in CdCl2 , CdCl2 +Rice-N, Rice-H, Rice-M, and Rice-L group were 27.50%, 20.78%, 21.90%, 26.90%, 36.46%, respectively, we found that the group of CdCl2 is significantly higher than CdCl2 +Rice-N and Rice-H ($p < 0.05$), while the targets hazard quotient (THQ) value of rice ingested without considering the in vitro bioavailability is 2.7-4.6 times than the THQ value with considered and the relative bioavailability (RBA) of Cd in Rice-L, Rice-M, Rice-H are 80.25%, 64.32%, and 60.91%, respectively. These results indicate that the rice substrate has impact on the bioaccessibility and bioavailability of Cd and might overestimate the health risks of Cd if bioavailability was not considered. PRACTICAL APPLICATION: Studying the bioaccessibility and bioavailability of cadmium in rice is a promising strategy to obtain a more accurate human health risk assessment of cadmium exposure in rice, as well as provide a theoretical basis for the formulation of cadmium limit standard in grain, which was also conducive to the rational and full utilization of rice resources in China.

Caffeine

Coffee Consumption, Health Benefits and Side Effects: A Narrative Review and Update for Dietitians and Nutritionists

Barrea L, Pugliese G, Frias-Toral E, El Ghoch M, Castellucci B, Chapela SP. *Crit Rev Food Sci Nutr*. 2021 Aug 28;p1-24. doi: 10.1080/10408398.2021.1963207. **Article link**

Significance: A review for dietitians finds that coffee may contribute to the prevention of inflammatory and oxidative stress-related diseases, such as obesity, metabolic syndrome and type 2 diabetes and that its consumption is associated with a lower incidence of several types of cancer.

Coffee is one of the most popular beverages worldwide; however, its impact on health outcomes and adverse effects is not fully understood. The current review aims to establish an update about the benefits of coffee consumption on health outcomes highlighting its side effects, and finally coming up with an attempt to provide some recommendations on its doses. A literature review using the PubMed/Medline database was carried out and the data were summarized by applying a narrative approach using the available evidence based on the literature. The main findings were the following: first, coffee may contribute to the prevention of inflammatory and oxidative stress-related diseases, such as obesity, metabolic syndrome and type 2 diabetes; second, coffee consumption seems to be associated with a lower incidence of several types of cancer and with a reduction in the risk of all-cause mortality; finally, the consumption of up to 400 mg/day (1-4 cups per day) of caffeine is safe. However, the time gap between coffee consumption and some drugs should be taken into account in order to avoid interaction. However, most of the data were based on cross-sectional or/and observational studies highlighting an association of coffee intake and health outcomes; thus, randomized controlled studies are needed in order to identify a causality link.

Food 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 Aug; 148(2): 67-632.e3. doi:10.1016/j.jaci.2021.03.028. **Article Link**

Significance: A multidimensional analysis of the oral cavity revealed distinct microbial and metabolic profiles linked with mucosal immune disturbances in peanut allergy.

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.