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Food Safety Briefs

Risk Assessment

Active Pharmaceutical Contaminants in Dietary Supplements: A Tier-Based Risk Assessment Approach

Bandara SB, Urban A, Liang LG, Parker J, Fung E, Maier A. *Regul Toxicol Pharmacol*. 2021 Jul;123:104955. doi: 10.1016/j.yrtph.2021.104955. **Article link**

Significance: A tiered framework for evaluating pharmaceutical elements is applied to five dietary supplements, providing a risk-based tool to address product safety concerns.

The presence of active pharmaceutical ingredients (APIs) in adulterated or contaminated dietary supplements is a current product safety concern. Since there are limited guidelines, and no published consensus methods, we developed a tier-based framework incorporating typical lines of evidence for determining the human health risk associated with APIs in dietary supplements. Specifically, the tiered approach outlines hazard identification and decision to test for APIs in products based on criteria for likelihood of contamination or adulteration, and evaluation of manufacturer production standards. For products with detectable levels of APIs, a variety of default approaches, including the use of fraction of the therapeutic dose and the threshold of toxicological concern (TTC), as well as health-based exposure limits (HBELs) are applied. In order to demonstrate its practical use, as well as any limitations and/or special considerations, this framework was applied to five dietary supplements (currently available to the public). We found that the detected levels of APIs in some dietary supplements were above the recommended dose of the drugs, and thus, pose a significant health risk to consumers and potentially workers involved in manufacturing of these supplements. The results support the value of increased product quality surveillance and perhaps regulatory activity.

Foodborne Pathogens

Functional Analysis of Deoxyhexose Sugar Utilization in Escherichia coli Reveals Fermentative Metabolism under Aerobic Conditions.

Millard P, Pérochon J, Létisse F. *Appl Environ Microbiol*. 2021 Jul 27;87(16):e0071921. doi: 10.1128/AEM.00719-21. **Article link**

Significance: This quantitative metabolic analysis elucidates 6-deoxyhexose sugar metabolism in E. coli under anaerobic and aerobic conditions. The findings point to the key role of fermentative pathways in 6-deoxyhexose sugar metabolism -- a trait shared by both a laboratory and a probiotic strain of E. Coli.

l-Rhamnose and l-fucose are the two main 6-deoxyhexoses Escherichia coli can use as carbon and energy sources. Deoxyhexose metabolism leads to the formation of lactaldehyde, whose fate depends on oxygen availability. Under anaerobic conditions, lactaldehyde is reduced to 1,2-propanediol, whereas under aerobic conditions, it should be oxidized into lactate and then channeled into the central metabolism. However, although this all-or-nothing view is accepted in the literature, it seems overly simplistic since propanediol is also reported to be present in the culture medium during aerobic growth on l-fucose. To clarify the functioning of 6-deoxyhexose sugar metabolism, a quantitative metabolic analysis was performed to determine extra- and intracellular fluxes in E. coli K-12 MG1655 (a laboratory strain) and in E. coli Nissle 1917 (a human commensal strain) during anaerobic and aerobic growth on l-rhamnose and l-fucose. As expected, lactaldehyde is fully reduced to 1,2-propanediol under anoxic conditions, allowing complete reoxidation of the NADH produced by glyceraldehyde-3-phosphate-dehydrogenase. We also found that net ATP synthesis is ensured by acetate production. More

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surprisingly, lactaldehyde is also primarily reduced into 1,2-propanediol under aerobic conditions. For growth on l-fucose, 13C-metabolic flux analysis revealed a large excess of available energy, highlighting the need to better characterize ATP utilization processes. The probiotic E. coli Nissle 1917 strain exhibits similar metabolic traits, indicating that they are not the result of the K-12 strain's prolonged laboratory use. IMPORTANCE E. coli's ability to survive in, grow in, and colonize the gastrointestinal tract stems from its use of partially digested food and hydrolyzed glycosylated proteins (mucins) from the intestinal mucus layer as substrates. These include l-fucose and l-rhamnose, two 6-deoxyhexose sugars, whose catabolic pathways have been established by genetic and biochemical studies. However, the functioning of these pathways has only partially been elucidated. Our quantitative metabolic analysis provides a comprehensive picture of 6-deoxyhexose sugar metabolism in E. coli under anaerobic and aerobic conditions. We found that 1,2-propanediol is a major by-product under both conditions, revealing the key role of fermentative pathways in 6-deoxyhexose sugar metabolism. This metabolic trait is shared by both E. coli strains studied here, a laboratory strain and a probiotic strain. Our findings add to our understanding of E. coli's metabolism and of its functioning in the bacterium's natural environment.

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

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: Mobile PCR and CRISPR-Cas tools may be coming for E. coli O157:H7 POC diagnostics with the potential for implementation by industry. Advances in the field of E. coli O157:H7 diagnosis with a focus on emerging high throughput point-of-care E. coli O157:H7 diagnostics is addressed.

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 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

Initial Reports of Foodborne Illness Drive More Public Attention Than Do Food Recall Announcements.

Jung J, Bir C, Widmar NO, Sayal P. *J Food Prot.* 2021 Jul 1;84(7):1150-1159. doi: 10.4315/JFP-20-383. **Article link**

Significance: New probabilistic models were developed and validated for growth and T-2 + HT-2 toxin production in relation to temperature × a_w conditions. When applied to stored oats, these models will help determine the risk of contamination from these toxins in the context of European Union maximum levels.

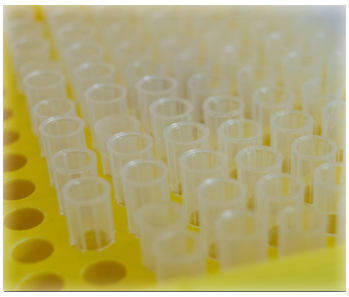
Recall announcements by the U.S. Food and Drug Administration (FDA) and Food Safety and Inspection Service (FSIS) are important communication tools. Nonetheless, previous studies revealed that the effects of recalls on consumer demand are small. Social media analytics can provide insights into public awareness of food safety-related incidents. This study included social listening data to analyze how the public, in social and online media spaces, responds to, interacts with, and references food safety recalls and/or initial announcements of foodborne illness outbreaks as reported by the Centers for Disease Control and Prevention (CDC). Analysis results suggest that mentions quantified in the social and online media searches moved closer in step with the CDC's initial reports of foodborne illness outbreaks than did FDA and FSIS recall announcements. Issuance of recalls may not be a popular source of food risk information in the social media space compared with reactions to the CDC's initial illness reports. This relative popularity reflects people more often sharing or posting about illness risk regardless of whether a recall occurs, suggesting that recall announcements by the FDA and FSIS may not induce changes in consumers' behavior, whereas initial illness reports by the CDC may.

Although recalls by the FDA and FSIS may not generate social media posts, their primary role is to take potentially unsafe food items off grocery shelves. Online media analytics provide policy makers with information to guide effective food risk communication; initial CDC reports drive immediate attention more than do FDA and FSIS recalls.

Current State of Development of Biosensors and Their Application in Foodborne Pathogen Detection.

Xu L, Bai X, Bhunia AK. DOI: 10.4315/JFP-20-464. *J Food Prot*. 2021 Jul 1;84(7):1213-1227. doi: 10.4315/JFP-20-464. **Article link**

Significance: Based on exposure assessments, it appears that food contact plastic materials such as PP, PE, PET, PCT, PLA and PBT are properly controlled by regulatory authorities in South Korea and the U.S.



Foodborne disease outbreaks continue to be a major public health and food safety concern. Testing products promptly can protect consumers from foodborne diseases by ensuring the safety of food before retail distribution. Fast, sensitive and accurate detection tools are in great demand. Therefore, various approaches have been explored recently to find a more effective way to incorporate antibodies, oligonucleotides, phages, and mammalian cells as signal transducers and analyte recognition probes on biosensor platforms. The ultimate goal is to achieve high specificity and low detection limits (1 to 100 bacterial cells or piconanogram concentrations of toxins). Advancements in mammalian cell-based and bacteriophage-based sensors have produced sensors that detect low levels of pathogens and differentiate live from dead cells. Combinations of biotechnology platforms have increased the practical utility and application of biosensors for detection of foodborne pathogens. However, further rigorous testing of biosensors with complex food matrices is needed to ensure the utility of these sensors for point-of-care needs and outbreak investigations.

Mycotoxins

Multidimensional Analysis of the Epigenetic Alterations in Toxicities Induced by Mycotoxins.

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

Significance: This review summarizes and analyzes the roles of DNA methylation, ncRNAs, and protein modifications after mycotoxin exposure and sheds light on the epigenetic alterations induced by the non-genotoxic effects of mycotoxin.

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.

Alternaria Mycotoxins: An Overview of Toxicity, Metabolism and Analysis in Food

Chen A, Mao X, Sun Q, Wei Z, Li J, You Y, Zhao J, Jiang B, Wu J et. al. *J Agric Food Chem*. 2021 Jul 21;69(28):7817-7830. doi: 10.1021/acs.jafc.1c03007. **Article link**

Significance: To effectively detect and determine the mycotoxins in food, accurate and sensitive analytical methods are needed to inform both the toxicity and metabolic mechanisms of Alternaria toxins.

The genus Alternaria is widely distributed in the environment. Numerous species of the genus Alternaria can produce a variety of toxic secondary metabolites, called Alternaria mycotoxins. In this review, natural occurrence, toxicity, metabolism, and analytical methods are introduced. The contamination of these toxins in foodstuffs is ubiquitous, and most of these metabolites present genotoxic and cytotoxic effects. Moreover, Alternaria toxins are mainly hydroxylated to catechol metabolites and combined with sulfate and glucuronic acid in in vitro arrays. A more detailed summary of the metabolism

of Alternaria toxins is presented in this work. To effectively detect and determine the mycotoxins in food, analytical methods with high sensitivity and good accuracy are also reviewed. This review will guide the formulation of maximum residue limit standards in the future, covering both toxicity and metabolic mechanism of Alternaria toxins.

Food Packaging

Tea Polyphenols (TP): a Promising Natural Additive for the Manufacture of Multifunctional Active Food Packaging Films

Zhang W, Jiang H, Rhim JW, Cao J, Jiang W. *Crit Rev Food Sci Nutr*. 2021 Jul 7;1-14. doi: 10.1080/10408398.2021.1946007. **Article link**

Significance: Adding Tea Polyphenols imparts antioxidant and antibacterial properties to active packaging films and can improve their mechanical and barrier functions.

As a bioactive extract from tea leaves, tea polyphenols (TP) are safe and natural. Its excellent antioxidant and antibacterial properties are increasingly regarded as a good additive for improving degradable food packaging film properties. This article comprehensively reviewed the functional properties of active films containing TP developed recently. The effects of TP addition to enhancing active food packaging films' performance, including thickness, water sensitivity, barrier properties, color, mechanical properties, antioxidant, antibacterial, and intelligent discoloration properties, were discussed. Besides, the practical applications in food preservation of active films containing TP are also discussed. This work concluded that the addition of TP could impart antioxidant and antibacterial properties to active packaging films and act as a crosslinking agent to improve other physical and chemical properties of the film, such as mechanical and barrier properties. However, the effect of TP on specific properties of the active packaging film is complex, and the appropriate TP concentration needs to be selected according to the type of film matrix and the interaction between the components. Notably, the addition of TP improved the efficiency of the active packaging film in food preservation applications, which accelerates the process of replacing the traditional plastic-based food packaging with active packaging film.

Chemical Contaminants

Probiotics as a Biological Detoxification Tool of Food Chemical Contamination: A Review

Średnicka P, Juszczuk-Kubiak E, Wójcicki M, Akimowicz M, Roszko M. *Food Chem Toxicol*. 2021 Jul;153:112306. doi: 10.1016/j.fct.2021.112306. **Article link**

Significance: Efforts are underway to reduce the risk of xenobiotics in foodstuffs through researching a biological detoxification process linked to probiotic strains and enzymes. Studies show that probiotics are effective, feasible and inexpensive for preventing xenobiotic-induced dysbiosis and alleviating their toxicity. The review also touches on probiotic-xenobiotic interactions with the gut microbiota and host.

Nowadays, people are exposed to diverse environmental and chemical pollutants produced by industry and agriculture. Food contaminations such as persistent organic pollutants (POPs), heavy metals, and mycotoxins are a serious concern for global food safety with economic and public health implications especially in the newly industrialized countries (NIC). Mounting evidence indicates that chronic exposure to food contaminants referred to as xenobiotics exert a negative effect on human health such as inflammation, oxidative stress, and intestinal disorders linked with perturbation of the composition and metabolic profile of the gut microflora. Although the physicochemical technologies for food decontamination are utilized in many cases but require adequate conditions which are often not feasible to be met in many industrial sectors. At present, one promising approach to reduce the risk related to the presence of xenobiotics in foodstuffs is a biological detoxification done by probiotic strains and their enzymes. Many studies confirmed that probiotics are an effective, feasible, and inexpensive tool for preventing xenobiotic-induced dysbiosis and alleviating their toxicity. This review aims to summarize the current knowledge of the direct mechanisms by which probiotics can influence the detoxification of xenobiotics. Moreover, probiotic-xenobiotic interactions with the gut microbiota and the host response were also discussed.

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 of Food Science*, 26 July. DOI: 10.1111/1750-3841.15829. **Article link**

Significance: The stomach and small intestine appear to absorb cadmium at a higher rate than exposure to the

metal in the oral cavity. Rice substrate impacts consumer exposure to Cd and should be part of risk assessments and policy guidance on the grain trade going forward.

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

Maternal Caffeine Consumption During Pregnancy and Risk of Low Birth Weight: a Dose-Response Meta-Analysis of Cohort Studies

Soltan S, Salari-Moghaddam A, Saneei P, Askari M, Larijani B, Azadbakht L, Esmaillzadeh A, et. al. *Crit Rev Food Sci Nutr*. 2021 Jul 5;1-10. doi: 10.1080/10408398.2021.1945532. **Article link**

Significance: Review of seven cohort studies on maternal caffeine intake finds a significant and dose-dependent positive association with the risk of low-birth weight infants.

Background & Objectives: Earlier published studies on maternal caffeine intake during pregnancy in relation to the risk of low birth weight (LBW) (birth weight <2500 g) have indicated conflicting findings. Therefore, the present systematic review and meta-analysis was conducted to examine the association between maternal caffeine intake and risk of LBW. **Methods:** We searched for relevant articles published up to Jan 2021 through PubMed and Scopus. For this purpose, we used MESH (Medical Subject Heading) and non-MESH keywords. Cohort studies that considered maternal caffeine intake as the exposure variable and LBW as the main outcome variable were included in the systematic review. Finally, seven cohort studies were considered in this systematic review and meta-analysis. **Results:** Combining seven effect sizes, we found a significant positive association between maternal caffeine intake and risk of LBW (RR: 1.70; 95% CI: 1.19-2.43). We also found that each additional 100-mg per day of maternal caffeine intake was significantly associated with an increased risk of LBW (RR: 1.12; 95% CI: 1.03-1.22; Pheterogeneity = 0.020). In addition, nonlinear dose-response analysis showed a significant relationship (Pnonlinearity < 0.001) between maternal caffeine intake and risk of LBW. **Conclusions:** In this systematic review and meta-analysis, we found a significant positive association between maternal caffeine intake and risk of LBW.

Food Allergens

Components of Plant-Derived Food Allergens: Structure, Diagnostics and Immunotherapy

Maruyama N. *Allergol Int*. 2021 Jul;70(3):291-302. doi: 10.1016/j.alit.2021.05.001. **Article link**

Significance: The links between allergen components and symptoms has been well characterized, making measures of specific IgE to these components key for the accurate clinical diagnosis and selection of optimal treatments for allergy-related conditions.

A large number of plant-derived food allergen components have been identified to date. Although these allergens are diverse, they often share common structural features such as numerous disulfide bonds or oligomeric structures. Furthermore, some plant-derived food allergen components cross-react with pollen allergens. Since the relationship between allergen components and clinical symptoms has been well characterized, measurements of specific IgE to these components have become useful for the accurate clinical diagnosis and selection of optimal treatment methods for vari

ous allergy-related conditions including allergy caused by plant-derived foods. Herein, I have described the types and structures of different plant allergen components and outlined the diagnosis as well as treatment strategies, including those reported recently, for such substances. Furthermore, I have also highlighted the contribution of allergen components to this field.