

# Food Safety Briefs

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## Risk Assessment

### In Silico Prediction of Input Parameters for Simplified Physiologically Based Pharmacokinetic Models for Estimating Plasma, Liver, and Kidney Exposures in Rats after Oral Doses of 246 Disparate Chemicals

Kamiya Y, Handa K, Miura T, Yanagi M, Shigeta K, Hina S, et al. *Chem Res Toxicol*. 2021 Jan 12. doi: 10.1021/acs.chemrestox.0c00336. [Article link](#)

**Significance:** In silico methods used to help model the impacts on gut, liver and kidney of 246 chemicals and food components correlated well with past results and show promise for predicting internal doses from physiologically based pharmacokinetic (PBPK) models.

Recently developed computational models can estimate plasma, hepatic, and renal concentrations of industrial chemicals in rats. Typically, the input parameter values (i.e., the absorption rate constant, volume of systemic circulation, and hepatic intrinsic clearance) for simplified physiologically based pharmacokinetic (PBPK) model systems are calculated to give the best fit to measured or reported in vivo blood substance concentration values in animals. The purpose of the present study was to estimate in silico these three input pharmacokinetic parameters using a machine learning algorithm applied to a broad range of chemical properties obtained from several cheminformatics software tools. These in silico estimated parameters were then incorporated into PBPK models for predicting internal exposures in rats. Following this approach, simplified PBPK models were set up for 246 drugs, food components, and industrial chemicals with a broad range of chemical structures. We had previously generated PBPK models for 158 of these substances, whereas 88 for which concentration series data were available in the literature were newly modeled. The values for the absorption rate constant, volume of systemic circulation, and hepatic intrinsic clearance could be generated in silico by equations containing between 14 and 26 physicochemical properties. After virtual oral dosing, the output concentration values of the 246 compounds in plasma, liver, and kidney from rat PBPK models using traditionally determined and in silico estimated input parameters were well correlated ( $r \geq 0.83$ ). In summary, by using PBPK models consisting of chemical receptor (gut), metabolizing (liver), excreting (kidney), and central (main) compartments with in silico-derived input parameters, the forward dosimetry of new chemicals could provide the plasma/tissue concentrations of drugs and chemicals after oral dosing, thereby facilitating estimates of hematotoxic, hepatotoxic, or nephrotoxic potential as a part of risk assessment.

## Foodborne Pathogens

### Whole-Genome Sequence Analysis of *Salmonella* Infantis Isolated from Raw Chicken Meat Samples and Insights into pESI-like Megaplasmid

Kürekcı C, Sahin S, Iwan E, Kwit R, Bomba A, Wasyl D. *Int J Food Microbiol*. 2021 Jan 16;337:108956. doi: 10.1016/j.ijfoodmicro.2020.108956. [Article link](#)

**Significance:** 22 *Salmonella* strains were sequenced in an attempt to understand increases in reports of contaminated chicken and other foods. The study found that pESI-like megaplasmid is common within the tested *S. Infantis* strains of chicken, warranting further genomic studies on clinical strains from humans and animals.



There has been an increase in the number of reports on *Salmonella enterica* subsp. *enterica* serovar *Infantis* (*S. Infantis*) isolated from animals and humans. Recent studies using whole genome sequencing (WGS) have provided evidence on the likely contribution of a unique conjugative megaplasmid (pESI; ~280 kb) to the dissemination of this serovar worldwide. In the present study, twenty-two unrelated *Salmonella* strains [*S. Infantis* ( $n = 20$ ) and *Salmonella* 6,7:r:- ( $n = 2$ )] and their plasmids were investigated using next generation sequencing technologies (MiSeq and MinION) to unravel the

significant expansion of this bacteria in Turkey. Multi-locus sequence typing, plasmid replicons, resistance gene contents as well as phylogenetic relations between strains were determined. According to the WGS data, all *S. Infantis* possessed the relevant megaplasmid backbone genes and belonged to sequence type 32 (ST32) with the exception of a single novel ST7091. Tetracycline and trimethoprim/sulfamethoxazole resistance were found to be widespread in *S. Infantis* strains and the resistant strains exclusively carried the *tetA*, *sul1*, *sul2* and *dfrA14* genes. One *S. Infantis* isolate was also a carrier of the plasmid-mediated ampC via *bla<sub>CMY-2</sub>* gene. Moreover, full genomes of four *S. Infantis* isolates were reconstructed based on hybrid assembly. All four strains contained large plasmids (240–290 kb) similar to previously published megaplasmid (pESI) and accompanied by several small plasmids. The megaplasmid backbone contained a toxin-antitoxin system, two virulence cassettes and segments associated with heavy metals resistance, while variable regions possessed several antibiotic resistance genes flanked by mobile elements. This study indicated that pESI-like megaplasmid is widely disseminated within the tested *S. Infantis* strains of chicken meat, warranting further genomic studies on clinical strains from humans and animals to uncover the overall emergence and spread of this serovar.

### Survey of *Salmonella* in Raw Tree Nuts at Retail in the United States

Zhang G, Hu L, Luo Y, Santillana Farakos SM, Johnson R, Scott VN, et al. *J Food Sci.* 2021 Feb;86(2):495-504. doi: 10.1111/1750-3841.15569. [Article link](#)

**Significance:** A total of 3,374 samples of eight tree nuts were collected from different types of retail stores and 0.44% were contaminated with diverse *Salmonella* strains.



The objective of this survey was to estimate the prevalence, contamination level, and genetic diversity of *Salmonella* in selected raw, shelled tree nuts (Brazil nuts, cashews, hazelnuts, macadamia nuts, pecans, pine nuts, pistachios, and walnuts) at retail markets in the United States. A total of 3,374 samples of eight tree nuts were collected from different types of retail stores and markets nationwide between September 2015 and March 2017. These samples (375 g) were analyzed using a modified FDA's BAM *Salmonella* culture method. Of the 3,374 samples, 15 (0.44%) (95% confidence interval [CI] [0.25, 0.73]) were culturally confirmed as containing *Salmonella*; 17 isolates were obtained. Among these isolates, there were 11 serotypes. *Salmonella* was not detected in Brazil nuts (296), hazelnuts (487), pecans (510), pine nuts (500), and walnuts (498). *Salmonella* prevalence estimates in cashews (510), macadamia (278), and pistachios (295) were 0.20% (95% CI [ $<0.01$ , 1.09]), 2.52% (95% CI [1.02, 5.12]), and 2.37% (95% CI [0.96, 4.83]), respectively. The rates of *Salmonella*

isolation from major/big-chain supermarkets (1381), small-chain supermarkets (328), discount/variety/drug stores (1329), and online (336) were 0.29% (95% CI [0.08, 0.74]), 0.30% (95% CI [0.01, 1.69]), 0.45% (95% CI [0.17, 0.98]), and 1.19% (95% CI [0.33, 3.02]), respectively. *Salmonella* prevalence in organic (530) and conventional (2,844) nuts was not different statistically ( $P = 0.0601$ ). Of the enumerated samples (15), 80% had *Salmonella* levels  $\leq 0.0092$  most probable number (MPN)/g. The highest contamination level observed was 0.75 MPN/g. The prevalence and contamination levels of *Salmonella* in the tree nuts analyzed were generally comparable to previous reports. Pulsed-field gel electrophoresis, serotype, and sequencing data all demonstrated that *Salmonella* population in nuts is very diverse genetically. **Practical Application:** The prevalence, contamination level, and genetic diversity of *Salmonella* in eight types of tree nuts (3,374 samples collected nationwide) revealed in this survey could help the development of mitigation strategies to reduce public health risks associated with consumption of these nuts.

## Foodborne Illness

### Emerging Applications of Machine Learning in Food Safety

Deng X, Cao S, Horn AL. *Annu Rev Food Sci Technol.* 2021 Jan 20. doi: 10.1146/annurev-food-071720-024112. [Article link](#)

**Significance:** Studying foodborne pathogen genomes and novel data streams could be enhanced by a machine learning approach, which could refine prediction of antibiotic resistance, source attribution of pathogens and foodborne outbreak detection and risk assessment.

Food safety continues to threaten public health. Machine learning holds potential in leveraging large, emerging data sets to improve the safety of the food supply and mitigate the impact of food safety incidents. Foodborne pathogen genomes and novel data streams, including text, transactional, and trade data, have seen emerging applications enabled by a machine learning approach, such as prediction of antibiotic resistance, source attribution of pathogens, and foodborne outbreak detection and risk assessment. In this article, we provide a gentle introduction to machine learning in the context of food safety and an overview of recent developments and applications. With many of these applications still in their nascence,

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general and domain-specific pitfalls and challenges associated with machine learning have begun to be recognized and addressed, which are critical to prospective use and future deployment of large data sets and their associated machine learning models for food safety applications.

## Mycotoxins

### Application of New Technologies in Decontamination of Mycotoxins in Cereal Grains: Challenges and Perspectives

Mir SA, Dar BN, Shah MA, Sofi SA, Hamdani AM, Oliveira CAF. *Food Chem Toxicol.* 2021 Feb;148:111976. doi: 10.1016/j.fct.2021.111976. [Article link](#)

**Significance:** Novel mycotoxin decontamination technologies such as cold plasma, irradiation and pulse light can be efficient for reducing mycotoxins in cereal with minimum adverse effects on quality and nutritional properties.

Emerging decontamination technologies have been attracted considerable attention to address the consumers' demand for high quality and safe food products. As one of the important foods in the human diet, cereals are usually stored for long periods, resulting in an increased risk of contamination by different hazards. Mycotoxins comprise one of the significant contaminants of cereals that lead to enormous economic losses to the industry and threats to human health. While prevention is the primary approach towards reducing human exposure to mycotoxins, decontamination methods have also been developed as complementary measures. However, some conventional methods (chemical treatments) do not fulfill industries' expectations due to limitations like safety, efficiency, and the destruction of food quality attributes. In this regard, novel techniques have been proposed to food to comply with the industry's demand and overcome conventional methods' limitations. Novel techniques have different efficiencies for removing or reducing mycotoxins depending on processing conditions, type of mycotoxin, and the food matrix. Therefore, this review provides an overview of novel mycotoxin decontamination technologies such as cold plasma, irradiation, and pulse light, which can be efficient for reducing mycotoxins with minimum adverse effects on the quality and nutritional properties of produce.

## Food Packaging

### Hydroxypropyl Methylcellulose or Soy Protein Isolate-Based Edible, Water-Soluble, and Antioxidant Films for Safflower Oil Packaging

Rosenbloom RA, Zhao Y. *J Food Sci.* 2021 Jan;86(1):129-139. doi: 10.1111/1750-3841.15543. [Article link](#)

**Significance:** Single-use pouches of sauce are common for seasoning instant and frozen foods but generate plastic waste. Edible, water-soluble packaging with antioxidant functionality would extend shelf life by preventing oxidation and increase consumer convenience.

Edible, water-soluble, heat-sealable, and antioxidant films were developed from hydroxypropyl methylcellulose (HPMC) or soy protein isolate (SPI) and applied as safflower oil packaging. A 0.1 or 0.2% DL- $\alpha$ -tocopherol acetate (VE) and 0 or 0.25% oleic acid were added into film formulations to provide antioxidant and hydrophobic properties, respectively, using a 23 factorial design. Films were analyzed for appearance, microstructure, water and oil sensitivity, mechanical properties, and antioxidant functionality. Subsequently, a completely randomized design was implemented for incorporating 2, 4, or 6% cellulose nanocrystals (CNCs, w/w dry weight polymer) for improving film mechanical and barrier properties. HPMC-based films achieved full dissolution in water at  $<55^{\circ}\text{C}$  under 5 min, while SPI-based films disintegrated in water up to  $90^{\circ}\text{C}$ . Oleic acid significantly increased ( $P < 0.05$ ) heat sealability of SPI film from 78 to 143 N/m and elongation at break from 36% to 88%, but decreased tensile strength and heat sealability of HPMC films by 55% and 41%, respectively. As safflower oil packaging, after 60 days of storage at  $35^{\circ}\text{C}$ , oil contained in SPI-based pouch had the lowest peroxide values,  $8.1 \pm 0.9$  mEq/kg. Based on barrier, mechanical, and antioxidant capacity evaluations, HPMC film with 0.1% VE and SPI film with 0.25% oleic acid and 0.1% VE were incorporated with CNC. SPI/CNC films did not show observable trends, but HPMC/2% CNC film exhibited significantly improved mechanical and barrier properties, with oxygen permeability of 5.0 mL mm/m<sup>2</sup> day kPa. The developed films are a promising packaging alternative to decrease plastic waste, extend shelf life of lipid-based foods, and increase consumer convenience. **Practical Application:** Individually packaged, single-use pouches of sauce or oil are common for seasoning instant and frozen foods, creating unnecessary plastic waste. Edible, water-soluble packaging with antioxidant functionality would reduce plastic waste, extend shelf life by preventing oxidation, and increase consumer convenience. The biopolymeric films and pouches developed in this study have unique properties from water solubility across a wide range of temperatures, resistance to oil, high oxygen barrier, and good heat sealability, providing a variety of potential applications for promoting sustainable food packaging.

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## Chemical Contaminants

### A Gene Expression Biomarker Identifies Chemical Modulators of Estrogen Receptor $\alpha$ in an MCF-7 Microarray Compendium

Rooney J, Ryan N, Liu J, Houtman R, van Beuningen R, Hsieh JH, et al. *Chem Res Toxicol*. 2021 Jan 6. doi: 10.1021/acs.chemrestox.0c00243. [Article link](#)

**Significance:** This study highlights a strategy with potential use for identifying environmentally relevant ER $\alpha$  modulators in future high-throughput transcriptomic screens.

Identification of chemicals that affect hormone-regulated systems will help to predict endocrine disruption. In our previous study, a 46 gene biomarker was found to be an accurate predictor of estrogen receptor (ER)  $\alpha$  modulation in chemically treated MCF-7 cells. Here, potential ER $\alpha$  modulators were identified using the biomarker by screening a microarray compendium consisting of ~1600 gene expression comparisons representing exposure to ~1200 chemicals. A total of ~170 chemicals were identified as potential ER $\alpha$  modulators. In the Connectivity Map 2.0 collection, 75 and 39 chemicals were predicted to activate or suppress ER $\alpha$ , and they included 12 and six known ER $\alpha$  agonists and antagonists/selective ER $\alpha$  modulators, respectively. Nineteen and eight of the total number were also identified as active in an ER $\alpha$  transactivation assay carried out in an MCF-7-derived cell line used to screen the Tox21 10K chemical library in agonist or antagonist modes, respectively. Chemicals predicted to modulate ER $\alpha$  in MCF-7 cells were examined further using global and targeted gene expression in wild-type and ER $\alpha$ -null cells, transactivation assays, and cell-free ER $\alpha$  coregulator interaction assays. Environmental chemicals classified as weak and very weak agonists were confirmed to activate ER $\alpha$  including apigenin, kaempferol, and oxybenzone. Novel activators included digoxin, nabumetone, ivermectin, and six progestins. Novel suppressors included emetine, mifepristone, niclosamide, and proscillaridin. Our strategy will be useful to identify environmentally relevant ER $\alpha$  modulators in future high-throughput transcriptomic screens.

## Heavy Metals

### DNA-Gated Graphene Field-Effect Transistors for Specific Detection of Arsenic(III) in Rice

Wang Y, Bi Y, Wang R, Wang L, Qu H, Zheng L. *J Agric Food Chem*. 2021 Feb 3;69(4):1398-1404. doi: 10.1021/acs.jafc.0c07052. [Article link](#)

**Significance:** Toxic inorganic arsenic bioaccumulates in global rice supplies warranting the development of rapid analytical detection methods. A novel electrochemical sensor was developed for successful detection of As(III) in practical rice samples with a high recovery rate.

As one of the most toxic forms of arsenic, inorganic As(III) is easy to accumulate in rice, leading to severe public health problems. Effective control of As(III) requires the development of fast analytical methods for its detection with high sensitivity and specificity. Toward this end, in this work, we report the fabrication of an As(III) electrochemical sensor based on a solution-gated graphene transistor (SGGT) platform with a novel sensing mechanism. The gold gate electrode of the SGGT was modified with DNA probes and then blocked with bovine serum albumin (BSA). The specific interaction between As(III) and gold disrupted the adsorption states of DNA probes, redistributing surface charges on the gate electrode, further leading to potential drop changes at the interfaces of the gate electrode and graphene active layer. This new mechanism based on DNA-charge-redistribution-induced SGGT current responses (denoted as “DNA-SGGT”) was found to greatly improve the selectivity of the sensor: the response of DNA-SGGT to As(III) was effectively enhanced fourfold, while to other interfering cations, it was significantly reduced. The optimized sensor showed a detection limit as low as 5 nM with superior selectivity to As(III). The as-prepared DNA-SGGT-based sensor has also been successfully applied to the detection of As(III) in practical rice samples with a high recovery rate, showing great potential for heavy metal detection in many types of food samples.



## Caffeine

### Coffee Consumption and Breast Cancer Risk: A Narrative Review in the General Population and in Different Subtypes of Breast Cancer

Nehlig A, Reix N, Arbogast P, Mathelin C. *Eur J Nutr*. 2021 Jan 13. doi: 10.1007/s00394-020-02465-0. [Article link](#)

**Significance:** This study found, in the general population, no association between coffee intake and breast cancer risk even at high dosages, but acknowledged that some subgroups may have different risk profiles.

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**Purpose:** Most of the existing literature reports no association or a slight negative association between coffee consumption and the risk of developing breast cancer. However, the level of risk differs when considering various subgroups, such as menopausal status, hormonal status of the tumor or genetic mutations. The present review based on a literature search sets the point on the potential influence of a common daily drink, coffee, on the risk of developing breast cancer in the general population, in different subgroups of women and the consequences of drinking coffee after breast cancer has been diagnosed and treated.

**Results:** This review confirms that in the general population, there is no association between coffee intake and breast cancer risk or a slight protective effect, even at high dosages. Coffee is inversely associated with breast cancer risk in postmenopausal women and in women carrying a BRCA1 mutation. Possible risk differences exist between slow and fast caffeine metabolizers and with weight. Coffee consumption after breast cancer diagnosis and surgery, associated with tamoxifen and/or radiotherapy, reduced the occurrence of early events. The effects of coffee intake are less clear in other subgroups, mainly premenopausal women, women carrying a BRCA2 mutation and tumors with variable hormonal status (positive or negative for ER/PR) and would need additional studies.

## Allergens

### Current Insights into the Genetics of Food Allergy

Kanchan K, Clay S, Irizar H, Bunyavanich S, Mathias RA. *J Allergy Clin Immunol*. 2021 Jan;147(1):15-28. doi: 10.1016/j.jaci.2020.10.039. [Article link](#)

**Significance:** The biggest challenge in the field of food allergy genetics is to identify the mechanisms of action of FA risk and the pathogenesis for these loci. New “-omics” tools will help integrate this information into results with pragmatic value.

Food allergy (FA), a growing public health burden in the United States, and familial aggregation studies support strong roles for both genes and environment in FA risk. Deepening our understanding of the molecular and cellular mechanisms driving FAs is paramount to improving its prevention, diagnosis, and clinical management. In this review, we document lessons learned from the genetics of FA that have aided our understanding of these mechanisms. Although current genetic association studies suffer from low power, heterogeneity in definition of FA, and difficulty in our ability to truly disentangle FA from food sensitization (FS) and general atopy genetics, they reveal a set of genetic loci, genes, and variants that continue to implicate the importance of barrier and immune function genes across the atopic march, and FA in particular. The largest reported effects on FA are from MALT1 (odds ratio, 10.99), FLG (average odds ratio, ~2.9), and HLA (average odds ratio, ~2.03). The biggest challenge in the field of FA genetics is to elucidate the specific mechanism of action on FA risk and pathogenesis for these loci, and integrative approaches including genetics/genomics with transcriptomics, proteomics, and metabolomics will be critical next steps to translating these genetic insights into practice.

### Age and Eczema Severity, but not Family History, Are Major Risk Factors for Peanut Allergy in Infancy

Keet C, Pistiner M, Plesa M, Szelag D, Shreffler W, Wood R, et al. *J Allergy Clin Immunol*. 2021 Jan 13;S0091-6749(20)31709-7. doi: 10.1016/j.jaci.2020.11.033. [Article link](#)

**Significance:** The findings of this study support screening infants with significant eczema for peanut allergy—but not those with another food allergy and no eczema—and introduction of peanut as early as possible in infancy.

**Background:** Whether to screen high-risk groups before early peanut introduction is controversial. **Objective:** We sought to determine the risk of peanut allergy (PA) before peanut introduction for infants with (1) moderate-severe eczema, (2) another food allergy (FA), and/or (3) a first-degree relative with peanut allergy (FH). **Methods:** Infants aged 4 to 11 months with no history of peanut ingestion, testing, or reaction and at least 1 of the above risk factors received peanut skin prick test and, depending on skin prick test wheal size, oral food challenge or observed feeding. **Results:** A total of 321 subjects completed the enrollment visit (median age, 7.2 months; 58% males); 78 had eczema only, 11 FA only, 107 FH only, and 125 had multiple risk factors. Overall, 18% of 195 with eczema, 19% of 59 with FA, and 4% of 201 with FH had PA. Only 1% of 115 with FH and no eczema had PA. Among those with eczema, older age (odds ratio [OR], 1.3; 95% CI, 1.04-1.68 per month), higher SCORing Atopic Dermatitis score (OR, 1.19; 95% CI, 1.06-1.34 per 5 points), black (OR, 5.79; 95% CI, 1.92-17.4 compared with white), or Asian race (OR, 6.98; 95% CI, 1.92-25.44) and suspected or diagnosed other FA (OR, 3.98; 95% CI, 1.62-9.80) were associated with PA. **Conclusions:** PA is common in infants with moderate-severe eczema, whereas FH without eczema is not a major risk factor, suggesting screening only in those with significant eczema. Even within the first year of life, introduction at later ages is associated with a higher risk of PA among those with eczema, supporting introduction of peanut as early as possible.