ILSI North America

Food Safety Briefs

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Methodology

How Well Can Carcinogenicity Be Predicted by High Throughput "Characteristics of Carcinogens" Mechanistic Data?

Becker RA, Dreier DA, Manibusan MK, Cox LAT, Simon TW, Bus JS. *Regul Toxicol Pharmacol*. 2017 Nov;90:185–196. Article Link

Significance: Using statistical analysis and machine learning prediction algorithms, the ability of ToxCast/Tox21 data to predict cancer hazard was found to be no better than chance.

IARC has begun using ToxCast/Tox21 data in efforts to represent key characteristics of carcinogens to organize and weigh mechanistic evidence in cancer hazard determinations and this implicit inference approach also is being considered by USEPA. To determine how well ToxCast/Tox21 data can explicitly predict cancer hazard, this approach was evaluated with statistical analyses and machine learning prediction algorithms. Substances USEPA previously classified as having cancer hazard potential were designated as positives and substances not posing a carcinogenic hazard were designated as negatives. Then ToxCast/Tox21 data were analyzed both with and without adjusting for the cytotoxicity burst effect commonly observed in such assays. Using the same assignments as IARC of ToxCast/Tox21 assays to the seven key characteristics of carcinogens, the ability to predict cancer hazard for each key characteristic, alone or in combination, was found to be no better than chance. Hence, we have little scientific confidence in IARC's inference models derived from current ToxCast/Tox21 assays for key characteristics to predict cancer. This finding supports the need for a more rigorous mode-of-action pathway-based framework to organize, evaluate, and integrate mechanistic evidence with animal toxicity, epidemiological investigations, and knowledge of exposure and dosimetry to evaluate potential carcinogenic hazards and risks to humans.

Highly Sensitive and High-Throughput Method for the Analysis of Bisphenol Analogues and Their Halogenated Derivatives in Breast Milk

Niu Y, Wang B, Zhao Y, Zhang J, Shao B. *J Agric Food Chem*. 2017 Nov 21. doi: 10.1021/acs.jafc.7b04394. Article Link

Significance: This is the first report describing the occurrence of BPF and BPAF in breast milk.

The structural analogs of bisphenol A (BPA) and their halogenated derivatives (together termed BPs) have been found in the environment, food, and even the human body. Limited research showed that some of them exhibited toxicities that were similar to or even greater than that of BPA. Therefore, adverse health effects for BPs were expected for humans with low-dose exposure in early life. Breast milk is an excellent matrix and could reflect fetuses' and babies' exposure to contaminants. Some of the emerging BPs may present with trace or ultratrace levels in humans. However, existing analytical methods for breast milk cannot quantify these BPs simultaneously with high sensitivity using a small sampling weight, which is important for human biomonitoring studies. In this paper, a method based on Bond Elut Enhanced Matrix Removal-Lipid purification, pyridine-3-sulfonyl chloride derivatization, and liquid chromatography electrospray tandem mass spectrometry was developed. The method requires only a small quantity of sample (200 μL) and allowed for the simultaneous determination of 24 BPs in breast milk with ultrahigh sensitivity. The limits of quantitation of the proposed method were 0.001-0.200 μg L-1, which were 1-6.7 times lower than the only study for the simultaneous analysis of bisphenol analogs in breast milk based on a 3 g sample weight. The mean recoveries ranged from 86.11% to 119.05% with relative standard deviation (RSD) ≤ 19.5% (n = 6). Matrix effects were within 20% with RSD < 10% for six different lots of samples. The proposed method was successfully applied to 20 breast milk samples. BPA, bisphenol F (BPF), bisphenol S (BPS), and bisphenol AF (BPAF) were detected. BPA was still the dominant BP, followed by BPF. This is the first report describing the occurrence of BPF and BPAF in breast milk.

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Heavy Metals

Metal(loid) Contamination in Seafood Products

Chiocchetti G, Jadán-Piedra C, Vélez D, Devesa V. *Crit Rev Food Sci Nutr*. 2017 Nov 22; 57(17):3715–3728. Article Link

Significance: This article reviews the occurrence of heavy metals in seafood products and health risks that could result from consumption.

Seafood products are important sources of proteins, polyunsaturated lipids and phospholipids, and also of numerous micronutrients (vitamins and minerals). However, they may also present chemical contaminants that can constitute a health risk and that must be considered when evaluating the risk/benefit associated with consumption of this group of foods. Toxic metals and metalloids in seafood, such as mercury (Hg), cadmium (Cd), arsenic (As), and lead (Pb), are subjected to legislative control in order to provide the consumer with safe seafood. This review provides an exhaustive survey of the occurrence of these toxic metal(loid)s in seafood products, and of the risk resulting from their consumption. Consideration is given to aspects related to speciation, food processing, and bioavailability, which are key factors in evaluating the risk associated with the presence of these toxic trace elements in seafood products.

Potential Adverse Effects of Engineered Nanomaterials Commonly Used in Food on the miRNome

Lim JP, Baeg GH, Srinivasan DK, Dheen ST, Bay BH. *Food Chem Toxicol*. 2017 Nov;109(Pt 1):771–779. Article Link

Significance: The article reviews potential toxic effects of nanomaterials commonly used in food products.

The emergence of nanotechnology has greatly impacted our daily lives. Multiple products, including cosmetics, pharmaceuticals, electronics and food, are produced with incorporation of nanomaterials (NMs). Nanotechnology has yielded many promising benefits, yet, there remains much uncertainty about the hazards of NMs to humans. Hence, it is important to ensure safety of the users. Although many in vitro and in vivo studies have been carried out on the potential toxicity generated by NMs in food, its effects on the microRNA genome (miRNome) involved in the regulation of gene expression have been poorly understood. Therefore, this review focuses on the types of commonly used NMs (containing silicon dioxide, titanium dioxide, silver or zinc oxide) in food products and their potential toxic effects, including how NMs can induce epigenetic toxicity mediated via altered miRNA expression.

Packaging

Food Contact Materials and Gut Health: Implications for Toxicity Assessment and Relevance of High Molecular Weight Migrants

Groh KJ, Geueke B, Muncke J. *Food Chem Toxicol*. 2017 Nov;109(Pt 1):1–18. Article Link

Significance: This review suggests that the molecular-weight–based cutoff for risk assessment should be reevaluated in light of potential effects of food contact materials on gut health.

Gut health is determined by an intact epithelial barrier and balanced gut microbiota, both involved in the regulation of immune responses in the gut. Disruption of this system contributes to the etiology of various non-communicable diseases, including intestinal, metabolic, and autoimmune disorders. Studies suggest that some direct food additives, but also some food contaminants, such as pesticide residues and substances migrating from food contact materials (FCMs), may adversely affect the gut barrier or gut microbiota. Here, we focus on gut-related effects of FCM-relevant substances (e.g. surfactants, N-ring containing substances, nanoparticles, and antimicrobials) and show that gut health is an underappreciated target in the toxicity assessment of FCMs. Understanding FCMs' impact on gut health requires more attention to ensure safety and prevent gut-related chronic diseases. Our review further points to the existence of large population subgroups with an increased intestinal permeability; this may lead to higher uptake of compounds of not only low (<1000 Da) but also high (>1000 Da) molecular weight. We discuss the potential toxicological relevance of high molecular weight compounds in the gut and suggest that the scientific justification for the application of a molecular weight-based cut-off in risk assessment of FCMs should be reevaluated.

Scientific Integrity

Disclosures in Nutrition Research: Why It Is Different

Ioannidis JPA, Trepanowski JF. *JAMA*. 2017 Dec 7. doi: 10.1001/jama.2017.18571. Article Link

Significance: This commentary discusses the bias that is unique to nutrition science.