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Food Toxicology: Principles, Toxicological Mechanisms, Risk Assessment, and Future Perspectives

Wenqin Jiang*

Minhang Crosspoint High School, Shanghai, China

**Corresponding author: Wenqin Jiang.*

Abstract

Food toxicology sits at the crossroads of toxicology, food science, biology, and public health. It focuses on the identification, source tracing, toxic action mechanisms, risk evaluation, and control strategies of all harmful toxic substances in food systems. These hazardous substances include both naturally occurring endogenous toxins and exogenous artificial pollutants generated in industrial production, agricultural cultivation, and food processing. With the continuous expansion of global food supply chains, the innovation of food deep-processing technology, the emergence of new food raw materials and packaging materials, as well as the increasing public attention to dietary health and food safety issues, food toxicology has gradually developed into an indispensable core discipline to guarantee global food security and human public health. This paper systematically combats the basic connotation and core research scope of food toxicology, classifies common food toxicants in detail, deeply analyzes the molecular and cellular toxicological mechanisms of food-harmful substances, summarizes the traditional and emerging food safety risk assessment and detection technologies, and discusses the current dilemmas, challenges, and future development trends of the discipline. The research aims to systematically elaborate on the practical value and scientific significance of food toxicology and provide a theoretical reference for the innovation and application of food safety supervision and toxicological risk prevention in the new era.

Keywords

food toxicology, food contaminants, toxic mechanism, risk assessment, food safety

1. Introduction

Food is the most basic material guarantee for human survival, physical development, and sustainable social progress. Food safety is closely linked to individual health, population quality, and public security. It has always been a key concern for governments and academic circles worldwide. In the whole industrial chain of food production, planting and breeding, processing, storage, transportation, and sales, various toxic and harmful substances may be introduced accidentally or inherently. These food toxicants cover natural biological toxins, chemical residual pollutants, unreasonable food additives, thermal processing toxic by-products, and microbial metabolic toxins. Different from acute food poisoning caused by high-dose toxic exposure in a short time, low-dose and long-term dietary exposure to food toxicants has stronger concealment and cumulative risk, which can induce chronic organ lesions, cellular genetic mutation, malignant tumor proliferation, endocrine

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disorder, and immune system damage, and bring long-term and potential hidden dangers to human public health.

The development of food toxicology originated from the early exploration and summary of natural food poisoning incidents. In the early stage of the discipline, researchers mainly focused on identifying acute toxic substances in food, analyzing the poisoning symptoms of accidental high-dose intake, and formulating simple food safety prohibition specifications. With the rapid development of modern analytical chemistry, molecular biology, cell biology, and computational science, food toxicology has overcome the limitations of traditional, phenotypically based research. The research focus has gradually shifted from simple hazard identification and acute toxicity judgment to in-depth exploration of molecular toxicological mechanisms, low-dose cumulative toxic effects, multi-toxicant combined exposure risks, and individualized population toxic responses.

At present, food toxicology has established a comprehensive scientific research system that integrates hazard detection, mechanism exploration, risk assessment, standard formulation, and risk control. It not only undertakes the basic research task of clarifying the toxic effects of harmful food substances, but also provides a core scientific basis for the formulation of national food safety standards, food quality supervision, foodborne disease prevention, and global food trade safety control. In the context of global food trade integration, cross-border food safety hazards are becoming increasingly prominent, and new pollutants and new toxic risks continue to emerge. Therefore, strengthening in-depth research on food toxicology is of great practical significance for addressing emerging food safety problems, eliminating potential dietary health risks, and building a comprehensive food safety guarantee system.

2. Core Research Scope and Classification of Food Toxicants

2.1 Definition and Core Research Content of Food Toxicology

Food toxicology is an important branch of applied toxicology that specifically studies the absorption, distribution, metabolism, excretion, and toxic pathogenesis of various toxic substances in food in human and other biological systems, as well as the quantitative relationship between toxicant dose and biological adverse effects. Its ultimate research goal is to evaluate food safety risks accurately, establish scientific safety limit standards, and formulate effective risk prevention and control measures to reduce the health damage caused by dietary toxic exposure.

The core research content of modern food toxicology exhibits systematic, multidimensional characteristics, encompassing six key research directions. First, qualitative and quantitative identification of food hazards, using analytical detection technology to screen and confirm unknown toxic substances in the food matrix and determine their levels. Second, dose-effect relationship research to establish a quantitative mathematical model relating the intake dose of toxicants to the severity of biological toxic reactions, and to distinguish threshold toxic effects from non-threshold genetic toxic effects. Third, multi-level exploration of toxic mechanisms, revealing the toxic action pathways of food toxicants at molecular, cellular, tissue, organ, and individual levels. Fourth, research and development of detection technology, developing efficient, sensitive, rapid, and high-throughput detection methods suitable for complex food matrix environments. Fifth, systematic food safety risk assessment, comprehensively evaluating the probability of health risks from toxicant exposure across different groups of people. Sixth, standard formulation and risk management, putting forward scientific toxicant limit standards, food processing specifications, and dietary risk prevention strategies to guide industrial production and market supervision.

2.2 Main Classification of Food Toxicants

According to the source, the generation pathways and chemical properties of toxic substances, including common food toxicants, can be systematically divided into five categories: natural endogenous toxins, environmental chemical pollutants, unreasonable food additives, processing-induced toxicants, and microbial toxins, each with unique occurrence characteristics and toxic hazard attributes.

Natural endogenous toxins are inherent secondary metabolites of food raw materials that cannot be eliminated by conventional food processing methods and are the main natural hazard sources in food. Common fungal toxins include aflatoxin B1, with strong hepatotoxicity and carcinogenicity; ochratoxin A, with

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nephrotoxicity; and zearalenone, with endocrine-disrupting effects, which are widely found in moldy grains, nuts, and feed. Plant-derived natural toxins include solanine in germinated and green potatoes, cyanogenic glycosides in fresh cassava and bitter almonds, and phytic acid and tannin in coarse cereals, which can cause gastrointestinal poisoning and nutrient absorption obstruction after excessive intake. Marine biotoxins are mainly produced by marine toxic algae, including saxitoxin, domoic acid, and tetrodotoxin, which are concentrated in shellfish, fish, and other aquatic products and can cause acute neurotoxic poisoning.

Environmental chemical pollutants are exogenous toxic substances introduced into the food chain through agricultural production, industrial emissions, and environmental pollution. Pesticide and veterinary drug residues are the most common agricultural pollutants, including organophosphorus and pyrethroid pesticides and antibiotic residues, which can cause cumulative toxicity over long-term exposure. Heavy metal pollutants such as lead, cadmium, arsenic, and mercury are persistent and toxic. They accumulate in the soil and water environment for a long time, migrate and enrich in crops and aquatic products, and cause irreversible damage to human organs. In addition, plasticizers, persistent organic pollutants, and other industrial pollutants in the environment will enter the food system and pose potential safety hazards.

Food additives are legal food processing auxiliary materials, but illegal addition, excessive use, or non-standard use may pose toxic hazards. For example, excessive addition of synthetic preservatives, artificial colorants, and sweeteners will increase the metabolic burden of the human body and induce chronic inflammation. The illegal addition of non-edible industrial substances such as melamine and industrial sulfur dioxide will cause serious organ damage and even life-threatening accidents.

Processing-induced toxicants are new toxic substances produced by chemical reactions of food components under high temperatures, high salt levels, fermentation, and other processing conditions. Starchy foods can form acrylamide, a known genetic toxicant, during high-temperature frying and baking. Meat products rich in protein and fat can form heterocyclic amines and polycyclic aromatic hydrocarbons, which are strongly carcinogenic, during high-temperature cooking. Pickled and smoked foods are prone to producing nitrosamine toxic substances during processing, which are important risk factors for digestive tract tumors.

Microbial toxins are toxic metabolites produced by pathogenic microorganisms that contaminate food. Botulinum toxin, produced by Clostridium botulinum, is one of the most toxic biological toxins in nature, which can cause severe neuroparalysis. Enterotoxins produced by Staphylococcus aureus and aflatoxins produced by Aspergillus flavus are the main pathogens causing mass acute food poisoning incidents, which seriously endanger public health.

3. Toxicological Mechanisms of Food-Harmful Substances

The toxic damage mechanism of food-harmful substances is extremely complex, involving multiple biological processes such as intracellular oxidative balance, genetic material stability, endocrine signal regulation, immune function, and cell metabolism. Different types of food toxicants have specific target organs and dominant toxic pathways, and multiple toxic mechanisms often interact and synergize to cause biological damage.

Oxidative stress reaction is the most common and basic toxic mechanism of food pollutants. A variety of food toxicants, such as aflatoxin B1, heavy metals, and pesticide residues, can stimulate cells to produce a large number of reactive oxygen species (ROS). Excessive ROS will disrupt the dynamic balance between oxidation and antioxidants, fail to be cleared by antioxidant enzymes in a timely manner, and further attack biological macromolecules. Lipid peroxidation of the cell membrane will lead to membrane structural damage and permeability imbalance; protein oxidative denaturation will cause enzyme activity inhibition and protein functional loss; DNA oxidative damage will induce base mutations and gene damage. Long-term oxidative stress will cause continuous damage to the liver, kidney, and other metabolic organs, and eventually induce tissue fibrosis and malignant lesions.

Genotoxicity is a key mechanism for food toxicants to induce cancer and genetic diseases. Processing toxicants such as acrylamide and benzo(a)pyrene can directly bind to intracellular DNA molecules to form DNA adducts, interfere with normal DNA replication and transcription processes, cause gene point mutation, chromosome aberration, and DNA strand breakage. The body's self-repair mechanism cannot completely repair this genetic damage, and the damaged genes will accumulate and mutate in cell proliferation, leading to

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abnormal cell proliferation and tumor formation, which is the core cause of food toxicant-induced malignant tumors.

Endocrine disruption has become a new hot spot in food toxicology research in recent years. New environmental pollutants, such as bisphenol A, phthalates, and low-dose residual pesticides, exhibit hormone-like effects. They can simulate the structure of endogenous estrogen in the human body, competitively bind to hormone receptors, or block the synthesis and secretion of androgen, interfering with the normal regulatory function of the endocrine system. The endocrine systems of infants and adolescents are in a critical period of development and differentiation, with limited tolerance to exogenous endocrine disruptors. Long-term low-dose exposure will lead to abnormal growth and development, reproductive system dysplasia, metabolic disorders, and precocious puberty, and even affect reproductive health in adulthood.

In addition, many food toxicants have immunotoxicity and metabolic toxicity. Toxic substances can inhibit the proliferation and differentiation of immune cells, reduce macrophage phagocytic ability and antibody secretion, resulting in decreased human immune defense function and increased susceptibility to infectious and autoimmune diseases. At the same time, toxicants can inhibit the activity of key metabolic enzymes in the liver and kidneys, disrupt the normal metabolism and energy circulation of the body, cause metabolic disorders, and further aggravate the cumulative damage from toxic substances.

4. Food Safety Risk Assessment and Detection Technology in Food Toxicology

4.1 Classic Risk Assessment Framework

Food safety risk assessment is the core applied technology of food toxicology research and also the scientific basis for governments to formulate food safety regulations and implement risk management. The internationally unified classic risk assessment framework formulated by the World Health Organization includes four standardized links: hazard identification, dose-response assessment, exposure assessment, and risk characterization, forming a complete closed-loop evaluation system from hazard confirmation to risk judgment.

Hazard identification is the primary link of risk assessment, which adopts experimental research, epidemiological investigation, and literature data analysis to confirm whether a certain food substance has adverse toxic effects on the human body, and clarify the types of toxicity such as acute toxicity, chronic toxicity, genetic toxicity, carcinogenicity, and endocrine toxicity. Dose-response assessment quantifies the correlation between toxicant intake dose and adverse health effects, determines the no-observed-adverse-effect level (NOAEL) and lowest-observed-adverse-effect level (LOAEL), and calculates the acceptable daily intake (ADI) of toxicants, thereby formulating safe dietary intake standards. Exposure assessment aims to comprehensively calculate the daily intake of food toxicants for different populations based on dietary habits, food consumption frequency, regional differences in food structure, and toxicant levels in food, and to clarify the actual exposure levels of the population. Risk characterization is the final link in the assessment, which integrates the results of the first three links, quantitatively evaluates the probability, severity, and population differences of health risks caused by toxicant exposure, and provides targeted risk control recommendations for risk managers.

4.2 Emerging Detection and Evaluation Technologies

With the progress of analytical chemistry and life sciences, food toxicology detection and evaluation technology has developed from traditional laboratory-precision detection to rapid on-site detection and intelligent simulation evaluation. Traditional chromatographic and mass spectrometry detection technologies such as high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS) are still the gold standard for food toxicant detection, offering high precision, high sensitivity, and good stability, enabling accurate detection of trace toxic residues in complex food matrices.

In order to adapt to the rapid supervision demand of the food market, emerging detection technologies such as high-resolution mass spectrometry, biological sensor detection, and rapid immunodetection have been widely applied. These technologies enable on-site, high-throughput, rapid screening of food toxicants, greatly improving the efficiency of daily food safety supervision and emergency response to poisoning incidents.

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In toxicological evaluation, traditional animal experiment models have limitations of long cycles, high costs, and ethical concerns. Modern toxicology has gradually replaced traditional animal experiments with in vitro cell models, organoid tissue models, and zebrafish models, which can more accurately simulate human toxic responses, shorten experimental cycles, and reduce costs. At the same time, computational toxicology has developed rapidly in recent years. In silico simulation technologies such as quantitative structure-activity relationship (QSAR) modeling, molecular docking simulation and physiologically based pharmacokinetic (PBPK) modeling can quickly predict the toxic activity, metabolic pathway and target of unknown food compounds, realize early hazard screening of new food raw materials and new pollutants, and fully comply with the modern toxicology 3Rs principles of Replacement, Reduction, and Refinement.

5. Challenges and Future Development Trends of Food Toxicology

5.1 Current Research Challenges of Food Toxicology

In the context of the rapid development of the modern food industry, food toxicology is facing many new challenges and difficulties. First, the globalization of the food supply chain leads to the cross-regional spread of food hazards. Food raw materials and processed products circulate globally, making regional food safety risks evolve into global public health problems, which increases the difficulty of unified supervision and risk prevention. Second, the emergence of new food technologies and new pollutants brings unknown toxic risks. New processing technologies, new packaging materials, and nano-food additives produce emerging pollutants such as nanoplastics and nanomaterials, whose toxic mechanisms and long-term health effects have not been fully clarified.

Third, the combined exposure risk of multiple low-dose toxicants is difficult to evaluate. The human dietary environment is complex, and the coexistence of multiple food toxicants will produce synergistic or antagonistic toxic effects. The traditional single-toxicant risk assessment model cannot accurately reflect the real human dietary exposure risk. Fourth, the individual differences in population toxic response increase the difficulty of precise risk assessment. Vulnerable groups such as pregnant women, infants, the elderly, and people with chronic diseases have different metabolic capacities and toxic tolerance compared with ordinary adults, and there is a lack of targeted personalized risk assessment standards at present.

5.2 Future Development Trends of the Discipline

In the future, food toxicology will develop toward precision, intelligence, interdisciplinarity, and international integration. First, multi-omics technology will be deeply applied in toxic mechanism research. Genomics, proteomics, and metabolomics technologies will be used to analyze the molecular regulatory networks of food toxicants acting on the human body, clarify the key target genes and protein pathways involved in toxic damage, and enable precise interpretation of toxic mechanisms.

Second, artificial intelligence and big data technologies will build an intelligent early-warning system for food safety risks. By integrating food toxicology data, dietary consumption data, and crowd health data, intelligent prediction of emerging food hazards and dynamic evaluation of crowd risks can be achieved, enabling proactive prevention and control of food safety risks. Third, interdisciplinary integration will promote the innovation of safety design concepts. The cross-integration of food toxicology, nutrition, food engineering, and public health will form a "safety-by-design" research model, which controls toxic risks from the source of food raw material selection, processing technology optimization, and formula design.

Fourth, international standardization and cooperation will be further strengthened. Unifying global food toxicant detection methods, risk assessment standards, and safety limit specifications can eliminate technical barriers to food trade and ensure the safety of global food supply chains. In addition, the popularization of food toxicology public science will be further promoted to improve consumers' ability to identify food safety and their self-protection awareness, and to form a joint supervision pattern of government oversight, industrial self-discipline, and public participation.

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6. Conclusion

Food toxicology is an indispensable basic discipline supporting global food safety and public health construction. It systematically explains the source characteristics, classification attributes, molecular toxic mechanisms, and risk control methods of food-harmful substances. It provides core theoretical support for the formulation of food safety standards, food quality supervision, new food technology safety evaluation, and foodborne disease prevention. Facing the challenges posed by global food trade integration, emerging food pollutants, and complex dietary exposure risks, modern food toxicology needs to continuously innovate detection and evaluation technologies, deepen multi-level research into toxic mechanisms, and build a precise and intelligent risk assessment system.

In the future, relying on interdisciplinary technological innovation and international cooperative research, food toxicology will further break through the limitations of traditional research models, realize the transformation from post-risk disposal to pre-source prevention, effectively resolve new and hidden food safety risks, protect the dietary health of global consumers, and provide solid technical guarantee and theoretical support for the sustainable and healthy development of the modern food industry.

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Conflicts of Interest

The authors declare no conflict of interest.

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