Combining analytical techniques, exposure assessment and biological effects for risk assessment of chemicals in food

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Humans today are exposed to a plethora of chemicals in food whether of anthropogenic or natural origin, and public-health agencies have developed risk-assessment methods to derive safe levels of exposure and to prevent adverse health effects. This review highlights analytical techniques used to measure chemical contaminants in food, how human exposure to such contaminants is assessed, and how contamination and exposure are combined with biological (toxicological) effects for risk assessment. We illustrate the whole process using recent examples of importance in public health and give perspectives on the future.

Keywords: Analytical chemistry; Biological effect; Chemical contaminant; Exposure assessment; Food contamination; Genotoxicity; Metabolism; Public health; Risk assessment; Toxicity

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1. Introduction

Modern man is exposed to a wide range of microorganisms and chemicals, the uptake of which by the human body is mainly through food, water, air and dermal contact. The European Food Safety Authority (EFSA) was created in 2002 to assess the risk of these hazards to human health when they are ingested via food. In theory, assessment of exposure to microbes is quite similar to that for chemicals with acute adverse effects but the former topic is beyond the scope of this article, which deals exclusively with chemicals or xenobiotics occurring in food.

Xenobiotics can be classified into broad categories, according to their relevance in terms of food safety, namely contaminants and chemicals that have been intentionally added to food or raw commodities. Man-made contaminants of importance include persistent organic pollutants [i.e. dioxins, polychlorinated biphenyls (PCBs), brominated flame retardants (BFRs)], melamine, phthalates, perfluoroalkyl acids [i.e. perfluoro-octanoic acid (PFOA) and sulfonate (PFOS)], a large number of pharmaceuticals, and natural toxins (i.e. mycotoxins, marine biotoxins and plant toxins). Other contaminants in food are produced from the Maillard reaction during frying and cooking at high temperature (i.e. acrylamide) or as a reaction product between ethanol and precursors (cyanide) (i.e. ethyl carbamate produced mainly in stone spirits). Food additives, flavorings and food-contact materials constitute the largest classes of chemicals that are intentionally added to food, whereas chemicals resulting from intentional treatment of raw commodities include mostly pesticides or biocides (e.g., herbicides, fungicides and insecticides) and veterinary residues (e.g., cocciodiostatics and antibiotics).

On a worldwide perspective, the World Heath Organization (WHO) is leading an initiative to provide reliable, accurate estimates of the global burden caused by all food-borne diseases caused by chemicals, parasites, and enteric infections by 2012 [1]. This program is expected to estimate and to compare on a common scale the respective burden for human health of various hazards from different origins.

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The United Nations Children's Fund (UNICEF) and the WHO have already estimated that over 1 billion people are currently deprived of safe water supplies and adequate sanitation. In 2005, they launched the ''International Decade for Action: Water for Life'' and the Millennium Development Goals (MDGs) to halve the proportion of the world's population without sustainable access to safe drinking water and sanitation by 2015 [2]. In such a context, standardized, powerful tools are needed in order to protect consumers from potential adverse health effects that may arise from exposure to chemicals.

Scientists and public-health agencies have developed risk-assessment methods to derive human safe levels of exposure. Risk assessment has been divided into four sequential steps: hazard identification, hazard characterization, exposure assessment and risk characterization [3]. In practice, once a chemical has been identified, its content in food measured through validated analytical techniques, its biological (toxicological) effects characterized and a safe level derived, one can relate exposure to biological effects for human risk assessment.

This review focuses on bridging the gap between chemical exposure and biological effects using analytical chemistry as a vehicle between the two. First, we review analytical techniques and exposure assessment applied to food contaminants together with biological and toxicological bases for setting safe levels of exposure in humans using recent examples of importance in public health. We then highlight the state of the art and the future of combining exposure and biological/toxicological effects with particular emphasis towards a multidisciplinary approach involving analytical chemistry, biology, toxicology and quantitative modeling.

2. Assessment of exposure to chemicals in food

Human dietary exposure to chemicals is mostly through ingestion of food and water, and reflects an external dose of the chemical entering the body. Assessing such exposure to chemicals is complex and depends on the availability of analytical techniques to provide the concentration of the chemical in a particular food item (occurrence data) and the corresponding patterns of food consumption in humans [4].

2.1. Analytical techniques

The occurrence data used for risk assessment are usually obtained from routine monitoring programs conducted at the level of a specific country to check compliance of contaminants for which maximum levels are laid down in European Union (EU) legislation. In addition, the implementation of the Rapid Alert System for Food and Feed (RASFF) in Europe has provided a helpful tool to perform systematic monitoring of specific notifications regarding either regulated contaminants or xenobiotics that may be above maximum levels or emerging contaminants or xenobiotics occurring in food and feed.

To obtain reliable occurrence data on contaminants in food, the availability of analytical methods for their determination is of utmost importance. The complexity of food samples, together with the low concentrations at which contaminants occur, requires highly sensitive, selective and reliable analytical techniques, which can also be applied to biological and environmental samples. Typically, the determination of contaminants in such matrices involves a number of steps (e.g., sampling, sample preparation, separation and detection, identification and quantification of the target compounds). Well-established separation techniques [e.g., gas chromatography (GC), liquid chromatography (LC) and capillary electrophoresis (CE)] are usually employed for the determination of food contaminants. Detection systems play a key role and should be sensitive and selective enough for the unequivocal determination of the target analytes. In particular, mass spectrometry (MS), coupled to GC, LC and CE, has become an essential tool to provide valuable structural information for identification of the compounds. The use of tandem MS (MS^2) is becoming frequent with the introduction of different mass analyzers that enhance MS^2 capabilities {i.e. improved designs of the triple-quadrupole (QqQ) and hybrid systems [e.g., the quadrupole-linear ion trap (Qq-LIT) and quadrupole time-of-flight (Qq-TOF)]}. The use of these systems allows not only for better sensitivity, but also provides further confirmation of the identity of the analytes [5,6]. While GC-MS is quite well established as a technique in many routine laboratories for the analysis of non-polar, semi-polar, volatile and semi-volatile contaminants, LC-MS or LC-MS^2 has experienced great development in recent years, with an increased number of applications in both food-safety and environmental fields. It has become a powerful tool for detection and quantification of polar and non-volatile contaminants, including pharmaceutical residues, veterinary drugs, as well as metabolites and degradation products of food contaminants [7]. However, despite all the advances in instrumental techniques and detection systems, the complexity of matrixes requires, in most cases, an extensive, time-consuming, sample-preparation step, which is often still the bottleneck of the whole analytical procedure [8]. The objective of this step is to extract the target compounds from the matrix and clean up the extract to remove possible interferences (i.e. matrix components or compounds co-eluting with the analyte) that might hinder the final instrumental determination. The selection of the sample-preparation methods depends on the matrix and the analyte. Currently, sample-preparation methods tend to move towards more environmental friendly approaches (less consumption of organic solvents), miniaturization, automation and, ideally, on-line coupling with the final instrumental