

Food Contaminants

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Abstract

Chemical contaminants may occur in our food from various sources. Contaminants can be present in foods mainly as a result of the use of agrochemicals, such as residues of pesticides and veterinary drugs, contamination from environmental sources (water, air or soil pollution), cross-contamination or formation during food processing, migration from food packaging materials, presence or contamination by natural toxins or use of unapproved food additives and adulterants.

They typically pose a health concern, resulting in strict regulations of their levels by national governments and internationally. Therefore, analysis of relevant chemical contaminants is an essential part of food safety testing programs to ensure consumer safety and compliance with regulatory limits. Modern analytical techniques can determine known chemical contaminants in complex food matrices at very low concentration levels. Moreover, they can also help discover and identify new or unexpected chemical contaminants.

Keywords: Agrochemical residues, Mycotoxins, Toxins in chemical processing, Packaging-derived chemicals

1. Introduction

Codex Alimentarius defines "contaminant" each substance not intentionally added to the food, but found inside as a result of the production process, farming practices, treatment, packaging, transport or storage of food, or result of environmental contamination. Foreign substances such as insect fragments, animal hair, etc. do not included in this definition.

The analysis of contaminants is a crucial step of food safety, essentially due to the high complexity of food matrices which generates chemical interactions that affect recoveries, and the low amount of analytes.

This chapter focuses on food contaminants, the presence of which is, sometimes, difficult to predict. They can be classified according to their chemical origin:

- agrochemicals (pesticides, veterinary drug residues),
- natural toxins (mycotoxins),
- toxins in industrial chemical processing (e.g., polycyclic aromatic hydrocarbons, phthalates, dioxins and polychlorinated biphenyls, acrylamide, perchlorate),
- packaging-derived chemicals (bisphenol A, semicarbazide)

2. Agrochemicals

2.1 Pesticides

The term "pesticides" is often used as a synonym for plant protection products; this category includes many compounds with different chemical nature and with a specific purpose for which they are produced. Pesticides are chemicals, natural or synthetic, used in agriculture for the systematic elimination of specific species considered harmful for crops, such as bacteria, molds, fungi, insects, mice and other species [1].

They are very different compounds, ranging from plant extracts (pyrethrum), to salts and mineral oils, to the most sophisticated organic compounds, which are not yet known interactions with the environment and with humans.

It is known that, the adverse health effects on humans caused by pesticides are obviously proportional to the amount of absorbed substance and the time of exposure, as well as to the chemical characteristics of each compounds. Exposure to certain pesticides leads to occurrence of liver disease, lung disease, skin and blood diseases and neurological disorders [2]. Several pesticides are carcinogenic to humans, including herbicides, for example, atrazine has been indicated as a possible cause of cancer. Some herbicides may play a role in ovarian cancer, while the arsenic-based pesticides appear to be associated with lung cancer [3,4].

Their extensive usage in agriculture involves considerable problems, related to the fact that they are commonly xenobiotic substances which are able to deeply modify all normal biological cycles and the dynamics of the trophic chain. Many pesticides are not biodegradable and accumulate in the environment causing the biomagnification phenomena.

The main source for human exposure is diet; in the world alarming levels of pesticides were found in the air, water, soil as well as in food and biological material, therefore, the concentration of pesticide residues should be monitored.

The legislation that deals with this topic has tried to limit the concentration of pesticides in foods for human consumption that did not involve a risk to consumer health. [5]

In this regard it is essential the determination of a dose without harmful effect or NOEL (No Observed Effect Level), i.e. the maximum amount of compound that does not give rise to any negative effect, if administered in the diet to laboratory animals for long periods.

NOEL is derived from the acceptable daily intake or ADI that represents the amount of xenobiotic that can be taken from a man every day, for a lifetime without appreciable risk to health. ADI is fundamental in this way to determine the maximum limit residual or MRL (Maximum Residue Limit) or the maximum concentration of residue of an active substance permissible in a food.

Regulation (EC) No 396/2005 establishes the MRLs of pesticides permitted in products of animal or vegetable origin intended for human or animal consumption. EU Member States were allowed to set MRL at the national level for the tens of thousands of food matrices for which, sometimes, no official MRL existed.

Pesticides can be distinguished according to the chemical class in:

- Organophosphorus pesticide group (OPPs) is the most widely used class of agricultural pesticides. Belong to the class of organophosphorus many structurally different compounds that have been synthesized in order to find highly toxic agents for insects and relatively harmless to non-target species. The broad spectrum of action of OPPs and their short persistence in the environment have favored their wide diffusion. Since the toxic action of OPPs is expressed at the level inhibition of the enzyme acetylcholinesterase, symptoms of poisoning resulting from the accumulation of acetylcholine in the synaptic cleft, and then by a continuous stimulation of cholinergic receptors. The extent and intensity of the observed effect depend on the type of pesticide, the dose and the exposure modes or intake. In recent years, many studies have proved OPPs to be mutagenic, carcinogenic, cytotoxic, genotoxic, teratogenic and immunotoxic.
- Carbamate pesticides: like organophosphate insecticides, carbamates are also cholinesterase inhibitors and in cases of double exposure, the effects would be additive. Carbamates cause the reversible carbamylation of the acetylcholinesterase enzyme, allowing accumulation of acetylcholine in the central nervous system. The accumulation of acetylcholinesterase in the brain due to carbamate poisoning may cause sensory and behavioral disturbances.
- Organochlorine insecticides (OCPs or chlorinated hydrocarbon) were commonly used in the past in agriculture as vector-borne disease control, but many have been removed from the market due to their health effects, residual activity and environmental persistence. OCPs are

known neurotoxins acutely toxic and bioaccumulate in the food chain. Studies in wildlife species and laboratory animals have demonstrated potent estrogenic and enzyme-inducing properties, which interfere with fertility and reproduction.

- Pyrethroid pesticides are the newest class of insecticides, a group of chemicals that entered the marketplace in 1980 but by 1982 accounted for approx. 30% of worldwide insecticide use. Pyrethroid pesticides are synthesized derivatives of naturally occurring pyrethrins, which are taken from pyrethrum, the oleoresin extract of dried chrysanthemum flowers. Some synthetic pyrethroids are toxic to the nervous system. Various formulations of these pesticides are often combined with other chemicals, known as synergists, to increase potency and persistence in the environment.
- Sulfonylurea herbicides were introduced in 1982 and have been used for control of nuisance broadleaf weeds and grasses. The sulfonylureas have soil half-lives that range from a few days to two months, and they are degraded by soil microbes and chemical hydrolysis. Specifically, these compounds interfere with a key enzyme required for weed cell growth, acetolactate synthase.

2.2 *Veterinary drugs*

Veterinary drugs are widely used at therapeutic levels to treat diseases in livestock, maintain the health in all animals treated, promote growth and improve the quality of the meat so as to reduce production costs.

Residues of veterinary drugs and their metabolic products are very small quantities of veterinary medicinal products which may remain in animal products and will appear in the food chain.

From a chemical point of view, they are very different substances as is their application. Tetracyclines, quinolones, macrolides and sulphonamides are some of the veterinary drugs that have been potentially used by farmers to fight against livestock infections. Furthermore, other families of veterinary drugs, such as acaricides or parasiticides, are often used for the treatment of parasitic diseases.

Most of these substances present in residual amounts in edible tissues, milk and eggs for human consumption have some important toxic effects. Some of them exert genotoxic, immunotoxic, carcinogenic or endocrine effects on consumers, constituting an important health risk.

In the livestock sector antimicrobials may also be added to animal feed to improve the conversion efficiency of nutrients, increase growth, reduction of the incidence or severity of animal diseases [6,7]. In these cases, antibiotics are administered at relatively low concentrations (doses "subtherapeutic"), from 2.5 to 125 mg/kg, depending on the drug and the species treated. Mounting evidence suggests a relationship between antimicrobial use in animal husbandry and an increase in bacterial resistance in humans. The use of antimicrobials in food animals leads to antibiotic resistance which can then be transmitted to humans

through the food supply. Antimicrobial resistance has emerged in zoonotic enteropathogens (*Salmonella* spp., *Campylobacter* spp.), commensal bacteria (*Escherichia coli*, enterococci), and bacterial pathogens of animals (*Pasteurella*, *Actinobacillus* spp.) [6]. In addition, the consumption of trace levels of antimicrobial residues in foods may have consequences on the indigenous human intestinal microflora which constitutes an essential component of human physiology [8]. In view of all these circumstances, surveillance programs, prudent use guidelines, and educational campaigns must be developed to minimize the further antimicrobial resistance [9].

The use of substances having hormonal or thireostatic action as well as β -agonists in animals breeding is controlled by Directive 81/602/EEC. Among the banned substances are 17 β -estradiol, testosterone, progesterone, zeranol, trenbolone acetate and melengesterol acetate. This prohibition includes all countries member and also meat imported from other states. The legal instruments used are the Directive 96/22/EC amended by Directive 2003/74/EC, and contributed to a sensible reduction in the number of growth promoting reported cases.

The following drugs were considered as the most likely to be detected in animal products.

- ✓ β -Agonists
- ✓ Corticosteroids
- ✓ Stilbenes and their derivatives
- ✓ Antithyroid agents
- ✓ Steroid hormones
- ✓ Antimicrobials
- ✓ Sulfonamides and quinolones
- ✓ Anthelmintics
- ✓ Anticoccidials
- ✓ Sedatives
- ✓ Nonsteroidal anti-inflammatory drugs

3. Natural toxins

3.1 Mycotoxins

Mycotoxin contamination of various foodstuffs and agricultural commodities is a major problem in the tropics and sub-tropics, where climatic conditions and agricultural and storage practices are conducive to fungal growth and toxin production.

Mycotoxins are small (MW~700) toxic products of secondary metabolism of filamentary micromycetes and represent the most important contaminants of natural origin. Three genera

are responsible for the majority of the mycotoxins: the *Aspergillus* spp., *Penicillium* spp., and *Fusarium* spp.

Mycotoxins have been reported to be carcinogenic, teratogenic, haemorrhagic and dermatotoxic to a wide range of organisms, and known to cause cancer.

The potential for a product to contain a naturally mycotoxin depends by food matrix and whether the optimum temperature and humidity are present. Their natural presence has been described worldwide in agriculture commodities such as cereals, spices, coffee, grapes and fruits and the risk of mycotoxin contaminations is an important world food safety.

In Europe, statutory levels of mycotoxins permitted in food and animal feed are set by a range of European directives and Commission Regulations [10,11] that include specific maximum levels for certain mycotoxins in individual foodstuffs. The U.S. Food and Drug Administration has regulated and enforced limits on concentrations of mycotoxins in foods and feed industries since 1985. It is through various Compliance Policy Guidance programs that FDA monitors the food chain to guarantee that mycotoxins are kept at safe levels in cereals, peanuts, tree nuts, corn and corn products, cottonseed, and milk [12].

Examples of mycotoxins of greatest public health and agro-economic significance include aflatoxins, ochratoxins, trichothecenes (deoxynivalenol, nivalenol), citrinin, zearalenone, fumonisins, tremorgenic toxins and ergot alkaloids.

The complete elimination of mycotoxin contaminated commodities is not achievable at this time.

It is important to realize that good agricultural practices represent the primary line of defense against mycotoxins contamination of foodstuffs, followed by the implementation of good manufacturing practices during the handling, storage, processing, and distribution of cereals for human food and animal feed.

National authorities should educate producers regarding the environmental factors that promote infection, growth and toxin production in crops. Emphasis should be placed on the fact that the planting, preharvest and postharvest strategies for a particular crop will depend on the climatic conditions of that particular year, taking into account the local crops, and traditional production conditions for that particular country or region.

There is also, considerable on-going research on methods to prevent preharvest contamination of crops. These approaches include developing host resistance through plant breeding and through enhancement of antifungal genes by genetic engineering, use of biocontrol agents, and targeting regulatory genes in mycotoxin development.

4. Toxins in industrial processing

4.1 Polycyclic Aromatic Hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) are a large class of organic compounds containing two or more aromatic rings. They are formed mainly from incomplete combustion or

pyrolysis of organic matter, characterized by chemical stability, poor degradation by hydrolysis, and susceptibility to oxidation and photodegradation.

Generally PAHs are present in complex mixtures that may include hundreds of compounds. PAHs are of health concern due to the carcinogenicity shown by many of them, and in particular by benzo[a]pyrene (BaP), the most studied compound, generally used as a marker of PAH class.

The sources of human exposure to PAHs are varied; natural sources of PAHs emissions are forest fires, volcanoes, hydrothermal processes, oil seepage, and carbonization. Nevertheless, they are present in the environment mainly due to anthropogenic sources: various industrial processes, refining of petroleum and coal, incinerators, domestic heating especially wood and coal, emissions from motor vehicles and tobacco smoke.

Humans can be exposed to PAHs through food. Food contamination can result from environmental sources, due to:

- atmospheric fallout which is located mainly on the waxy surface of vegetables;
- technological processing, in particular, heating processes (i.e., grilling and smoking);
- contact with mineral oils which, if not for food purposes (food-grade quality).

Foods mostly contributing to PAH intake are cereals, vegetables, oils and fats; a high level of contamination has been found in smoked meat and fish, which was related to the smoking method [13,14]. Leafy vegetables grown in areas heavily exposed to air pollution may present large levels of PAHs. The crustaceans and bivalve molluscs do not metabolize PAHs and can therefore accumulate high amounts of contaminants.

Maximum limits have been set for PAHs in key foodstuffs, e.g. meat and meat products, fish and fishery products, milk and milk products, oils and fats, infant formulae and follow-on formulae and processed cereal based foods and baby foods for infants and young children via Commission Regulation (EC) No 1881/2006 [10].

4.2 Phthalates

Phthalic acid esters (PAEs), commonly known as phthalates, are a group of organic and synthetic chemical compounds with a wide spectrum of industrial applications. Phthalates are used in the plastics industry as plasticizers, or as substances added to the polymer to impart the characteristics of flexibility and elasticity.

A very important aspect regarding PAEs present in plastic materials is that they are not chemically bound to the polymeric matrix, but remain as a freely mobile phase. PAEs are present in a wide range of consumer products including building materials, packaging material, everyday objects (PVC gloves, toys) and medical devices.

Ingestion, inhalation, intravenous injection, and skin absorption are potential pathways of human exposure to PAEs. The inhalation exposure is in particular for the worker (for example of plastic industry), which is highly exposed to emissions of phthalates during

normal industrial activities, such as the operations of mixing, loading / unloading of plastic materials.

The ingestion instead is very important if, as "actor" is considered the child, which tends to bring any object to the mouth. This route of exposure leads to consider children the population most exposed, as well as the most susceptible. Data provided by the National Health and Nutrition Examination Survey (NHANES) show that the concentration of phthalate metabolites in the urine of children between 6-11 years is higher than that of adolescents and adults. The dermal exposure, in general, plays a minor role, and the absorption of phthalates through the skin is very slow [15].

Overall, foods represent one of the most important sources of PAE exposure for humans [16]. Foods can be contaminated during the entire life of a product, from the collection of raw materials, during the whole production chain, to storage and consumption. Possible contamination sources are represented by the air, objects and parts of industrial plant (tubes, conveyor belts, plastic connections, etc.), as well as plastic foils in contact with food and gloves during meal preparation; the transfer of the phthalates from the packing increases as a function of contact time, temperature, and the fat content of the packaged food.

Since 1999, with the Decision of the European Parliament and now included in Annex XVII of REACH are in force, the legal regulations governing the maximum concentration of phthalates in toys. In particular, there is the restriction of the use of phthalates because they are suspected to cause cardiovascular, liver, urologic and endocrine diseases. There is sufficient evidence in short- and long-term rodent studies, but not yet in humans, that phthalate exposure causes developmental and reproductive toxicity [17].

It was observed that phthalates migration occurs in particular in foods with high fat content (milk, milk powder and infant formulas). However, even some wine samples were found positive at traces of PAEs; they may be derived from raw materials and from tanks coated with polymeric materials, tubes and plastic containers. In beer samples presence of PAEs can result from metal crown caps, which are equipped with a gasket, currently consists of plasticized PVC. The Commission Regulation (EU) No 10/2011 on materials and articles intended to come into contact with food, provides specific PAEs migration limits apply to different plasticizers.

4.3 Dioxins and polychlorinated biphenyls

Dioxins and Polychlorinated biphenyls (PCBs) are two series of organic compounds having similar chemical-physical and toxicological behaviour. Dioxins are tricyclic planar compounds, which is formed by two rings benzene rings joined by oxygen bridges (two for the polychlorinated dibenzo-p-dioxins PCDDs, one only for polychlorinated dibenzo furans PCDFs), and characterized by substitution of one or more hydrogen atoms with chlorine atoms [18]. Depending on the number of chlorine atoms and their positions at the rings, 75 PCDDs and 135 PCDFs, termed "congeners", can occur. Dioxins haven't technological applications, but are generated as unwanted and often unavoidable in different thermal and

industrial processes. Dioxins are semivolatile substances, thermostable, slightly polar, insoluble in water, highly liposoluble, resistant to chemical and biological degradation.

Dioxins, consider global contaminants, are from a variety of emission sources: combustion processes, solid urban wastes, incineration, hazardous wastes, hospital wastes, burning tires, vehicle fuels, coal, oil, production of pesticides and herbicides, production of chlorinated solvents and vinyl chloride. Soils and sediments contaminated releasing into atmosphere small concentrations of contaminants. Dioxin toxicity depends on number and position of the chlorine atoms, and the 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), was classified in 1997, by the International Agency for Research on Cancer (IARC) as a human carcinogen. Based on the information available to date, the primary mechanism of entry of dioxins in the food chain seems to be the deposition on plant leaves and subsequently ingested by animals. If contaminated grass and soil are ingested by herbivores is an accumulation of these substances in meat and in milk produced.

Unlike dioxins, PCBs are a series of bicyclic aromatic compounds variously chlorinated, produced by chemical by industrial processes. The physico-chemical properties of PCBs vary significantly with direct effects on persistence and bioaccumulation. The PCB congeners are divided into two groups according to the different possibilities that have chlorine atoms to be arranged on a single biphenyl ring or on both. PCBs are characterized by low solubility in water (approximately, inversely proportional to the degree of chlorination), heat resistance, high lipophilicity which favors environmental persistence.

Due to their lipophilic properties, they accumulate in the food chain and are stored in fatty tissues.

Investigations of the different pathways have indicated that dietary intake represents the main route of human exposure to dioxins and PCBs, with the exception of specific cases of accidental or occupational exposure. The major food sources for dioxin exposure include fish, poultry, meats, milk, and milk products.

Dioxins and PCBs exposure at significant dose levels has been linked to a large number of adverse health effects [19]: acute exposures, resulting from chemical accidents or occupational exposure to dioxins, have caused a severe skin effects and liver damage. Concerns from chronic exposure to dioxins include cancer, reproductive effects, and developmental effects. Due to potential high dietary exposure in some population groups, dioxins and PCBs represent an important public health issue at the European level [20]. Commission Regulation EC No 1881/2006 sets out the maximum allowable limits of dioxins and PCBs for certain food products deemed of risk (including meats and meat products, liver, fish and fishery products, milk and dairy products, some animal fats and vegetable oils). These limits apply to the edible foodstuffs. This includes an assessment of the dietary intake of dioxins and dioxin-like PCBs by the EU population, identifying the main contributors. Given the persistent nature of these compounds the Directive has established a tolerable weekly intake (TWI) of 14 picogram toxic equivalents (TEQ) per kilogram body weight for dioxins and dioxin-like PCBs.

Animal feed and additives are regulated under ‘the undesirable substances in products intended for animal feed’ Commission Directive 2006/13/EC and ‘feed additives’ Commission Regulation EC No 1831/2003.

4.4 Acrylamide

Acrylamide is an industrial chemical widely used. Most acrylamide is used to synthesize polyacrylamides, which find many uses as water-soluble thickeners. These include use in wastewater treatment, gel electrophoresis, and the manufacture of permanent press fabrics.

Acrylamide was accidentally discovered in foods in April 2002 by scientists in Sweden when they found the chemical in starchy foods, such as potato chips, French fries, and bread that had been heated. It was not found in food that had been boiled or in foods that were not heated [21].

The acrylamide synthesis pathway isn’t completely clear, but the most reliable hypothesis seems to be the close relationship with the Maillard reaction, also called non enzymatic browning. In particular, the synthesis depends on the presence in food matrix of the amino acid asparagines. The formation of acrylamide, also, appears to be linked to the presence of reducing sugars such as glucose and fructose. Potatoes are high in asparagine and in reducing sugars, and are commonly prepared for consumption by frying or baking; all of these factors help explain the relatively high levels of acrylamide in heated potato products. In other words, the amount of acrylamide in food products can be formed from precursors in the matrix, and depends to some physical parameters such as temperature, pH, etc.

The International Agency for Research on Cancer (IARC) has classified acrylamide as a probable carcinogen to humans. Hence, it is necessary to know the presence of this compound in various food products and to limit the amount as much as possible.

Laboratory toxicology studies have indicated that acrylamide is carcinogenic and also has been associated with the development of reproductive toxicity, genotoxicity and neurotoxicity, leading to nervous system damage, weakness, and incoordination of limbs [22]. Several epidemiology studies have been conducted to examine the relationship between dietary acrylamide exposure and cancer. In particular, in 2013 EFSA accepted a request from the European Commission to carry out a full assessment of the potential risks for human health of acrylamide in food. The Scientific Panel on Contaminants in the Food Chain of EFSA adopted on 19 April 2005 a statement on acrylamide in food in which it endorsed the risk assessment on acrylamide in food carried out by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in February 2005. In that assessment JECFA concluded that the margins of exposure for average and high consumers were low for a compound that is genotoxic and carcinogenic and that this may indicate a human health concern. On 3 May 2007 the European Commission adopted a Recommendation on the monitoring of acrylamide levels in food. This recommendation has been extended by Commission Recommendation 2010/307/EU of 2 June 2010. By December 2012 Member States are recommended to carry out investigations in cases where the levels of acrylamide in a foodstuff, tested in the

monitoring exercise, exceeds certain acrylamide indicative values. No US federal legislation limiting acrylamide currently exists.

4.5 Perchlorate

Current interest in the food analysis of perchlorate is primarily due to its presence as a contaminant in groundwater and drinking water. The negatively charged perchlorate ion (ClO_4^-) is composed of one chlorine atom surrounded by four oxygen atoms arranged in tetrahedral geometry.

The perchlorate anion commonly originates as a contaminant in the environment from the improper disposal of solid salts of ammonium, potassium, or sodium perchlorate. These salts are very soluble in water, and the perchlorate ion is kinetically inert to reduction and has little tendency to adsorb to mineral or organic surfaces. Therefore the perchlorate anion persists in groundwater, and its mobility in surface or groundwater is so high that perchlorate essentially moves with the flow of water. Compounds containing perchlorate are used as the primary ingredient of solid rocket propellant as well as that in fireworks, flares, airbags, and other applications where an energetic oxidant is required. A report on the occurrence of perchlorate in drinking water by the American Water Works Association indicates that perchlorate contamination is a national problem.

The presence of perchlorate in groundwater and drinking water is a potential health concern because perchlorate can impair proper functioning of the thyroid gland by interfering with iodide uptake. Impairment of the pituitary–hypothalamic–thyroid axis by perchlorate may lead to serious effects such as carcinogenicity, neuro-developmental and developmental changes, reproductive toxicity, and immunotoxicity [23]. Specific concerns relate to the exposures of infants, children, and pregnant women because the thyroid plays a major role in fetal and child development. Currently there are no US federal regulatory standards for perchlorate materials under the Clean Water Act (maximum contaminant level or discharge limits),

The 1996 amendments to the Safe Drinking Water Act required EPA (United States Environmental Protection Agency) to establish criteria for a monitoring program for unregulated contaminants which included perchlorate. EPA concluded in 1998 that it could not regulate perchlorate because the EPA lacked both a risk assessment and occurrence data.

California Office of Environmental Health Hazard Assessment has set a state Public Health Goal (PHG) for perchlorate of 6 ppb. This accounted for exposure from water, farm products and cow's milk. The PHG is only a goal, not a standard.

5. Packaging-derived chemicals

5.1 Bisphenol A

Bisphenol A (BPA) is the common name for 4,4-dihydroxy-2,2-diphenylpropane. BPA is a white solid (available in crystals or flakes) with a mild phenolic odour under ambient conditions. Chlorinated BPA can be found in both wastewater and drinking-water, as BPA can be easily chlorinated by sodium hypochlorite, a bleaching agent in paper factories and a

disinfection agent in sewage treatment plants, and chlorine, a chemical used in the disinfection of drinking-water.

Major application of BPA is in the production of polycarbonate plastics, a high performance transparent, rigid plastic, frequently used to produce food packaging materials such as plastic containers for food and drinks, baby bottles, and lining materials for food and beverage cans. Residues of BPA are also present in epoxy resins used to make protective coatings and linings for food and beverage cans and vats. BPA can migrate in small amounts into food and beverages stored in materials containing the substance.

Since BPA showed estrogenic properties in a large number of studies, it is described as an endocrine disruptor chemical. It is in particular able to bind and activate the human estrogen receptor. Moreover, BPA has been shown to interact with other endocrine receptors, e.g., thyroid hormone receptors, peroxysome proliferator-activated receptor gamma [24,25].

EFSA completed its full risk assessment of BPA in 2006 and set a Tolerable Daily Intake (TDI) of 0.05 milligrams/kilogram of body weight (mg/kg bw/day) for this substance. The TDI is an estimate of the amount of a substance, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable risk. At the same time, EFSA also evaluated intakes of BPA through food and drink, for adults, infants and children and found that they were all below the TDI. EFSA reviewed new scientific information on BPA in 2008, 2009, 2010 and 2011: On 24 April 2012, EFSA announced that it has started work on a new risk assessment of BPA used in food contact materials (such as packaging and containers, kitchen equipment, cutlery and dishes), focusing specifically on its exposure to vulnerable groups. BPA is permitted for use in food contact materials in the European Union (EU) under Regulation 10/2011/EU, relating to plastic materials and articles intending to come into contact with foodstuffs. In January 2011, the European Commission adopted Directive 2011/8/EU, prohibiting the use of BPA for the manufacture of polycarbonate infant feeding bottles. In July 2013, EFSA launched a public consultation on the first part of its draft scientific opinion, specifically on its assessment of consumer exposure to BPA. All stakeholders and interested parties will be able to provide their comments on the draft exposure assessment before the end of 2013.

5.2 Semicarbazide

Semicarbazide (SEM) is considered to be a characteristic protein-bound side-chain metabolite of the banned veterinary drug nitrofurazone. It is therefore used as a marker for nitrofurazone abuse. The presence of SEM in foods, including baby foods, fruit juices, jams and preserves, preserved in jars and glass bottles, initially discovered by the industry, is due to the degradation of azodicarbonamide, the foaming agent present in the plastic gaskets used to seal the lids metal with glass packaging. Limited toxicological data are available for semicarbazide. SEM has been shown to be carcinogenic in mice, but not rats. Literature data on genotoxicity together with the results of recent studies indicate that SEM is mutagenic but not clastogenic in some test systems *in vitro*. *In vivo*, negative results were reported in studies on DNA damage in liver and lung of mice [26]. From 2005, the EU directive 2004/1/EC prohibits the use of azodicarbonamide in any materials that may come into contact with food.

6. Determination by analytical methods

The rapid and reliable detection methods of chemical contaminants are extremely important in managing the safety of food.

Developments in analytical techniques have led to the emergence of a wide range of rapid methods to complement the traditional methods that have some typical drawbacks which include: high costs of implementation, long time of analysis and low samples throughput, and the need for highqualified manpower.

The availability of fast, reliable and simple to use detecting tools for food commodities is therefore a target both for the safeguard of customer's health and production improvement.

Methods of analysis with high sensitivity and accuracy to meet the regulatory requirements that provide qualitative or semiquantitative results for many chemical and microbiological applications are now available.

A large variety of analytical approaches are used, often with diverse aims and using complementary technologies.

Bioanalytical methods such as immunoassays, immunosensors, and immunoaffinity chromatography are providing information regarding the presence and concentration of contaminants that may impact human health and the environment [27].

Chromatography technics combined on line with mass spectrometry is among the most sensitive and selective analytical methodologies. The most significant development of recent years has been the integration of ultra-high pressure liquid chromatography (UHPLC), coupled to tandem mass spectrometry (MS/MS), in the field of food contaminant analysis. Selectivity is of prime advantage; while sensitivity is a key issue to identify trace components [28].

Other technologies have also been shown to identify potentially food contaminants. Some examples of use of nuclear magnetic resonance are reported in literature [29,30]. Near-infrared analysis with chemometric data analysis is being used in the food industry as a quality assurance tool, and this technology has been expanded to monitor for food adulteration.

7. Conclusions

Food security aims to protect human health and the interests of consumers while ensuring the orderly functioning of the market. The application of advanced technologies to food contaminants and residues has made possible the analysis of broader range of compounds with higher sensitivity, selectivity and specificity. Consequently, a modern analytical approach permitted more comprehensive assessment of food safety with the determination of trace level in accordance with international rules and legislation.

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