


A perspective on the potential risks of emerging contaminants to human and environmental health

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Abstract Technological, agricultural, and medical advances have improved the lifestyle of humankind. However, these advances have caused new problems that affect the environment and future generations. Emerging contaminants display properties such as low degradation potential and environmental persistence. In addition, most contaminants are lipophilic, which culminates in high bioaccumulation. The disposal of pharmaceuticals and personal care products into the environment underlies microbial and bacterial resistance. Plasticizers change several characteristics of industrialized materials, such as flexibility, but they are potentially carcinogenic and disrupt the endocrine system. Pesticides prevent the propagation of numerous kinds of pests; nevertheless, they exert neurotoxic and mutagenic effects, and they impact the environment negatively. Addition of flame retardants to a number of materials prevents flame propagation; however, after their release into the environment, these chemicals may bioaccumulate in organisms and disrupt the endocrine system, too. Surfactants can change the surface and interfacial properties of liquids,

but their presence in the environment can interfere with countless enzymes and can even impair the endocrine system of various organisms and induce the feminization of species. Hence, gaining knowledge about emerging contaminants is increasingly important to minimize future damage and enable proper monitoring of each class of compounds in the environment which will help to improve legislation on this matter.

Keywords Pharmaceuticals · Plasticizers · Pesticides · Flame retardants · Surfactants · Nanomaterials

Introduction

The environment consists of the surroundings where the body is, including air, water, land, natural resources, flora, fauna, humans, and their interrelation. In recent decades, environmental problems have become critical and frequent. Population growth has called attention for increasing human action and industrial development, and the need to meet the demands of the modern world has culminated in catastrophic consequences to the environment. Indeed, the continuous release of chemicals seen in recent decades can induce acute toxicity, and the bioaccumulation and biomagnification of contaminants can give rise to undesirable long-term effects, as represented in Fig. 1 (Kunz et al. 2002; Logar and Vodovnik 2007).

Public concern about the dangers that chemicals cause to the environment, humans, and animals started to arise in 1962, when Rachel Carson published the book entitled *Silent Spring*. This milestone raised public awareness of the impact of chemicals on wildlife and reproduction. Earlier, this impact originated mainly from chlorinated hydrocarbons, i.e., the PCB family of compounds, which included the pesticide dichlorodiphenyltrichloroethane (DDT). Recently, researchers have focused on a number of consumer products that can

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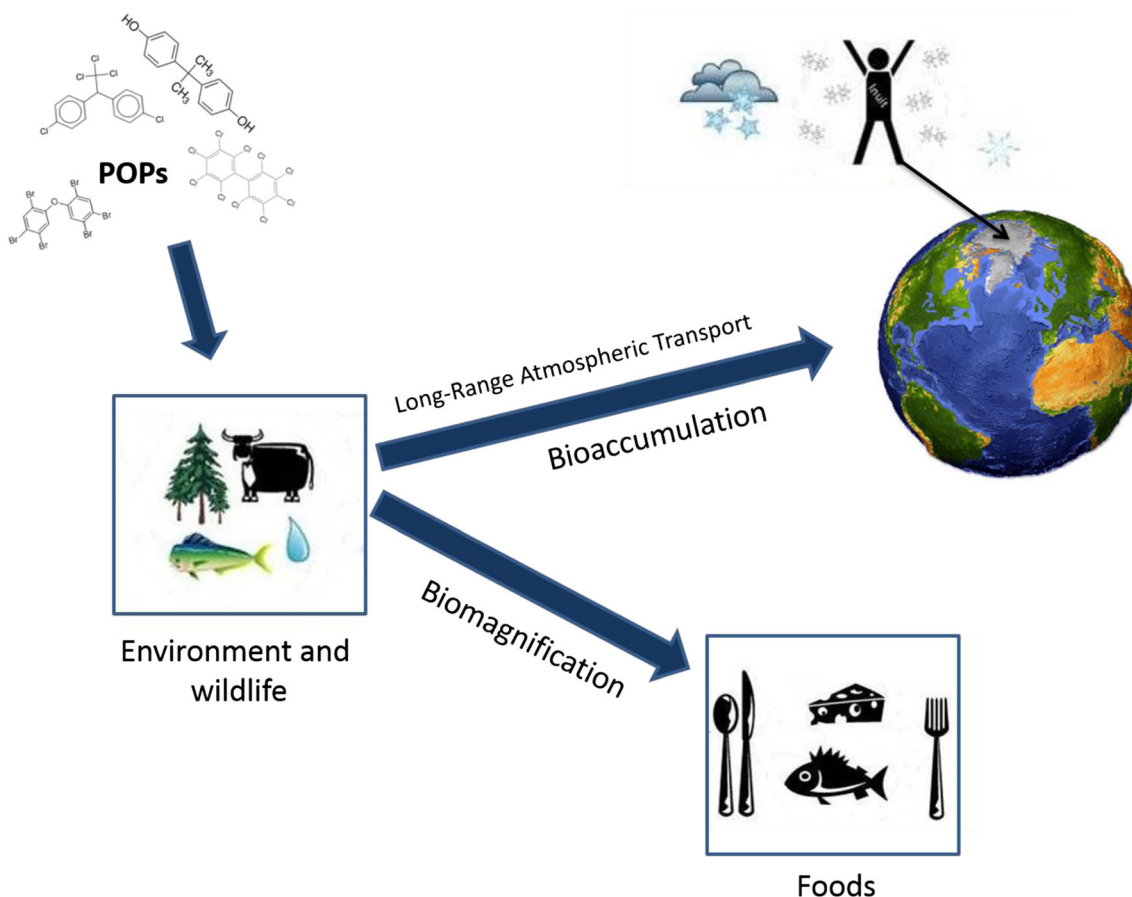


Fig. 1 The diverse persistent organic pollutants (POPs) released into the environment may bioaccumulate and exert toxic effects on animals and humans. Moreover, they can reach regions far apart from their initial

production, even affecting the Inuit population through bioaccumulation. They can also biomagnify and impact different trophic levels of the food chain

interfere in the endocrine system (Rosner and Markowitz 2013). Endocrine disruptors are exogenous substances that alter the functions of the endocrine system and adversely affect the health, growth, reproduction, and progeny of organisms, even at concentrations in the order of *microgram* and *nanogram* per liter (Bila and Dezotti 2003). This class of compounds can mimic, antagonize, or modify the levels of endogenous hormones by altering their synthesis, metabolism, expression, transport, or action. Unfortunately, discussions on this topic go against industrial interests, even though Henry F. Smyth Union clearly stated the responsibilities of industries in his statement in 1946: “it is the duty of the brake manufacturer to produce a chemical with well-known health risks” (Smyth 1946).

When DDT and other chlorinated hydrocarbons came into general use in the 1940s and 1950s, scientific evidence pointed to the chronic toxicity of chlorinated hydrocarbons in animals and humans. In general, authors noted that this class of chemicals accumulated in fat tissue and existed in the milk of lactating animals, and many researchers mentioned the possibility of chronic poisoning. Fitzhugh and Nelson reported the chronic oral toxicity of DDT in their study on rats fed with

diets containing DDT from 100 to 800 ppm for a period of 2 years. These authors found that DDT produced chronic toxicity in the animals at all the concentrations. Their experiment concluded that chronic poisoning with small amounts of DDT elicited degenerative changes in rat liver as well as other organs (Fitzhugh and Nelson 1947).

According to recent estimates, the society currently uses about 100,000 compounds. Over 40,000 of these compounds have been identified as persistent organic pollutants. This number becomes even more worrying when one considers technological advances and the rampant discharge of these pollutants into the environment (Ginebreda et al. 2012a, b; Rodil et al. 2012). The US Environmental Protection Agency defines “emerging contaminant” as a chemical or material with perceived, potential, or real threat to the human health or the environment or for which published health standards are lacking (USEPA 2008). Emerging contaminants include a long list of routinely employed products such as pharmaceuticals, cosmetics, plasticizers, and flame retardants, among others. This list has grown rapidly in recent years, to include an array of compounds with reported presence in the environment. Immune toxicity, neurotoxicity, endocrine disruption,

and carcinogenicity are among the consequences of exposure to these contaminants (Balducci et al. 2012).

Several experimental models such as different organisms, cells, and/or organelles can serve as “analytical devices” can help to assess how pollutants affect the environment. The biological response of tested organisms after exposure to these substances may provide data on the toxicity, genotoxicity, and estrogenicity of a compound or even aid identification of the biomarkers of exposure or of the compounds that become toxic only after bioactivation (Rand 1995; Pereira et al. 2012; Bandele et al. 2012). The toxicity of environmental pollutants relates not only to the chemical structure of the pollutant but also to the characteristics of each compartment that receives the pollutant (soil, sediment, air, surface water, and groundwater), the nature and the physical and chemical properties of these compounds (solubility, volatility, biodegradation, and adsorption properties), and biological targets (fish, birds, and humans, among others) (de Oliveira et al. 2013).

In this scenario, this review addresses relevant characteristics and summarizes the data that is available on the sources and toxicity of compounds considered as emerging pollutants. Despite not being exhaustive, this review describes state-of-the-art knowledge about emerging environmental contaminants and highlights their known toxic effects on human and environmental health.

Pharmaceuticals and personal care products

General information

The impact of pharmaceuticals and personal care products (PPCPs) on the environment is a hot topic. Numerous research works have reported that drug residues occur in the environment worldwide, mainly in water resources. Table 1 summarizes some examples of drug residues and their main effects on human health and other organism. Environmental contamination due to PPCPs may occur due to improper disposal of prescription drugs, cosmetics, and veterinary antibiotics (Zuccato et al. 2005; Jjemba 2008), which continuously enter the environment.

Initially, several researchers reported on the presence of clofibrac acid, a breakdown product of many blood lipid regulators and salicylic acid, in the environment (USEPA 2008). Advances in technology and analytical techniques have contributed to the identification and quantification of a large number of pharmaceutical compounds in ambient water, wastewater, and drinking water (Collier 2007; USEPA 2008). Scientists have sought to monitor these pharmaceuticals because they often contain chemicals such as sulfamethazine, diclofenac, ibuprofen, salicylic acid, carbamazepine, propranolol, fluoxetine (Collier 2007; Drewes et al. 2007),

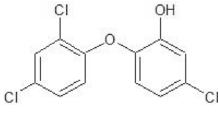
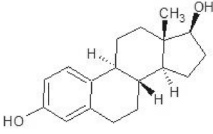
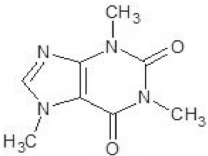
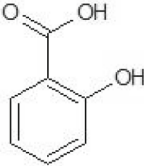
bezafibrate, sulfamethoxazole, iopamidol (Zwiener and Frimmel 2004), trimethoprim, sulfamethoxazole, and diazepam (Madureira et al. 2010). Many studies have also indicated that natural hormones like estrones, 17 β -estradiol, and the synthetic hormone 17 α -ethinyl estradiol, the main active substance of oral contraceptives, exist in waters (Pessoa et al. 2012). Early studies on the occurrence of estrogens excreted by human involved assessment of sewage treatment plants in England. The main finding was that the hormone 17 β -estradiol stimulated feminization of male fish with consequent production of vitellogenin (Fent et al. 2005; Lopes et al. 2010).

Countless pharmaceuticals undergo biological degradation to active metabolites that still require evaluation. Because these pharmaceuticals exert negative effects on humans and/or aquatic organisms, are difficult to decompose, and can spread and contaminate soil and water (Milic et al. 2013; Olofsson et al. 2013; de Lorenzo and Fleming 2008), they constitute emerging pollutants (Olofsson et al. 2013).

Despite having short half-lives, many PPCPs can persist in the environment due to their continual disposal and release into aquatic ecosystems (Jasim et al. 2006). Even after being metabolized by the human organism and animals, drugs and metabolites can still be excreted into the environment, to reach the sewage. Besides the fact that PPCPs display the characteristics of persistent organic pollutants (POPs), sewage treatment stations (STPs) may not be able to remove them completely (Stumpf et al. 1999). According to Rahman et al. (2009), some important properties like water solubility, adsorption coefficient ($\log K_{OC}$), bioconcentration ($\log K_{OW}$), and Henry's law constant decide the fate and behavior of PPCPs. These properties can also define whether these compounds sediment or associate with biota (Birkett and Lester 2003). Moreover, PPCPs are biologically active and not readily biodegradable (Kummerer 2001). Finally, the ability of these compounds to interact with particles in the environment can also determine their fate (natural clays, sediments, colloids, and microorganisms, among others) (Filali-Meknassi et al. 2004).

Although wastewater treatment efficiently removes impurities from effluents, ensuring total removal of toiletries and pharmaceutical waste from wastewater is not possible (Mitjans and Ventura 2005). In addition, the presence of contaminants in drinking water reveals that the methods used to treat water are flawed (Ternes et al. 1999). The commonest preservatives in cosmetics, skin creams, tanning lotions, and hygiene products are parabens alkyl-*p*-hydroxybenzoates, which display estrogenic activity. The use of the antiseptic agent triclosan is also widespread. In fact, triclosan has been incorporated in formulations for at least 30 years, being part of the formulation of various products, like soaps, cream, and shoe insoles. This compound can be discharged into sewage systems (Daughton and Ternes 1999).

Table 1 Data summary for the main PPCPs detected in environmental samples

Emerging contaminant	Structure	Physical and chemical properties	Known effects to organisms	References
triclosan [5-chloro-2-(2,4-dichlorophenoxy)]		The poor solubility and high value of log K_{ow} (4.76) presented by triclosan suggest high potential for bioaccumulation in sewage sludge. This chemical is non-volatile (5.3×10^{-4} Pa at 20 °C)	Microbial resistance, dermal irritations, and endocrine disruption in human and mice. Acute toxicity values range from 1.4 to 3,000 $\mu\text{g L}^{-1}$ (<i>Daphnia magna</i> , <i>Chironomus tentans</i> , <i>Pimephales promelas</i>).	Dhillon et al. (2015), Kumar et al. (2009)
17 β -Estradiol		This compound is used as benzoate and palmitate esters of estradiol. The body hydrolyzes them to 17 β -estradiol.	Disruption of fish population dynamics and endocrine system at low concentrations. A single exposure is enough to disrupt the development of brown trout. Potential formation of complexes with nucleic acids.	Kunz et al. (2014), Schuberts et al. (2014), Heger et al. (2014), Casey et al. (2013)
Caffeine		Caffeine has density of 1.2g/cm ³ , volatility of 0.5%, and vapor pressure of 101 kPa at 178 °C. It is soluble in water and organic solvents.	Decrease in HepaRG cell viability after oral or dermal administration of caffeine. Evaluation in Sprague-Dawley rats, Wistar rats, and female adult rhesus monkeys showed that caffeine did not induce carcinogenicity or changes in fertility, reproduction, or lactation.	Agyemang-Yeboah Oppong (2013), Gajewska et al. (2015), IARC (1991)
Salicylic acid		Salicylic acid occurs as colorless or white needle-like crystals or white crystalline powder; it is odorless or almost odorless. It is soluble in water and organic solvents.	Dose-dependent increase in the incidence of upper gastrointestinal toxicity. Impact on the gastric mucosa, with possible irritation, ulceration, and bleeding in the stomach.	IARC (1997)

Occurrence and course in the environment

Several studies have investigated the occurrence of pharmaceuticals in the aquatic environment. Results have revealed the presence of estrogenic hormones and industrial chemicals in surface water and groundwater in Austria, for example

(Hohenblum et al. 2004). In the Billings dam in Sao Paulo, Brazil, a study conducted in 2005 detected the substances diclofenac, ibuprofen, and caffeine (Almeida and Weber 2005). According to Heberer (2002), over 80 compounds of various classes of existing drugs have been detected in reclaimed wastewater, surface and ground water, sludge,

agricultural soils, aquatic and terrestrial biota, and raw and finished drinking water (De Lorenzo and Fleming 2008; Kumar and Xagorarakis 2010; Hedges et al. 2012; Bondarenko et al. 2012).

Among a wide variety of pharmaceuticals, antibiotics have gained special significance for their extensive application in human therapy and veterinary medicine. They also promote the growth of animals in livestock production. Concern about the presence of pharmaceutical residues in the environment is associated with their potential role in the widespread resistance of bacterial pathogens and post-therapeutic effects (Xu et al. 2007). The occurrence of drug residues in the environment could escalate their adverse effects on aquatic and terrestrial organisms and their levels in cells, organisms, and populations (Bila and Dezotti 2003).

A significant amount of PPCPs and their metabolites are excreted in urine, feces, or manure. They may undergo biodegradation or partial degradation or even occur in their original form. They can enter water through flushing of unused medications down the toilet or sink, excretion of unabsorbed medications into the sewage system, excretion of veterinary drugs into fields by farm animals, and improper commercial disposal methods (Richardson and Bowron 1985; USEPA 2008). In addition, the female body excretes natural estrogens (estrone, estradiol, and 17β -estradiol). Even though these estrogens are inactive when conjugated to glucuronic acid, fecal coliforms present in water bodies can activate them (D'Ascenzo et al. 2003; Lopes et al. 2010).

In 1997, in the state of Rio de Janeiro, Brazil, authors detected antilipemics, anti-inflammatories, and some metabolites in the effluent of wastewater treatment plants and river waters (Stumpf et al. 1999). Another study published in the same year identified natural estrogens and synthetic contraceptives, such as 17β -estradiol, 17α -ethinyl estradiol, and estrone, in sewage treatment plants (Ternes et al. 1999). Some studies noted the presence of contaminating substances in five points of the Tama River, Japan, including ethinyl estradiol, estrone, and 17β -estradiol. 17β -Estradiol and estrone also emerged in water samples in Austria. Synthetic hormones like 17α -ethinyl estradiol and natural hormones like 17β -estradiol were some of the organic contaminants that prevailed in surface waters of the USA (Kolpin et al. 2002; Bursch et al. 2004; Furuichi et al. 2009).

Toxicity

Although the measured concentrations of PPCPs in the environment were low, for example, in the order of 5 μg of ciprofloxacin per liter (5 $\mu\text{g}/\text{L}$) and 500 ng of diclofenac per liter (500 ng/L), the extent to which these compounds may pose a risk to human health is unclear. Therefore, further studies on toxicity level and antibiotic resistance, among other issues, after long-term exposure to these contaminants are essential.

Additional investigations into bioaccumulation and cumulative or synergistic effects of pharmaceutical compounds are also welcome (Lopes-Serna et al. 2012; Parrot 2007; Collier 2007).

Researchers have collected some ecotoxicological data to identify drugs that are potentially hazardous to the environment, but the currently available data are not sufficient. Scientists have usually evaluated the toxic effects of residual drugs on aquatic biota (Bila and Dezotti 2003). Migliore et al. (1998) investigated the effects of sulfonamide antibiotics on plant species; they observed how these antibiotics modified plant development modified modification of microbial and bacterial resistance (Migliore et al. 1998).

Exposure to PPCPs, classified as compounds that disrupt the endocrine system, can result from a chronic dose rather than bioaccumulation, which makes them toxic to the receptor organism (CEC 1999). Larsson et al. (2000) noted these effects in their study on fish species such as *Cyprinus carpio*, *Rutilus rutilus*, and *Oryzias latipes*; these authors detected increased synthesis of vitellogenin, a protein related to the development of ova and regulated by estrogen. The occurrence of such chemicals in the aquatic environment probably impairs reproduction and elicits sexual anomalies. Exposure to estrogens can also cause fish feminization during sexual differentiation (Bila and Dezotti 2003). However, all the consequences of the presence of estrogens in aquatic organisms still need unveiling (Bila and Dezotti 2003; Rahman and Brazel 2006).

Plasticizers

General information

Plasticizers are organic compounds of low molecular weight; their addition to polymeric materials allows for efficient plastic processing and formulation. Plasticizers enable the fabrication of a wide variety of plastics, and they have found multiple applications in areas such as the automobile industry, medical products, and commodities. The production of plasticizers has reached 100,000,000 t/year, as a result of the great demand by the plastic industry (Yan et al. 2010).

There are many types of plasticizers: phthalates, phosphates, adipates, benzoates, trimellitates, esters of sulfonic acids, sulfonamides, and elastomers, among others (Wypych 2004; Rahman and Brazel 2006). Phthalic acid esters (phthalate) (Viecilli et al. 2011) such as di-(2-ethylhexyl) phthalate (DEHP), diethyl phthalate (DEP), and dibutyl phthalate (DBP) are the most often employed; they exist in medicines, perfumes, nail polish, shampoos and lotions, paints, and adhesives for printers (Gómez-Hens and Aguilar-Caballeros 2003; Andrady and Neal 2009). However, phthalates

exhibit adverse effects on human and organisms, as summarized in Table 2.

Bisphenol A (BPA) is another widely used plasticizer. The production of this monomer is primarily intended for the manufacture of polycarbonate plastic and the synthesis of epoxy resins. Polycarbonates have also found application in consumer electronics, automotive equipment, food packaging, plastic bottles, and water bottles (CEC 1999). Epoxy resins are employed in coatings for beverage and food cans, pharmaceutical packaging, adhesives, and dental sealants (Andrady and Neal 2009).

According to the Environmental Protection Agency of the USA and some of its international counterparts, most plasticizers constitute priority organic pollutants (Birkett and Lester 2003; Chang et al. 2007). They can also act as endocrine disruptors by negatively impacting the hormonal system of animals and humans (Nagel and Bromfield 2013).

According to Horn et al. (2004), plasticizers consist of clear, colorless, oily liquids. Plasticizer incorporation into a material increases flexibility, or distensibility, facilitating material handling. Plasticizers can reduce the viscosity, lower the temperature of the second-order transition, or reduce the elastic modulus of the final product (Horn et al. 2004; Biermann et al. 2012). In some cases, plasticizers provide transparent materials that are highly resistant to heat and chemicals (Simmchen et al. 2012).

Because plasticizers have relatively low molecular weight, they easily spread around the environment (water, foods, etc.). Some plasticizers contain a high amount of fat; as a result of their lipophilic nature, they display high mobility and pass through natural barriers such as the skin, lung, and gut tissues without difficulty (Yan et al. 2010; Simmchen et al. 2012). Factors like temperature, plasticizer concentration, and other characteristics (solubility and diffusion coefficient) commonly influence plasticizers leaching and migration (Wypych 2004; Rahman and Brazel 2006; Goulas et al. 2007).

Occurrence and course in the environment

Nearly 25 years ago, the presence of plasticizers in the environment was already a matter of concern (Wams 1987). Numerous studies have identified phthalates in soils (Bauer and Herrmann 1997; Cartwright et al. 2000; Fries and Mihajlovic 2011), surface water (Taylor et al. 1981; Horn et al. 2004), indoor air (Butte et al. 2001; Becker et al. 2004), and the atmosphere (Thuren and Larsson 1990). DEHP, DEP, DBP, and BPA are the plasticizers that commonly arise in the environment (Quan et al. 2006).

Understanding the potential environmental pathways followed by plasticizers may aid proper management of

their production and use, to ensure health and environmental safety. Plasticizers enter the environment not only through loss during production and distribution but also by leaching from the finished product or through ineffective wastewater treatment (Matamoros et al. 2012). Plasticizers like phthalates do not chemically bind to the polymer matrix, which culminates in their facile release into the environment as well as animal and human exposure to these contaminants (Zimmer et al. 2012).

The main routes through which plasticizers enter the environment are direct transfer (building materials), urban runoff, emission by industries and deposition in atmospheric air, deterioration of water supply and sewage pipes, solid waste disposal (from which plasticizers leach into landfills), industrial activities, wastewater and sewage treatment plants (effluent discharge, waste disposal activities like incineration, waste discharge into landfills), and application of fertilizers (Liu et al. 2009; Wagner and Oehlmann 2009; Yan et al. 2010).

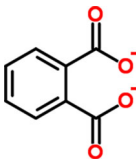
The widespread use of plasticizers makes human exposure to these compounds and their release into the environment unavoidable. Both biotic and abiotic factors, such as adsorption and volatilization of organic matter in aquatic and terrestrial systems, influence environmental contamination with these substances (Yan et al. 2010). Plasticizers may undergo degradation by aerobic and anaerobic organisms, but their adsorption onto particles slows the degradation rate. Plasticizers may adsorb onto soil and sediments and spread through the terrestrial environment, which will depend on their carbon content (Yan et al. 2010).

Toxicity

Some plasticizers are potential disruptors of the endocrine system (Arcadi et al. 1998; Mlynarciková et al. 2005; Robinson and Hellou 2009; López-Casas et al. 2012). One of such endocrine disruptors, BPA, is one of the most often used plasticizers worldwide. It accounts for several endocrine disorders in multiple systems, such as changes in salivary glands (Folia et al. 2013), thyroid, and the male reproductive system (Zhou et al. 2013). BPA is also neurotoxic (Kundakovic et al. 2013) and impairs cell division as well as plant growth (Adamakis et al. 2013).

Most tissues contain enzymes that can hydrolyze the diester to its monoester mono-(2-ethylhexyl) phthalate (MEHP), whereas complete hydrolysis seems to require enzymes present in phase I biotransformation in the liver. This metabolism generates other metabolites such as mono-(2-ethyl-5-hydroxy) phthalate, mono-(2-ethyl-5-oxo-hexyl) phthalate, mono-(2-ethyl-5-carboxypentyl) phthalate, and mono-(2-carboxymethylhexyl) phthalate. According to the results of

Table 2 Physical and chemical properties of plasticizers and data on their biological effects

Emerging contaminant	Structure	Physical and chemical properties	Biological effects	References
Phthalates		<p>Phthalates have a clear syrupy liquid consistency, low volatility, low water solubility, and high oil solubility. They consist of colorless and odorless liquids.</p> <p>Phthalates usually bear a 4-13 carbon, which originates from esterification of 2 mol of monohydric alcohol with 1 mole of phthalic anhydride.</p>	<p>Teratogenic effects, endocrine disruption (especially in sexual organs) and hepatocellular carcinomas in rodents.</p> <p>ROS production, apoptosis, and changes in gene expression, mainly in the case of genes linked to brain development, as attested by assays on cell culture treated with phthalates.</p> <p>Adverse effects on fetal health after crossing of the placental barrier and alterations in the endocrine function.</p> <p>Insidious behavioral effects in adulthood in the case of both animals and humans.</p>	<p>Rosado-Berrios et al. (2011), Gallinger and Nguyen, (2013), Benjamin et al. (2015), Rosenfeld, (2015), Martinez-Arguelles and Papadopoulos, (2015),</p>

Horn et al. (2004), these metabolites are more toxic than their parent compounds (Horn et al. 2004). Glucuronidation facilitates their removal from the body. In this way, the body excretes most of the adsorbed DEHP within 24 h, avoiding its accumulation in the tissues. In children, particularly infants, metabolism is not mature, so glucuronidation and excretion are lower at the same time that MEHP hydrolysis increases. The latter situation is especially problematic because DEHP toxicity stems from its conversion into MEHP (Albro and Thomas 1973; Kluwe 1982; Garcia et al. 2002; Simmchen et al. 2012).

In rats and mice, both DEHP and MEHP produce toxic effects in the liver, kidneys, and testicles. Reports on carcinogenicity and reproductive toxicity also exist (Rossi and Schettler 2000; Tickner et al. 2001).

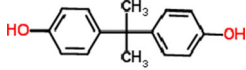
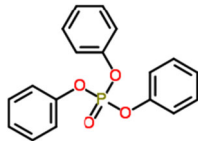
Pesticides

General information

According to the Environmental Protection Agency of the USA, pesticides constitute any substance or mixture of substances that can prevent, destroy, repel, or mitigate a pest (USEPA 2007). In addition, the Food and Agriculture Organization of the United Nations says that the term pesticide also covers substances used to control disease vectors in humans or animals, regulate plant growth, and maintain the ideal conditions for the use of vegetation (FAO 2012).

The classification of pesticides relies on the pattern of use and the pests they combat. In the latter case, the main classes are insecticides, herbicides, fungicides, and

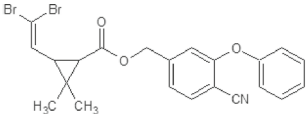
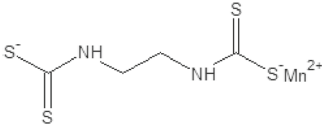
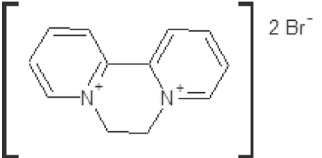
Table 2 (continued)

<p>Bisphenol A (BPA)</p>		<p>BPA is a white solid (powder or flake), with a mild phenolic odor. It is soluble in organic solvents and has low water solubility. It consists of two phenolic rings connected by a bridging group originating from the reaction of phenol with acetone.</p>	<p>Endocrine disruption and adverse effects on immune, reproductive, renal, cardiovascular, and nervous systems, in both animals and humans.</p> <p>Cytotoxicity, oxidative stress, lipoperoxidation, mutagenicity, and hepatotoxicity.</p> <p>Possible teratogenic and carcinogenic effects.</p> <p>Clear negative effects on embryonic and infant development.</p> <p>Insidious behavioral effects after early exposure of animal and humans.</p>	<p>Hassan et al. (2012), Gowder (2013), Michałowicz (2014), Srivastava et al. (2015), Rosenfeld (2015)</p>
<p>Triphenyl phosphate</p>		<p>Triphenyl phosphate is a colorless, crystalline powder with a phenol-like odor. It has high volatility, low water solubility, moderate ethanol solubility, and good solubility in organic solvents.</p>	<p>Low toxicity. Toxicological data on the effects of using triphenyl phosphate as plasticizer and flame retardant on humans are inconclusive.</p> <p>Toxic effects on aquatic ecosystems, as revealed by laboratory assays on fish, shrimps, daphnia, and algae, with consequent endocrine disruption.</p>	<p>Lassen and Lokke (1999), van der Veen and de Boer (2012), Kim et al. (2015)</p>

rodenticides (USEPA 2007; Nougadère et al. 2012). Grouping many compounds on the basis of similarities in their chemical structures is possible (Alonzo and Corrêa 2003), e.g., organochlorines (including aldrin and DDT), organophosphates (diazinon and malathion), carbamates (carbaryl and propoxur), pyrethrins and pyrethroids (tefluthrin), triazines (atrazine), phenoxyacid (2,4-

dichlorophenoxyacetic acid), chloroacetanilides, also called chloroacetamides (metolachlor and alachlor), and phenylureas (diuron) (Barr 2008). Organochlorines, organophosphorus, and pyrethroids (which are synthetic analogues of pyrethrins) serve mainly as insecticides, acaricides, or nematicides. Table 3 lists some data and peculiar characteristics for some compounds of these classes.

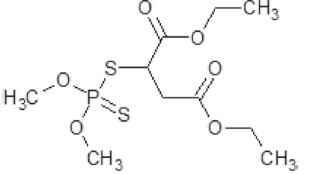
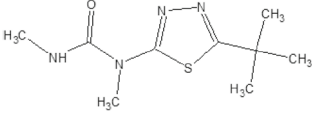
Table 3 Data and characteristics of the main classes of pesticides

Pyrethroids and pyrethrins (Deltamethrin)		Both pyrethroids and pyrethrins bear an acid moiety, a central ester bond, and an alcohol moiety in their structure. Generally, they have low vapor pressures, low Henry's law constants, and large octanol/water coefficients ()	Accumulation in aquatic ecosystems and negative effects on aquatic organisms like invertebrates and fish.	Pérez-Fernández et al. (2010), Bjorling-Poulsen (2008),
Dithiocarbamates (Maneb)		The properties of dithiocarbamates can vary depending on their structure. The two main examples of this class, Maneb and Zineb, are soluble in water and slightly soluble in water, respectively.	Toxicity to aquatic organisms. Induction of thyroid cancer, modification of thyroid hormones, and inhibition of acetaldehyde dehydrogenase	Van Wezel and Van Vlaardingen (2004), Belpoggi et al. (2006)
Dipyridyl derivatives (Diquat dibromide)		Diquat, for example, is a dipyridylium quaternary ammonium salt that is practically nonvolatile, has a vapor pressure lower than 0.013 mPa, and is soluble in water.	Necrosis in the gastrointestinal tract, kidney tubules, liver, and lung upon oxidative stress.	Krieger (2001), Ronnen et al. (1995)
Organophosphorus (Malathion)		The properties of organophosphorus vary depending on	Muscarinic syndrome and nicotine syndrome as a result	Ellenhorn, Barceloux, 1998; Barr, Needham

The use of pesticides has provided many public benefits. For example, food supply has become safer and more plentiful, and the occurrence of vector-borne disease has diminished (Barr and Needham 2002; Cooper and Dobson 2007; Pacioni and Veglia 2007). Unfortunately, because

pesticides are stable in the environment, they bioaccumulate, and the excessive use of these substances can easily cause poisoning through various toxicity mechanisms (Fenik et al. 2011). The widespread application of pesticides contaminates the soil, air, and water, as well as

Table 3 (continued)

		<p>size and structure. In general, all the organic compounds containing phosphorus are more soluble in organic solvents than water.</p>	<p>of the establishment of covalent bonds between organophosphorus and the serine residue in the active site of acetyl cholinesterase (reversibly or irreversibly), to afford excess acetylcholine in organisms.</p>	<p>2002.</p>
<p>Phenylureas (Tebuthiuron)</p>		<p>Phenylureas are stable upon exposure to light. Phenylureas have low vapor pressure and log K_{ow}, which indicate that they are non-volatile and relatively hydrophilic, respectively. Due to their water solubility, relatively strong persistence, and low absorption in soil particles, phenylureas like tebuthiuron can reach aquatic environments.</p>	<p>Increased phase I biotransformation enzymes in small and larger fish, with increased production of reactive intermediates. Genotoxicity in small fish.</p>	<p>Caux et al. (1997), Franco-Bernardes et al. (2014)</p>

fruits and vegetables, which increases the human vulnerability to contamination and may even affect the fauna and flora (Pimentel 2005; Fenik et al. 2011; Hernández et al. 2013). In addition, the synergies between pesticides are worrisome. Understanding the fate and occurrence of these compounds, mainly at low levels, requires analytical methods with much lower detection limits than traditional methods (Pacioni and Veglia 2007; Andreu and Picó 2012).

Physical and chemical properties can vary depending on the chemical characteristics of the compounds. Organochlorines are persistent pesticides belonging to the group of POPs: they have long environmental half-lives and tend to bioaccumulate in the food chain. They are liposoluble, have low volatility, and may spread to various places via exposed animals or physicochemical processes (Borga et al. 2001;

Alonzo and Corrêa 2003; Barr 2008; Andreu and Picó 2012). In general, organophosphates, carbamates, synthetic pyrethroids, triazines, phenoxyacid, and chloroacetanilides, among others, are considered nonpersistent. Most decompose within several weeks under exposure to sunlight and water, so they do not tend to bioaccumulate, except in cases of unfavorable degradation conditions. However, extensive use of these products has culminated in constant human exposure to pesticides via domestic use or the food chain (Barr 2008; Andreu and Picó 2012).

Occurrence and course in the environment

Organisms may take up pesticides through ingestion of food and water, inhalation, and contact with the skin or exoskeleton (Van Der Werf 1996; Hernández et al. 2013). Geographical

location also influences exposure to pesticides. As a result of crop spraying, pesticide detection prevails in rural residents as compared with inhabitants of urban zones. Pesticide concentrations found in rural residents are also higher (Mckinlay et al. 2008).

Most pesticides are often applied as mixtures to crops. Because they are either directly applied to the soil or sprayed onto crops, they are directly released into the environment (Biziuk et al. 1996; Hernández et al. 2013). Their application in the liquid form contaminates the environment more than their application as powder (Fenik et al. 2011). Rain and wind transport the applied pesticides to the surroundings. The quantities found in a given region usually reflect the intensity and frequency of pesticide use (Biziuk et al. 1996; Fenik et al. 2011). The persistence of pesticides in the soil will largely depend on the physical and/or chemical reactions that they undergo with other substances and microorganisms present in the soil, which should culminate in different environmental behavior. Relatively degradation-resistant and water-soluble pesticides can be transported to water bodies, where they have been found in significant amounts (Konstantinou et al. 2006). Pesticides can come into direct contact with water upon their application to control aquatic plants in the environment. They can also reach water indirectly through draining of agricultural land, soil permeation, and water and waste discharge into water bodies (Biziuk et al. 1996; Guzzella et al. 2006). In surface waters, pesticides can travel long distances, leading to extensive contamination (Yan et al. 2010).

Toxicity

Solvent constituents favor the absorption of pesticides, regardless of their structure (Alonzo and Corrêa 2003). Human exposure to pesticides results in a series of health problems, which range from irritation to serious diseases that may ultimately lead to death (Simonelli et al. 2007).

Pesticides are generally highly soluble, and organisms can absorb them by various routes. After absorption, these compounds are rapidly distributed throughout the body, to undergo biotransformation reactions (Ecobichon 1996; Timchalk 2006). The US Environmental Protection Agency has already issued a document demonstrating that some of these compounds can act as endocrine disruptors, to modify the levels of hormones (USEPA 2006; Ji et al. 2008).

Poisoning by pesticides directly alters the endocrine system (Colburn et al. 1993; Ji et al. 2008; Mckinlay et al. 2008; Yan et al. 2010). Occupational exposure is linked to neurotoxic effects, like Parkinson's disease (Franco et al. 2010), various genotoxic effects (Bolognesi 2003; Sailaja et al. 2006), cytogenetic damage (Bolognesi 2003), and induction of carcinogenic (Sailaja et al. 2006; George and Shukla 2011) and mutagenic effects (Ruiz and Marzin 1997).

Flame retardants

General information

The addition of flame retardants to different products, especially polymeric materials, makes them more resistant to high temperatures, prevents the ignition process, and reduces the probability that flame spread rapidly during the combustion process. Flame retardants can be classified as reactive and non-reactive compounds, depending on the mechanism through which they are added to materials. Their non-reactive addition favors their emergence in air, water, and food and leads to their accumulation in the organism.

Over 175 substances serve as flame retardants, which include organic halogenated flame retardants (the compound contains chlorine and bromine atoms in its chemical structure), flame retardants displaying nitrogen, and flame retardants bearing inorganic phosphorus (Birnbbaum and Staskal 2004).

Brominated flame retardants are divided into additives and reagents, depending on how they are added to materials. The industry employs tetrabromobisphenol A (TBBPA), hexabromocyclodecane (HBCD), and polybrominated diphenyl ether (PBDE) the most often (Table 4 depicts the main representatives of this class). Brominated flame retardants are efficient and less costly. For these reasons, this type of flame retardant is the most frequently applied worldwide. However, these compounds account for adverse effects on the human health and the environment (Strandman et al. 2000). Moreover, there are no laws to monitor their use in some countries, except in Europe and some states of the USA, where reduced use of brominated flame retardants occurs because the legislation has banned the manufacture of products containing some representatives of PBDEs in their formulation (Hale et al. 2001).

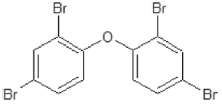
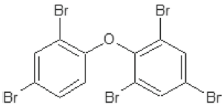
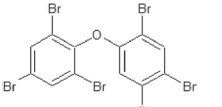
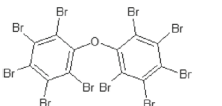
The basic differences between the compounds of this class, such as molecular weight and physicochemical properties, define their behavior in the environment (Cetin and Odabasi 2011) and regulate their accumulation and magnification in humans, wildlife, and ecosystems.

In general, the distinguishing physicochemical properties of flame retardants are their hydrophobic potential, low vapor pressure, and high octanol–water partition coefficient ($\log K_{OW}$). Therefore, most flame retardants persist in the environment, have the potential to bioaccumulate in the organism and the environment, are potentially toxic, and are prone to long-range atmospheric transport, which raises the levels of these compounds in remote areas like the Arctic regions (Hale et al. 2001; Abb et al. 2011).

Occurrence and course in the environment

TBBPA, with application in electrical and electronic equipment, furniture, and construction materials (Geens

Table 4 Main representatives of the polybrominated diphenyl ether class of flame retardants and their known effects

Emerging Contaminant	Structure	Physical and chemical properties	Biological effects	References
Tetrabromodiphenyl ether – BDE 47		<p>BDE 47 is a viscous liquid or white solid. It bears four bromine atoms in its structure. Among its congeners BDE is the one with the highest solubility in water.</p>	<p>Modified bioenergetic parameters and damaged mitochondria.</p> <p>Potential endocrine system disruption.</p> <p>Induction of apoptosis, ROS accumulation, DNA damage, and LDH release.</p> <p>Thyroid hormone disruption and impaired energy metabolism (oxidative phosphorylation) upon exposure of zebrafish during larval development to 6-OH-BDE-47.</p>	<p>Pazin et al., 2014; Pestana et al., 2008; He et al., 2008; Macaulay et al., 2015.</p>
Pentabromodiphenyl ether – BDE 100		<p>BDE 100 is highly lipophilic and can potentially bioaccumulate in human tissues and in the biota</p>	<p>Neurodevelopmental and neurobehavioral effects. Interference in calcium homeostasis on isolated mitochondria and cells culture.</p>	<p>Huang et al., 2010; Pereira et al., 2013;</p>
Hexabromodiphenyl ether – BDE 154		<p>BDE 154 is a white solid that is soluble in acetone and benzene and slightly soluble in water.</p>	<p>Potential hepatotoxic and neurotoxic effects. Induction of mitochondrial permeability transition. Mitochondrial bioenergetics impairment.</p>	<p>Huang et al., 2010; Madia et al., 2004; Pereira et al., 2014</p>
Decabromodiphenyl ether – BDE 209		<p>BDE is a crystalline powder/solid bearing ten bromine atoms in its structure. It is very slightly soluble in water.</p>	<p>Group C carcinogenicity (“possible human carcinogen”)</p>	<p>Pestana et al., 2008; USEPA, 1986;</p>

et al. 2009), has emerged in food, air, dust (Thomson and Grounds 2005; Wilson et al. 2007; Geens et al. 2009; Abb

et al. 2011), water, fish, and sediments (Yang et al. 2012) as well as in human fluids like urine (Calafat et al. 2007a,

b), serum (Dirtu et al. 2008), breast milk (Ye et al. 2008; Shi et al. 2009), and human amniotic fluid (Cariou et al. 2008). PBDEs are another class of flame retardant that has arisen as contaminant. PBDEs comprise chemical compounds added to consumer goods during or after the manufacturing process. Because PBDEs do not establish effective chemical bonds with the material during the fabrication process, the products can release these contaminants during handling and disposal. Consequently, different levels of PBDE congeners have emerged in the human blood, adipose tissue, breast milk, placental tissue, brain, marine mammals, fish, and bird eggs (Hopper and McDonald 2000; Siddiqi et al. 2003; Sjödin et al. 2014; Kodavanti and Ward 2005).

Evidence of the toxicity of classic flame retardants has led to the use of new compounds, e.g., organophosphorus (OP) flame retardants (Van der Veen and De Boer 2012), as alternatives to the aforementioned emerging contaminants (Stapleton et al. 2008). Nevertheless, OP can also persist in the environment. Indeed, researchers have already detected them in several environmental samples (Andresen et al. 2004; Hartmann et al. 2004; Reemtsma et al. 2008) and animals (Kim et al. 2011). Some research teams have reported that their levels and the levels of PBDEs in indoor dust are comparable (Reemtsma et al. 2008; Stapleton et al. 2008).

Toxicity

Strandman et al. (2000) have shown that exposure to PBDEs could begin even before birth, during gestation in the maternal womb, since there are reports on the presence of PBDEs in placenta samples. Recently, many studies have demonstrated the toxic potential of PBDEs, including hepatic, immune, neurotoxicity, endocrine actions, and the development of cancer (Pestana et al. 2008). More precisely, PBDEs induce cell death in hepatic cell lines via the mitochondrial pathway (Souza et al. 2013), leading to dysfunction in rat liver mitochondria (Pereira et al. 2012, 2014). Furthermore, potential reproductive toxicity such as induction of abnormal growth in female reproductive organs, breast, and liver has resulted from disrupted thyroid hormone receptors, estrogen, progesterone, and androgen caused by the action of PBDEs as antagonists or agonists of androgen, progesterone, and estrogen receptors (McDonald 2002; Legler and Brouwer 2003; Madia et al. 2004; Stoker et al. 2005; Hamers et al. 2007; Costa and Giordano 2007; Costa et al. 2008; Talness 2008).

TBBPA exerts toxic effects on both animals and humans. It affects the endocrine system: in the thyroid hormonal system, it binds to the thyroid hormone transport protein, transthyretin (Kitamura et al. 2005; Fini et al. 2007), and causes endocrine disruption and oxidative stress in aquatic species (de Wit 2002; Roniz et al. 2004; Hamers et al. 2006; Shi et al. 2010). Recently, the

thyroid effect elicited by TBBPA has been reported to have teratogenic effects on *Xenopus tropicalis* embryos (Shi et al. 2010). Neurotoxic effects due to exposure to TBBPA include increased ROS production and higher basal intracellular calcium concentration (Hendriks et al. 2012; Mousa and Michelangi 2012).

The toxicity of hexachlorobutadiene (HCB) affects the thyroid function, brain development, neuron function, reproduction, and general development (Marvin et al. 2011). This compound has low toxicity in different animals, but distinct administration modes can enhance toxicity and favor mutagenicity (Danerub 2003).

Alternative flame retardants are also toxic. Meeker and Stapleton (2010) have described associations between organophosphorous flame retardants present in indoor dust and changes in T4 and prolactin levels as well as decreased sperm concentration. Hence, the rising levels of these novel flame retardants cannot be overlooked.

Surfactants

General information

Surfactants are emerging contaminants belonging to a diverse group of chemicals with distinct solubilization properties. These chemicals are present in household cleaning detergents, personal care products, textiles, paints, polymers, pesticide formulations, and pharmaceuticals; they also find application in mining, oil recovery, and the pulp and paper industries (Ying 2006).

The classification of these emerging contaminants usually relies on their ionic behavior in solution: anionic, cationic, nonionic, or amphoteric (Yan et al. 2010). The commonest classes of surfactants are the following: (1) anionic: linear alkylbenzene sulfonic acid (LAS), sodium dodecyl sulfate (SDS), alkyl sulfate (AS), sodium lauryl sulfate (SLS), and alkyl ethoxysulfate (AES); (2) cationic: quaternary ammonium compound (QAC), benzalkonium chloride (BAC), cetylpyridinium bromide (CPB), cetylpyridinium chloride (CPC), and hexadecyltrimethylammonium bromide (HDTMA); (3) nonionic: alkylphenol ethoxylate (APE), alcohol ethoxylate (AE), and fatty acid ethoxylate (FAE); and (4) amphoteric: amine oxide (AO) (Ivanković and Hrenović 2010).

Surfactants generally consist of a polar head group (either charged or uncharged) and a nonpolar hydrocarbon tail (Ying 2006), but the development of new surfactants has generated dimeric (gemini) surfactants bearing two amphiphilic moieties linked together at the level of the head group by a spacer group (Zana 2002a; Yang et al. 2010). The properties of dimeric surfactants have stimulated the synthesis and investigation of

even longer homologues, the oligomeric surfactants (Zana 2002b).

A fundamental property of surfactants is their ability to form micelles in solution, because each molecule contains both hydrophobic and hydrophilic groups, which provide surfactants with excellent detergency and solubilization properties. At low concentration in water, surfactant molecules exist as monomers. The concentration of the surfactant at which the thermodynamics of the surfactant–solvent system favors micelle formation is called the critical micelle concentration (CMC) (Haigh 1996).

CMC can be regarded as the maximum solubility of surfactants (Könnecker et al. 2011). Nonionic surfactants have lower CMC levels than anionic and cationic surfactants (Ying 2006), and dimeric surfactants can exhibit superior solution properties to the traditional ones, such as lower CMC (Menger and Littau 1993; Zhu et al. 2012).

Occurrence and behavior in the environment

The extensive use of surfactants has led to the release of some of these chemicals into rivers (Odokuma and Okpokwasili 1997), and they can accumulate in sludge sewage treatment flow (Holt et al. 1995; Cserháti et al. 2002). After their use, surfactants can enter the environment through sewage discharge into surface water, pesticide application, or sludge disposal on land (Ying 2006).

After release into the environment, surfactants undergo many processes. One of such processes is biodegradation, which enhances their removal and reduces their impact on biota. Degradation of surfactants by microbial activity is the first transformation that they experience (Ying 2006). Biodegradation depends primarily on the chemical structure of the surfactant and on the physicochemical conditions of the environment (Ivanković and Hrenović 2010).

Even though a major proportion of surfactants undergo degradation in wastewater treatment plants, some surfactant may end up in surface waters, soil, or sediment (Holt et al. 1995). In surface waters, the dilution process can minimize the toxic effects of surfactants on aquatic organisms, so the concentrations of surfactants allowed in this environment are below the effective concentrations that are toxic to aquatic organisms (Ivanković and Hrenović 2010).

In soil or sediment, sorption is one of the processes that will determine whether a contaminant will persist (Haigh 1996). Sorption on soil or sediment can reduce the toxicity of surfactants in the environment. Data on sorption can help to estimate the distribution of a surfactant in different environmental compartments and its bioavailability. In addition, sorption significantly affects the biodegradation of a surfactant (Ying 2006).

Sorption depends on the nature of the adsorbent and on the concentration of the surfactant (Adeel and Luthy 1995; Ou et al. 1996). In the presence of increasing surfactant

concentrations, fewer active sorption sites are available on the surface of the solid and more hemimicelles arise. Surfactants have relatively high sorption on sludge, sediment, and soil, and their sorption is higher in cationic, followed by non-ionic and anionic surfactants (Ying 2006). The effective CMC of surfactants in soils and sediments is generally much higher than their CMC in clean water systems (Haigh 1996).

Toxicity

Surfactants are toxic to organisms. High levels of these chemicals can affect the ecosystem (Ivanković and Hrenović 2010), as shown in Table 5. Surfactants are widely dispersed in the environment, so concern regarding their ultimate environmental fate and effects (Haigh 1996) as well as their biodegradation products is large.

Anionic surfactants can bind to bioactive macromolecules such as peptides, enzymes, and DNA, to modify their biological function through changes in the polypeptide chain folding and the surface charge of a molecule (Ivanković and Hrenović 2010). In addition, anionic surfactants can link to phospholipids on the cell membrane and proteins, to increase permeability and reduce selectivity, which may culminate in cell death.

In general, anionic, nonionic, and cationic surfactants can modify microorganisms such as *Vibrio fischeri*, *Ceriodaphnia dubia*, *Carassius auratus*, *Artemia salina*, and *Daphnia magna*, among others, to elicit luminescence (in the case of *V. fischeri*), immobilization, and changes in cell density (Sütterlin et al. 2008; Mariani et al. 2006; Singh et al. 2002; Liwarska-Bizukojc et al. 2005; Warne and Schifko 1999; Garcia et al. 2007).

Biodegradability is a desirable characteristic to prevent pollution; however, partial biodegradation may result in intermediates that may be more harmful to the environment than the parent compound (Haigh 1996). For example, the biodegradation of APE generates nonylphenols (NOP) and octylphenols (OP), but NP is approximately ten times more toxic than its ethoxylate precursor (Renner 1997; Scott and Jones 2000). Besides, NP and OP can induce vitellogenin production in male fish, a protein that by sexually mature females generate under the influence of estrogens (Pedersen et al. 1999). Hence, NP and OP act as endocrine disruptors in fish (Jobling and Sumpter 1993; Ivanković and Hrenović 2010).

Nanomaterials

General information

Nanotechnology is often regarded as “enabling technology” (Mann 2006). It exploits properties and phenomena developed

Table 5 Toxicity data for different types of surfactants. Adapted from Ivanković and Hrenović (2010)

Surfactant	Test species	Endpoint	Concentration (mg/L)	References
LAS	<i>Vibrio fischeri</i>	EC50—luminescence 30 min	109.7	Sütterlin et al. (2008)
	<i>Dunaliella</i> sp.	EC50—24 h	3.5	Utsunomiya et al. (1997)
	<i>Ceriodaphnia dubia</i>	EC50—immobilization 48 h	5.96	Warne and Schiffko (1999)
	<i>Carassius auratus</i>	EC50—immobilization 48 h	5.1	Singh et al. (2002)
SDS	<i>Vibrio fischeri</i>	EC50—luminescence 15 min	2.36	Mariani et al. (2006)
	<i>Raphidocelis subcapitata</i>	IC50—cell density 72 h	36.58	Liwarska-Bizukoje et al. (2005)
	<i>Artemia salina</i>	LC50—larvae mortality 24 h	41.04	Liwarska-Bizukoje et al. (2005)
	<i>Gambusia affinis</i>	EC50—immobilization 48 h	40.15	Singh et al. (2002)
QAC	<i>Vibrio fischeri</i>	EC50—luminescence 30 min	0.5	Sütterlin et al. (2008)
	<i>Dunaliella</i> sp.	EC50—24 h	0.79	Utsunomiya et al. (1997)
	<i>Salmo gairdneri</i>	EC50—immobilization 48 h	1.21	Singh et al. (2002)
AE	<i>Microcystis aeruginosa</i>	Estimated EC10—cell density	0.154	Belanger et al. (2006)
	<i>Navicula pelliculosa</i>	Estimated EC10—cell density	0.140	Belanger et al. (2006)
	<i>Ceriodaphnia dubia</i>	EC50—immobilization 48 h	0.39	Warne and Schiffko (1999)
	<i>Pimephales promelas</i>	NOEC—survival>	4.35	Belanger et al. (2006)
AO	<i>Phosphobacterium phosphoreum</i>	EC50—luminescence 15 min	2.4	Garcia et al. (2007)
	<i>Daphnia magna</i>	EC50—immobilization 48 h	6.8	Garcia et al. (2007)

LAS linear alkylbenzene sulfonic acid, SDS sodium dodecyl sulfate, QAC quaternary ammonium compound, AE alcohol ethoxylate, AO amine oxide, EC50 half maximal effective concentration, IC50 half maximal inhibitory concentration, LC50 half maximal lethal concentration, EC10 effective concentration at 10 % inhibition

at the nanoscale. “Nano” derives from the Greek word nanos, which means a dwarf. The invention of the first tool to manipulate atomic structures, a scanning tunnelling microscope (STM), is one of the most important milestones in nanotechnology development (Piotrowska et al. 2009). Since the 1990s, implementation of nanotechnologies has escalated and has found many practical applications in the industry and daily life (Nanonet 2014). A large number of new nanoproducts are expected to appear in the market within the next few years. Over 800 products based on nanotechnology exist (Maynard et al. 2006; Rejeski and Lekas 2008).

Nanoparticles reach dimensions of up to several dozens of nanometers and resemble large complexes of protein molecules. However, they differ from proteins in terms of chemical composition, shape, size, density, aggregation, type of surface, and physicochemical properties (e.g., magnetic, optical, and electrochemical properties) (Piotrowska et al. 2009).

One of the side effects of the large-scale use of nanotechnology is the release of nanomaterials into the environment. Because the industry has employed nanotechnology, it also accounts for the production of waste containing residual nanomaterials. Indeed, the amount of “nanowaste” should increase in the future.

Nanomaterials offer a wide range of applications in the medical, technological, and scientific areas. Nanotechnology constitutes an interdisciplinary area that involves physics, chemistry, and biology from the start; this area includes the

manipulation of nanoparticles (NP). NPs usually measure less than 100 nm, and their physical, chemical, electrical, magnetic, and biological properties differ from those of other materials. In this context, because of the application of NPs in biomedicine, their fundamental characteristics are size and format. Indeed, the uptake of organic NPs by cells depends on these characteristics (Faramazi and Sadighi 2013).

Various chemical, physical, and biological methods exist to synthesize nanomaterials. Physical methods have disadvantages such as low production rate. Although chemical methods are generally inexpensive, they require solvents that produce toxic and hazardous by-products (Faramazi and Sadighi 2013). In contrast, biological methods are sustainable: they occur in living systems including bacteria, fungi, algae, viruses, and plants (Ahmad et al. 2003; Sweeney et al. 2004; Singaravelu et al. 2007; Thakkar et al. 2010; Shakibaie et al. 2010; Mishra et al. 2010). Moreover, they are generally cost-effective, biocompatible, nontoxic, and eco-friendly (Krumov et al. 2009).

Toxicity

Adverse effects of NPs on the human health depend on individual factors such as genetics and existing disease, exposure, and NP chemistry, size, shape, agglomeration state, and electromagnetic properties. Recent epidemiological studies have shown a strong correlation between particulate air pollution

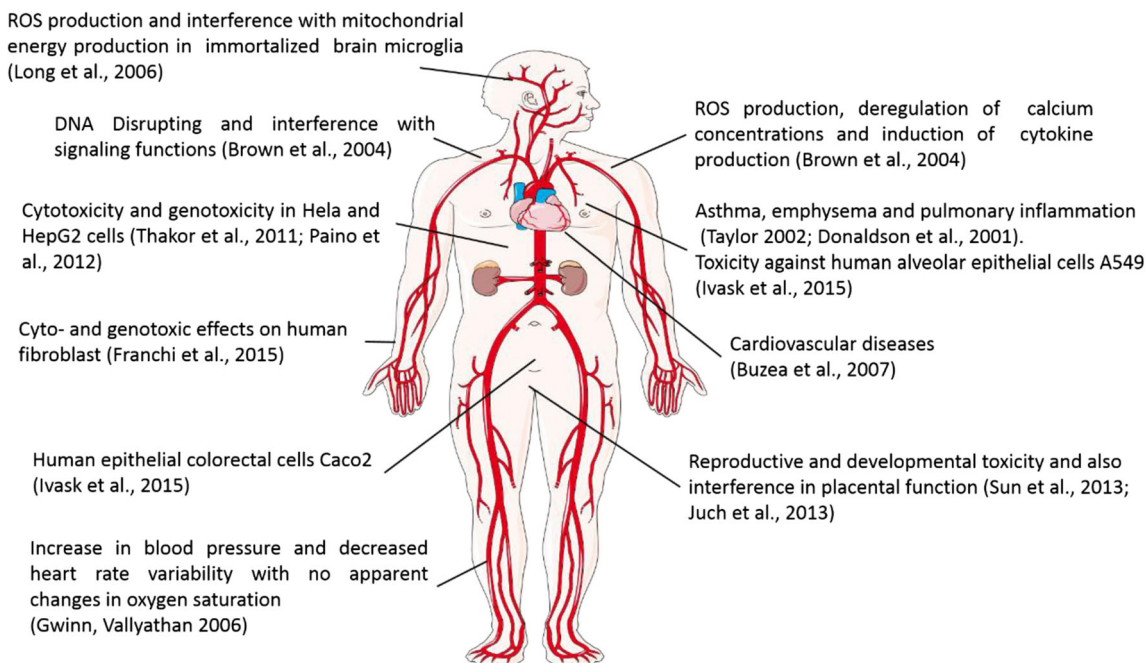
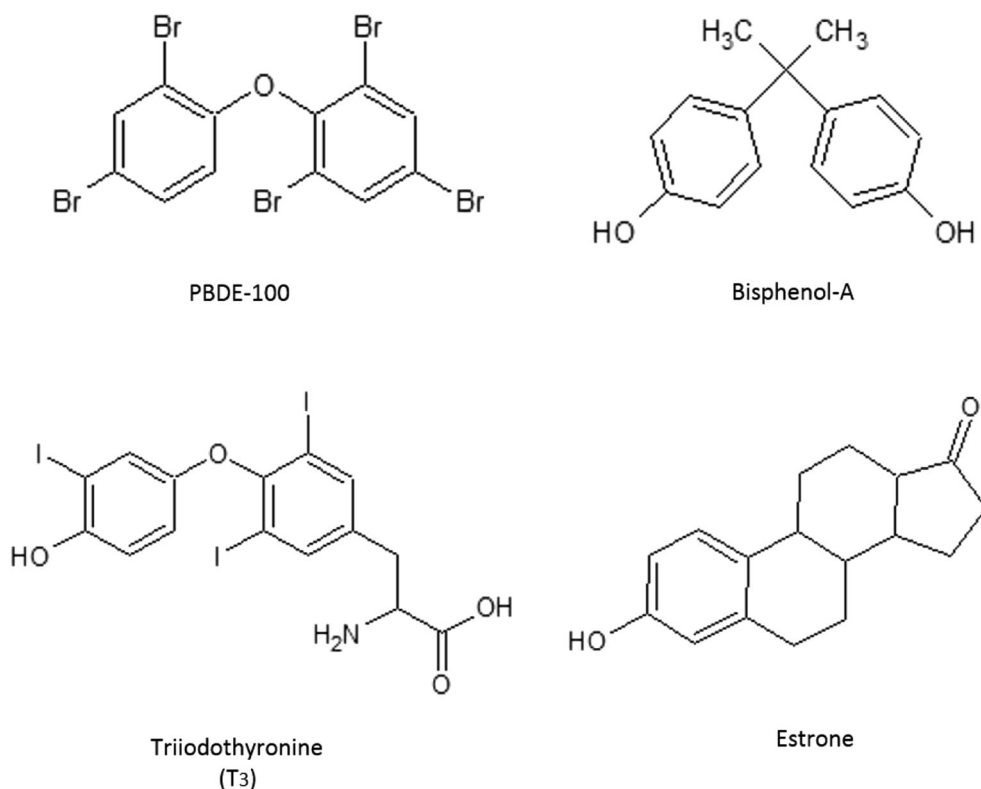


Fig. 2 Adverse effects caused by exposure to nanoparticles. Figures were produced by using Servier Medical Art: www.servier.com

levels, respiratory and cardiovascular diseases, various cancers, and mortality (Buzea et al. 2007). Orrenius et al. recently discussed the implications of different mechanisms of cell death in toxicology (chemicals, drugs, and environmental pollutants) (Orrenius et al. 2011). In the same way, increased understanding of the complexities of nanomaterial-induced

perturbation of different cell death pathways will allow better prediction of the consequences of human exposure to these materials. In the majority of the cases, the key to understanding the toxicity of nanomaterials is that their smaller size (smaller than cells and cellular organelles) allows them to penetrate these basic biological structures and disrupt their

Fig. 3 Similarity between the structures of PBDE-100 (flame retardant) and bisphenol A (plasticizer) as compared with triiodothyronine thyroid hormone (T3) and the endogenous hormone estrone



normal function (Buzea et al. 2007). Figure 2 summarizes some adverse effects caused by exposure to nanoparticles.

According to Andón and Fadeel (2012), evaluating the cell death pathways helps to assess nanotoxicology. Assessing and quantifying each specific biochemical signal of cell death induced by nanomaterials can aid this investigation. The literature reports that NPs impact cells through three mechanisms of programmed cell death.

A number of studies have described how carbon nanotubes (CNTs) at doses of 10 and 50 $\mu\text{g/mL}$ affect apoptosis. CNTs can induce apoptosis in A549 lung carcinoma cells. Carbon black NPs (13 nm) elicit apoptosis in bronchial epithelial cells via intrinsic apoptosis signaling with Bax activation and release of cytochrome c from mitochondria. TiO_2 NPs (15 nm) induce apoptosis by destabilizing lysosomal membrane and releasing cathepsin B, which suggests that the apoptosis pathway varies depending on the chemical nature of the NPs (Srivastava et al. 2011; Schrand et al. 2010). Several other classes of NPs including fullerenes, gold NPs, iron core-gold shell nanoparticles, and iron oxide NPs activate autophagy in vitro (Johnson-Lyles et al. 2010; Li et al. 2010; Wu et al. 2011). Some nanomaterials can produce reactive oxygen species as well as in vitro cytotoxicity; they can also pass through cell membranes and biological barriers such as the blood–brain barrier (Xia et al. 2006; Foley et al. 2002; Kashiwada 2006; Kim et al. 2006). In addition, NPs constitute potent inducers of micronuclei, which attest to their genotoxicity and mutagenicity (Lindberg et al. 2009; Totsuka et al. 2009).

Future perspectives

A large number of toxic compounds, mostly originating from excessive population growth and industrial and agricultural activities, are continuously entering the environment. In some cases, these toxic compounds can have serious acute effects on the organisms exposed to them. In addition, because they can induce chronic effects, exposure to low doses of these chemicals is also important (USEPA 2008; Ginebreda et al. 2012a, b). A problem common to all of the emerging classes of contaminants presented in this article, which covered a large number of chemicals with different structures such as synthetic and natural hormones, phytoestrogens, organochlorine pesticides (DDT), plasticizers (bisphenol A), and flame retardants (PBDEs), among others, is their ability to disrupt the endocrine system (Bila and Dezotti 2007; Bergman et al. 2012). This happens because their chemical structures are very similar to the structure of human endogenous hormones, as shown in Fig. 3. However, this similarity is not required for the effect to occur.

Until recently, concern about environmental toxicology focused on toxic compounds that were present in large quantities in the environment. Nowadays, major concern

resides on emerging contaminants, for which toxicological data are lacking. Little knowledge about associated biomarkers coupled with lack of legislation is also a worrying issue. In this context, some chemicals that are potentially toxic to humans have been extensively investigated. Other chemicals that harm the biota and pose risks to humans have also received researchers' attention. Finally, some other pollutants that are not directly toxic to human beings or whose environmental concentrations in the biota are not high have also been the object of several investigations. This is because they can modify environmental characteristics and bring about major environmental damage (Pierre-Marie et al. 2011). Thus, researchers have produced considerable knowledge that will assist the management of emerging contaminants. Unfortunately, people, animals, and the environment have actually been exposed to multiple chemicals from a variety of sources at once, while current risk assessment is most often carried out on one chemical substance only, at low doses (EFSA 2013; Pierre-Marie et al. 2011).

“Chemical mixtures” refers to combined exposure to multiple chemicals (EFSA 2013). For example, freshwater sources contain hundreds of measurable emerging contaminants. Of the 16 contaminants present at the highest concentrations in Lake Michigan, 11 of them are pesticides, including diazinon, chlorpyrifos, endosulfan, melathion, atrazine, permethrins, dichlorvos, manganese, zinc, imidacloprid, and naphthalenes (Raley-Susman 2014). Thus, single chemical risk assessment has proven to be efficient but fail to extrapolate the data to the contaminants existing in real life.

In conclusion, the need for high-quality information on emerging contaminants is evident. Assessing exposure to multiple chemicals is crucial, in order to estimate the effects of emerging pollutants more accurately. This will require technological improvements and the design of sensitive and selective methods for the identification, confirmation, and quantification of these compounds (Aguera et al. 2013). Biomarkers of effects, environmental monitoring, and surveillance are also essential for accurate assessment. Furthermore, legislation and more data on the occurrence, distribution, uptake, and consequences of the exposure to these compounds are welcome.

Conflict of interest The authors declare that they have no competing interests.

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