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Water Quality and Contaminants of Emerging Concern (CECs)

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1.1 Introduction: Water Quality and Emerging Contaminants

Water is a scarce resource globally and the pollution-driven deterioration of its quality further limits its availability. Freshwater pollution is mainly caused by the discharge of large amounts of untreated or insufficiently treated wastewater into aquatic environments, like aquifers, rivers, lakes, and coastal waters. Therefore, water quality is an important concern around the planet and during the twenty-first century will represent one of the main challenges for our societies. This challenge will be of huge proportions in both industrialized and developing countries. However, water quality is actually not just a health issue. According to UNESCO, public health, sustainable livelihoods, gender equality, poverty reduction, conservation of the ecosystems, and equitable social and economic developments are highly dependent on water quality [1]. This should justify why in 2010 the United Nations General Assembly (RES/64/292) recognized access to clean and safe drinking water and sanitation as a human right for our health and well-being.

The water quality survey carried out in 2002 by the US Geological Survey revealed the omnipresence of pharmaceuticals and hormones in the environment [2]. Almost 30 years before, organic compounds including pharmaceuticals had already been identified in domestic wastewaters by gas chromatography/mass spectrometry (GC/MS) [3]. However, the significant increase in the number of studies on the so-called emerging contaminants (ECs) has only been possible thanks to the technological advances in high-performance liquid chromatography/mass spectrometry (HPLC/MS) during the last two decades, achieving sufficient sensitivity to quantify organic compounds at concentrations below $\mu g\,l^{-1}$ [4].

Broadly speaking, ECs could be defined as any chemical product, whether synthetic or natural, or any microorganism with potential to induce adverse health effects on human and the environment, and for which there are no controls or regulations on their presence in the environment. Therefore, ECs constitute a heterogeneous class of pollutants, which includes different groups of contaminants such as pharmaceuticals, personal care products (PCPs), pesticides, flame retardants, industrial additives, surfactants, plasticizers, nanomaterials, and mycotoxins, among others (Table 1.1). Metabolites and natural hormones should also be included. In addition, it should be kept in mind that ECs suffer different processes (biodegradation, oxidation, hydrolysis, chemical reduction, and photolysis) generating other transformed products that, in some cases, are more toxic or more persistent than the parent compound [4, 5]. There are many technological obstacles to remove them with immediate effectiveness from wastewater treatment plants (WWTPs), releasing them at residual concentrations into surface and

Chemometrics and Cheminformatics in Aquatic Toxicology, First Edition. Edited by Kunal Roy.

Table 1.1 List of emerging contaminants of concern in water environments.

Group of contaminant	Type of compound	Examples
Pharmaceuticals	Human and veterinary antibiotics	Trimethoprim, ciprofloxacin, enrofloxacin, erythromycin, amoxicillin, lincomycin, sulfamethoxazole, chloramphenicol, triclosan
	Analgesics, anti-inflammatory drugs	Ibuprofen, diclofenac, paracetamol, codein, acetaminophen, acetylsalicylic acid, fenoprofen, ketoprofen, paracetamol, phenazone, and propyphenazone
	Psychiatric drugs	Diazepam, carbamazepine, primidone, salbutamol, fluoxetine
	β-Blockers	Metoprolol, propranolol, timolol, atenolol, sotalol
	Lipid regulators	Bezafibrate, clofibric acid, fenofibric acid, etofibrate, gemfibrozil
	X-ray contrasts	Iopromide, iopamidol, diatrizoate
	Hormones and steroids	Estradiol, estrone, estriol, diethylstilbestrol (DES)
Personal care products (PCPs)	UV filters	4-Methyl-benzylidene-camphor (4MBC), ethylhexyl-methoxycinnamate (EHMC), benzophenone-3 (BP-3), octocrylene (OC)
	Fragrances	Nitro (e.g. ketone or xylene), polycyclic (e.g. galaxolide, tonalide, celestolide, phantolide), macrocyclic, and alicyclic musks
	Preservatives	Parabens (alkyl esters of *p*-hydroxybenzoic acid)
	Antiseptics	Triclosan, triclocarban, chlorophene
	Insect repellents	*N*,*N*-Diethyl-*m*-toluamide (DEET)
Nanomaterials	Metals and metal oxides, carbonaceous, silicon nanomaterials, organics, ceramics, polymers	Silver (Ag), titanium dioxide (TiO_2), zinc oxide (ZnO), carbon-based nanomaterials
Plasticizers	Phthalates, bisphenol A (BPA)	
Surfactants and surfactant metabolites		Alkylphenol ethoxylates, 4-nonylphenol, 4-octylphenol, alkylphenol carboxylates
Flame retardants	Chlorinated flame retardants	Polychlorinated biphenyls, dechlorane plus, polychlorinated dibenzodioxins, and polychlorinated dibenzofurans
	Brominated flame retardants	Polybrominated diphenyl ethers (PBDEs): polybrominated biphenyls (PBBs), TBBPA, HBCD, decabromodiphenyl ethane or 1,2-bis (pentabromodiphenyl) ethane (DBDPE), 1,2-bis (2,4,6-tribromophenoxy) ethane (BTBPE), 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB or EHTBB), bis(2-ethylhexyl)-3,4,5,6-tetrabromo-phthalate (TBPH or BEHTBP), tetrabromobisphenol A–bis (2,3-dibromopropylether) (TBBPA–DBPE), and hexachlorocyclopentadienyldibromo-cyclooctane (HCDBCO)
	Fluorinated flame retardants	Perfluorotoctane sulfonate (PFOS), perfluoroctanoic acid (PFOA)
	Organophosphate flame retardants and plastizicers	Tris(2-chloroethyl) phosphate (TCEP), tris(2-chloro-1-methylethyl) phosphate (TCPP), and tris(1,3-dichloro-2-propyl) phosphate (TDCP)
Industrial additives and agents	Volatile organic carbons (VOCs)	$CHCl_3$, trichloroethylene (TCE) and tetrachloroethylene (PERC)
	Polycyclic aromatic hydrocarbons (PAHs)	Indeno[1,2,3-*cd*]pyrene, benz[*a*]anthracene, dibenz[*a*,*h*]anthracene, benzo[*a*]pyrene (BaP), chrysene, benzo[*b*]fluoranthene, and benzo[*k*]fluoranthene

Table 1.1 (Continued)

Group of contaminant	Type of compound	Examples
	Siloxanes (silicones)	Octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5)
	Gasoline additives	Dialkyl ethers, methyl-*t*-butyl ether (MTBE)
	Anticorrosives and antifouling agents	Benzotriazoles (1*H*-benzotriazole (BTri), (4-methyl-1*H*-benzotriazole (4-TTri), 5-methyl-1*H*-benzotriazole (5-TTri), the mixture of 4- and 5-methyl-1*H*-benzotriazole (TTri), 5,6-dimethyl-1*H*-benzotriazole (XTri) and 5-chloro-1*H*-benzotriazole (CBT) and benzothiazoles (benzothiazole (BTH), 2-hydroxy-benzothiazole (2-OH-BTH), 2-amino-benzothiazole (2-NH2-BTH), 2-methyl-benzothiazole (2-Me-BTH), 2-methyl-thio-benzothiazole (2-Me-S-BTH), 2-mercapto-benzothiazole(2-SH-BTH), 2-thiocyanomethylthio-benzothiazole (2-SCNMeS-BTH), and 2-benzothiazole-sulfonic acid (2-SO_3H-BTH), organotins, zinc pyrithione (ZnPT), antifouling biocides (irgarol, diuron, sea-nine 211, dichlofluanid, chlorothalonil, thiram, busan, densil, pyridine–triphenylborane, capsaicin, econea, medetomidine, and tolylfluanid)
	Chelating agents (EDTA), aromatic sulfonates	
Natural emerging contaminants	Mycotoxins	Trichothecenes: Deoxynivalenol or vomitoxin (DON), deepoxy-deoxynivalenol (DOM-1), 3-acetyl-deoxynivalenol (3AcDON), 15-acetyl-deoxynivalenol (15AcDON), nivalenol (NIV), and T2-toxin. Zearalenone (ZEN) and its metabolite β-ZEN. Fumonisins: fumonisin B1 (FB1), B2 (FB2), and B3 (FB3). Beauvericin (BEA)
	Phytotoxins	Phenolic acids, quinones, benzoxazinones, terpenoids, glycoalkaloids, glucosinolates, isothiocyanates, phytosterols, flavonoids, coumestans, lignans, and chalcones

groundwater. This is a cause of concern because some of them may trigger the development of antibiotic resistance in pathogen bacteria, chronic toxicity, and endocrine disruption in humans and aquatic wildlife [1, 6].

These contaminants usually have an anthropogenic origin, with special relevance in discharges from urban and industrial WWTPs, livestock production, and aquaculture. Urban wastewater collects the discharges of ECs from households, hospitals, and veterinary establishments, so a very important part of the burden of ECs are pharmaceuticals and PCPs. On the other hand, industrial wastewater receives a more specific load depending on the industries located in each area, being the pharmaceutical and chemical ones especially relevant.

In any case, these compounds reach aquatic ecosystems in different ways, including effluents of WWTPs or directly from water activities (e.g. gasolines, sunscreen products), having been detected at a global scale in WWTP effluents [7], surface and groundwater, and even in drinking water [8–11].

Although the ECs concentrations vary depending on the type of water, concentrations in surface waters are usually lower than those detected in WWTPs [6], mainly due to dilution processes, but also to natural processes such as volatilization, biodegradation, sorption, or photolysis.

According to Petrie et al. [12], several factors influence concentrations of ECs in wastewater:

- *Sampling*: inappropriate sampling strategies have been considered as one of the main weaknesses of reported occurrence data.
- *Spatial variation*: climate associated to each geographical area, including rainfall distribution and temperatures, affects dilution processes of ECs in aquatic environments.
- *Intra-day variation*: for example, levels of antibiotics in rivers are usually higher early in the morning (7:00–9:00, a.m.), mainly due to their concentration in urine overnight.

- *Inter-day variation*: concentrations of illicit drugs in influents of wastewater are generally higher at weekends than at working days.
- *Seasonality*: for example, concentrations of antihistamines are higher in spring, but, on the contrary, levels of anti-cough and decongestant medicines are higher during the cold months of the year, and especially in winter.
- Some occasional events, such as festivals, local fairs or exam periods, can induce concentration peaks of certain type of drugs.

In general, these contaminants provoke few acute toxicity events as they are found at low concentrations in aquatic ecosystems. However, significant reproductive effects have been observed after long-term exposures to mixtures of very low doses of pharmaceuticals [13]. Currently, there are a great number of analytical and experimental tools available to detect and assess toxicity of emerging pollutants in aquatic compartments, including WWTPs. This allows to link chemical measurements with the toxicity exhibited by a sample [14].

In summary, slightly modifying the Noguera-Oviedo and Aga's proposal [4], research on ECs in aquatic ecosystems have taught us six lessons:

1) No part of the world is free from ECs.
2) There is no single water treatment capable of removing all ECs.
3) Metabolites and transformation products should be taken into account in terms of toxicity.
4) Demonstration of effects and toxicity induced by ECs need unconventional tests.
5) In spite of modern and advanced analytical tools, the target of detecting and quantifying ECs in water may not be achieved.
6) The extent and consequences of the risks associated to mixtures of ECs is still far from being known.

1.2 Contaminants of Emerging Concern

1.2.1 Pharmaceuticals

Pharmaceuticals are natural or man-made chemicals used in human and veterinary drugs. Their consumption in developed countries is very high, rising up to 50–150 g per capita with an annual global mean of 15 g [15]. More than 600 active pharmaceutical ingredients (APIs) have been identified in the environment, mainly in sewage effluents and surface waters, but also in groundwater and soils [16]. Their presence in drinking water is of particular concern for the scientific community, mainly due to the ignorance of their effects after chronic exposure to low doses [4]. However, they are present in all types of waters, being, together with PCPs, the most frequently detected group of ECs in surface and groundwater [17]. In groundwater, the most frequently detected pharmaceuticals are non-steroideal anti-inflammatory drugs (NSAIDs) (ibuprofen, diclofenac, salicylic acid, and ketoprofen), analgesics (paracetamol, phenazone, and propyphenazone), antibiotics (lincomycin, triclosan, sulfamethoxazole, and erythromycin), barbiturates (primidone), antiepileptics (carbamazepine), X-ray contrast agents (iopamidol), and clofibric acid (a metabolite of clofibrate, a lipid regulator) [6, 17]. On the other hand, the most frequently detected pharmaceuticals in drinking waters are meprobamate, atenolol, sulfamethoxazole, carbamazepine, ibuprofen, naproxen, gemfibrozil, phenytoin, estrone, and trimethoprim [18, 19].

The first step to understand the toxic effects of pharmaceuticals in the environment is to identify the different sources and entry routes into the environment [16]. The main point sources of pharmaceuticals as ECs in aquatic environment are [6, 16]:

- *Pharmaceutical industry*: residual pharmaceuticals in industrial wastes, in spite of Good Manufacturing Practices (GMP) and storm water runoff carrying them.
- *Hospital wastewater outflows*: discharges containing pharmaceuticals, X-ray contrast, solvents, disinfectants, and expired medicines. Some of these substances (e.g. iopromide, iopamidol, diatrizoate) are highly persistent in aquatic environments and are also detected in groundwater.

- *Livestock production and veterinary medicine*: pharmaceuticals are highly present in waste discharges. In the case of intensive livestock farming, veterinary medicines, particularly antibiotics, are of special concern and they have to be exclusively prescribed for veterinary use. Urine and feces of livestock animals contaminate soil and surrounding surface and groundwater. Some of these drugs are sulfamethazine, frequently detected in groundwater in the United States and Europe, as well as tylosin and monensin [17].
- *Domestic outflows*: these mainly include unused and expired medicines and metabolites eliminated in urine.
  - *Agriculture*: Sludge from sewage treatment plants (STPs) is frequently used as fertilizer, and antibiotics have been used in the United States to control bacteria in flowers and fruits.
  - *Aquaculture*: Antibiotics have been employed for both preventive and therapeutic purposes.

Human and animal metabolism of pharmaceuticals results in new molecules (metabolites) due to structural changes of the parent compounds mostly by oxidation, hydrolysis, or reduction, being then eliminated, mainly by urine, together with the unchanged fraction of the parent chemical. In this sense, antibiotics, one of the most frequently used pharmaceutical classes, are poorly metabolized, being released from the body in an unchanged form at rates from 25% to 75% after ingestion [20]. Once in the environment, pharmaceuticals and metabolites may suffer both transformation and removal processes like sorption, dilution, or degradation, among others [6]. Both pharmaceuticals and their transformation products can persist in the environment [21].

Although the presence of pharmaceuticals and related compounds in the environment, and especially in aquatic ecosystems, is unquestionable, they are considered as micro-pollutants because their usual concentrations are in most cases very low, ranging between $\mu g\,l^{-1}$ and $ng\,l^{-1}$. In this sense, the typical concentrations detected in drinking water (below $0.05\,\mu g\,l^{-1}$) are considerably lower than the lowest therapeutic doses [6]. According to the World Health Organization (WHO), the exposure to individual pharmaceuticals at this level may not be a direct threat to human health, which explains the initial lack of guidelines regulating their presence in the environment [22]. A first positive step toward regulating pharmaceuticals in water environments was already taken by the European Union approving the Directive 2013/39/EU of the European Parliament amending Directives 2000/60/EC and 2008/105/EC regarding priority substances for water policy. Article 8c of this Directive treats the specific provisions for pharmaceutical substances in water [23].

Some studies have suggested that pharmaceuticals acting, for example, on cardiovascular (as propranolol) or central nervous systems (for example, antiepileptic drugs as carbamazepine or clofibrate), as well as antibiotics, may pose high risk to the environment [24]. In this sense, the presence of antibiotics in aquatic environments may cause considerable impacts, mainly due to the generation and transmission of resistances among microorganisms [25]. This is especially relevant in treated wastewater effluents as they can disrupt the microbial community structure and, thus, alter the microbial populations as well as their ecological function within their ecosystem. Therefore, antibiotics are a cause of concern considering the high risks associated to their presence in the aquatic environment. In addition, effects on human health related to antibiotic resistances are also being a cause of special attention worldwide [26].

Although there are no regulations for concentrations of pharmaceuticals in the environment, there are some for pharmaceuticals in human food. Recently, a survey of 47 antibiotics in seafood in the United States was published [27] reporting that five antibiotics (virginiamycin, oxytetracycline, sulfadimethoxine, ormetoprim, and 4-epioxytetracycline) were detected at doses ranging between 0.3 and $8.6\,ng\,g^{-1}$ (fresh weight). Although they were below US regulatory limits in seafood, chronic exposure could trigger antibiotic resistance genes (ARG) [4] with the corresponding risks to human health.

In addition to ARG, some antibiotics, together with other pharmaceuticals such as sex hormones, veterinary growth hormones, and glucocorticoids are known for their endocrine disrupting properties [4, 6]. This is especially important for chronic exposure, because there is still much uncertainty concerning the impact of ECs in scenarios of long-term exposure at low doses on human, terrestrial, and aquatic wildlife and ecosystems [28]. Moreover, a majority of the scientific research focuses on certain groups such as antineoplastics, antibiotics, or hormones, whereas other groups such as anti-ulcerants and some of the non-prescribed drugs with a potential to impact the environment negatively have not received the due attention yet. In this sense, different aquatic organisms have been found to be susceptible to a variety of pharmaceuticals (including antineoplastics, antibiotics, cardiovascular drugs, and hormones), being sex hormones and antibiotics considered as the most dangerous compounds for both human and aquatic life health [29].

1.2.2 Personal Care Products

PCPs represent a group of heterogeneous emerging pollutants of concern due to their extensive use and ubiquity in water environments. This group of compounds includes a wide variety of substances mainly used as ultraviolet (UV) filters, fragrances, preservatives in cosmetics, antiseptics in creams, soaps and toothpaste, and insect repellents. Current wastewater treatment systems are not efficiently removing some PCPs [30], and a variety of them may persist in ecosystems and can be accumulated in wildlife, inducing a wide range of adverse effects in organisms (e.g. endocrine disruption, reproductive and neurotoxic alterations, growth and development impairment) [31]. They are detected in different water compartments worldwide, including influent/effluent wastewaters, groundwater, rivers, lakes, marine environments, and sediments [4, 12, 31–35]. However, less attention has been placed on these compounds compared with other groups of contaminants.

UV filters are the active ingredients in sunscreen products and other cosmetics, and they are also used in different products (e.g. textile, plastics, packages, and paints). There are many different filters, and some of the most frequently investigated are 4-methyl-benzylidene-camphor (4MBC), ethylhexyl-methoxycinnamate (EHMC), benzophenone-3 (BP-3), and octocrylene (OC). UV filters show environmental stability and lipophilicity, and some reports suggest that they can bioaccumulate at similar levels than some legacy organochlorine compounds (dichlorodiphenyltrichloroethane, DDT and polychlorinated biphenyls, PCBs) [31]. UV filters have been found in different organisms such as crustaceans, molluscs, fish, birds, and marine mammals [31, 36–38]. The potential for trophic magnification of some UV filters (e.g. BP3, EHMC, and OC) has been recently observed in freshwater ecosystems [38, 39]. These compounds have shown estrogenic activity and effects on growth, behavior, and reproduction [31, 40, 41], but further research is needed to evaluate additional environmental concentration data and related effects in different wild species.

Fragrances area broadly used in different products (e.g. soaps, lotions, perfumes, deodorants, and detergents), and are divided in different groups including nitro, polycyclic, macrocyclic, and alicyclic musks. Nitro musks (e.g. ketone or xylene) are persistent and some of them have been found to be weakly estrogenic. Some compounds in this group are banned or restricted in their use due to their toxicity [42]. Synthetic polycyclic musks are frequently used (e.g. galaxolide, tonalide, celestolide, and phantolide), being galaxolide and tonalide the fragrances most widely used. They are water soluble and persistent, they can be accumulated in sediments and have high bioaccumulation potential in aquatic species. Their toxicity varies depending on the species; growth and development-related effects are the main alterations reported [31]. Some evidences suggest that they may produce endocrine disruption [43]. Effects associated to long-term exposure to fragrances due to industrial and domestic discharges need further evaluation in aquatic organisms. Different studies show that these chemicals are not efficiently removed by conventional WWTPs and are present in their effluents and receiving aquatic ecosystems. In addition, galaxolide may biotransform into galaxolidone in activated sludge WWTPs [44, 45], and the concentrations of this product may increase in the final effluent [46].

Parabens (alkyl esters of *p*-hydroxybenzoic acid) are chemicals with antimicrobial preservative properties that are widely used in cosmetics (e.g. lotions, creams, and shampoos), but also in pharmaceuticals, beverages, and food. Some studies have identified these chemicals in surface water. The parabens most commonly used in PCPs are methyl-, ethyl-, propyl-, and butyl-paraben. Studies seem to indicate that increased chain length and chlorination increase the toxicity of parabens [31]. Although additional studies are required to assess concentrations in the environment and elucidate chronic effects, results show that some parabens may cause negative effects on aquatic wildlife, including estrogenic responses at low concentrations, while effects on spermatogenesis have also been reported [31, 47].

Two antiseptics used in soaps, toothpaste, creams, and deodorants are triclosan and triclocarban. They are frequently detected in surface water worldwide. These chemicals, as well as the methyl derivative of triclosan (methyl triclosan) are lipophilic, and although some contradictions are found in the literature regarding triclosan bioaccumulation capacity, these compounds seem to bioaccumulate in aquatic biota. Algae seem to be the most sensitive trophic group to triclosan toxicity and algal growth being the main endpoint affected. Algae, invertebrates, and fish seem to be more sensitive to triclosan than mammals [48]. Triclosan has shown to induce oxidative and genetic damage, and can affect development, behavior, reproduction, and survival. In addition, some studies show its potential for endocrine disruption [31, 48–50].

N,*N*-Diethyl-*m*-toluamide (DEET) is the active ingredient most commonly used in insect repellents worldwide. This compound is relatively persistent and has been detected in WWTPs effluents and surface waters. However, it has a low bioconcentration factor suggesting low accumulation capacity in aquatic organisms [31]. Acute toxicity studies have reported that DEET is slightly toxic to some aquatic organisms [31, 51]. Published results on chronic toxicity show that DEET can affect growth and survival, as well as biochemistry (e.g. cholesterol) [31, 51, 52]. The toxicity data available has indicated that exposure to DEET poses higher toxicity to some algae than other aquatic species, and crustaceans were more sensitive than insects and fish [51].

1.2.3 Nanomaterials

The use of nanomaterials into different commercial products (e.g. PCPs, clothing, cosmetics, sporting goods, home and garden products, electronics, food and beverage, medicine, construction, etc.) has rapidly increased [53]. Nanomaterials include nanoparticles defined as having at least one dimension of 1–100 nm of length and displaying novel properties different from those of molecules or material of the same composition [54]. They are expected to provide benefits such as antimicrobial properties, protective coatings, cosmetic and health applications, hardness and strength, miniaturization, etc. [53]. Continental and marine waters are important receiving compartments through direct or water discharge and routine use of products containing them [55].

There are different types of nanomaterials depending on their chemical composition, including metals and metal oxides, carbonaceous and silicon nanomaterials, among others (e.g. organics, ceramics, polymers, etc.) [53]. Some of the nanomaterials most frequently incorporated in products are silver (Ag), titanium dioxide (TiO_2), zinc oxide (ZnO), and carbon-based nanomaterials [53, 55]. These nano-scale materials can be used in combination, such as Ag–TiO_2 in electronics and cosmetics, TiO_2–ZnO in cosmetics and paints, calcium (Ca)–magnesium (Mg) in dietary supplements, or Ag–nano-ceramics in water filtration products and cosmetics [53]. Therefore, it is essential to evaluate potential synergistic, additive, and antagonistic effects of multiple exposures from a combination of nanomaterials [53]. However, current knowledge on their potential deleterious effects on animal and human health is limited.

Nanomaterials have special characteristics due to their size, surface area, and physicochemical properties, and they may produce unpredictable interactions in the organism compared to larger equivalents. Therefore, nanotoxicology is an important research area within toxicology assessing the complex interactions between these materials and cells, tissues, and organisms [56]. For example, studies using mammal cells have reported that fullerenes can produce oxidative damage, and their toxicity is related to their lipophilicity since modifying fullerenes surface to reduce their lipophilicity also reduces their cytotoxicity [57]. Nanomaterials have the potential to produce reproductive, developmental, cardiovascular, immunological, neural, and hepatic toxicity in aquatic organisms [58]. A variety of studies have shown that oxidative stress, inflammation and oxidative damage in lipid membranes, proteins and DNA can be the mechanism for their toxicity [58, 59]. Further studies are needed to properly evaluate the toxic effects, underlying mechanisms, size-dependent properties and potential risks of nanomaterials.

1.2.4 Plasticizers

Plasticizers are widely used in commercial applications as they provide special characteristics (e.g. flexibility, transparency, longevity, workability) to plastics. However, they are not well chemically bonded and can migrate from the product during its use or after disposal, being present in effluents, sludges and in surface waters, posing a risk to ecosystems and human health [60, 61]. These plastic additives include bisphenol A (BPA) present in polycarbonate plastics and phthalates frequently used as plasticizers in polyvinyl chloride (PVC) plastics and in consumer products (e.g. PCPs, packaging and medical products) [62]. Diethylhexyl phthalate (DEHP) is the most commonly used plasticizer and an important organic pollutant, and it can be partially biodegraded by soil microorganisms into more toxic metabolites [63].

Plastics are resistant to degradation, but can break up into small fragments over time due to abrasion, UV radiation, photodegradation and biological processes, producing the so-called microplastics. They are defined as particles smaller than 5 mm in diameter, and can derive from primary sources (e.g. material added to PCPs such as toothpaste or cosmetics) or secondary sources (from degradation of larger plastic materials). Microplastics have been found in marine environments and are a global environmental issue [64].

Different studies have reported plastic ingestion by wildlife [65–67], which may put some populations at risk. Together with the physiological effects due to the ingestion of pieces of plastic, there are other hazards related to chemicals found in plastic. Besides the additives intentionally included and the unintentional chemicals from the production process [62], plastics can sorb and concentrate environmental contaminants such as persistent organic pollutants [68–70]. In this sense, exposure to microplastics has been related to negative physical/mechanical effects on growth, reproduction, and survival of marine organisms [62]. On the other hand, chemicals from plastics such as some phthalates and BPA may produce endocrine disruption affecting development and reproduction, although there is an important knowledge gap regarding the potential health impacts that needs to be covered [62].

1.2.5 Surfactants and Metabolites

Surfactants are other of the groups of ECs in aquatic environments of special concern in scientific community due to their hazards to human, animal, plant, and environmental health. According to the nature of their head group they can be classified in four main groups: anionic, cationic, nonionic, and amphoteric. They have been widely used in different domestic and industrial applications and for a variety of purposes such as emulsion stabilization, wetting, foaming, detergency, separations, pharmaceutical formulation, among others [71].

Anionic surfactants, commonly used in detergents, account for 60% of the total annual production (15 MT), whilst the remaining 40% is distributed between nonionic (30%) and cationic and amphoteric surfactants (10%) [72, 73]. Because of their persistence and solubility in water, they can reach drinking water resources after passing through wastewater treatment processes [74]. In domestic wastewaters, concentrations of surfactants are usually ranging between 1 and 10 mg l^{-1}, while typical concentrations in wastewater from surfactant industries are about 300 mg l^{-1} [75]. Although sewage treatments are effective in reducing these concentrations, there are always residual concentrations posing health risk to humans, terrestrial and aquatic animals, and ecosystems [71].

Surfactants affect ecosystems at different levels. For example, they can alter soil physics, chemistry, and biology, kill the roots of plants and reduce their photosynthetic capacity, and they may alter growth and physiology of algae. In aquatic systems, surfactants can produce several deleterious effects related to chronic and sublethal toxicity in both invertebrate and vertebrate fauna. Humans are also adversely affected by surfactants, although only under chronic-exposure scenarios, since an acute exposure is unlikely to occur [76].

Once used and released into the environment, surfactants enter the water bodies and the majority are degraded or removed in WWTPs. However, depending on the physic-chemical characteristics of each compound, some of them will persist long, increasing the likelihood of accumulation and toxicity [76–78]. In some cases, surfactant degradation processes generate products that are more toxic than the original compound, gaining capacity to disrupt the endocrine system [78]. Endocrine disruption is one of the main mechanisms of toxic action of nonylphenols [79], which are precursors to the nonionic surfactants alkylphenol ethoxylates and nonylphenol ethoxylates [80].

1.2.6 Flame Retardants

PCBs were mainly used as coolants and lubricants, plasticizers, in pigments and copy paper [81]. Although they were banned decades ago, they can still be found in the environment, including aquatic ecosystems, due to their high persistence [82]. Experimental and epidemiological studies have linked environmental and occupational exposures to PCBs to liver, kidney, endocrine, and neurodevelopmental adverse effects [83]. Dechlorane plus (DP) is a highly chlorinated flame retardant used to replace older dechloranes in wires coating, computer connectors and monitors, furniture, and plastic roofs [84]. *In vitro* and *in vivo* experiments found some neurotoxicity, oxidative stress, and endocrine disruption after exposure to DP, although more research is needed [85].

Brominated flame retardants (BFRs) can be either additives (in electronic devices, polystyrene foams, carpets, and upholstery) or reactives (in epoxy resins and polycarbonate polyesters) [86]. Due to legal restrictions [87, 88], they have been substituted by other “novel” BFRs (NBFRs) [87]. However, these NBFRs share most of their physical–chemical properties with the legacy ones and therefore their environmental fate [86]. Liver, kidney, and thyroid are the main target organs for polybrominated diphenyl ethers and there is enough evidence about the ability of BFRs to alter endocrine, central nervous and reproductive systems [89]. The low exposure levels to tetrabromobisphenol A and its rapid metabolism in humans may indicate that it is safe for the population, but its potential effects on early developmental stages should be further evaluated [90]. In the case of NBFRs, several compounds can cause adverse effects such as endocrine disruption, genotoxicity, and behavioral modification. Ecological risk assessments did not find significant environmental risk, but it should be taken into account that the toxicity data is still limited [87].

Thermal decomposition of brominated and chlorinated flame retardants leads to the production of polybrominated dibenzo-*p*-dioxins/dibenzofurans and polychlorinated dibenzodioxins/dibenzofurans. Dioxins and furans are highly lipophilic and resistant to degradation and metabolism, which leads to bioaccumulation and biomagnification. They are also ubiquitous as they can suffer long-distance transport, mainly through the atmosphere [91]. Dioxins can activate the aryl hydrocarbon receptor (AhR) causing skin and immune toxicity, carcinogenicity and alteration of reproduction, development, and endocrine functions [91].

Per- and polyfluoroalkyl substances (PFASs) wide use (e.g. nonstick cookware, textiles, firefighting foams, etc.) has raised concerns as many of them are persistent, bioaccumulative, and toxic (PBT). Volatile PFASs precursors reach remote areas due to long-range atmospheric transport while ionic PFASs are transported via the aquatic system and in marine aerosols as well as from air–sea exchange [92]. Although epidemiologic data that links human exposure to perfluorotoctane sulfonate and perfluoroctanoic acid to adverse effects are usually inconsistent, experimental studies in different animal species have found hepatotoxicity, immunotoxicity, endocrine disruption, metabolic disorders, cancer, and developmental toxicity [93].

Organophosphate esters (OPEs) comprise a large group of compounds that share a central phosphate molecular group. Usually, the chlorinated and brominated OPEs are used as flame retardants (organophosphorus flame retardants, OPFRs) in consumer products, and the non-halogenated ones are used as plasticizers and performance additives to engine oils [94]. Most OPEs are lipophilic and additives, being easily released to the environment and detected in indoor air and dust, drinking water, sediments, and biota [94]. Experimental studies found neurotoxic, developmental, reproductive and endocrine effects at doses higher than those environmentally relevant. Thus, more studies about molecular targets in benthic species and new OPFRs are needed [95].

1.2.7 Industrial Additives and Agents

Organic compounds that are readily evaporated at room temperature are classified as volatile organic compounds (VOCs) and also called solvents. The main exposure route is inhalation although they can be easily absorbed by gastrointestinal tract and skin [96]. VOCs are widely used both in household and industrial products (e.g. paints and waxes, cleaning and disinfecting products, cosmetics, moth repellents, air fresheners, automotive products, degreasers and intermediates in chemical synthesis, fuels, printers, and craft materials). Due to an inappropriate discharge of these products and the presence of disinfection by-products such as chloroform ($CHCl_3$), drinking water has become a common source of solvent exposure [96]. Together with their toxicity and bioaccumulation potential, VOCs were included in water regulations in Europe and in the United States as the main group of synthetic organic contaminants [97]. However, the aforementioned widespread use and properties of VOCs contributes to the wide distribution of these compounds in the environment, being released during production, processing, storage, use, and elimination [96]. Acute exposure to VOCs causes central nervous system depression and irritation of membranes and tissues. In addition, VOCs can cause toxic effects on liver, kidney and heart, and carcinogenicity has been evidenced after intense exposure to benzene and vinyl chloride in humans, while some chlorinated VOCs (CCl_4; $CHCl_3$; trichloroethylene, TCE; tetrachloroethylene, PERC; etc.) are potentially carcinogenic in animals [96].

Polycyclic aromatic hydrocarbons (PAHs) originate from the incomplete combustion and pyrolysis of fossil fuels, wood and waste, automobile exhaust, and petroleum spills [98]. As number of fused rings increases, their volatility decreases and hydrophobicity and environmental stability increase. As they are lipophilic, they can easily cross biological membranes and accumulate in lipids, while they are also easily mixed with air, water, soil, sediments, and food due to their good volatile properties [99]. The greatest public health concern for PAHs is related to airborne chronic exposure to low levels, due to their carcinogenic potential, but immunosuppression, teratogenicity, cytotoxicity, and genotoxicity may also happen [100, 101]. However, acute intoxication symptoms include nausea, vomits, DNA and proteins damage and mutation, and skin and eye irritation [100].

Siloxanes are a heterogeneous group of organosilicon compounds formed by a polymer backbone with repeating silicon–oxygen atoms (–Si–O–) and different substituents. Siloxanes can be universally applied in different fields such as construction, electronics, baking, clothing, sports equipment, chemicals [13, 23]. Studies have shown that some low molecular siloxanes can travel long distances, being found in the Arctic [102]. Frequently considered safe [102], low molecular ones are more dangerous, as they are lipophilic [103] and may accumulate in the organism leading to chronic effects [104], and alter the structure of the lipid bilayer [105]. In addition, as they are volatile, they can enter the organism by respiration [102]. Octamethylcyclotetrasiloxane (D4) was classified as a PBT and both D4 and decamethylcyclopentasiloxane (D5) were classified as very persistent and very bioaccumulative (vPvB) substances [106]. On the other hand, the information about toxic effects of siloxanes is scarce, especially in regards to the molecular mechanisms of action [107]. Animal studies found that D4, D5, and D6 are endocrine disruptors [108]. Assessing the aquatic toxicity of these volatile compounds is difficult due to the low water solubility and the limited number of studies that have been sponsored by industry [109]. However, D4 causes narcosis and has been classified as very toxic to sensitive aquatic organisms [104].

1.2.8 Anticorrosives and Antifouling Agents

Benzotriazoles and benzothizoles are ubiquitous compounds as they are soluble in water, resistant to biodegradation, and only partially removed in wastewater [97]. They are two groups of heterocyclic aromatic compounds widely used in industrial and consumer products, including rubber production, fungicides, corrosion inhibitors, herbicides, algicides, UV light stabilizers in textiles and plastics, and also as precursors of pharmaceuticals [110]. Sublethal effects of benzotriazoles and benzothizoles include endocrine disruption, hepatotoxicity, neurotoxicity, mutagenicity, and carcinogenicity, while acute toxicity includes respiratory irritation and dermal sensitization [110–112].

Organotin compounds are chemicals with at least one covalent Sn–C bond. Bioaccumulation has been found along aquatic and terrestrial food webs [113]. They can be used as heat stabilizers, catalysts, biocides, and as drugs to treat cancer, inflammation, tuberculosis, leishmaniasis and bacterial infections [114]. Toxicity is also influenced by the number of alkyl groups in organotin compounds [113], turning to be very broad and complex. Tributyltin (IV) (TBT) is considered one of the most toxic environmental contaminants of anthropogenic origin, mainly due to its toxicity to aquatic but also terrestrial ecosystems [115]. Moreover, the differences are also due to the type of organism. Acute exposure causes damage to liver, kidney, and central nervous system, while chronic effects include immunotoxicity, endocrine disruption, carcinogenicity, and genotoxicity [113].

To substitute organotin compounds in antifouling paints, copper(I) salts (Cu_2O, CuCHNS), non-metallic organic compounds (i.e. irgarol, diuron, thiram ortolylfluanid), and organometallic compounds (copper pyrithione, zinc pyrithione (ZnPT), zineb, and maneb) have been proposed [116]. According to their intended use, these compounds are expected to cause detrimental effects in the aquatic biota. In the case of copper, its use in antifouling paints can cause a risk for the marine ecosystem [116]. ZnPT is the most frequently used alternative to organotins as antifouling. Although marine organisms are very sensitive to ZnPT, its environmental concentrations may only pose a risk at shipping ports, shipyards, and hull cleaning sites [117]. On the other hand, because ZnPT may be degraded to persistent metabolites, further studies are needed [117]. The list of potential organic biocides is large and not all the compounds have been used, and the amount and types of compounds used worldwide is unknown [116]. In fact, due to their high toxicity and environmental persistence, diuron, and irgurol were banned as antifouling in the European Union, but can be still used in other countries [118].

1.2.9 Natural Emerging Contaminants: Mycotoxins and Phytotoxins

Mycotoxins and phytotoxins are naturally occurring chemical compounds derived from a wide variety of fungal and plant species, respectively, some of them are well known by their estrogenic activity [119, 120]. Mycotoxins are produced by fungal species, such as Fusarium, Aspergillus, and Claviceps, that grow under warm and humid conditions on cereals, nuts, dried fruits, spices and similar foodstuffs [121]. It has been hypothesized that there are thousands of potential toxic metabolites of fungi, from which around 400 have been identified, a few tens have been analyzed in environmental aquatic compartments, and approximately only 10–15 are priority food contaminants due to their toxic effects [122–124].

Although the information about environmental distribution of mycotoxins and phytotoxins is scarce, their presence has been described in all type of waters, such as agricultural, industrial and urban WWTP influent and effluent, rivers, streams, runoff waters, spring snowmelt, soil, sediment, manure, and sewage sludge [122, 125–127], and even in drinking water [128].

In general, there is limited information about the different chemical forms in which each mycotoxin can be detected in aquatic environments (unchanged form, metabolites or transformation products). In the case of zearalenone (ZEN), it is known that it may be excreted by animals in unchanged form or after reduction to α- and β-zearalenol, so that these compounds are likely to reach aquatic compartments passing through WWTPs [126].

Mycotoxins in rivers, lakes, streams and irrigation ditches are detected at very low concentrations (tens of $\mathrm{ng\,l^{-1}}$), usually below $50\,\mathrm{ng\,l^{-1}}$ [126, 129], while phytoestrogens in WWTPs in Italy ranged from 7 to $384\,\mathrm{ng\,l^{-1}}$ [126]. In some occasions, mycotoxins and phytoestrogens have reached the $\mu\mathrm{g\,l^{-1}}$ range in water compartments [126, 130]. The concentrations of mycotoxins and phytotoxins are influenced by several factors, but it has been observed that, in general, the highest concentrations are reached during spring and summer [120, 130].

Researchers have mainly focused their studies on myco- and phyto-estrogens due to their potential estrogenic effects on human and animals [126]. There is a considerable body of evidence linking detrimental reproductive disorders on humans and wildlife with certain natural endocrine disrupters such as the mycotoxin ZEN or the phytoestrogens isoflavones, lignans, and coumestans [120]. These natural estrogenic compounds are able to induce reproductive effects on all living beings, including freshwater species, livestock, wildlife, and humans [126]. The structural analogy of ZEN and its derivatives (α-zearalenol and β-zearalenol) with estrogens allows them to bind to estrogen receptors, which explains their estrogenic activity in both *in vivo* and *in vitro* experiments [131, 132]. ZEN, and particularly its derivatives, are also able to induce oxidative stress and damage in DNA in *in vitro* cell cultures [133].

These natural compounds are rarely controlled by regulatory rules. In the European Union, maximum levels have been established in some foodstuffs only for ZEN [134]. Currently, the priority list of chemicals in water policy does not include limits for ZEN in water [23].

A better understanding of the spatiotemporal occurrence of natural ECs is needed to adequately assess potential cumulative impacts of such natural compounds and their mixtures on freshwater biota, humans, and animals due to their presence in drinking water. In any case, there is enough evidence on mycotoxins and phytoestrogens to consider these findings as an alert of possible endocrine-driven effects on wildlife and human reproduction.

1.3 Summary and Recommendations for Future Research

- Water quality is intrinsically associated to the health and well-being of the society and it essentially depends on the level of aquatic pollution. The so-called ECs have been detected in water bodies globally, which raises concern on water safety and quality, including drinking water. The current knowledge of the potential effects of polluted waters on living beings and ecosystems, as well as its control and regulation, represent a great challenge for societies in the twenty-first century.
- ECs include a broad range of compounds differing in their properties, such as persistence, bioaccumulation and, in some cases, biomagnification capacity, and toxicity. They are mainly associated with anthropogenic production, use and disposal (e.g. pharmaceuticals, PCPs, plasticizers, flame retardants, industrial additives, surfactants, nanomaterials, natural toxins, etc.), and the major sources into water bodies are effluents from urban and industrial WWTPs, alongside livestock and agricultural runoffs and aquaculture.
- Nowadays, WWTPs are not capable of completely removing all ECs, and they ultimately reach different water compartments. Consequently, these compounds are detected in aquatic environments and biota at a global scale at concentrations from ng l^{-1} to mg l^{-1}, which raises concerns about the potential effects on humans and wildlife. Therefore, new advances in WWTP technologies are clearly needed, so that effluents discharged into water bodies may contain lower or even null residue levels.
- Metabolites and transformation products generated from ECs, can be, in some cases, more toxic and/or persistent than parent compounds. Further research is warranted to clarify the underlying mechanisms and toxic effects of ECs and their generated compounds to elucidate potential risks of exposure to complex mixtures of this heterogeneous group of contaminants.
- The chronic exposure to low doses of these chemicals may provoke accumulative impacts in a mid- and long-term basis. To date, information about the deleterious effects related to EC exposure is still limited. Endocrine disruption in humans and aquatic wildlife, development of bacterial pathogen resistance, and chronic toxicity are currently the main effects that are being assessed to understand the risk associated to ECs exposure.
- In the last two decades there has been a significant increase of scientific studies and research regarding the broad diversity of the scientific and technological fields related to ECs and water quality. In spite of this, additional studies are still required evaluating different issues: ECs presence and persistence in water compartments and biota, toxicity and adverse human health consequences, effects in wildlife populations and ecological impacts, removal of ECs from water bodies, especially from WWTPs, relevance of natural contaminants (mycotoxins and phytotoxins) in the accumulative impacts on health, etc. This, undoubtedly, will improve water quality.

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