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REVIEW

A global overview of endocrine disrupting chemicals in the environment: occurrence, effects, and treatment methods

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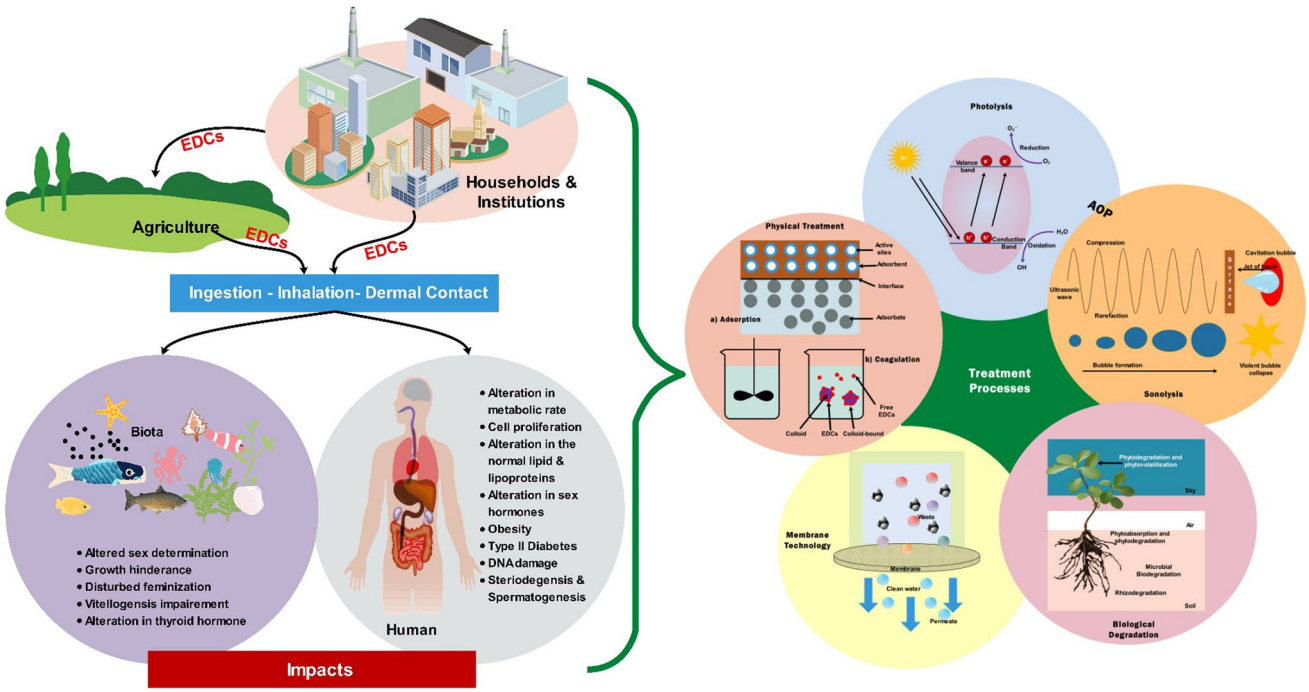
Abstract

Various chemicals are known to impact biological systems disrupting normal homeostasis, especially the endocrine system, called endocrine disrupting chemicals. Endocrine disrupting chemicals are universal in the environment, and a low concentration (µg/L to ng/L) severely impacts human health and wildlife due to transgenerational and multigenerational effects. The present review analyzed original research articles (109), review articles (76), short communication (20), article report (1), monograph (1), and scientific reports (2) via PubChem, science direct, National Center for Biotechnology Information, web of science on the source and fate of endocrine disrupting chemicals in the environment which are a prime concern to public health. A thorough investigation of the fate of these contaminants in environmental matrices such as air, water, soil, and biota is prioritized to form a clear link between the exposure and its effect on humans and biota. Environmental guidelines for these chemicals in environmental matrices and their treatment methods are also discussed in the review.

Graphical abstract



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Extended author information available on the last page of the article

Keywords Phthalate · Bisphenol A · Pharmaceuticals and personal care products · Sources · Advanced oxidation processes · Physical processes · Biological degradation and membrane technology

Introduction

Endocrine disrupting chemicals (EDCs) are exogenous in origin and potentially harm human and wildlife health even at a low concentration. The increased demand and consumption have resulted in the global existence and pseudo-persistence of these chemicals in the environment. Chemicals disrupting growth, reproduction, and the equilibrium of the body system include industrial chemicals, plasticizers, pharmaceuticals and personal care products (PPCPs) (Bergman et al. 2012).

The primary source of EDCs contamination in the environment is wastewater effluent, as conventional treatment technologies are ineffective and insufficient in removing the pollutants (Ebele et al. 2020). Concentrations from a few nanograms per litre (ng/L) to 15 µg per litre (µg/L) cause severe acute and chronic toxic effects raising serious environmental health concerns (Kasonga et al. 2021). Scientific studies and research reveal that exposure to endocrine disrupting chemicals can lead to permanent developmental damage, such as diethylstilbestrol (DES), an artificial nonsteroidal estrogen used by medical practitioners to treat menopause-related problems in females, affecting follicular growth, fertilization, and implantation in females, also cause abnormality in reproductive tracts with reduced sperm production causing infertility in males. Other classic examples including organochlorines like dicofol, methoxychlor, and dichlorodiphenyltrichloroethane (DDT) cause thinning of eggshells leading to deformity in the oviducts of female birds. Even the metabolites of dicofol cause additional effects such as the feminization of male alligators, non-formation of vitellogenin in fishes, and neurological disorders in humans. Pharmaceuticals such as ciprofloxacin, sulfamethoxazole, azithromycin, and acetaminophen, with long-term exposure to infants through their mothers, cause DNA methylation defects (Montrose et al. 2018). Further, the in vivo studies on the mixture of EDCs revealed the impact on the physiology of the hypothalamic-pituitary-thyroid axis, growth stress, and immune system in humans (Hamid et al. 2021).

Currently, occasional legislation and policies are being released in countries globally challenging to achieve water security, ensuring better quality and healthier. Waterborne disease outbreaks and the growing number of new pollutants have prompted regulatory agencies to formulate legislation and policies.

Figure 1 represents the roadmap taken up by the European and Non-European countries to combat the occurrence of EDCs in the environment. It could be observed that 205 substances fall under the category of "Substances of Very High Concern" (SVHC), with only 16 of them with the potential to cause endocrine disrupting chemicals. Currently, registration, evaluation, authorization, and restriction of chemicals (REACH) 2006 formed by the European Union (EU) identifies the risks and restricts the usage of the substances. Forty-three substances have been included in Annex XIV of REACH (two recognized as EDCs), indicating the intent to ban their use as soon as their technically and economically appropriate alternatives are available. In the USA, the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA), along with Toxic Substances Control Act (TSCA) identify the risks of the chemicals, controlling and regulating the strict compliance of the laws and legislation (Kassotis et al. 2020). Organizations such as United Nations Environment Programme (UNEP) and World Health Organization (WHO) reported and commissioned the International Panel on Chemical Pollution, identifying the twenty-eight policies to address and evaluate the EDCs and other substantial chemicals globally. Exposure to EDCs was observed in treated drinking water ranging from 0.2 to 5510 ng/L, with a maximum concentration of 280,000.0 ng/L reported in groundwater (wells) in India. WHO drinking water guidelines are inadequate compared to the exposure of the EDCs (Wee and Aris 2018). Table 1 presents the global view of the concentration ranges in diverse environmental matrices such as water and solids. This infers the ubiquitous and consistent presence of EDCs in low concentrations worldwide daily. The twelve countries or regions have regulated drinking water standards for few selected EDCs namely, 17β-estradiol (E2), 17α-ethinylestradiol (EE2), bisphenol a (BPA), 4-n-nonylphenol (NP), di-2-(ethylhexyl) phthalate (DEHP), benzyl butyl phthalate (BBP), di-butyl phthalate (DBP), di-ethyl phthalate (DEP), and di-2-(ethylhexyl) adipate (DEHA). The twelve countries include the EU, USA, UK, Australia, China, Israel, Japan, Korea, New Zealand, Oman, Philippines, Singapore, and UAE. Japan, China and the USA have been successful in regulating six, four, and two EDCs, respectively, according to their drinking water standards, while the other eight countries have only considered DEHP in their national drinking water standards. The EU has regulated only BPA in their drinking water standards (Liu et al. 2021). India follows drinking water standards for pesticides, halogenated

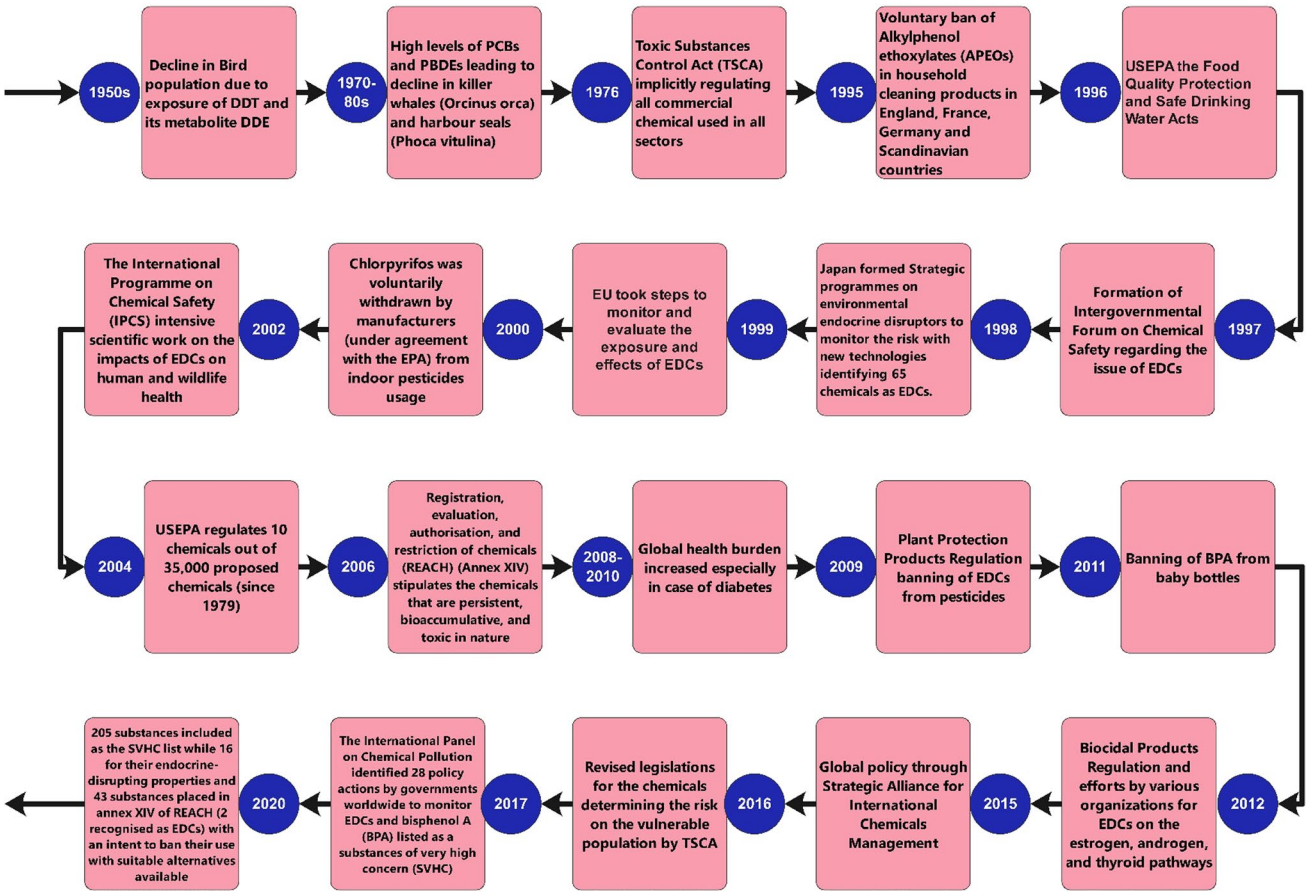


Fig. 1 Roadmap representation of regulatory measures taken for combating issues on EDCs Globally

compounds, and a few pharmaceuticals and personal care products (Wee and Aris 2018). These indicate that regulations for EDCs in environmental matrices are region-specific and lack universal guidelines without consistent monitoring.

Figure 2 explains the different point and non-point sources of EDCs entering the environment, like volatilization, precipitation, and evapotranspiration. Further, the uptake of EDCs via ingestion and inhalation has resulted in various reproductive and genotoxic effects via physicochemical and biochemical disruptions.

The present review focuses on comprehensively summarizing the current state of knowledge regarding the various classes of EDCs, some of which the EPA has identified as "the priority pollutants" primarily used in production and manufacturing processes. These EDCs also end up in various industrial effluents as a byproduct. Further, the study discusses the sources, fate, and adverse effects of various EDCs on human and biota, jeopardizing public health and the sustainable development goals (SDGs) globally. The review compares various EDC degrading methods and offers corrective actions to reduce EDC emissions into the environment.

Endocrine disrupting chemicals (EDCs)

EDCs are exogenous substances that can affect the endocrine and homeostatic systems by interfering with endogenous hormone synthesis, secretion, transport, metabolism, receptor binding, or elimination. USEPA defines them as "exogenous chemicals or mixture of chemicals that interfere with any aspect of hormone action" (Kasonga et al. 2021). EDCs enter the human body through different routes. The most frequent exposure modes are inhalation, food consumption, and direct contact. These routes suggest that EDCs could enter the food chain and build up in animal tissues and humans. Because most EDCs seem extremely lipophilic and accumulate in adipose tissue, they often have a long half-life. Being at the top of the food chain, humans, large mammals, and top predators may accumulate higher dosages of EDCs due to bioaccumulation and bioamplification. These could form a "cocktail" of effects with unknowable effects.

Figure 3 and Table 2 explain the physicochemical characteristics of EDCs based on the origin, which are broadly divided into five main categories to highlight the prevalence of these target categories in daily use.: natural and synthetic

Table 1 Global comparison of concentration range of commonly detected EDCs in different matrices

Chemicals	Location	Environmental Matrix	Concentration	References
Wastewater (ng/L)				
Triclosan (TCS)	Switzerland		Influent: 11–98	Dhillon et al. (2015)
Diethylstilbestrol (DES)	China		1.46–12	Lv et al. (2016)
∑6 parent parabens	India		Influent- 131–920 Effluent- 16–67	Karthikraj et al. (2017)
Alkylphenols	Serbia		1.1–78.3	Celi et al. (2020)
Nonylphenol (NP)	South Africa		Influent- 6720	Farounbi (2020)
Bisphenol A (BPA)	China		Influent- 100.0–10,566.7 Effluent- 15.5–1210.7	Ye et al. (2012)
4-tert-octylphenol (OP)	Canada		Influent- < 10–195,000*	Lee et al. (2019)
Estradiol	New Zealand		Effluent- 19–1360	Sarmah et al. (2006)
s∑3 hormones = 17β-estradiol (E2), estrone (E1), ethynylestradiol (EE2)	Australia		Influent- 20–54	Leusch et al. (2005)
Surface/Ground/Drinking water (ng/L)				
Butyl Paraben (BuP)	Portugal	Estuarine	7.1	Haman et al. (2014)
Estrone (E1)	Europe	River	12.5	Adeel et al. (2017)
Estradiol (E3)	China	Groundwater	3.5–7.6	Lu et al. (2020)
Methyl Paraben (MeP)	Egypt	Drinking water	47.2	Radwan et al. (2020)
Bisphenol A (BPA)	Iran	Drinking water	2–1000	Jafari et al. (2009)
Caffeine	China	Swimming pool	Indoor- ∑ average = 11.15 Outdoor- ∑ average = 1.90	Zhou et al. (2019)
Sediments/ Sludges (ng/g dry weight (dw))				
Bisphenol A (BPA)	Malaysia	Sediments	0.072–0.389	Ismail et al. (2019)
Σ7 plasticizers (PAEs + DEHA)	India	Sediments	Adyar riverine sediment- 51.82–1796 Coum riverine sediment- 28.13–856	Mukhopadhyay (2020)
∑6 EDCs	China	Sediments	ND t-492	Huang et al. (2018)
Organochlorine pesticides (DDE/DDT)	Turkey	Sediments	1.281 ± 0.754	Oguz et al. (2013)
Diclofenac (DCF)	Greece	Sludge	30	Samaras et al. (2013)

*Reported value in µg/L

hormones (estradiol, testosterone and ethinylestradiol); industrial (furans-dioxins, perfluoroalkyl, polychlorinated biphenyls (PCBs), heavy metals, and alkylphenols); agricultural (pesticides, phytoestrogens, and fungicides); household (phthalates, polybrominated biphenyls, and bisphenol A); and pharmaceutical and personal care products (parabens, antibiotics, sunscreen blockers).

Phthalates (PAEs)

PAEs are a group of compounds that include alkyl, aryl, and dialkyl esters of phthalic acid (1,2-benzene dicarboxylic acid). They are produced by the reaction of phthalic anhydride with an appropriate alcohol. PAEs lack a covalent bond between them and the polymer and are available in the free and mobile form in the environment (Baloyi et al. 2021). Hence, PAEs enter the environment through several pathways, including losses during manufacturing processes, leaching or volatilization from final products, waste, and treated effluents (with minute concentration) from wastewater treatment plants (Das et al. 2021, Przybylinska and Wyszkowski 2016). Table 3 summarizes the physicochemical properties of PAEs that play a crucial role in determining the fate and transportation in environmental matrices and the effectiveness of the treatment methods for maximum removal efficiency. The presence of PAEs in the air is determined by the Henry constant value and the log Kow parameters. Long-chain PAEs with a higher log Kow value have lower water solubility and vapour pressure and are unlikely to evaporate. In the case of moist soil, PAEs are moderately volatile and are not likely to bioaccumulate except in the case of DEHP. Low molecular weight (LMW) PAEs in a pure state have a high value of the air–water partitioning (log K_{AW}) and hence evaporate more rapidly from water than in the aqueous form. Many PAEs absorb the aerosol particles due to the high value of octanol–air partitioning (log K_{OA}). Biodegradation is more dominant in PAEs than hydrolysis and photolysis, which are proven to have gradual degradation in nature, such as the half-life for BBP is > 100 days, DMP is three years, and DEHP is 2000 years.

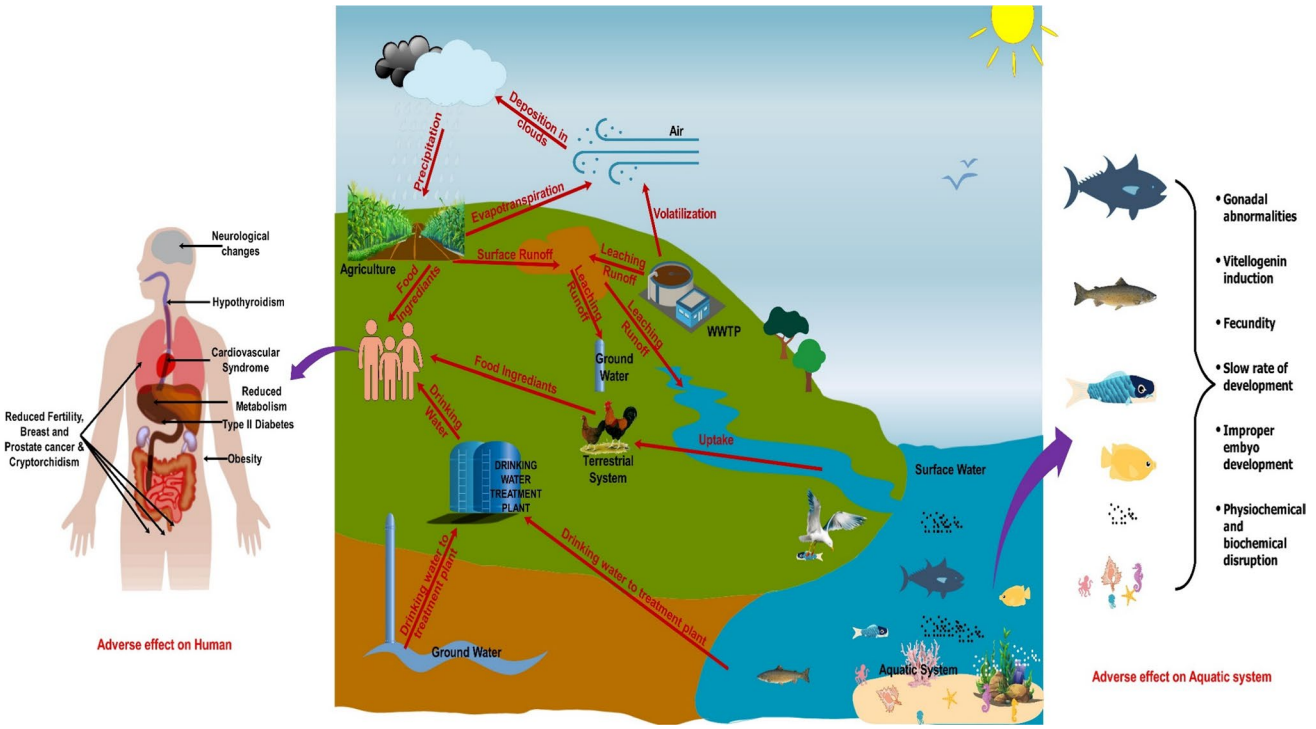


Fig. 2 Sources, Fate, and adverse effect of endocrine disrupting chemicals (EDCs) on humans and biota

Since the 1930s, PAEs have been widely used in synthetic organic chemicals due to increased economic and commercial interests in agriculture, packaging materials, and personal care goods (Heo et al. 2019). Global production of PAEs has increased from 2.7 to 6 million tons per year (approximately) from 2007 to 2017 (Bu et al. 2020). Among various PAEs, compounds such as dibutyl phthalate (DnBP), di-iso-butyl phthalate (DBP), benzyl butyl phthalate (BBP), and di(2-ethyl-hexyl) phthalate (DEHP) are classified under reproductive toxicants (Class 1B). According to the United States Environment Protection Agency (USEPA) 2B and C group, BBP and DEHP are regarded as potential human carcinogens (Lee et al. 2019). The route of exposure in humans and biota is through dermal, ingestion, and inhalation. (Teil et al. 2016) detected 10-100 ng/m^3 PAEs concentration in air of surrounding urban area, 74 µg/L of DEHP concentration in leachate, which was 1.7-56 times higher than recommended by the EU limit for surface water, i.e., 1.3 µg/L (Wowkonowicz and Kije 2017) and 4000 ng/L of PAEs in drinking water (Net et al. 2015).

The direct and indirect release of the PAEs into the environment risks human and wildlife species. PAEs mimic the normal homeostasis and estrogenicity (mediated by two estrogen receptors, alpha and beta) and disrupt the hypothalamic-pituitary-gonadal (HPG) axis pathway in vertebrates. A recent review by Mohammadi and Ashari reported the mechanism of toxicity associated with PAEs via mimicking on the nuclear surfaces (such as erythroid 2–related factor 2 (Nrf2), nuclear factor-κB (NF-κB), and phosphatidylinositol-3-kinase (PI3K)/AKT), resulting in the inexpression of genes, leading to alterations in cell hemostasis and toxic effects such as reproductive, cardio, hepato, nephro, teratogenicity, and tumor development (Mohammadi and Ashari 2021). It is evident that PAEs and their metabolites interact and disrupt several endocrine molecular signalling pathways, proving toxic (Kahn et al. 2020; Ribeiro et al. 2020). Agencies like USEPA have established the tolerated daily intake (TDI) (g/kg body weight per day) values for monomethyl phthalates (3500 g/kg body weight per day) with PAEs (i.e., DEHP, BBP, DNBP, and DIBP) listed as "Substances of Very High Concern." by the EU.

Parabens

Parabens are p-hydroxybenzoic acid alkyl esters (p-HBA) which are inert, odourless, tasteless, colourless, lipophilic, and stable in a wide pH range (Fransway et al. 2019; Nowak et al. 2020). Parabens have antimicrobial properties and are used in various processed and packaged foods, such as fruit juices, pickles, sauces, soft drinks, in cosmetic products like lotions, deodorants, hair gels, shampoos, creams, and toothpaste. Parabens are ubiquitous in environmental matrices, and the main sources of parabens in the aquatic environment have been identified as municipal wastewater that enters via

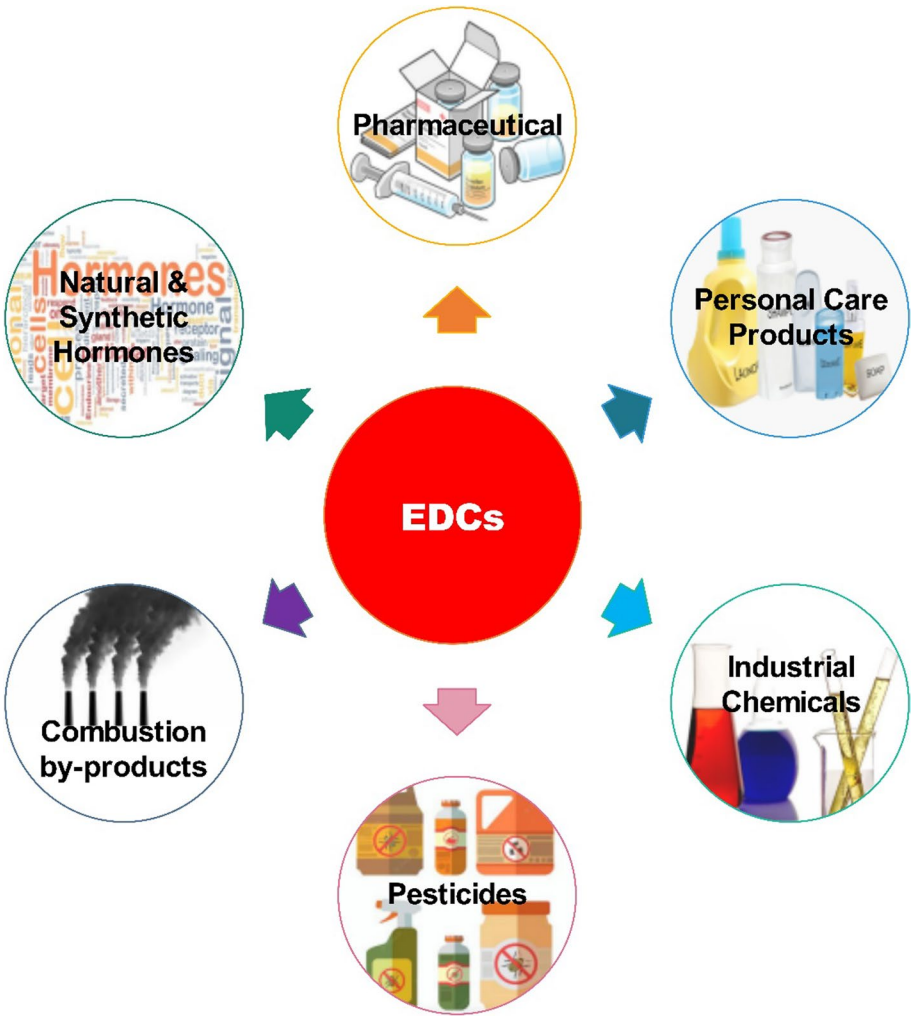


Fig. 3 Categories of EDCs on basis of origin

sewage and industrial discharge, surface runoff via urban drainage, or atmospheric deposition. Moderately soluble in water and hence detected in the dissolved or sorbed in the form of sludge or organic-rich floating particles in WWTPs (Haman et al. 2014). Five WWTPs detected $\sum_6$ parent parabens and $\sum_5$ paraben metabolites in influent, effluent, and sludge samples, ranging from 131–920 ng/L, 16–67 ng/L, and 104–1090 ng/g dry weight (dw) in influent, effluent, and sludge samples, respectively, with a removal efficiency of 80–100%. While $\sum_5$ Paraben metabolites ranged from 4110 to 34,600 ng/L in influent, 2560–3800 ng/L in effluent, and 1220–35,900 ng/g dw in sludge with 28–76% removal efficiency. The study signifies the presence of transformed products or metabolites are more dangerous than the original compounds (Karthikraj et al. 2017). Chen et al. studied 80 indoor dust samples for parabens in the U.S. due to personal care products with a maximum concentration of 140–39,090 ng/g (Chen et al. 2018).

Human and animal exposure to parabens is due to inhalation, ingestion, and dermal contact. The toxicity of parabens is debatable, as a recent review by Fransway et al. mentioned that parabens are transformed into a less toxic compound by the cutaneous carboxyesterases enzyme (Fransway et al. 2019). However, previous scientific evidence does depict the toxicity of parabens. Dobbins et al. studied the lethal concentration (LC_{50}) of *Daphnia magna* and *Pimephales promelas*. Paraben concentrations of 0.12–25 mg/L showed negative growth in both species, causing toxicity in their normal body functioning. Other studies, such as Yamamoto et al. (2011), Tersaki et al., Nagar et al. (2020), and Gouukon et al. (2020), all reflect the toxicity of parabens on different species (Gouukon et al. 2020; Nagar et al. 2020). Humans observe several negative impacts on synthesis and metabolism. Parabens' interaction with various steroid-sensitive tissues causes malfunctioning the central nervous system and immune system (Raza et al. 2017). The aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor employed as a toxin indicator, the activation of which by xenobiotics in the environment is called a toxicity sensor (Irigaray and Belpomme 2010). Gouukon et al. (2020) studied the AhR agonist activity of mono-brominated parabens mediating

Table 2 Physicochemical characteristics and classification of endocrine disrupting chemicals (EDCs) on the basis of their origin

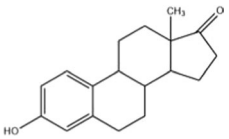
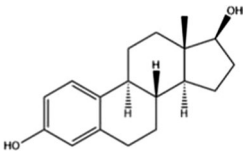
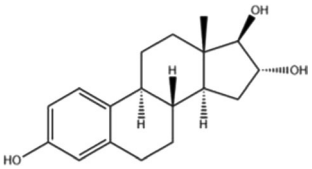
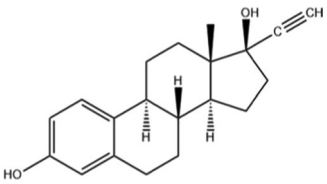
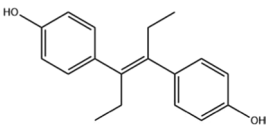
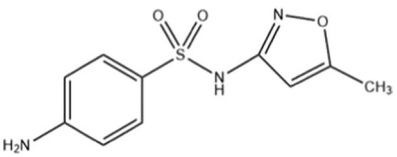
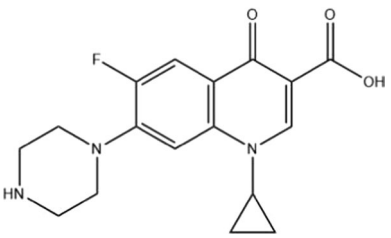
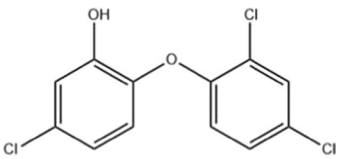
Compounds	Formula	Chemical Structure	Molecular weight (g/mol)	Log Kow	References
Natural Hormones					
Estrone (E1)	$C_{18}H_{22}O_2$		270.4	3.1–4.0	Shareef et al. (2006)
17β-Estradiol (E2)	$C_{18}H_{24}O_2$		272.4	3.1–4.0	Holbrook et al. (2004)
Estriol (E3)	$C_{18}H_{24}O_3$		288.4	2.6–2.8	Sarmah et al. (2006)
Synthetic hormones					
17α-ethinylestradiol (EE2)	$C_{20}H_{24}O_2$		296.4	4.15	Shareef et al. (2006)
Diethylstilbestrol (DES)	$C_{18}H_{20}O_2$		268.4	5.64	Zhang et al. (2011)
Pharmaceuticals and personal care products					
Sulfamethoxazole (SMX)	$C_{10}H_{11}N_3O_3S$		253	0.89	Giang et al. (2015), Nagulapally et al. (2009)
Ciprofloxacin	$C_{17}H_{18}FN_3O_3$		331.3	0.28	Ratola et al. (2012)
Triclosan (TCS)	$C_{12}H_7Cl_3O_2$		289.54	3.5–4.8	Bedoux et al. (2012)

Table 2 (continued)

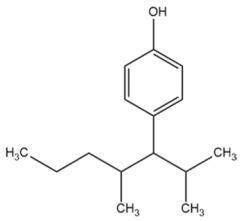
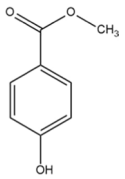
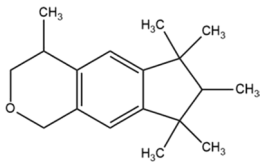
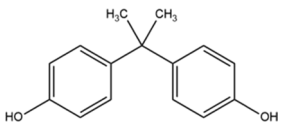
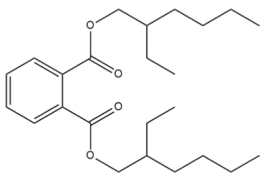
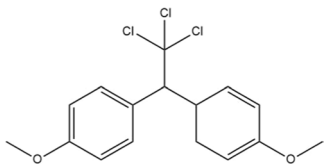
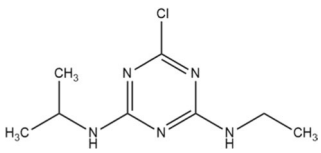
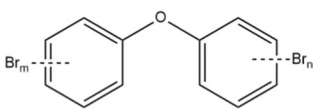
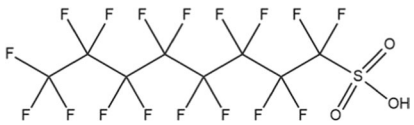
Compounds	Formula	Chemical Structure	Molecular weight (g/mol)	Log Kow	References
Nonylphenol (NP)	$C_{15}H_{24}O$		220.4	4.48	Zhang et al. (2011)
Methyl Paraben	$C_8H_8O_3$		152.15	1.96	Haman et al. (2014)
Galaxolide	$C_{18}H_{26}O$		258.40	5.9–6.30	Lefebvre (2016)
Industrial and agricultural chemicals					
Bisphenol A (BPA)	$C_{15}H_{16}O_2$		228.3	3.32	Choi et al. (2005)
di(2-ethylhexyl) phthalate (DEHP)	$C_{24}H_{38}O_4$		390.54	4.5	Peijnenburg and Struijs (2006)
Methoxychlor	$C_{16}H_{15}Cl_3O_2$		345	5.08	Abbasi and Mannaerts (2020)
Atrazine	$C_8H_{14}ClN_5$		215.7	2.5	Aslam et al. (2013)
Polybrominated diphenyl ether (PBDE's)	$C_{12}Br_{10}O$		959.17	6.27	Wee and Aris (2018)
Perfluorooctanesulfonic acid (PFOS)	$C_8HF_{17}O_3S$		500.13	6.28	Wee and Aris (2018)

Table 3 Physico-chemical Properties of PAEs

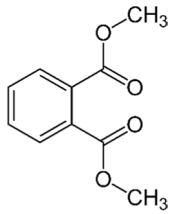
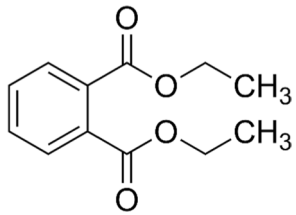
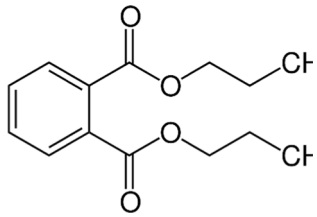
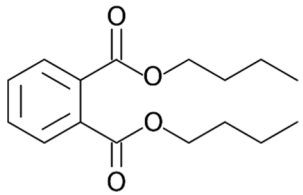
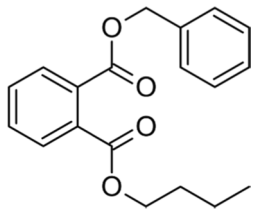
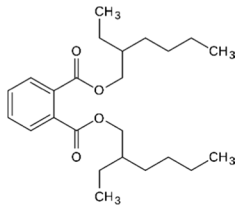
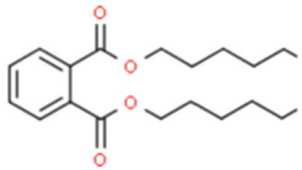
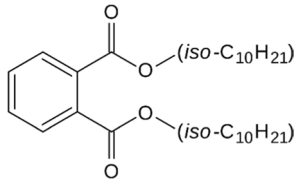
PAEs	Chemical Structure	Mol. Wt. (g/mol)	Sw at 25°Cmg/L	Vapour pressure at 25 °C (Pa)	Henry constant (at 25 Pa. m^3/mol)	Log Kow	Log Koc	References
Dimethyl phthalate (DMP)		194	5220	0.26	9.78×10^{-3}	1.61	55–360	Cao (2010), Clara et al. (2010), Net et al. (2015)
Diethyl phthalate (DEP)		222	591	6.48×10^{-2}	2.44×10^{-2}	2.54	69–1726	Cao (2010), Net et al. (2015)
Di-n-propyl phthalate (DnPrP)		250	77	1.74×10^{-2}	5.69×10^{-2}	3.40	–	Net et al. (2015)
Di-n-butyl phthalate (DnBP)		278	9.9	4.73×10^{-3}	0.13	4.27	1375–14,900	Cao (2010), Net et al. (2015)
Butyl benzyl phthalate (BBzP)		312	3.8	2.49×10^{-3}	0.21	4.70	9×10^3–17×10^3	Cao (2010), Net et al. (2015)

Table 3 (continued)

PAEs	Chemical Structure	Mol. Wt. (g/mol)	Sw at 25°Cmg/L	Vapour pressure at 25 °C (Pa)	Henry constant (at 25 Pa. m^3/mol)	Log Kow	Log Koc	References
Di(2-ethylhexyl) phthalate (DEHP)		390	2.49×10^{-3}	2.52×10^{-5}	3.95	7.73	–	Cao (2010), Net et al. (2015)
Di-n-octyl phthalate (DnOP)		390	0.2[a]	1.44×10^{-4}*	3.95	7.73	–	Cao (2010), Net et al. (2015), Srivastava et al. (2010)
Diisodecyl phthalate (DiDP)		446	3.81×10^{-5}	1.84×10^{-6}	–	9.46	–	Cao (2010)

Sw: Water solubility, Mol. Wt.: Molecular weight, Log Kow: octanol–water partitioning, Koc: organic, carbon partitioning

[a]Water solubility at 20 °C mg/L

*: Vapour pressure at 23 °C mmHg

similar toxicity by polychlorinated biphenyls (PCBs) due to similar structures, supporting Sasaki and Terasaki's findings (Gouukon et al. 2020).

Bisphenol A

Bisphenol A (BPA), also known as 2,2-(4,4′-dihydroxyphenyl) propane, is an organic synthetic chemical with two phenol moieties linked together by functional groups in construction materials and consumer products, including plastics and resins. Even canned foods and beverages, medical equipment, toys, and thermal receipts contain it (Iribarne-durán et al. 2019; Molina-Molina et al. 2018). The European Chemicals Agency recently designated BPA as a reproductive toxin and a chemical of high concern (ECHA 2017). Many structural counterparts have been introduced to replace BPA, such as bisphenol S (BPS), bisphenol F (BPF), bisphenol AF (BPAF), bisphenol AP (BPAP), bisphenol Z (BPZ), and bisphenol B (BPB) which induce estrogenic and neurobehavioral disruption as BPA (Chen et al. 2016; Rosenfeld 2017; Soto et al. 2017).

The physicochemical properties of bisphenol A and analogues determine the fate and transportation in the environment. Bisphenol A is moderately soluble due to its two non-polar methyl groups. At the same time, its analogues range from low to high as presence of non-polar groups have equal distribution of electron charge between C–C and C–H bonds making then unreactive (i.e., poor polarity), resulting in decreased water solubility (BPP). In contrast, the vice-versa behaviour results in improved water solubility (BPS). Bisphenols tend to partition in soil, vegetation, and aerosols more than gases due to the moderate to high log K_{ow} (Morin et al. 2015). Bisphenols being low volatile ($H < 1.01 \times 10^{-2}$ Pa·m^3/mol) do not evaporate in the air. Bisphenol A and its mixture of analogues cause the breaking of the double DNA strands by up-regulation of *CYP1A1* and *UGT1A1* and *CDKN1A* and *GADD45a* genes and down-regulation of *GST1A* (Hercog et al. 2019). BPA is a known EDC to cause geno- and cytotoxicity in humans. USEPA has set a maximum TDI of 50 µg/kg body weight per day, and the Canadian government has also banned the use of BPA in the import and sale of BPA-containing bottles. Furthermore, the European Union replaced BPA with its equivalents, which are more dominant EDCs than bisphenol A (Pelch et al. 2019; Zhu et al. 2020).

Pharmaceuticals and personal care products

Many pharmaceuticals and personal care products (PPCPs) have been continuously found in aquatic habitats worldwide in recent decades. Antibiotics, analgesics, steroids, antidepressants, disinfectants, scents, and various other compounds are among the many chemicals used daily for various purposes. PPCPs are frequently used (pseudo persistent) to help improve the overall health and well-being of humans and animals, with a rare potential to cause physiological distress at low concentrations, making them dangerous enough to alter the biological processes (Ebele et al. 2020; Sangion and Gramatica 2016).

Anthropogenic activities such as sewage discharge, animal breeding, and leachate can release PPCPs into the environment, causing them to be present in surface water and groundwater at ng/L to mg/L concentrations. Continuous exposure to low, subtoxic doses of certain PPCPs has unforeseen repercussions and unintended impacts on non-target. Recent studies have indicated that drugs are present in all environmental matrices from 71 nations (Beek et al. 2016; Fischer et al. 2021; Patel et al. 2018). The physicochemical features of PPCPs determine their environmental route and movement through the aquatic ecosystem. Pollutants enter surface water by runoff from agriculture, rainfall, and direct waste discharge into water bodies. They then leach into the groundwater, adding to the pollution load in the system (Puri et al. 2022). There were concentrations of ofloxacin, norfloxacin, and azithromycin in Spain that ranged from 10.2 to 367 ng/L, BDL-2 ng/L in the aquifer (karst system), and BDL-68 ng/L in the Danube River, Serbia, respectively (Tijani et al. 2016). In 148 samples, caffeine and other stimulants were found in the urban catchment area of Singapore at a concentration of BDL-16249 ng/L with a detection frequency of 80–83% (Tri et al. 2016). In Lagos, Nigeria, drinking water samples included amoxicillin concentrations of 1614, 238 and 358 ng/L, respectively. With detection rates above 70%, acetaminophen, nicotine, ibuprofen, and codeine are some of the most frequently found drugs (Limousy et al. 2016). E1, E2, and EE2 are estrogenic chemicals found in low concentrations in Northern America and Europe, ranging from 0.1 to 12.5 ng/L, 0 to 5.5 ng/L, and 0.1 to 4.3 ng/L, respectively (Adeel et al. 2017).

PPCPs aim to maximize biological activity at low dosages while targeting specific metabolic, enzymatic, or cell-signalling pathways. The probability that these medications will be pharmacologically active in organisms other than the targets is increased by the evolutionary conservation of these molecular targets in a particular species. The concept of the mode of action (MoA) can be applied to any aquatic biota that unintentionally comes into contact with pharmaceuticals in its natural environment, raising the risk of ecotoxicological effects and what is sometimes referred to as antimicrobial resistance. The antidepressant fluoxetine, which targets the serotonin (5-HT) signalling system, was used to evaluate the MoA conceptual framework. Because 5-HT is a top-tier physiological controller in aquatic species,

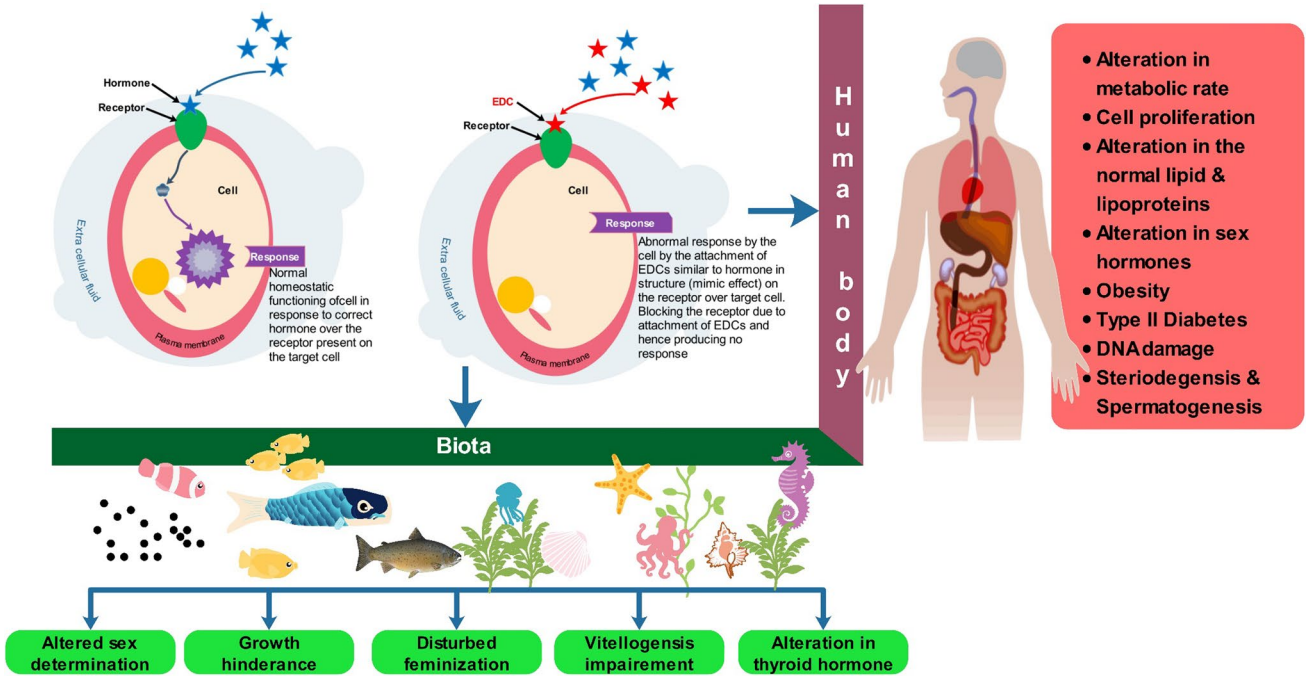


Fig. 4 Impacts of EDCs on human and biota

fluoxetine changes had many adverse effects on essential physiological activities in mussels, including reproduction, metabolism, and motility, at concentrations close to or even below environmental limits (Fabbri et al. 2016; Ford et al. 2018). The compounds diphenhydramine, thioridazine, sertraline, and dextropropoxyphene were shown to have the highest potential for acute toxicity in the populations of algae, invertebrates, and fish. The acute toxicity of analgesic drugs was shown to be relatively insensitive to bacteria, fish, and amphibians but most sensitive to phytoplankton and invertebrates. Another study investigated the sublethal and cytotoxic effects of PPCP, both singly and in combination, by measuring cell viability, oxidative stress, cellular senescence, and activation of CYP1A in the RTG-2 rainbow trout cell line. Cashmeran and galaxolide had EC_{50} values for the β-galactosidase assay of 40 µg/L, whereas most of the individual studied compounds had EC_{50} values of 150 µg/L or above. Contrarily, in this assay, the mixture of pharmaceuticals and EDCs had an experimentally observed EC50 value of 32.23 µg/L and a predicted EC_{50} value of 489.21 µg/L for β-galactosidase. (Fernández et al. 2012). Drinking water or ingesting organisms are two possible sources of human exposure to pharmaceuticals. Some PPCP molecules can persist in the drinking water system for extended periods (Liu et al. 2019). In recent investigations, drugs in urine have been studied, and the health hazards associated with them have been analyzed. The detection of many low-dose antibiotics in the urine of adults (21–75 years old) demonstrated health hazards caused by antibiotic-induced gut microbial disruption (Wang et al. 2018).

Impacts of EDCs

Impact of EDCs on humans

EDCs, when present in nanomolar or micromolar concentrations, activate receptors and change the body's feedback mechanism causing chromosomal instability. Figure 4 demonstrates that the hormones produced activate receptor cells where they bind to the target cell. Further, the EDCs attach to ligands, mimic the normal function, and changes occur in the process, leading to alterations in the transcription of the newly synthesized proteins. EDCs also interact with steroid hormones via distinct pathways. The membrane oestrogen receptor (mER) releases Ca2 + ions along with changes in prolactin secretion, which impairs immunological response and causes cell proliferation. Even receptors such as cAMP, kinases, and cyclases are impacted (Annamalai and Namasivayam 2015).

The in vivo test with 750–1000 mg/kg/day of DEP (0.71–4.6 µg/kg/day permissible limit) for 12–30 days causes testicular & epididymal atrophy, haemorrhagic testis, foetal death, respiratory distress, and pathological changes (Annamalai and Namasivayam 2015). A study by Yawer et al. (2020) reported that EDCs disrupt testicular homeostasis due to the testicular gap junctional intracellular

communication (GJIC). Disruption in the early phase of steroidogenesis in prepubertal Leydig cells contributes to the prolonged damage to male reproductive health (Yawer et al. 2020). The effect of EDCs is not limited to the in vivo and in vitro studies but is also observed in infants because of the affected mothers. Since the infant is attached to the mother's umbilical cord, the transportation of compounds from the mother to the infant becomes easy, disrupting DNA-methylation. Compounds such as Bisphenol A (BPA) and phthalates are known for causing these disruptive effects (Montrose et al. 2018).

The severity of effects of EDCs is dependent on variable factors such as the age of exposure, modification of DNA genes, the delay between exposure and onset of symptoms, the concentration of EDCs, and low dose effect. EDCs exposure at a young age has its severe impacts evident in adulthood. Some substances are 100 times more potent in low concentration than in high (low-dose effect), and direct exposure to the same causes DNA mutations in generations (Kabir et al. 2015). Infants are vulnerable to getting affected through the umbilical cord of the mother. BPA and phthalates effects are sex-specific and affect the foetal liver enzymes, which control the β- oxidation process, responsible for the infant's growth and normal homeostatic development. Due to BPA and phthalates in the first trimester, changes in DNA occur, disrupting the ability of gene expression and bringing toxic-epigenetic changes (Montrose et al. 2018).

Numerous experimental research data have substantiated the disruption in the growth, function, hormone production, action, and metabolism of mammalian endocrine systems due to the increase in the number of EDCs. Additionally, the results inferred from both animal and human model studies support the hypothesis that exposure to EDCs during foetal development and puberty causes an increase in cases of reproductive disorders, endocrine-related cancers, infections, asthma, and possibly obesity and diabetes, as well as behavioural and learning problems like attention-deficit/hyperactivity disorder (ADHD). They can afflict abnormalities up to 5–10% in babies and cause autism spectrum disorders up to 1% among children. Hence, it can be concluded that these complex non-communicable diseases have both a genetic and an environmental component (up to 24%) that contribute to the development of human diseases and disorders following exposure to EDCs (Bergman et al. 2012; Nuttal et al. 2013).

Impact of EDCs on biota

The effects of EDCs on the biota are different in terms of function, growth, reproduction, and metabolism. The unspecified sources, concentration, and biotransformation products of EDCs in the environmental matrices increase toxicity impacting the biota (Miller et al. 2019). Castro-català et al. (2016) studied a series of approaches to detect the ecotoxicological effects in the organism and identified the variables responsible for the toxicity in rivers. The organophosphate chlorpyrifos resulted in toxicity in *Daphnia magna* and mortality in *Chironomus riparius* as long-term toxicity (Castro-català et al. 2016). Exposure to EDCs during the critical developmental stages induces changes in both reproductive and non-reproductive organs. A study on the effect of BPA and Vinclozolin (Vz) on the terrestrial isopod *Porcellio scaber* (common rough woodlouse) was performed by Lemos et al. (2010). The chemicals affect the developmental toxicity in the species by decreasing the overall growth and inducing chronic sensitivity (Lemos et al. 2010). The estrogenic chemicals affect specific genes due to the absence of ER receptors in cells, resulting in ligand-independent gene activation, such as in octopus and sea slugs. Pesticides, namely pyriproxyfen (3–30 nM) and TCDD, lead to increased mortality in *Eucypris virens* (freshwater ostracod) and reproductive dysfunction in lake trout, respectively (Watanabe et al. 2018).

Wang et al. (2019) studied the endocrine disrupting effect of pesticide thiamethoxam and its metabolite clothianidin on gonads in *Eremias argus* (farmland lizard). The 28 days of exposure to the pesticide and its metabolite on the male and female farmland lizard led to the endocrine disruption of gonads by the up-regulation of cyp17 & cyp19 genes in testis and hsd17β gene in ovaries resulting in a decrease of testosterone levels with an increase in 17-estradiol concentration in plasma in males and increased levels of testosterone in plasma in females (Wang et al. 2019). EDCs alone and in a mixture creates a cocktail of effects in an intact organism with possible antiandrogen and antithyroid behaviour. The mixture tends to have more toxicity than the individual EDCs. Rainieri et al. (2017) studied the toxic effects of the perfluorinated compounds (PFCs), namely perfluoro-octane sulfonate (PFOS), perfluoro-octanic acid (PFOA), and perfluorononanoic acid (PFNA) in a human macrophage cell line (TLT cells) and zebrafish embryos. Depending on the concentration, the mixture of PFCs showed more acute toxicity than the individual compounds in the zebrafish (Rainieri et al. 2017).

Further, exposure to EDCs has compromised the endocrine system function in wildlife species, such as PCB contamination in the Baltic Sea, and high levels of POP observed in very high rates of reproductive failures and disruption in the thyroid and bone health in grey seals, respectively. Additionally, the antifouling agent tributyltin has disrupted mollusc sexual development worldwide. The most current research on PCB-exposed animals has revealed vital details on exposure levels, early and subclinical impacts, and the clinical neurotoxicity of these chemicals, shedding light on the mechanisms underlying the effects and results of EDCs exposure identical to those

in humans. EDCs affect behaviour, fecundity, growth, survival, and immunological function, making vertebrates—especially marine mammals—more vulnerable to infectious illnesses (Bergman et al. 2012; Nuttal et al. 2013).

The data demonstrate that exposure to EDCs significantly impacts trends in wildlife and human health, as shown in Table 4.

Treatment methods

Several contaminants originating from industrial sources observe endocrine activity. Many issues about these compounds remain unanswered, and their long-term persistence makes them a significant hazard for future generations.

In nature, most EDCs are persistent, widespread, lipophilic, and bio-accumulative. They are hydrophobic and do not disintegrate quickly in the environment (Chen et al. 2019). Its widespread presence in the environment, even at low amounts, poses a threat. This section deals with the removal methods for the group of EDCs. Table 5 represents the currently available methods employed in degrading different categories of EDCs with their removal efficiencies obtained for various treatment processes at optimal conditions. While Fig. 5 signifies the mechanism of action involved in the discussed treatment methods for the target categories of EDCs.

Physical treatment

Coagulation/flocculation and adsorption are used to reduce suspended solids, ions, colloid particles, floating materials, oil and grease, colour, heavy metals, and other persistent and non-persistent substances. However, there are some downsides to these processes, including the production of sludge, the release of metal ions, the difficulty of regenerating adsorbents, the absence of suitable low-cost adsorbents, and the poor mineralization of harmful organic molecules into safe byproducts (Gu et al. 2021).

Coagulation/flocculation

In order to destabilize the colloidal dispersion and encourage agglomeration of the individual colloidal particles through charge neutralization, the process is carried out by adding various kinds of coagulants or floc-forming chemical reagents to the wastewater. Sedimentation is then performed after the sedimentation. In order to evaluate the removal of PAEs from landfill leachate, three coagulants—ferric chloride, aluminium sulphate, and polyaluminum chloride—were utilized. The results show that the coagulation-flocculation method simultaneously eliminates compounds with log $K_{OW} > 4$ and dissolved organic matter with a removal rate better than 50%, while aluminium chloride only removes 30% (Bhatnagar and Sillanpää 2011). The processes are known to be ineffective for removing parabens and bisphenols (Barzegari et al. 2015; Tufail et al. 2020). Pharmaceuticals, namely acetaminophen, atenolol, antipyrine, indomethacin, roxithromycin, sulfamethoxazole, tiamulin, and trimethoprim, were all treated, with only indomethacin removed at better than 40% efficiency. Pollutant-specific parameters, such as the octanol–water partition coefficient (Kow) and the weak acid-hydrolysis coefficient (pKa), would influence the removal efficacy of coagulation-flocculation and sedimentation. The greater pKa value of a contaminant during treatment would help to exchange PPCPs into ionic states, where they may be easily adsorbed onto particles and the flocs generated in coagulation by electrostatic interactions (Vieno et al. 2007).

Higher Kow values are linked to increased hydrophobicity improving target contaminant removal through hydrophobic interactions. Kow had a lower contribution than pKa, to the removal efficiency of combined coagulation-flocculation and sedimentation, which is consistent with previous research that found Kow to be a limited and unstable predictor of the removal of some PPCPs, such as polar compounds, example, tiamulin (Kim et al. 2010).

Adsorption

Adsorbate builds up on a solid or liquid surface due to the surface phenomenon known as adsorption. The adsorbent's available surface area, or active sites, is the most important factor regulating the adsorption process. Two more important factors that determine the adsorption process are temperature and the medium's pH, which regulates the surface charge of adsorbents and the process's thermodynamics. Additionally, the adsorption of an organic molecule is governed by its chemical makeup and polarity. Moreover, the availability of different functional groups affects how much the chemical structure is involved. In the context of the octanol–water system, the partitioning coefficient K_{OW}, a quantitative measure of polarity, establishes a molecule's hydrophobicity (lipophilicity). As a result, the substance's capacity to adsorb depends on the value of Log K_{OW} (Gao et al. 2017).

Ester groups operate as electron acceptors when adsorbing PAEs with long alkyl chains from an aqueous medium, interacting with the adsorbent's electron donor to create the electron–donor–acceptor (EDA) interaction (Ye et al. 2020). Additionally, some functional groups with which the ester group can form hydrogen bonds can help the adsorption process. As a result, depending on the pH, phthalates interact

Table 4 Impacts of EDCs on humans and biota

EDCs	Species	Chemical Exposure	Effect	References
Genistein	Fishes	50–100 µM	Alteration in the sex steroid levels and reproductive dysfunction	Ingham et al. (2004)
Triclosan	*Daphnia magna*	390 µg/l	Mortality	Dhillon et al. (2015)
Dioxins, Furans, Phytoestrogens	Human	–	Development of breast cancer	Lauretta et al. (2019)
Musks, BPA, herbicides, fungicides	Human and animals	–	Disrupts female sexual development by targeting progesterone receptor (PR)	Encarnação et al. (2019)
17α-ethynylestradiol	Bullfrog tadpole	10 ng/L	Heart issues	Adeel et al. (2017)
2,3,7,8-Tetrachlorodibenzodioxin (TCDD)	Guinea pig and rats (in vivo)	–	Pancreatic cell death by autophagy in β cell line (INS-1E) and insulin resistance observed by decreasing the cellular component (RNA/protein)	Lind and Lind (2018)
Perfluoroalkyl acids	5 months old adult *Danio rerio*	0.01, 0.1, and 1 mg/L chronic long-term 180 days exposure	Reduction in egg production in females and gonad somatic index (GSI) in males	Shen and Zuo (2020)
Lindane	*Caenorhabditis elegans*	1 ng/L	Altered insulin and gene expression resulting in multigenerational changes	Chen et al. (2019)
Diethyl phthalate (DEP)	Rats (in vivo)	750–1000 mg/kg/day 0.001–4.2 mg/hour for 12–30 days	Testicular & epididymal atrophy, haemorrhagic testis, foetal death, Respiratory distress and pathological changes. In semen (0.08–1.32 mg/l) infertility and reduced sperm quality	Annamalai and Namasivayam (2015)
Butyl Paraben (BuP)	In utero rats (male/female)	100–200 mg/kg/day Male mice (27–29 days): 14, 150, 1500 mg/kg/day	Low sperm count, increase of epididymis, decrease of spermatids, decrease in daily sperm production	Golden and Gandy (2005)
Diethylstilbesterol (DES)	Human and wildlife	–	Vagina adenocarcinoma in females, pseudo hermaphroditism, epididymal cysts in males, foetal disorder, breast cancer and testicular cancer Reduced fertilization, immune dysfunction, breast and prostate cancer	Kabir et al. (2015)
Mixture of Parabens	Humans and rodents	–	In rats' metabolic alterations observed with decrease in birth weight (prenatal) and obesity (post- natal)	Xin et al. (2015)

Table 5 Removal methods of EDCs

Chemicals	Source	Process	Dose	Detection	Observation	References
Physical treatment						
Triclosan (TCS)	Waste water effluent	Coagulation/flocculation Sand filtration and chlorination	–	–	89% (coagulation) 86.6% (Sand filtration + chlorination)	Yang et al. (2017)
Hormones (E1, E2, EE2)	Waste water effluent	Coagulation/flocculation Sand filtration and chlorination	–	–	E1- 87–93.8%, E2- 95.2%, EE2- 90%	Yang et al. (2017)
Primidone	Synthetic water	Adsorption	Graphene, Conc. 10 mg/L	UV at 276 nm	97%	Rizzo et al. (2015)
Octylphenol	Surface water	Adsorption	PAC, dose: 5 mg/L, conc. 100 ng/L	GC/MS/MS	65%	Snyder et al. (2007)
Chemical or advanced oxidation processes						
Bisphenol A (BPA)	Aqueous solution	Fenton/UV	10 mg/l	GC–MS	BPA removal 90% in 9 min. Mineralisation occur above 90% to carbon dioxide	Liu et al. (2008)
Ciprofloxacin	Wastewater	UV/H_2O_2	550 W/m^2, pH 2.5, temp 17 °C, H_2O_2 50 mg/L, 30 min, conc. 129 ng/L	–	100%	Esplugas et al. (2007)
17α-ethnylestradiol (EE2)	Surface water	Dark ozonation	Initial conc. of ozone: 0.1,0.2,0.5,1 & 2 mg/l	–	At 0.2 and 0.5 mg/L of ozone concentration removal efficiency obtained 97%	Esplugas et al. (2007)
Diethylstilbestrol (DES)	Aqueous solution	Ultrasonic induced radiation with iron (II) as a catalyst	Conc. of H_2O_2: 450 mM with ultrasonic radiations: 665 kHz for 1 h	–	Addition of Fe (II) catalyst enhanced the degradation of DES faster	Abderrazik et al. (2005)
		Ozonation	pH 9.0, Ozone conc. 0.38 mg/min	HPLC	100% degradation within 6 min process time. Increase of conc. of EDC's hence lower degradation efficiency	Lin et al. (2009)
Diethyl phthalate (DEP)	Aqueous solution	Ultraviolet (UV) with ultrasound frequency. UV-induced with H_2O_2	UVC: 254 nm, VUV: 185 nm and 254 nm with ultrasound frequency: 283 kHz	–	Faster degradation observed in combined UVC and VUV process than UVC alone. More energy production with high number hydroxyl radical (OH^-) due homolysis of water. H_2O_2 enhances DEP degradation	Na et al. (2012)

Table 5 (continued)

Chemicals	Source	Process	Dose	Detection	Observation	References
Butyl paraben (BuP)	Aqueous solution	Ozonation process	Conc. O3: 0.67 g/h for 12 min, pH range: 2.5–10 at T°: 25 °C	–	99% Paraben degradation observed. In 500 µM paraben solution additional removal of 61% Chemical oxygen demand (COD) and 32% Total organic carbon (TOC) with same conditions with 3 h of ozonation time	Soo et al. (2010)
Galaxolide		H_2O_2/UV, photolysis	–	HPLC	8% degradation by H_2O_2/UV and light visible photolysis by 16% and photosensitized oxidation degraded 36%	Gmurek and Olak-kucharczyk (2015)
	Waste water effluent	UV photolysis	UV lamp (254 nm) with low pressure. Flow rate of effluent 760m^3/h and TSS 25 mg/l	LC–MS	22% musk removed alone with UV photolysis	Salgado et al. (2012)
Biological and membrane treatment						
Methyl and propyl parabens	Wastewater and aqueous solution	Magnetic waste tyre activated carbon chitosan (MWTACC)	Conc. 2 mg/L, pH 6.5, dose 1.2 g/L. time 35 min	–	100% removal efficiency	Pertunia et al. (2020)
Carbamazepine (CBZ)	Wastewater	MBR-NF	–	–	81–93%	Beshaa et al. (2017)
Sulpiride, amisulpride and lamotrigine	Wastewater	ASP	Conc. 1.1–1.6 µg/L	LC/MS/MS	85%	Franka et al. (2016)
Hormones (E1, E2, EE2)	Wastewater	ASP + Trickling filters	Aerobic	GC/MS	E1-81%, E2-28% and EE2-18%	Liu et al. (2008)
BPA	Hazardous waste landfill	*Stereum hirsutum* and *Heterobasidium insulare*	Conc. 200 mg/L	HPLC	*Heterobasidium insulare* and *Stereum hirsutum* are 64.1 and 62.8 mg/L, respectively	Chouhan et al. (2013)
Triclosan (TCS)	Waste water and sludge	Anaerobic, aerobic or anoxic (denitrifying and sulphate reducing)	Conc. 10 mg/L, 5 days incubation, Tolerance of 1 g/l of TCS by *Pseudomonas sp.* (3 strains)	–	95% aerobically and 87% in anaerobically or anoxic	Gangadharan and Veetil (2012)
DMP + DEP + DBP	Soil samples from electronic and plastic waste contaminated site	Aerobically	Conc. 300 mg/L, *Variovorax sp.*, Temp 30 °C, 30 h incubation	HPLC	> 99% with no production of toxic metabolites	Prasad and Suresh (2012)

Table 5 (continued)

Chemicals	Source	Process	Dose	Detection	Observation	References
Butyl Paraben (BuP)	Aqueous solution	*Trametes versicolor*	laccase-10nkat/ml, HBT, pH-4.5, temp-30 °C, 150 rpm, 2 h	HPLC	5% treatment by laccase alone. Addition of HBT, reduction levels by 95% and 100% after 4 h, decreased estrogenic activity observed in laccase-HBT than laccase alone	Mizuno and Hirai (2009)
Galaxolide (HHCB)	Activated sludge	*Bjerkandera adusta* and *Phanerochaete chrysosporium* mycelium	Conc. 1 mg/L, 2 weeks incubation, Temp 30 °C	GC–MS	The musk was not detectable after 14 days due to volatilization	Feijoo et al. (2011)
Genistein	Wood, paper and pulp waste	Yeast strain (*Phanerochaete sordida YK-624*)	3 different enzymatic conditions. MnP, laccase and laccase mediator (HBT)	HPLC	90% estrogenic activity in 1 h and 100% in 4 h incubation period	Tamagawa et al. (2005)

with charged adsorbents through electrostatic attraction or repulsion (Lu et al. 2017; Gao et al. 2017). DEP sorption was studied on activated carbon isolated from the aqueous phase with a surface area of 500 m2/g and a geometric mean size of 70 mm. They studied, among other things, the effects of starting concentration, contact time, carbon dose, and operating pH. The trials showed that DEP was quickly eliminated and gradually decreased over time until equilibrium was established. The author came to the conclusion that the existence of active surface spots was responsible for the high initial removal rate. Additionally, the DEP concentration had an impact on the rate of adsorption. Using single-walled carbon nanotubes (SWCNTs) with outer diameters of 1–2 nm and MWCNTs (MWCNT10: outer diameters of 10–10 nm, MWCNT20: outer diameters of 10–20 nm, and MWCNT40: outer diameters of 10–40 nm) as an adsorbent, they have demonstrated the adsorption of three phthalate compounds (DMP, DEP, and DBP). Additionally, they found that the hydrophobicity of particular DEPs affects adsorption capacity in the following ways: DMP, DEP, and DBP. They also found that when CNTs' external diameter rose, the effectiveness of adsorption was reduced in the following ways: MWCNT10 > MWCNT20 > MWCNT40 SWCNT > M WCNT10 > MWCNT20 > MWCNT40 (Wang et al. 2015).

It has been extensively discussed how to eliminate parabens for maximum adsorption using magnetic nanoparticles. The parabens were eliminated using magnetite (PS/Fe3O4) covered in polystyrene (PS). As the alkyl groups on the paraben grew, PS/sorption Fe_3O_4's capacity increased. After five reuse cycles, the parabens' adsorption capacities for MeP, EtP, and PrP were 19.5%, 42.4%, and 63.7%, respectively, while their desorption capacities were 42.5%, 77.5%, and 99.7%. Since the parabens' adsorption on PS/Fe_3O_4 was mediated via electron-donor acceptor interactions, it was pH-independent. For methylparaben and propylparaben, the adsorbent demonstrated high adsorption capacities of 85.9 mg/g and 90.0 mg/g, respectively. The magnetic adsorbent remained constant for up to seven adsorption/desorption cycles before dropping to 87% (Chen et al. 2017). In a different study, a porous N grafted graphene-NiO (NiO@N-G) nanoparticle was utilized as an adsorbent to remove parabens. NiO was chosen as an ingredient in this adsorbent because it may prevent the aggregation of graphene layers by acting as a stabilizing agent. Methyl, ethyl, propyl, and butylparaben were all reduced by the NiO@N-G nanoparticle adsorbent by 39.2%, 56.6%, 69.5%, and 79.3%, respectively. An equilibrium between adsorption and desorption was attained after three hours. The adsorbent was stable for four adsorption/desorption cycles with 100% ethanol, and the desorption efficiency was 50.1%, 81.1%, 99.0%, and 99.9%, respectively. Paraben molecules are adsorbed by interactions through double bonds in parabens (Husein 2019).

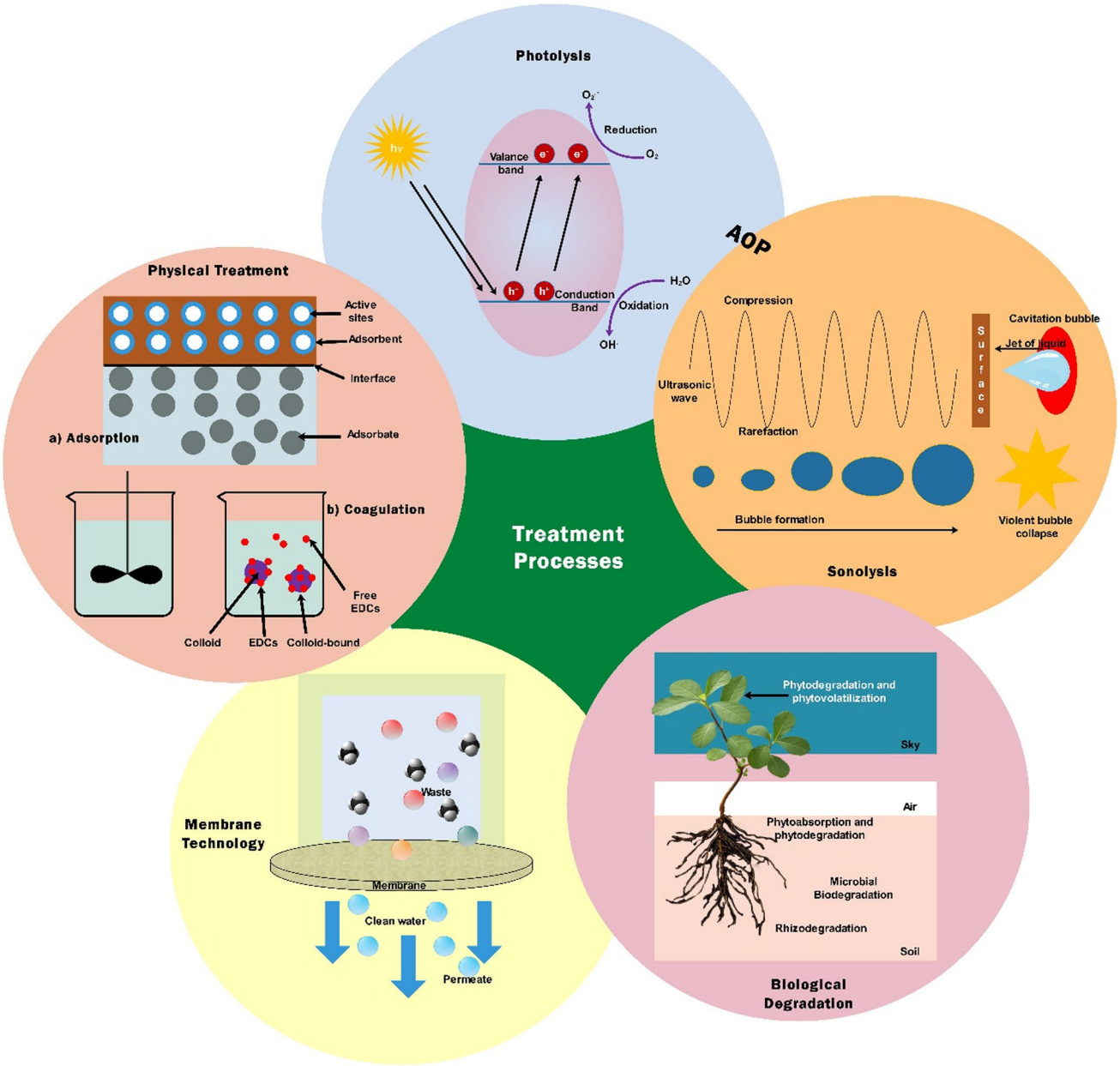


Fig. 5 Various treatment methods in degradation of EDCs

As a BPA sorbent, ultrafine powdered activated carbon (SPAC) with a particle size of 1.38 ± 0.03 µm was used to study the breakdown of BPA by oxidized manganese (Mn) species. BPA was strongly sorbed by SPAC, necessitating the use of organic solvents to remove it. No degradation of adsorbed BPA (278.7 ± 0.6 mg BPA g^{-1} SPAC) was detected with synthetic, solid-MnO2 with a particle size of 15.41 ± 1.35 µm; however, an 89% mass reduction was noticed after the addition of 0.5 mM liquid Mn (III). Results from small-angle neutron scattering indicated that BPA adsorption and breakdown occurred in SPAC pores. The results contradict the widely held belief that contaminant desorption and diffusion out of pore structures are essential steps in degradation by demonstrating that Mn (III) triggered the oxidative transformation of both liquids and adsorbed BPA (Sun et al. 2021).

PPCPs adsorption characteristics differ from chemical to compound and are difficult to anticipate due to interactions with specific functional groups or intricate pH-dependent speciation. Clofibric acid, ibuprofen, naproxen, triclosan, diclofenac, and bisphenol A sorptive and degradation properties in 4 US agricultural soils with varied physicochemical parameters were studied. The Freundlich equation could represent the adsorption of all compounds

studied in soils, and their adsorption affinities on soil were as follows: Triclosan > bisphenol A > clofibric acid > naproxen > diclofenac > ibuprofen, according to a batch equilibrium test. According to the retardation factor, triclosan and bisphenol A were easily delayed in soils, while ibuprofen might travel downhill with percolating water (RF). Selected PPCPs had half-lives in soils that ranged from 0.81 to 20.44 days, and they degraded using the kinetics of first-order exponential decay. The amount of organic matter and clay in the soil affected how quickly PPCP degraded**.** The removal of triclosan, ibuprofen, acetaminophen, carbamazepine, caffeine, prometryn, carbendazim, and 4-Acetylamino-antipyrine by multiwalled nanotubes is efficient. As feeding concentration decreased, the elimination of PPCPs increased. Through hydrogen bonding, multiwalled nanotubes absorbed acetaminophen. Additionally, they found that larger inner diameter carbon nanotubes did not outperform smaller inner diameter carbon nanotubes in the adsorption competition between PPCPs and the fulvic acid in the river (Wan and Wang 2016). Physical treatment alternatives are efficient in removing the set mentioned above of substances, but they do not accomplish total removal, necessitating the development of more effective options.

Chemical treatment or advanced oxidation processes

The shortcomings of conventional wastewater treatment plants, including incomplete organic pollutant breakdown, sludge formation, secondary pollutant generation, and high costs, are eliminated by chemical oxidation or advanced oxidation processes (AOPs). The generation of highly reactive species, notably the hydroxyl radical (˙OH), which can degrade organic pollutants in water and cause their mineralization, is necessary for the AOP processes (Zanias et al. 2020).

Ultraviolet irradiation and Photocatalysis

The principal degradation process of PAEs is believed to be the hydrolytic photolysis of the carbon in the and-position of the ester chain. PAEs were photo-degraded using 254 nm UV in a relatively rapid and orderly manner. The photolysis of PAEs were examined, numerous studies have employed artificial irradiation sources such as mercury lamps, Xenon arc lamps, and UV light. However, there is little information on the utilization of natural UV irradiation, such as sunlight (Mailhot et al. 2002; Rastkari et al. 2018). After 28 days of natural UV irradiation, less than 5% BBP was degraded (Gledhill et al. 1980). In the photocatalysis process, the utilization of ROS in the degradation of PAEs is explained below.

$$\text{Photocatalyst} + hv \rightarrow h^+ + e^{\cdot} \quad (1)$$

$$h^+ + e^{\cdot} \rightarrow \text{heat} \quad (2)$$

$$h^+ + \text{OH}^- \left(\text{or } \text{H}_2\text{O}\right) \rightarrow {}^{\cdot}\text{OH} \quad (3)$$

$$\text{O}_2(\text{free}) \rightarrow \text{O}_2^-(\text{ads}) \quad (4)$$

$$e^{\cdot} + \text{O}_2^-(\text{ads}) \rightarrow \text{O}_2^- \quad (5)$$

$$\text{O}_2^- + \text{H}^+ \rightarrow {}^{\cdot}\text{HO}_2 \quad (6)$$

$${}^{\cdot}\text{HO}_2 + {}^{\cdot}\text{HO}_2 \rightarrow \text{H}_2\text{O}_2 + \text{O}_2 \quad (7)$$

$$\text{H}_2\text{O}_2 + e^- \rightarrow {}^{\cdot}\text{OH} + \text{OH}^- \quad (8)$$

$${}^{\cdot}\text{O}^{2-} + \text{pollutant} \rightarrow \text{products} \quad (9)$$

$${}^{\cdot}\text{OH} + \text{pollutant} \rightarrow \text{products} \quad (10)$$

Hollow glass microspheres (HGM) and magnetic poly (methyl methacrylate) (mPMMA) were utilized as catalyst support structures by Jiang et al. (2013) to improve filtration and catalyst recovery, respectively. In both experiments, DMP was successfully broken down; however, Jiang et al. reported a 20–60% improvement in removal when Pt was added. Additionally, the PtTiO2/mPMMA composite material was verified to be functional in numerous experimental runs after being recovered (Jiang et al. 2013). Huang et al. (2013) employed TiO_2 immobilized on hydrophobic layered double hydroxides to create a support structure that might enhance the procedure and increase substrate adsorption (LDHs). LDHs were shown to have significant adsorption characteristics, combined with photocatalytic degradation via TiO2, for the first time to eliminate DMP (Huang et al. 2013). Another typical technique for degrading parabens is the use of photosensitizers. This method combined benzyl-, n-butyl-, propyl-, ethyl-, and methylparabens with tetrasulfonic acid and aluminium phthalocyanine as photosensitizers, a light source to break them down. Singlet oxygen has been shown to degrade when photosensitizers are applied under light and produce singlet oxygen. In a study, singlet oxygen generated from tetraphenylporphyrin, zinc phthalocyanine, and electrospun nanofibers degraded the parabens butyl and benzyl (Gmurek and Olak-kucharczyk 2015). An oxygen stream was used to facilitate the reaction, and benzylparaben and butylparaben degradation was monitored with a UV diode array detector and high-performance liquid chromatography. It was found that the rate of decay increases as the amount of photosensitizer used for the reaction also

does. When exposed to UV light, the parabens may undergo de-esterification, hydroxylation, or breakdown (Gmurek and Olak-kucharczyk 2015; Gryglik and Gmurek 2015). For photocatalytic destruction of BPA, the TiO_2 nanoparticles have been examined. Zhao et al. reported a 91.2% treatment efficacy using a titania/titanate (TiO_2/TNTs) composite for BPA breakdown. However, several investigations have been devoted to the photocatalytic oxidation of BPA using graphitic carbon nitride (g-C_3N_4). BPA in surface waters was transformed into chlorinated intermediates using solar photodegradation (Ohore and Zhang 2019). Photolysis occurs when light (natural or artificial) interacts with a molecule, causing photochemical processes that result in the molecule's disintegration into intermediate products and, eventually, complete mineralization. As in case of 17α-ethinylestradiol (EE2), diclofenac, sulfamethoxazole, and iopromide. In dilute solutions of buffered water undergoing photolysis at pH 7.0, only minor removals (0.4–27%) were observed. Alone UV exposure of 2768 mJ/cm^2 in 15 min, several macrolide antibiotics (clarithromycin, azithromycin, and erythromycin) was degraded with a low 4–7% efficiency (Hu and Oakes 2015). For usage in a slurry reactor with 385 nm LEDs, Hossaini et al. (2014) created and studied brand-new TiO2-based catalysts doped with N, NS, FeNS, and FeNFS. The outcomes showed that FeFNS-doped TiO_2 exhibited the best photocatalytic activity for the mineralization and degradation of diazinon, making it a promising material for use in real applications (Hossaini et al. 2014). Under flow-through UVA LED/TiO_2 conditions, the antibiotics sulfamethoxazole and trimethoprim decomposed in Milli Q-water, causing significant chronic toxicity with reduced residual antibacterial action and no acute toxicity (Cai and Hu 2016).

Oxidation using sulfate radicals ($SO_4^{\cdot-}$) and hydroxyl radical (OH·)

The substrates' chemical characteristics strongly influence $SO_4^{\cdot-}$ and degradation OH· efficiency. In theory, the non-selective actions of the OH· and $SO_4^{\cdot-}$· radicals on organic and organometallic contaminants in the aqueous medium lead to their total mineralization into CO_2, water, and inorganic ions. The four main ways that hydroxyl radicals assault organic pollutants are radical addition, hydrogen abstraction, electron transfer, and radical combination. When interacting with organic molecules, they produce radicals (R· or R·–OH) containing a carbon nucleus. With the aid of oxygen, these carbon-centred radicals can be transformed into organic peroxyl radicals (ROO·). These organic molecules experience chemical degradation and even mineralization due to all of the radicals' further reactions, which form more reactive species like H_2O_2 and super oxide (O2·) (Qi 2010). Sulfate radicals are highly reactive substances with a limited life period, similar to hydroxyl radicals, although they react differently. Hydroxyl radicals can either contribute to C=C bonds or abstract H from C–H bonds when interacting with organic molecules. On the other hand, sulfate radicals frequently absorb electrons from organic molecules, leading to the creation of organic radical cations. It should be noted that sulphate radicals can also form hydroxyl radicals as follows:

$$SO_4^{\cdot-} + H_2O \rightarrow OH^{\cdot} + SO_4^{2-} + H + SO_4^{\cdot-} + H_2O \rightarrow OH^{\cdot} + SO_4^{\cdot-} + H^+ \quad (11)$$

$$SO_4^{\cdot-} + OH^- \rightarrow OH^{\cdot} + SO_4^{2-} \quad (12)$$

Studies such as Fang et al. (2015) studied the 3 stages mechanism of action by producing OH· radical from biochar suspensions: (a) In biochar suspensions, free radicals (FRs) transfer electrons to O_2 to make O_2^- (b) O_2^- receives an electron from FRs or dismutates to form H_2O_2 (c) H_2O_2 combines with FRs to form OH· radical via a single-electron transfer process (Fang et al. 2015). Wang et al. (2020) studied that the primary radical in the CuS/PMS system was found to be hydroxyl radical (·OH), which performed better than an alternate ·OH-based oxidation system (CuS/H_2O_2) for DEP degradation than sulphate radical-based PMS activation procedures. Furthermore, anions such as Cl^- and NO_3^- have only a minor inhibitory effect on DEP breakdown (Wang et al. 2020).

Biological degradation and membrane technology

The biological degradation process is more or more important than the AOPs. Microbes are accessible to culture, have more removal efficiency and have estrogenic potency for the complex compounds. Consortia of microbes can be more effective and target many xenobiotic compounds under the same conditions, with less toxic intermediates and no more chemicals in the environment.

Many experiments successfully remove and reduce estrogenic potency and its presence in the environment. Maximum studies are conducted with fungi mainly used due to their intracellular enzymes. Compounds like triclosan, 4-nonylphenol, nonylphenol, BPA, and 17-α-ethinylestradiol (EE2) were studied for biodegradation by eight different strains of fungi (Cajthaml and Kr 2009). All eight strains could degrade BPA and nonylphenol entirely within three days of incubation. In EE2, the degradation achieved was 60% with *P.magnoliae*, and estrogenic potential was reduced entirely. Bacteria like Bacillus sp, *Sphingomonas bisphenolicum*, *Pseudomonas sp*, etc., have also been used. *Sphingomonas bisphenolicum* has been regarded as a novel pathway for BPA degradation (Chouhan et al. 2013). The bacterial strain was isolated for the vegetable field. It was

the DNA-DNA hybridized strain that made it unique for the removal. 100 mg/L concentration of BPA was degraded aerobically in 10 days by the bacterial strain. Majorly P450 is responsible for degrading the BPA and coenzymes like NAD^+, NADH, NADPH, and $NADPH^+$. The drawback of the strain was that the intermediate of 4,4'-dihydroxy-α-methylstilbene (DHMS) was formed with a similar structure (Chouhan et al. 2013).

Algae *Monoraphidium braunii* was tested for the complete removal of the BPA. Non-living organic matter (NOM) is added to algae to enhance degradation. The removal efficiency of BPA + NOM addition in aqueous solution concentrations of 2, 4, and 10 mg/L obtained was 39, 48 and 35%. A study showed an increase in removal efficiency in aerobic conditions than in anaerobic conditions (Gattullo et al. 2012).

Due to their high efficiency, ability to conserve space, and simplicity of use, membrane filtration techniques using different types of membranes have much potential for eliminating EDCs. The pollutant that can be retained depends on the membrane's pore size, surface charge, and hydrophobicity, which vary depending on the material used to make it. Pore size, hydrophobicity, functional groups, pKa of membrane materials and pollutants, and the quality of the water treated are a few of the many factors that affect removal. Despite the large pore size of the microfiltration membrane, the combined system successfully removed almost all of the endocrine disruptors from the effluent (Rodriguez et al. 2017). Three membranes were used to study the degradation of DEP and DEHP: the RO-DS3SE reverse osmosis membrane, the NF-DS5DK nanofiltration membrane, and the UF-DSGM ultrafiltration membrane. Under regulated conditions (RO, NF 2.0 MPa, UF 0.3 MPa), all membranes eliminated a sizable portion of PAEs from water, varying from 97.6% to nearly 99.9% (Miriyam et al. 2022). Similar or higher quantities of these compounds were found in ultrafiltration (UF) effluent with 3.1–9.9% removal efficiency compared to paraben concentrations in secondary effluent. Because the UF membrane pores are more significant than the molecules of target compounds and the high pH variations. This could be explained because parabens are challenging to retain by size exclusions (Li et al. 2015).

It could be concluded that EDCs may still be present in final effluents depending on various factors, such as the physicochemical properties (pKa, Kow) of the target pollutants and wastewater characteristics, despite using conventional and advanced oxidation processes. Physical treatments are usually pH-dependent interactions such as electrostatic and speciation specific that can remove EDCs up to 97%. At the same time, chemical or advanced oxidation processes have the potential to deal with the chemical properties of substrates, resulting in the breaking down of the parent molecule more quickly for the effective degradation of EDCs. The drawback of using these processes is forming residual breakdown products that tend to cause chronic toxicity. Hence, biodegradation is critical in efficiently mineralizing the parent and residual degraded products into carbon dioxide and water. In an environmentally and economically sustainable manner, the employment of microorganisms can benefit the degradation of broad classes of EDCs, either as individual compounds or in combination.

Research in the last few years has concentrated chiefly on modelling AOP remediation of wastewater without considering strategies combining them with biological treatments. Based on the current state of the art, emphasis must be laid on the need for combined treatment methods focussing on oxidizing the persistent or non-biodegradable components chemically to yield biodegradable byproducts, which the microbes can further take up to achieve enhanced or complete mineralization. When designing or modelling the combined treatment methods at optimal operating parameters, the focus must be on the effects of waste characteristics, flow rates, reactor volumes, organic and inorganic loads, and reactor configurations to achieve maximum removal degradation efficiency. In addition to modelling, generic measures like chemical oxygen demand (COD) and total organic carbon (TOC) lack specificity in presenting the whole wastewater treatment. Nevertheless, these parameters are essential, and ecotoxicity testing could be used as an alternative to assess mineralization.

Though the aforementioned factors are significant when working on combined treatment processes, a thorough economic evaluation of the proposed process that promotes environmental sustainability should still be carried out before implementation. Additionally, the microbes used in biodegradation must adhere to biosafety norms while prioritizing public health.

Recommendations and future directions

It is evident from data reported in the papers and scientific assessments by WHO and UNEP that these low-concentration substances pose a risk to people and the environment. More than 1,000 compounds have been recognized as endocrine disrupting properties. The UN-IPCC is monitoring the most recent version of 2021 lists 45 chemicals and 77 after the global meeting on July 5, 2018. The USEPA has stated a framework for legal limits and estimated daily dietary intakes (EDI) for a small number of substances, such as BPA and phthalates, among others. Additionally, toxicity tests for the intermediates or byproducts from degradation studies are required. In order to meet the Sustainable Development Goals (SDGs) 2050, water should be safe and clean; the biota above and below should not be in danger. Small levels of substances that are present in groundwater, drinking

water, and the air must be treated. Even minute amounts of a substance taken continuously can have physiological, neurological, and endocrinological effects that completely dominate the usual homeostatic regulation systems. Thus, the promise of improved public health welfare is essential. It is recommended to frequently monitor the release of these man-made toxins and investigate these substances posing significant physicochemical properties with sophisticated instruments in quantification and detection. Studies on EDCs in various matrices with potential removal or reduction treatment processes must be investigated for cleaner, economic, and sustainable development.

The emission of EDCs can be controlled by the mechanism of 'downstream regulations' that focuses on the inclusion of the harmful chemicals used in production in industrial settings and their presence in final products, as well as in the environment and waste. Though EDCs are addressed in many circumstances under European Union (EU) law, including the Water Framework Directive, Registration, Evaluation and Authorization of Chemicals (REACH), Plant Protection Products Regulation (PPPR), and Cosmetic Regulation, even though there is no consensus on their regulation. Therefore, the government and regulatory authorities can focus on enforcing rigorous compliance with EDCs across diverse industries. However, the fundamental problem is that the wide range of chemicals generated are not evaluated for endocrine disrupting properties, nor are their combination interactions and ensuing consequences studied.

Conclusion

EDCs are ubiquitous and disrupt the hormonal-receptor activity affecting humans' reproductive and non-reproductive organs. Rapid industrialization and the increasing demand for drugs lead to the discharge of excretes and secretions in the environment in metabolites and other unknown conjugates. It is crucial to comprehend the genetic and epigenetic pathways with differing phenotypic responses of vertebrates and invertebrates to provide a unique perspective in toxicological investigations. The experimental set-up is crucial when determining the quantity and length of human exposure to EDCs. The mixture of EDCs causes severe malfunctions even at low concentrations; hence, it is vital to comprehend the genotoxic effect on humans' HPA and thyroid axis. Data availability and a universal approach to regulating the production and the release of chemicals is the way forward. The ensurity of the legislation will significantly impact the environment and vulnerability. Screening of hazardous chemicals can aid research in achieving SDG 2050.

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Declarations

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