



## Review

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# Endocrine-disrupting chemicals in aquatic ecosystems and their impacts on aquatic organisms and humans with advances in detection and remediation

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**Abstract:** The increasing anthropogenic burden, driven by population growth and intensified industrial and agricultural practices, has led to the widespread release of endocrine-disrupting chemicals (EDCs) into aquatic ecosystems, with significant implications for both environmental and human health. Many studies have reported the concentrations and toxicological effects of EDCs in aquatic environments, but few have addressed detection methods and remediation techniques. This review aims to highlight the sources, dynamics, and bioaccumulation of EDCs in aquatic ecosystems, along with their toxic effects on aquatic species and associated health risks in humans. Additionally, we provide an overview of advanced detection and remediation techniques. Our review found that EDCs, particularly phthalates and bisphenols, included in industrial effluents, domestic waste, and agricultural runoff, are frequently discharged into aquatic bodies through human activities. EDCs are associated with various toxic effects in aquatic organisms, such as bioaccumulation, transgenerational effects, reduced growth, immunotoxicity, DNA damage, and abnormal hormonal release, which impair reproductive development. Among the detection methods, biosensors, surface-enhanced Raman spectroscopy (SERS), and nuclear magnetic resonance (NMR) spectroscopy are promising tools for EDC detection relative to conventional analytical methods in aquatic systems. Emerging remediation techniques, such as hybrid activated carbon systems and N-doped carbon-based adsorbents, are recommended for their high removal efficiency. This review serves as a valuable resource for advancing research on EDC toxicity, detection, and remediation technologies.

**Key words:** Endocrine-disrupting chemical; Bioaccumulation; Health risk; Biosensor-based detection; Hybrid activated carbon; N-doped carbon adsorbent

## 1 Introduction

Rapid industrialization and urbanization have increased the occurrence of emerging contaminants, including endocrine-disrupting chemicals (EDCs), in aquatic ecosystems (Xiao et al., 2023). These

contaminants tend to exist in surface water, groundwater, industrial effluent, and even drinking water sources and have gained significant attention due to their potential environmental and human health implications (Hercog et al., 2019). Synthetic EDCs interfere with endocrine functions by altering hormone synthesis, secretion, and receptor signaling (Pan et al., 2024). While natural EDCs such as steroid hormones have a role in development and reproduction, synthetic EDCs, which are widely used in consumer products like plastics, cosmetics, and cleaning agents, contribute significantly to long-term aquatic contamination.

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Notable examples include bisphenol A (BPA), a major component in plastics and epoxy resins, and phthalic acid esters (PAEs), found in a diverse range of personal care items, plastic products, and medical devices. These synthetic EDCs have been linked to adverse effects on aquatic biota and pose increasing concerns for ecosystem and human health (Careghini et al., 2015). In aquatic environments, EDCs disrupt hormone receptors, including androgen, estrogen, and thyroid hormone receptors, which can lead to a wide range of adverse effects such as impaired growth, altered sex ratios, and developmental abnormalities (Hong et al., 2020; Razak et al., 2023). Even at low concentrations, EDCs can induce embryo mortality (Pu et al., 2020), posing an ecological threat across aquatic trophic levels (e.g., zooplankton and fish) (Zhou et al., 2020).

Numerous studies have explored the prevalence and toxicological impacts of EDCs, particularly bisphenols and phthalates, with a significant portion focusing on their toxicological effects and detection (Zhang Y et al., 2021; Czarny-Krzywińska et al., 2023). However, most studies have neglected the transgenerational effects, mechanistic pathways, and health risks associated with the consumption of aquatic organisms contaminated by EDCs. Moreover, while traditional detection methods such as gas chromatography coupled with mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), and liquid chromatography coupled with mass spectrometry (LC-MS) are commonly used, these techniques are expensive, time-consuming, and unsuitable for real-time monitoring (Benigni et al., 2015; Lazofsky and Buckley, 2022). Despite the growing use of electrochemical and nanomaterial-based biosensors in EDC detection (Scognamiglio et al., 2016), their full potential has not been realized. In terms of remediation, techniques like activated carbon adsorption, membrane filtration, and advanced oxidation have proven effective in removing EDCs from aquatic environments (Ahmed et al., 2021), with activated carbon and biochar adsorption emerging as the primary focus of research (Cheng et al., 2021; Liao et al., 2022). However, these methods are energy-intensive and costly in terms of resources, operations, and maintenance. Hybrid systems that combine the strengths of various techniques have been proposed as cost-effective alternatives, showing potential in addressing these challenges. The use of innovative

advanced detection methods, such as surface-enhanced Raman spectroscopy (SERS) and nuclear magnetic resonance (NMR) spectroscopy, alongside hybrid remediation techniques like hybrid activated carbon systems and N-doped carbon-based adsorbents, remains an underexplored area of research.

In this review, we explore the sources and complex dynamics of EDCs, particularly phthalates and bisphenols, in aquatic ecosystems, focusing on aspects such as bioaccumulation, transgenerational effects, mechanistic pathways, general toxicity mechanisms, and health risks to humans through trophic transfer, mainly via consumption of contaminated aquatic organisms. Additionally, we examine current remediation techniques, evaluate emerging detection methods, and propose innovative solutions to enhance the cost-effectiveness and efficiency of EDC removal from aquatic environments.

## 2 Sources and environmental dynamics of EDCs

### 2.1 Sources of EDCs in the aquatic ecosystem

Despite the intricate transit and accumulation pathways of EDCs in the environment, research indicates that most are significantly linked to anthropogenic activities. Industrial and wastewater treatment plant (WWTP) effluents and intensively farmed agricultural runoff are the primary sources of EDC pollution in aquatic systems (Chaturvedi et al., 2023). These chemicals also come from consumer products like plastics and personal care items, which are widely used in food production and industrial operations (Khalid and Abdollahi, 2021). A significant portion of these chemicals are excreted in urine and feces due to incomplete metabolism and enter the wastewater system, eventually reaching WWTPs (Rodríguez-Hernández et al., 2022). Despite the development of alternative technologies for EDC removal, such as membrane bioreactors and nanotechnologies (Katibi et al., 2021; Liang et al., 2024), the high costs of these methods have made them difficult to implement on a full scale, meaning that many EDCs still pass through conventional WWTPs and are discharged into the aquatic environment (Tran et al., 2022). They can enter water systems via sewer leaks or direct discharge from households or industries (Puri et al., 2023), while intense rainfall and floods

can further transport them from agricultural, industrial, and residential areas into surface water bodies (Gałązka and Jankiewicz, 2022). In rural regions lacking proper sewerage systems, untreated wastewater often flows directly into rivers, where it spreads through river networks to remote locations, exacerbating the contamination (Williams et al., 2019). Fig. 1 illustrates the complex pathways of EDCs from anthropogenic sources like industrial discharges, wastewater, and landfills through environmental compartments (surface water, groundwater) to their bioaccumulation in aquatic organisms, demonstrating how these persistent contaminants biomagnify up the food chain and ultimately pose human health risks through consumption of contaminated seafood.

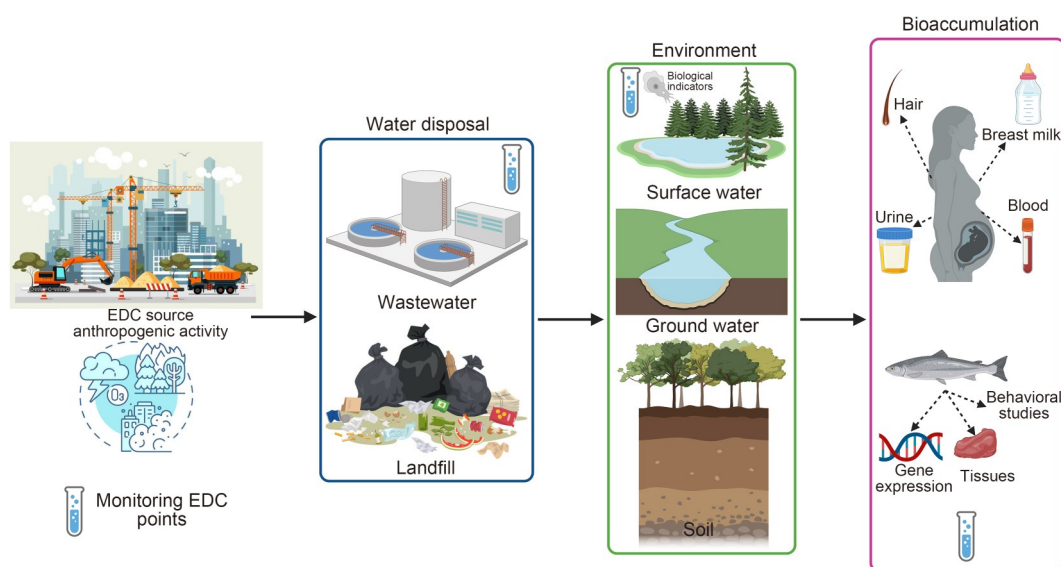
## 2.2 Transmission of EDCs in the aquatic ecosystem

The transmission of EDCs in aquatic ecosystems occurs through a complex interplay of anthropogenic inputs and environmental processes (Xiao et al., 2023). EDCs enter water bodies mainly via industrial effluents, municipal wastewater, agricultural runoff, landfill leachates, and the improper disposal of pharmaceuticals and personal care products (Puri et al., 2023). Conventional WWTPs frequently fail to completely remove these pollutants, resulting in their persistent release into surface waters. Once introduced, EDCs can disperse through the water column, adsorb onto suspended particles, and accumulate in sediments,

which serve as long-term reservoirs and potential secondary sources under dynamic environmental conditions (Rodríguez-Hernández et al., 2022). Aquatic organisms are exposed to EDCs through direct uptake from water and sediments, as well as through dietary intake via trophic transfer. This leads to bioaccumulation and, in some cases, biomagnification, raising the risk of endocrine disruption at higher trophic levels, including fish and humans (Pironti et al., 2021). The physicochemical properties of EDCs, such as low water solubility, high lipophilicity and chemical stability, facilitate their persistence and mobility, allowing for long-range environmental transport. Furthermore, seasonal variations, hydrological events, and physicochemical changes in aquatic systems influence the fate, distribution, and transformation of EDCs, often resulting in the formation of metabolites with equal or higher endocrine-disrupting potential (Thakur et al., 2025). Understanding these transmission pathways is imperative for developing effective monitoring, risk assessment, and remediation strategies to protect aquatic ecosystems and human health.

## 2.3 Distribution and concentration of EDCs in the aquatic ecosystem

Endocrine disruptors are widely detected in surface water and sediment samples from aquatic environments globally. Table S1 provides a comprehensive summary of the concentrations of key EDCs like bisphenols

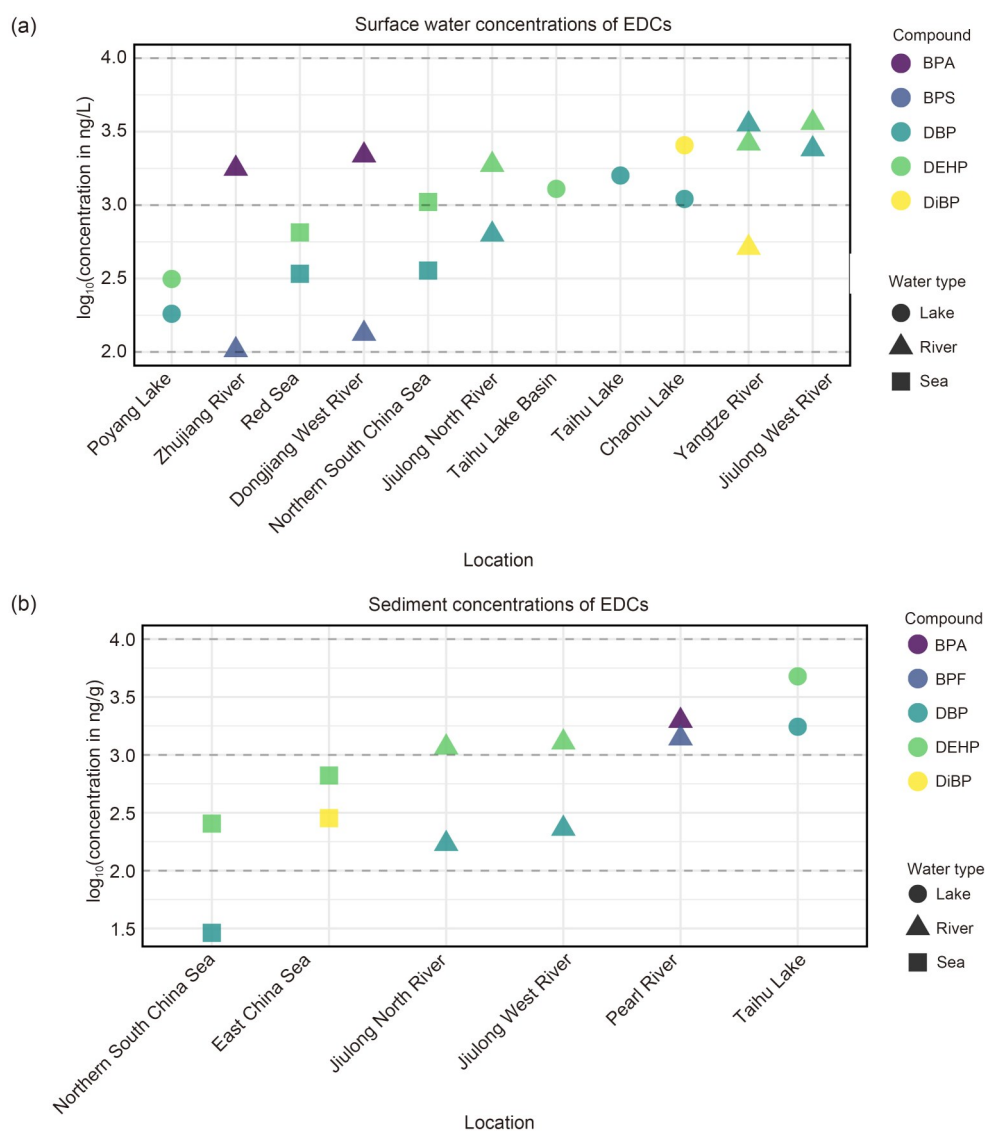


**Fig. 1 Migration pathway of contamination and proposed sample points for endocrine-disrupting chemical (EDC) monitoring. Created with BioRender.com.**

and phthalates in both surface water and sediments across various global aquatic ecosystems. These data underscore the widespread occurrence and variable concentrations of these chemicals in different environments, which can be associated with human activities and regional industrial practices. Fig. 2 shows the distribution of these EDCs in surface water and sediment samples, revealing the pervasive nature of compounds like di(2-ethylhexyl) phthalate (DEHP) and BPA in various aquatic environments (Koniecko et al., 2014; Yamazaki et al., 2015; Gao et al., 2019, 2023; Zhao et al., 2019, 2020; Hu et al., 2020b; Huang et al., 2020; Liu et al., 2020; Xie et al., 2020, 2022; Cao

et al., 2022; Dhavamani et al., 2022; Nurulnadia et al., 2023; Mei et al., 2024).

DEHP predominates in both surface water and sediments, owing to its high solubility and widespread usage, and can have adverse environmental consequences. The increasing use of BPA substitutes has led to their frequent availability in surface water and sediments, with bisphenol AF (BPAF) and bisphenol F (BPF) being the most prevalent bisphenol analogs to increase the environmental load of EDCs (Ballesteros-Gómez et al., 2007; Song et al., 2012). Their lipophilic nature tends to promote their accumulation in sediments, especially in areas with high water retention



**Fig. 2** Surface water (a) and sediment (b) concentrations of endocrine-disrupting chemicals (EDCs) across different locations. BPA: bisphenol A; BPS: bisphenol S; BPF: bisphenol F; DBP: dibutyl phthalate; DEHP: di(2-ethylhexyl) phthalate; DiBP: diisobutyl phthalate. Created with R version 4.4.1.

or reduced flow (Zhao et al., 2019). Despite the rise of other substitutes, BPA is frequently detected in sediments due to its large-scale historical and ongoing presence in consumer products (Careghini et al., 2015). Bisphenol analogs are abundant in river and lake sediments in areas with high plastic manufacturing (e.g., China) (Zhao et al., 2020). Likewise, higher concentrations of phthalates, especially DEHP, are detected downstream, reflecting the impacts of industrial activities, agricultural runoff in urbanized areas, and wastewater discharge (Xu et al., 2022).

Most EDC compounds are persistent and accumulate in sediments, raising concerns about their long-term environmental health impact (Rocha et al., 2019; Shen et al., 2020). Additionally, the distribution of EDCs is strongly influenced by human activities, such as the release of industrial effluents, and hydrological factors. For example, phthalate concentrations are frequently higher in coastal areas, mainly due to land-based inputs such as wastewater (Zhang et al., 2020; Wang LY et al., 2021). In areas near agricultural fields or industrial activity, elevated EDC concentrations are associated with industrial wastewater discharge, the use of plastic films, and irrigation water from polluted rivers (Arfaenia et al., 2019). Although bisphenol distribution in coastal areas is less studied, higher seawater concentrations of tetrabromobisphenol A (TBBPA) can be linked with industrial effluents (Gong et al., 2017).

Similarly, human activities, more specifically their associated industrial effluents, elevate EDC concentrations in inshore marine regions (Heo et al., 2019; Zhang et al., 2020). In such regions, phthalate esters are frequently detected at higher concentrations in both surface water and bottom layers of marine habitats. This distribution pattern is related to the poor solubility of these compounds, which favors their accumulation in sediments (Paluselli and Kim, 2020). DEHP, a prominent component of plastic waste, exhibits higher concentrations in bottom seawater, most likely due to its gradual release from litter deposited on the seafloor. Furthermore, EDC levels vary seasonally and tidally. For instance, higher concentrations of DEHP and diisobutyl phthalate (DiBP) have been detected during the dry season and under stronger tidal conditions in Hangzhou Bay, China (Paluselli and Kim, 2020). This spatiotemporal pattern illustrates the complexity of EDC dispersion in marine systems and highlights the need for context-specific monitoring strategies (Wang LY et al., 2021).

The bioavailability of EDCs differs significantly between water and sediments, influencing their potential for environmental exposure and ecological risks. In aquatic environments, EDCs like DEHP and BPA remain more bioavailable in water than in sediment mostly as suspended particles (Wang K et al., 2020). This enables these compounds to interact more easily with micro and aquatic organisms, making them readily available for absorption (Zhang et al., 2020). Hydrophobic compounds like PAEs are more likely to adsorb to organic and inorganic particles in sediments and water, which significantly reduces their bioavailability (Mi et al., 2019; Sun et al., 2021). The strong affinity of these chemicals for sedimentary particles leads to their accumulation in the sediment phase, making them less available for uptake by aquatic organisms, as observed with high molecular weight PAEs such as DEHP and di-*n*-butyl phthalate (DnBP) (Liu et al., 2014). In sediments, factors like the presence of organic colloids, black carbon, and sediment organic matter content further enhance their adsorption capacity, thereby limiting their bioavailability (Zhang et al., 2012; Xiao et al., 2023). Similarly, EDCs degrade slowly in sediments, especially under anaerobic or fluctuating redox conditions, which also limits their transformation and bioavailability in the sedimentary phase (Adeogun et al., 2015). In contrast to water, where EDCs are more mobile and bioavailable, sediments act as both a long-term reservoir and a potential source of contamination when disturbed by events such as floods or increased turbulence. These disturbances can remobilize the adsorbed compounds back into the water, increasing their bioavailability and exposure risk (Arfaenia et al., 2019).

### 3 Bioaccumulation and transgenerational effects of EDCs in aquatic species

#### 3.1 Bioaccumulation

For decades, EDCs have been found in surface waters, yet their biological activity, ecological impacts, and trophic transmission routes are poorly understood (Meador et al., 2016). Although data on the bioaccumulation of these contaminants in aquatic organisms are limited, studies suggest that bioaccumulation occurs through various exposure routes, influenced by the balance between uptake and elimination

(Savoca and Pace, 2021). Bioaccumulation of EDCs, particularly BPA, has been observed across various aquatic species, including vertebrates and invertebrates (Ismail et al., 2017; Jasrotia et al., 2021). Marine organisms such as mussels are particularly effective bio-accumulators, with elevated concentrations of BPA found in both laboratory and field studies (Gatidou et al., 2010), positioning mussels as valuable indicators for detecting contamination levels in seawater. Similarly, benthic species, such as filtering mollusks and sediment-dwelling amphipods, accumulate significant amounts of plasticizers, with bioconcentration factors reaching higher limits (Oehlmann et al., 2008). Studies on fish species in the Yangtze River Delta, China, further support the idea of widespread bioaccumulation across aquatic food webs, with contaminants migrating from primary producers to higher trophic levels (Hu et al., 2016). EDCs like BPA, as well as their metabolites, accumulate in primary producers and are subsequently biomagnified through the food chain, potentially affecting top consumers, including humans in the food web. This is particularly concerning given the harmful effects of EDCs even at low concentrations. For instance, BPA levels in freshwater

fish have been reported to range from non-detectable (ND) to 25.2  $\mu\text{g}/\text{kg}$ , with marine species exhibiting similar or higher concentrations of this compound (Lee et al., 2015).

The findings in Table 1 summarize the reported occurrence and accumulation levels of EDCs in different aquatic organisms. Once ingested by primary producers, these contaminants can accumulate at higher trophic levels, potentially inducing toxicological effects. Compounds like BPA, in particular, have high bioaccumulation and biomagnification potential that may impact a wide spectrum of aquatic life, including those consumed by humans. The increasing evidence demands more research into the ecological and toxicological effects of these pollutants, especially considering their potential to disrupt aquatic food webs and pose health risks through the consumption of contaminated aquatic organisms.

### 3.2 Transgenerational effects

Several studies have reported negative effects of EDCs on the male reproductive system, such as abnormal sperm morphology and reduced sperm motility (Jeng, 2014; Thacharodi et al., 2023). Paternal exposure

**Table 1 Bioaccumulation of various endocrine-disrupting chemicals in aquatic organisms**

Compound	Species/group	Tissue accumulated	Reported concentration	Location/study area	Reference
DBP, DiNP	Mangrove fish	Muscle	Across the trophic level	Freshwater, Dongzhai Harbor, China	Chen et al., 2024
DBP, DEHP	Zooplankton, phytoplankton	Whole organism	Wide BAF range	Lake Taihu, China	Liu and Tao, 2024
BPA	Fish	Muscle	5.28 ng/g dry weight	Dongjiang River Basin, China	Yang et al., 2024
BPA	Mussels	Whole body	Lab>field (2.5 times)	Greece	Gatidou et al., 2010
BPA	Bivalves, fish	Whole body	High bioaccumulation noted	Persian Gulf, Guangdong, China	Chen et al., 2021
BPA analogs	Common carp	Liver, kidney		Not specified	Wang Q et al., 2020
BPA, triclosan	Freshwater fish	Liver, fat	Triclosan biomagnified	Pearl River catchment, China	Peng et al., 2018
BPA, alkylphenols	Mussels	Whole body	Alkylphenols exhibit a 6–8 times higher accumulation potential than BPA	Gulf of Gdansk, Poland	Staniszewska et al., 2017
BPA, DBP	Bivalves, holothurians	Soft tissues	Enhanced by microplastics	Balearic Islands, Spain	Rios-Fuster et al., 2022
NP, OP	Carnivores, filter-feeding fish	Whole body	Higher than herbivores	Pearl River, China	Xie et al., 2020

DBP: dibutyl phthalate; DiNP: diisononyl phthalate; BPA: bisphenol A; DEHP: di(2-ethylhexyl) phthalate; NP: nonylphenol; OP: octylphenol; BAF: bioaccumulation factor.

to these chemicals can induce adverse reproductive effects in their offspring (Wan et al., 2013). The reproductive effects of BPA were first reported in Japanese medaka fish (Ramakrishnan and Wayne, 2008). These effects were evaluated in a multi- and transgenerational context in the same species (Bhandari et al., 2015). These studies consistently revealed a reduction in fertilization and embryo survival due to 100 µg/L BPA, which was comparable to the estrogenic effect observed with 0.05 µg/L ethinyl estradiol, following crossbreeding experiments associated with this effect on male subfertility (Thayil et al., 2020). For instance, Akhter et al. (2018) observed consistent declines in fertility and embryo development in F<sub>1</sub>, F<sub>2</sub>, and F<sub>3</sub> offspring from parental exposure lineages in zebrafish. These effects were observed using various exposure routes such as dietary intake during multiple developmental periods (adults, 3–9 months post-fertilization).

The intergenerational toxic effects of EDCs affect not only reproductive health but also embryonic development. A study evaluated the developmental outcomes of F<sub>1</sub> embryos after exposing 120-d-old zebrafish (F<sub>0</sub>) to 10 µg/L BPAF for 28 d. The results showed that paternal BPAF exposure led to higher mortality, reduced hatchability, and smaller body size in F<sub>1</sub> larvae, along with changes in DNA and N<sup>6</sup>-methyladenosine (m<sup>6</sup>A) RNA methylation gene expression in both F<sub>0</sub> testes and F<sub>1</sub> larvae (Zhang YY et al., 2022). In another study, paternal exposure of zebrafish to DBP for 30 d before mating with untreated females resulted in an increase in deformities in F<sub>1</sub> embryos, including edema, trunk curvature, and disrupted primordial germ cell migration. Some F<sub>1</sub> adults exhibited abnormalities in their axial bones (Hu et al., 2021). This is consistent with findings from another study that assessed the chronic toxicity of DEHP in *Daphnia magna* across three generations. In this case, DEHP exposure enhanced reproduction in the F<sub>0</sub> and F<sub>1</sub> generations, but by the F<sub>2</sub> generation, survival rates in the DEHP-exposed groups decreased significantly to only 45%–50% of the control group, with smaller body lengths observed after the DEHP 500 µg/L treatment (Le et al., 2019). Additionally, single and combined exposure of *D. magna* to polystyrene nanoplastics (PSNPs) and DEHP resulted in the regulation of developmental and reproductive genes in the F<sub>0</sub>–F<sub>3</sub> generations. Survival rates in all treatment groups decreased and did not recover until the F<sub>2</sub> generation, while growth

rates were reduced in the F<sub>1</sub> and F<sub>2</sub> generations (Liao et al., 2023). In a study by Lombó et al. (2015), adult male zebrafish were exposed to BPA during spermatogenesis and mated with untreated females. This exposure led to a higher incidence of heart failure in F<sub>2</sub> offspring and downregulated five genes critical for cardiac development in F<sub>1</sub> embryos. Additionally, BPA exposure reduced sperm residual messenger RNA (mRNA) linked to early development in both F<sub>0</sub> and F<sub>1</sub> generations. The downregulation of insulin receptor β mRNA suggests that paternal BPA exposure may alter the insulin signaling pathway, potentially contributing to heart development disorders in offspring.

Thus, paternal EDC exposure causes transgenerational reproductive and developmental defects in offspring, linked to sperm epigenetic alterations. Compared to controls, exposed offspring show disrupted gene expression and organ dysfunction across generations. These findings reveal that paternal environmental exposures can heritably impact offspring health via germline epigenetic changes.

#### 4 Mechanism of action of EDCs in aquatic organisms

Endocrine disruptors can bind to estrogen receptors (ERs) and disrupt endocrine signaling in aquatic organisms, although the receptor specificity and mechanisms differ significantly between vertebrates and invertebrates. The estrogenic effects of EDCs are mediated through ERs in vertebrates, including nuclear ERα/β, estrogen-related receptor α/β/γ (ERRα/β/γ), and the membrane-bound G protein-coupled estrogen receptor (GPER) (Yuan et al., 2023). EDCs act as both agonists and antagonists of ERα/β, causing displacement of α-helices in the ERα ligand-binding domain while preventing proper conformation in ERβ, which leads to different regulatory effects depending on the tissue's ERα/ERβ ratio (Acconcia et al., 2015; Fitzgerald et al., 2015). ERRs, unlike ERα/β, do not bind estrogen but can still interact with estrogen-responsive elements (EREs), resulting in functional overlap (Ascenzi et al., 2006). EDCs such as BPA can also activate GPER, triggering signaling pathways such as extracellular signal-regulated kinase (ERK)/mitogen-activated protein kinase (MAPK), phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT), and cyclic adenosine

monophosphate (cAMP)/cAMP response element-binding protein (CREB) (Yuan et al., 2023). In contrast, invertebrates have ERs with constitutive activity, meaning they do not require estrogen binding to be activated. These receptors are mutated to remain active, and even without estrogen binding, some mollusks show increased ER mRNA expression when exposed to exogenous estrogens, suggesting that estrogen signaling can also occur through receptor-independent pathways or non-nuclear forms of ERs (Tran et al., 2016). This highlights the complexity of estrogenic signaling in aquatic organisms, where alternative mechanisms in invertebrates can come into play.

In aquatic invertebrates, EDCs disrupt endocrine-regulated developmental processes, including molting and metamorphosis, mainly via the ecdysteroid signaling pathway. For example, butyl benzyl phthalate (BBP) exposure in *Chironomus riparius* larvae upregulates ecdysone receptor (*EcR*) gene expression, indicating endocrine disruption at environmentally relevant concentrations (Herrero et al., 2015). Likewise, bisphenol S (BPS) exposure increased *EcR* gene expression in multiple tissues of *Procambarus clarkii*, with elevated concentrations (100 µg/L) also inducing oxidative stress and inflammatory responses (Pu et al., 2024b). Phthalates, such as diisodecyl phthalate (DiDP), disrupt lipid and androgen signaling by activating the peroxisome proliferator-activated receptor (PPAR)/retinoid X receptor (RXR) pathway, resulting in dysregulation of fatty acid metabolism (Cocci et al., 2017). Moreover, long-chain phthalates like DEHP and diisononyl phthalate (DiNP) have higher binding affinities to sex hormone-binding globulin than short-chain phthalates, signifying a greater endocrine-disrupting potential (Sheikh et al., 2016). Such interference with lipid and androgen pathways may induce metabolic dysfunctions, ultimately impairing growth and reproductive success in exposed aquatic species.

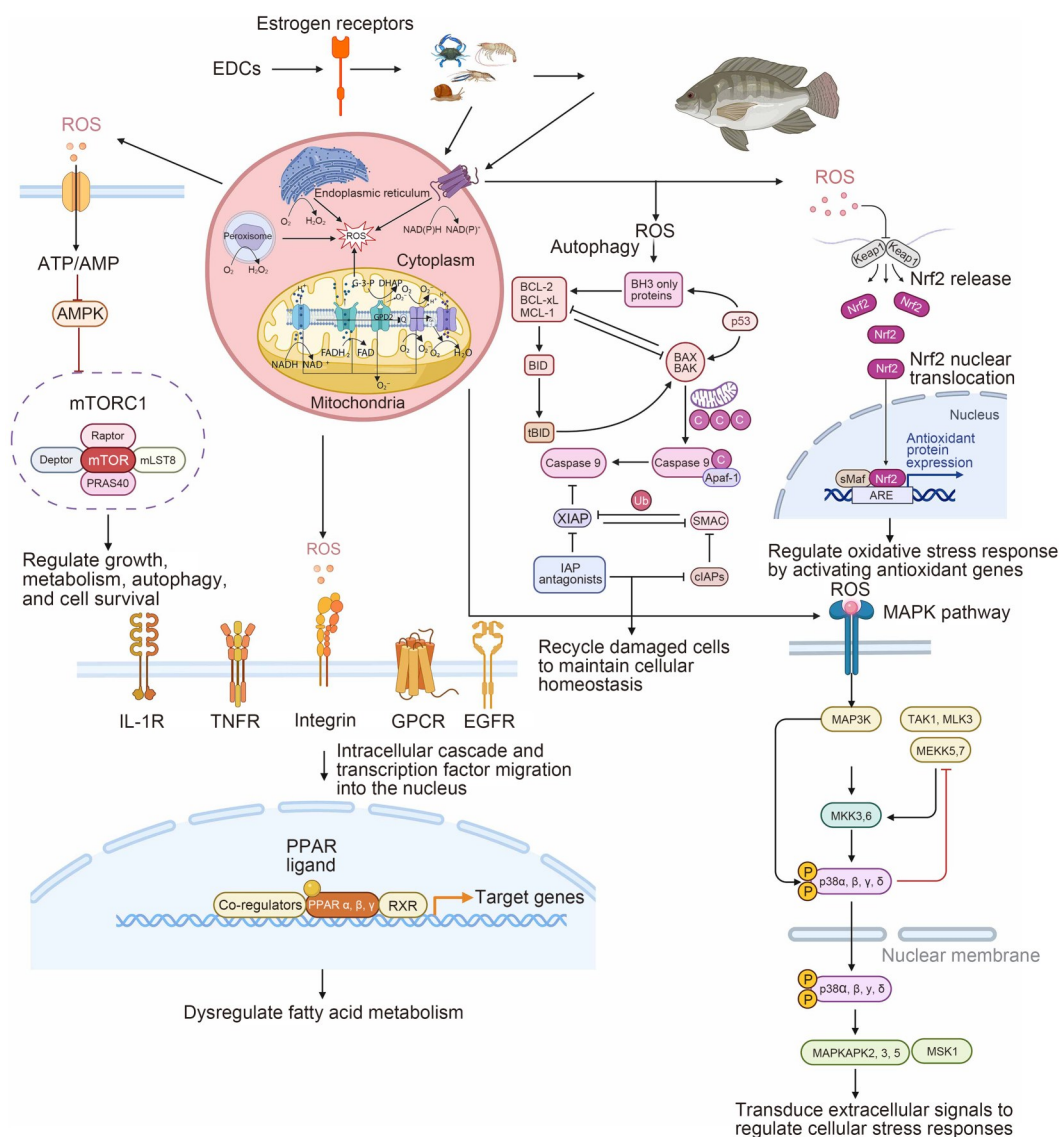
## 5 Toxicity mechanisms of EDCs in aquatic organisms

EDCs are pervasive pollutants in aquatic environments, posing significant risks to the health and functioning of aquatic ecosystems (Table S2). These chemicals cause disruptions in key physiological functions such as oxidative stress, developmental toxicity, immunotoxicity, and reproductive toxicity.

### 5.1 Oxidative stress

Environmental pollutants, including EDCs, generate oxidative stress via reactive oxygen species (ROS) production (Virant-Klun et al., 2022). Oxidative stress occurs when there is an imbalance between pro-oxidant and antioxidant mechanisms, leading to an oxidizing cellular environment (Subaramaniyam et al., 2023). Oxidative stress has either adaptive or toxic consequences in the organism or the whole population. Oxidative stress is linked with several cellular pathways such as nuclear factor erythroid 2-related factor 2 (Nrf2)/Kelch-like ECH-associated protein 1 (Keap1), PPAR, nuclear factor-κB (NF-κB), autophagy, MAPK, and mechanistic target of rapamycin (mTOR) (Fig. 3). Nrf2/Keap1 is a central regulatory pathway linked with antioxidant metabolism (Silvestre, 2020). These pathways regulate the expression of catalase (*CAT*) and superoxide dismutase (*SOD*) genes, but pollutants affect their normal function. For example, in crayfish, BPS exposure decreased antioxidant enzymatic activities and suppressed the key genes of the Nrf2/Keap1 pathways, leading to obvious oxidative stress (Pu et al., 2024a). BPA and DEHP induce similar effects on the Nrf2/Keap1 pathways, resulting in high ROS concentrations (Chen et al., 2022; Lei et al., 2023).

Oxidative stress also activates the PPAR pathway related to lipid metabolism and anti-inflammatory responses, helping the cells to cope with inflammation due to stressors. For instance, in common carp, the PPAR pathway mediates liver inflammation induced by oxidative stress following BPS exposure (Qiu et al., 2019). Oxidative stress also affects the mechanistic activity of the NF-κB pathway related to several physiological activities, including inflammation, bacterial resistance, and apoptosis (Morgan and Liu, 2011). However, the interrelationship between the NF-κB pathway and oxidative stress through ROS is highly complex and time-dependent (Nakajima and Kitamura, 2013). For example, Cui et al. (2019) reported that benzo[a]pyrene (BaP) affected the NF-κB pathway in medaka fish via changes in ROS concentration and exposure time. The relationship between oxidative stress and the NF-κB pathway is intricate, with ROS influencing the NF-κB pathway, while the transcription of NF-κB-related genes also regulates ROS levels within the cells (Guo et al., 2019). The mTOR pathway, which regulates cell growth and metabolism, is also affected by oxidative stress. Oxidative stress



**Fig. 3** Schematic overview of endocrine-disrupting chemicals (EDCs) and their impact on oxidative stress-relevant pathways. This figure illustrates the complex interactions between EDCs, estrogen receptors (ERs), and reactive oxygen species (ROS). It shows how EDCs can influence oxidative stress responses through the nuclear factor erythroid 2-related factor 2 (Nrf2)/antioxidant response element (ARE) pathway, modulating antioxidant protein expression. Additionally, it highlights the regulation of growth, metabolism, and autophagy via adenosine 5'-monophosphate (AMP)-activated protein kinase (AMPK) and mechanistic target of rapamycin complex 1 (mTORC1), and their involvement in apoptosis through mitogen-activated protein kinase (MAPK) and caspase cascades. The figure also depicts how oxidative stress dysregulates fatty acid metabolism and activates key transcription factors, ultimately affecting cell survival and homeostasis. ATP: adenosine triphosphate; mLST8: mammalian lethal with SEC13 protein 8; PRAS40: proline-rich Akt substrate of 40 kDa; G-3-P: glycerol-3-phosphate; DHAP: dihydroxyacetone phosphate; FAD: flavin adenine dinucleotide; FADH<sub>2</sub>: reduced flavin adenine dinucleotide; BCL-2: B-cell lymphoma 2; BCL-xL: B-cell lymphoma-extra large; MCL-1: myeloid cell leukemia 1; BID: BH3-interacting domain death agonist; tBID: truncated BID; BH3: BCL-2 homology domain 3; BAX: BCL-2-associated X protein; BAK: BCL-2 antagonist/killer; XIAP: X-linked inhibitor of apoptosis protein; SMAC: second mitochondria-derived activator of caspases; IAP: inhibitor of apoptosis protein; cIAPs: cellular inhibitor of apoptosis proteins; sMaf: small musculoaponeurotic fibrosarcoma protein; MAP3K: mitogen-activated protein kinase kinase kinase; TAK1: transforming growth factor- $\beta$ -activated kinase 1; MLK3: mixed-lineage kinase 3; MEKK: mitogen-activated protein kinase/extracellular signal-regulated kinase kinase; MKK: mitogen-activated protein kinase kinase; MAPKAPK: mitogen-activated protein kinase-activated protein kinase; MSK1: mitogen- and stress-activated protein kinase 1; IL-1R: interleukin-1 receptor; TNFR: tumor necrosis factor receptor; GPCR: G protein-coupled receptor; EGFR: epidermal growth factor receptor; PPAR: peroxisome proliferator-activated receptor; RXR: retinoid X receptor; Keap1: Kelch-like ECH-associated protein 1. Created with BioRender.com.

downregulates the PI3K/AKT/mTOR signaling pathway, leading to decreased cell survival and increased apoptosis (Li et al., 2025). Autophagy, a process essential for cellular homeostasis, is often regulated by oxidative stress. It is involved in the clearance of damaged organelles and proteins, but excessive autophagy can lead to autophagic cell death. BPA and microplastic (MP) exposure has been reported to suppress autophagy through the AMPK/mTOR signaling axis (Wu et al., 2022). Autophagy may either protect cells by promoting cell survival or, when dysregulated, contribute to cell death (Redza-Dutordoir and Averill-Bates, 2021). BPA notably elevates oxidative stress, reduces Nrf2 translocation into the nucleus, and inhibits the activation of the Wnt/ $\beta$ -catenin pathway, leading to increased apoptosis, reduced autophagy, and immunosuppression (Chen et al., 2022). Furthermore, the MAPK pathway, involved in cell survival and apoptosis, is activated by oxidative stress and plays a significant role in the response to environmental pollutants like DEHP (Liu et al., 2022). Thus, oxidative stress induced by EDCs suppresses the inflammation, growth, survival, and reproductive efficacy of aquatic organisms, but in-depth studies are required to elucidate the complex cross-talk between oxidative stress and various molecular pathways.

## 5.2 Developmental and reproductive toxicity

Endocrine disruptors pose significant threats to aquatic species, causing a wide range of toxic effects across various biological processes. For instance, exposure to phthalate esters impacts embryo development in abalone by decreasing hatching rates, increasing developmental deformities, and impeding metamorphosis (Zhou et al., 2011). Yang et al. (2018) also reported that DEHP toxicity affects fish growth through a combination of oxidative stress and apoptosis pathways, leading to reduced body weight (BW) and length. Studies have also indicated that bisphenols such as BPF and other BPA analogs affect cardiovascular development in aquatic species. Ji et al. (2022) reported deformities in heart and vascular development, showing that the cardiovascular system is highly susceptible to EDC toxicity. Zebrafish larvae exposed to 700  $\mu\text{g/L}$  BPF showed morphological abnormalities in the brain, including vacuolization, linked to neurotoxicity and behavioral abnormalities (Gu et al., 2020). The cardiotoxicity of PAEs has also been confirmed in aquatic animals,

with effects including a decreased heart rate and lower expression of *T-box5* and *Nkx2.5* transcription factor genes, which are crucial for heart development (Sun and Liu, 2017; Sun and Li, 2019). Once PAEs enter cells, ROS production is triggered, leading to apoptosis and immunosuppression, which result in various adverse effects on the development of aquatic organisms, such as embryo malformations and abnormal heart development (Zhang Y et al., 2021).

Chen et al. (2020) explored reproductive toxicity in male zebrafish exposed to a combination of DBP and DiBP. The combined phthalates disrupted spermatogenesis by inhibiting steroid hormone signaling pathways, which severely affected the male reproductive system. A study on DnBP exposure in male Murray rainbowfish increased spermatogonia proliferation and upregulated ER genes, but DEHP exposure negatively impacted oocyte growth, maturation, and ovulation in female zebrafish (Bhatia et al., 2013). In zebrafish larvae, exposure to BPA increased the expression of ER $\alpha$  at 100  $\mu\text{g/L}$  and ER $\beta$  subunits at 1  $\mu\text{g/L}$ , but did not affect ER $\beta$  expression at 100  $\mu\text{g/L}$ . Additionally, luteinizing hormone  $\beta$  subunit (LH $\beta$ ) expression was elevated, consistent with increased LH secretion (Qiu et al., 2021). This suggests that BPA's reproductive effects may be mediated through ER pathways. Similarly, BPF has been shown to affect reproductive processes, although through a different mechanism. One study indicated that BPF's reproductive effects may occur mainly through the *cyp19a2*-mediated pathway, rather than via *cyp19a1*. Zebrafish embryos exposed to environmentally relevant concentrations of 0.5  $\mu\text{g/L}$  BPF over 150 days post-fertilization (dpf) showed adverse effects at both the gene and hormone levels in juvenile and adult males and females. In females, exposure to 0.5  $\mu\text{g/L}$  BPF altered the expression of steroidogenic genes and receptors in the ovary, with dose-dependent suppression of *cyp19a1a*, *hsd3b2*, *hsd17b1*, and *fshr*. Gene expression patterns in the ovary at higher concentrations of BPF indicated dose-dependent effects on steroidogenesis. Conversely, in males, exposure to 0.5  $\mu\text{g/L}$  BPF increased steady-state mRNA levels of *vtg1*, *cyp17a1*, *cyp19a1a*, and *cyp11a1* in the testes, suggesting sex-specific regulation of steroidogenesis by BPF (Mu et al., 2022). DEHP exposure in marine medaka fish also resulted in gender-specific reproductive effects, but in this case, males were more sensitive than females

(Ye et al., 2014), highlighting the variable sensitivity to reproductive disruption between compounds and genders.

### 5.3 Immunotoxicity

Many studies have confirmed the immunotoxicity of PAEs. Diethyl phthalate (DEP) can significantly decrease the serum antibacterial activity, phagocytic activity, and phagocytic index of carp in vivo, thereby impairing their nonspecific immune function (Zhang and Wang, 2014). Wang et al. (2010) observed that exposure to DEP, DBP, and dioctyl phthalate (DOP) in the shrimp *Litopenaeus vannamei* reduced immune activity, impairing physiology, increasing their susceptibility to pathogens, and resulting in lower survival rates and slower growth. In the green mussel *Perna viridis*, exposure to BPA (11 ng/L) led to a reduction in the number of circulating hemocytes and a decrease in extracellular lysozyme concentration. Phagocytosis remained unaffected at this concentration, but it was significantly reduced at a higher concentration of 760 ng/L (Juhel et al., 2017). In contrast, hemocytes of the blood clam, *Tegillarca granosa*, exposed to 10 ng/L BPA showed no significant change in their count. However, when exposed to 100 ng/L BPA, a significant decrease in total hemocyte count was observed. The cell-type composition of the hemocytes also showed pronounced alterations in clams exposed to 100 ng/L BPA. The phagocytic activity of the hemocytes was suppressed in a dose-dependent manner, with a marked decrease in red granulocytes and a significant increase in basophil granulocytes. These toxic effects were further exacerbated when BPA was combined with 100 ng/L MPs, indicating evident dose-dependent immunotoxicity in the clam (Tang et al., 2020). These findings highlight the broad range of toxic effects that EDCs have on aquatic biota, including developmental defects, hatching rates, oxidative stress, and immunotoxicity.

## 6 Human health risk assessment

The evaluation of health risks associated with EDCs is crucial for understanding their impact on human health, particularly in light of bioaccumulation observed in aquatic organisms. As top consumers in the food chain, humans are vulnerable to higher EDC exposure due to biomagnification at higher trophic

levels (Akhbarizadeh et al., 2020). EDCs, such as bisphenols and phthalates, have been linked to reproductive toxicity, hormonal imbalances, and other adverse health effects. To assess these risks, the estimated daily intake (EDI) is calculated using the following formula:  $EDI = cr/w$ , where  $c$  is the concentration of the chemical,  $r$  is the consumption rate, and  $w$  is the BW. This metric is used to evaluate exposure from contaminated aquatic food sources, such as fish and shellfish. The European Food Safety Authority (EFSA) initially set the tolerable daily intake (TDI) for BPA at 4  $\mu\text{g}/\text{kg}$  BW per day, which has since been revised to 0.2 ng/kg BW per day (EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) et al., 2023). The TDI represents the maximum amount of a compound that a person can be exposed to daily over their lifetime without significant health risks. Furthermore, the target hazard quotient (THQ) is defined as the ratio between chemical exposure and respective reference values (e.g., acceptable daily intake or TDI) (EFSA Scientific Committee et al., 2019). The THQ compares chemical exposure to reference values like TDI, with THQ values above 1 indicating potential health risks (Pawelczyk, 2013). Studies have shown that toddlers are particularly exposed to phthalates, with worst-case estimates reaching 333.78 ng/kg BW per day for DBP and 193.34 ng/kg BW per day for DEHP (Squillante et al., 2023). In Hong Kong, China, fish consumption exceeds recommended levels, leading to increased phthalate exposure, particularly to DEHP (Chen et al., 2012). The EDI for bisphenols in shellfish varies regionally, ranging from 1.1 ng/kg BW per day in Europe to 7.1 ng/kg BW per day in Asia (Baralla et al., 2021), with some regions reporting EDI values for BPA exceeding 20.5 ng/kg BW per day, far surpassing EFSA's TDI limit of 0.2 ng/kg BW per day (EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) et al., 2023). These values suggest a significant risk to human health, particularly in high-consumption regions such as China and South Africa, where the mean exposure for sum of BPs ( $\Sigma\text{BPs}$ ) reaches 27.5–33.0 ng/kg BW per day, and maximum values can reach 135 ng/kg BW per day (Liao and Kannan, 2019; Castro et al., 2022). A recent study found low human health risks from consuming fish muscle in the Tagus estuary, Portugal, based on the margin of exposure for  $\Sigma\text{BPs}$ , but such assessments often overlook cumulative exposure to multiple EDCs (Lestido-Cardama et al., 2023). The

existing regulatory framework typically evaluates single compounds, potentially underestimating cumulative toxicological risks. For instance, cumulative exposure to sum of PAEs ( $\Sigma$ PAEs) and  $\Sigma$ BP often exceeds safety limits, highlighting the need for a more comprehensive risk assessment approach (Karrer et al., 2019; Payne-Sturges et al., 2023). The disparity between adult and child exposure is significant, with children's higher BW relative to intake resulting in proportionally greater exposure to EDCs. For example, the EDI for  $\Sigma$ PAEs in children is 1600.6 ng/kg BW per day, compared to 1100.1 ng/kg BW per day in adults (Hu et al., 2020a). EDCs such as phthalates are more harmful to young children, who are significantly more vulnerable to EDC exposure, including during fetal development (Przybylińska and Wyszowski, 2016). Moreover, maternal exposure to EDC compounds derived from plastics such as bisphenols and phthalates during early developmental stages can impact pregnancy outcomes by modifying embryo and placental development, even at sub-TDI exposure levels (Basak et al., 2020). This analysis underscores the need for a more comprehensive approach to risk assessment that considers both individual compound risks and cumulative effects from simultaneous exposure to multiple EDCs, especially for vulnerable populations such as children and pregnant women.

## 7 Advanced detection and remediation-based techniques

### 7.1 Biosensor-based EDC detection techniques

The EDC concentrations in wastewater are minimal, often in the range of ng/L or  $\mu$ g/L, and the predominant methods for their identification and quantification refer to conventional analytical methods like high-performance liquid chromatography tandem mass spectrometry (HPLC-MS/MS), ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS), and gas chromatography time-of-flight mass spectrometry (GC-TOF-MS) (Rodríguez-Hernández et al., 2022). These approaches have excellent sensitivity and repeatability in detection, but they need extensive sample preparation, substantial sample volumes, prolonged analysis, costly consumables, and sophisticated equipment. Electrochemical sensors have been identified as a novel and expedited method for the detection and screening of EDCs and other hazardous

substances in wastewater, exhibiting minimal detection thresholds, elevated sensitivity, and cost-effectiveness (Fig. S1) (Patel et al., 2022).

Biosensors have been engineered using cells, specific compounds, aptamers, antibodies, DNA, and model organisms, and have been used for the detection of several EDCs. Transducer sensors have been developed using carbon nanomaterials, including graphene oxide (GO) and carbon nanotubes (CNTs), as well as metal oxide nanoparticles, noble metal nanomaterials, and polymers (Jaffrezic-Renault et al., 2020; Lu et al., 2020). Kim et al. (2021) developed an electrochemical approach for detecting, measuring, and eliminating BPA using inexpensive carbon felt, with a detection limit of  $4.78 \times 10^{-4}$   $\mu$ mol/L. The CTpPa-2/GCE (a highly porous crystalline covalent organic framework (COF, CTpPa-2)-modified glassy carbon electrode (GCE)) sensor detected BPA and BPS with LODs of 0.02  $\mu$ mol/L and 0.09  $\mu$ mol/L, respectively. The sensor achieved recoveries of 87.0%–92.2% for determining BPA and BPS in bottle samples (Pang et al., 2020). Most research on biosensor development for the detection of EDCs emphasizes BPA and its analogs, as well as certain estrogens such as  $17\beta$ -estradiol (Zhu et al., 2020).

### 7.2 Spectroscopy-based advanced techniques for EDC detection

Newer bioanalytical techniques allow more effective methods for identifying and tracking EDCs in environmental samples. These advanced techniques offer major improvements in accuracy, efficiency, and the ability to handle complex environmental samples with greater precision. Among the leading advancements are SERS and NMR spectroscopy.

#### 7.2.1 SERS-based EDC detection techniques

SERS has emerged as a powerful tool for detecting low concentrations of EDCs in complicated environmental samples. Using plasmonic nanoparticles (gold and silver), SERS provides quick, sensitive, and cost-effective detection of EDCs at ultralow concentrations, outperforming standard approaches like HPLC (Yang et al., 2020). Recent innovations have further improved SERS capabilities through the use of advanced nanomaterials and hybrid methodologies. For example, Au-molecularly imprinted nanofiber (Au-MINF) combined with SERS exhibited exceptional sensitivity and specificity for phthalates like dimethyl

phthalate (DMP) in water, achieving detection limits as low as 0.01  $\mu\text{mol/L}$  (Li et al., 2019; Hu et al., 2023; Rong et al., 2024). These systems show low error rates (approximately 6%) in real-world applications like lake water monitoring. However, issues persist due to nanoparticle size variation and interference by dissolved organic matter (Rong et al., 2024).

Other advances include SERS-based immunochromatographic assay (SERS-ICA), which uses antibody-functionalized  $\text{Ag}_2\text{SiO}_2$  nanoparticles to detect diclofenac at concentrations as low as 0.07  $\text{pg/mL}$  within 15 min, indicating high stability and cost-effectiveness, despite minor nanoparticle instability (Zhou et al., 2019). To overcome sensitivity limitations, three-dimensional (3D) monolithic SERS substrates with aptamer recognition have been developed, producing high-density Raman hotspots designed for detecting EDCs at ultra-trace levels (e.g., limit of detection (LOD) of  $9.12 \times 10^{-4}$   $\text{ng/L}$ ), exceeding conventional GC-MS and HPLC in speed and precision (Li ZX et al., 2024).

A remarkable application of SERS-ICA was reported by Zhang L et al. (2021) for BPA detection in water samples. This approach coupled immunochromatographic test strips with SERS measurement, achieving an LOD of 0.1  $\text{ng/mL}$ , which was one three-hundredth of the LOD obtained using conventional ICA. Over two weeks, the test remained highly specific (4.1% relative standard deviation (RSD)) and stable, with HPLC validation revealing spiking recoveries of 90.80%–117.80% in river, tap, and bottled water. Dipole-enhanced SERS (DE-SERS) uses LiCl co-adsorbates on silver nanoparticles to increase signals, enabling BPA detection at 1  $\text{ng/mL}$ , far below standard SERS limits, although matrix impacts and LiCl optimization require further development (Yu et al., 2024).

Magnetic molecularly imprinted polymers (MIPs) have also improved SERS performance by adding ferromagnetic nanoparticles for selective EDC adsorption. This approach optimizes sample preparation through magnetic separation and reaches an LOD of  $8.7 \times 10^{-9}$   $\text{mol/L}$  for DMP (Feng et al., 2025). However, challenges in Raman enhancement and substrate fabrication persist. Overall, these SERS-based techniques provide quick, sensitive, and selective alternatives to existing analytical methods, but challenges in substrate design and matrix interference must be addressed to unleash their full potential for environmental monitoring.

## 7.2.2 NMR spectroscopy-based EDC detection techniques

NMR spectroscopy has emerged as a potent analytical method for detecting and quantifying EDC substances in environmental and biological samples. Its main advantage pertains to providing extensive molecular information without demanding sample derivatization, thereby making it particularly suitable for both targeted and untargeted analysis of complex mixtures (Shumilina et al., 2016). The non-invasive nature of NMR allows for the identification and structural characterization of contaminants such as BPA in environmental samples, while maintaining sample integrity.

One prominent method for BPA detection is the use of low-field NMR (LF-NMR) with a DNA-hydrogel (LNDH) nanoprobe. This biosensor integrates  $\text{Fe}_3\text{O}_4$  superparamagnetic iron oxide nanoparticles ( $\text{Fe}_3\text{O}_4$ -SPIONs) with a DNA-hydrogel system to achieve a detection range of 10–20  $\text{ng/mL}$  and an LOD as low as 0.07  $\text{ng/mL}$ , providing higher sensitivity for environmental applications (Wang JY et al., 2020). In contrast to other analytical techniques, LF-NMR stands out for its non-invasive performance and user-friendly application, making it especially suited for regular evaluation of trace-level EDCs (Mo et al., 2019; Yao et al., 2019). Despite limitations in nanoparticle dispersion, LF-NMR is a promising technique for EDC detection with minimal sample preparation and high reliability.

Among the methods for detecting environmental contaminants, particularly EDCs, SERS offers high sensitivity, making it ideal for trace detection and real-time monitoring, with high spatial resolution, especially for localized detection. However, it faces challenges with reproducibility due to nanoparticle-based enhancement and its sensitivity to matrix interference, limiting its consistency in field applications. In contrast, NMR provides detailed molecular and structural information with minimal sample preparation and high reproducibility, making it highly reliable for pathway analysis. Despite its strengths, NMR has lower sensitivity than SERS for low-abundance metabolites, requires larger sample volumes, and has longer acquisition time, which may hinder its use for high-throughput or real-time monitoring. Thus, while SERS excels in speed and sensitivity for field-based analysis, NMR is more suited for in-depth, reproducible

analysis of complex samples in controlled environments. Table S3 shows a direct comparative analysis of SERS and NMR under real-world scenarios, highlighting clear trade-offs (Deriu et al., 2023; Mitschke et al., 2023; Usman et al., 2023; Sloan-Dennison et al., 2024; Balasubramani et al., 2025).

### 7.3 Techniques for removing EDCs from the aquatic ecosystem

#### 7.3.1 Conventional wastewater treatment techniques for EDC removal

The challenge presented by EDCs in wastewater is the absence of efficient degradation mechanisms. In poor nations, most WWTPs are equipped with only fundamental treatment stages that are incapable of eliminating a broad spectrum of pollutants, including EDCs (Recsetar et al., 2021). WWTPs generally have two phases: primary treatment and secondary treatment. Nonetheless, many pollutants remain uneliminated throughout these phases, necessitating tertiary treatment (Fig. S2) (Mandal et al., 2020). In the initial phase of treatment, physical methods are used to separate solids from water. In conventional WWTPs, initial treatment consists of screening, grit removal, and sedimentation (Bakhtyari et al., 2020). During the screening process, solid waste is segregated using a device with consistent apertures that capture coarse materials. Grit chambers facilitate the sedimentation of sand and gravel to prevent additional buildup or harm to mechanical equipment. Ultimately, during the sedimentation process, sedimentation tanks or main settlers are used to facilitate the settling of organic suspended materials as sludge (Sikosana et al., 2019).

Following basic treatment, most pathogens and pollutants remain in the stream. Secondary treatment emphasizes the breakdown of biological matter, mainly via aerobic and anaerobic treatment techniques. The predominant aerobic systems are trickling filters and activated sludge. In trickling filters, a stationary medium supports microbial growth, resulting in biofilms that break down organic matter, whereas in the activated sludge process, a high concentration of microorganisms aggregated as minute suspended particles decompose the organic material (Rajasulochana and Preethy, 2016). The anaerobic systems used in secondary treatment rely on anaerobic digestion. The organic matter is converted into a combination of biogas and sludge. The predominant anaerobic treatment methods

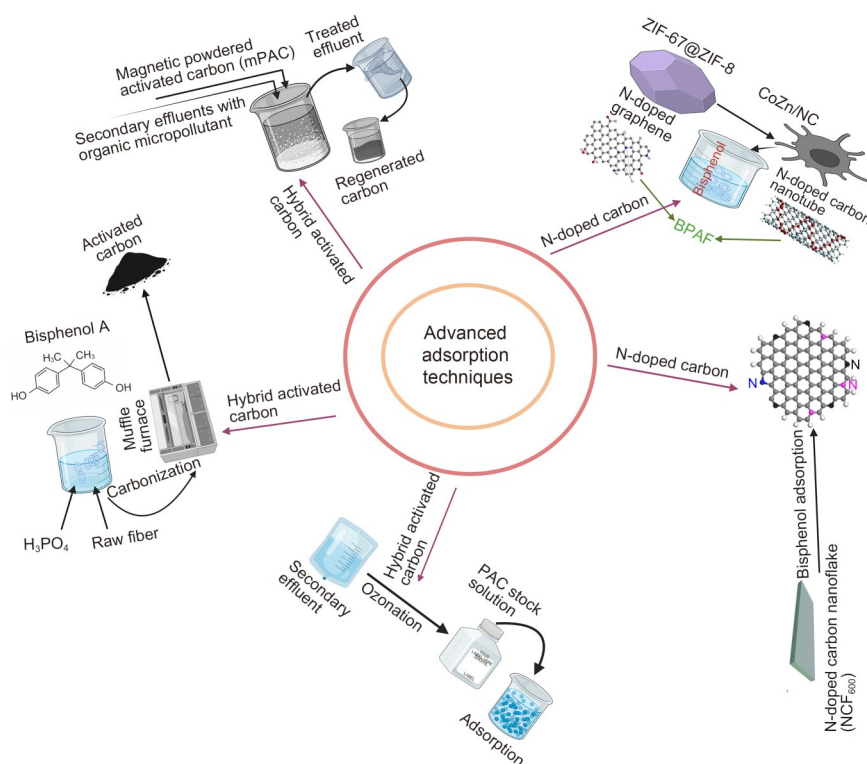
are the up-flow anaerobic sludge bed (UASB), expanded granular sludge bed (EGSB), and anaerobic fixed film reactor (AFFR). The concentration of organic pollutants in the effluents post-treatment varies based on several aspects, including the starting concentration and the degradability of each pollutant by the methods used (Mandal et al., 2020). In most instances, the concentration of contaminants in treated wastewater has been reported ranging from 10 ng/L to 20 µg/L (Prieto-Rodriguez et al., 2012). Nonetheless, for pollutants such as EDCs, even minimal quantities may pose an environmental threat due to their propensity for bioaccumulation. Tertiary treatment has been instituted to improve the elimination of residual pollutants in wastewater.

#### 7.3.2 Advanced adsorption-based EDC removal techniques

While conventional techniques have limited efficacy in EDC removal, new adsorption techniques have been developed as promising solutions for addressing these gaps. Adsorption has gained popularity for treating EDCs due to its cost-effectiveness, simplicity, and limited byproduct generation. This technique purifies water by transferring pollutants to the surface of an adsorbent substance (Rezania et al., 2024). This section explores advanced adsorption approaches for EDC removal, including hybrid activated carbon systems and N-doped carbon methods (Fig. 4).

##### 7.3.2.1 Hybrid activated carbon systems for EDC removal

Hybrid activated carbon systems show remarkable performance in removing EDCs, including BPA and phthalates, from wastewater streams. These systems capitalize on the combined advantages of powdered activated carbon (PAC) and granular activated carbon (GAC), which have excellent adsorption capacity due to their high surface area and microporous structure, allowing effective pollutant removal through both physisorption and chemisorption methods (Sudhakar et al., 2016). Current technological advancements have centered on integrating activated carbon with complementary treatment processes to improve the overall removal efficiency. For example, the integration of ozonation with activated carbon systems has proven effective, as ozone pretreatment breaks down complex pollutants into more adsorbable forms. This synergistic



**Fig. 4** Advanced adsorption techniques for the removal of endocrine-disrupting compounds from aquatic ecosystems. The diagram illustrates the integration of hybrid activated carbon systems, N-doped carbon-based materials, and ozonation processes for enhanced removal efficiency. Specific adsorbents, such as powdered activated carbon (PAC) solutions, are highlighted alongside carbon adsorbent regeneration pathways. The effectiveness of N-doped carbon materials in adsorbing bisphenol and related pollutants is emphasized, demonstrating their potential in treating contaminated effluents. ZIF: zeolite imidazolate framework; BPAF: bisphenol AF; CoZn/NC: CoZn/N-doped carbon. Created with BioRender.com.

approach has achieved removal rates of up to 98% for persistent EDCs such as BPA and nonylphenol when combining GAC with coagulation and ozonation (Fang et al., 2014). Similarly, PAC dosage in activated sludge systems can remove more than 80% of phthalates and BPA (Wirasmita et al., 2018), while PAC-ozone systems in secondary effluent treatment show comparable performance for atrazine removal (Zhang et al., 2025).

Biological amplification of activated carbon systems is emerging as another promising strategy. Biological activated carbon (BAC) systems use indigenous microbial communities that develop biofilms on carbon surfaces, enabling simultaneous adsorption and biodegradation of contaminants. These systems retain high removal efficiency for diverse EDCs regardless of the self-sustaining biofilm formation (Sbardella et al., 2018). Further advances include magnetic PAC (mPAC), which combines iron oxide nanoparticles to facilitate magnetic separation and regeneration. A recent study by Drenkova-Tuhtan et al. (2024)

indicated that mPAC can remove up to 85% of 28 distinct contaminants during five regeneration cycles with negligible efficiency loss (<5%). However, these systems have limitations, including a reduced surface area and pore volume compared to conventional activated carbon, prompting adjustment of regeneration techniques to retain performance. Kim et al. (2021) extended hybrid activated carbon applications to include integration with gravity-driven membrane (GDM) filtering systems. The GAC-GDM configuration offers significant potential for eliminating emerging pollutants, including MPs and perfluorinated chemicals, while also providing practical advantages for low-resource situations due to its small design and minimum maintenance requirements. Concurrently, research on sustainable activated carbon sources has found doum fiber-derived carbon as a promising, low-cost adsorbent for phenolic EDCs, showing high adsorption capability and stability for chemicals like BPA and  $\alpha$ -naphthol (Grich et al., 2024).

While activated carbon systems show significant promise for EDC removal, their environmental impacts require careful consideration. Studies have shown that ingestible activated carbon particles, such as PAC, can cause adverse effects in benthic invertebrates, including reduced dry weight, carbon assimilation, and damage to gut microvilli in species like the clam (Rämö et al., 2021). These negative effects are attributed to physical abrasion of the gut wall by activated carbon particles, leading to starvation, reduced foraging, and impaired nutrient assimilation (Nybom et al., 2015). Apart from adverse effects, the use of activated carbon in treatments has shown valuable benefits in reducing toxicity in aquatic organisms, as shown by a 68% decrease in mussel toxicity after detoxification with activated carbon for 3 d (Qiu et al., 2018). Following a previous study, non-ingestible activated carbon particles, such as GAC, have also shown positive biological responses in benthic organisms, possibly due to contaminant sequestration and improved sediment habitability (Janssen and Beckingham, 2013). This highlights the potential of activated carbon systems not only in enhancing the removal of EDCs from wastewater but also in mitigating toxic effects on marine life, making activated carbon a promising tool for ecological management. However, it remains crucial to consider the potential ecological risks of activated carbon use, particularly in benthic environments, to ensure a sustainable and effective application in future remediation strategies.

### 7.3.2.2 N-doped carbon-based techniques for EDC removal

N-doped carbon-based materials are promising in their ability to remove EDCs due to their adjustable porosity, abundant active sites, and eco-friendly properties. There is high potential for BPA removal by N-doped carbon produced from poly-dopamine, with a capacity of 1351 mg/g and quick adsorption kinetics, mostly through  $\pi$ - $\pi$  interactions and hydrophobic forces involving pyridinic nitrogen (Sun et al., 2020). Wu et al. (2021) found that magnetite/hollow core-shell N-doped mesoporous carbon sphere ( $\text{Fe}_3\text{O}_4/\text{N-HCSCs}$ ) composites effectively remove EDCs, with recovery rates of 88%–97% and LODs of 0.05–0.10  $\mu\text{g/L}$  due to their wide surface area and nitrogen content. CoZn/N-doped carbon (CoZn/NC), synthesized from zeolite imidazolate framework ZIF-67@ZIF-8, removes over 96.5% BPA in just 1 min with less than

10% efficiency lost after five cycles, while remaining stable across a wide pH range and exhibiting magnetic characteristics for simple separation from water (Zhang H et al., 2022). Additionally, Cu-Mn spinel oxide nanospheres on N-doped carbon may activate peroxymonosulfate to fully degrade BPA with a rate constant of  $0.557 \text{ min}^{-1}$ , exceeding other catalysts and revealing strong anti-interference properties (Wang XB et al., 2024).

N-doped carbon nanoflakes ( $\text{NCF}_{600}$ ) also show high BPA adsorption (200 mg/g) and reusability with minimal efficiency loss after five cycles (Lai et al., 2023). Likewise, ultra-edge N-doped hierarchically porous carbon-based materials with rich vacancy defects (HENDC) have a high BPA adsorption capacity (870.1 mg/g) and rapid adsorption kinetics with 81%–93% removal efficiency, exhibiting excellent stability, with only a 9.74% efficiency loss after five regeneration cycles (Wang T et al., 2024). Other materials, such as N-doped framework carbons and dual-doped N/S carbon adsorbents, have fast adsorption and substantial capacities (Wang T et al., 2021). Furthermore, N-doped pyrocarbons from seaweed show 91.48% BPA removal and a maximum BPA adsorption capacity of 270.581 mg/g, offering a cost-effective water treatment option; however regeneration cycles led to a gradual decline in efficiency with up to a 5%–25% loss after just five cycles due to surface fouling, structural degradation, and pore blockage over time (Marrakchi et al., 2022). Additionally, the potential nanotoxicity risks posed by leaching nanoscale fragments into treated water, which may induce oxidative stress or bioaccumulation in aquatic organisms, further complicate their sustainable application (Suji et al., 2025). These nanomaterial fragments can induce oxidative stress and bioaccumulate in aquatic organisms, leading to detrimental effects on their health. For example, carbon quantum dots and CNTs have been shown to cause toxicity and behavioral alterations in aquatic species, particularly affecting embryonic development (Chousidis et al., 2020). Moreover, GO nanoparticles have been linked to developmental disruptions in zebrafish embryos, including altered locomotor activity, increased malformation rates, and elevated oxidative stress (Yang et al., 2019). Additionally, CNTs have been shown to alter immune signaling pathways, raising concerns about their environmental persistence and impact on aquatic health (Rahman et al., 2025).

These findings underscore the need for rigorous ecotoxicological assessments and improved material stability, secure recovery methods, and minimal environmental leaching to ensure the safe large-scale adoption of N-doped carbon-based nanomaterials for water treatment.

Based on these studies, N-doped activated carbon stands out as the most field-practical and cost-effective method for EDC removal. Derived from sustainable biomass, N-doped activated carbon techniques offer low production costs and high adsorption capacity, with some materials showing BPA removal rates as high as 1351 mg/g (Sun et al., 2020). In addition, they benefit from rapid adsorption kinetics and magnetic properties, making it easy to separate BPA and rendering them ideal for large-scale wastewater treatment (Wu et al., 2021). However, these techniques show a 5%–25% efficiency loss after five cycles. In contrast, hybrid activated carbon systems require additional treatments like ozonation and face challenges such as biofouling and surface area reduction, particularly in biological activated carbon systems, contributing to higher operational and maintenance costs. While advanced adsorbents like metal-organic frameworks (MOFs) and CNTs show excellent lab-scale performance for EDC removal, their real-world efficacy is hindered by high synthesis costs, regeneration difficulties, and poor mechanical stability under environmental stresses, making them less practical for large-scale use (Hashemi et al., 2017; Meskher et al., 2023). In comparison, modified biochar and activated carbon offer more viable and scalable solutions. Although they show lower adsorption metrics in controlled studies, their cost-effectiveness and sustainability make them suitable for field applications (Dixit and Ahammed, 2023). Consequently, future research should prioritize hybrid adsorbents that optimize performance, stability, and reusability in practical aquatic environments.

## 8 Regulatory policies

Regulatory measures controlling the release of EDCs are imperative to mitigating their effects on ecosystems and public health. In the USA, the Environmental Protection Agency (EPA)'s Endocrine Disruptor Screening Program (EDSP) assesses the potential of chemicals to disrupt endocrine systems, guiding water contamination decisions. The European Union (EU)'s Registration, Evaluation, Authorization

and Restriction of Chemicals (REACH) regulation designates substances like BPA and phthalates as substances of very high concern (SVHCs), requiring risk assessments (Andersson et al., 2018). The EU's Water Framework Directive (WFD) also enforces quality standards for EDCs in surface water to prevent harm to aquatic life (Xiao et al., 2023).

In North America and the EU, BPA is banned from use in the production of children's cups and bottles due to health concerns. Tariffs incentivize plastic recycling, and European Norm EN 13432 ensures biodegradability standards. Despite these efforts, challenges persist in fully controlling EDCs, and global mandatory screening protocols for water bodies should be implemented. The precautionary principle, already adopted in the EU and Canada, must expand to ensure that suspected endocrine disruptors undergo thorough risk assessments before approval (Attina et al., 2016).

A collaborative approach involving government bodies, non-governmental organizations (NGOs), and international organizations can provide effective implementation of policies to reduce EDC exposure. Canada was the first to regulate BPA in plastic baby bottles in 2009, followed by similar actions in the US and Europe. The EFSA reduced the BPA TDI from 50  $\mu\text{g}/\text{kg}$  BW per day in 2006 to a temporary TDI of 4  $\mu\text{g}/\text{kg}$  BW per day in 2015, and later established a much lower TDI of 0.2  $\text{ng}/\text{kg}$  BW per day (EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) et al., 2023). However, there are several countries (e.g., Japan, India) that lack comprehensive regulations on BPA in food-contact plastics, underscoring the need for further research on the effects of low-dose BPA and stricter regulations in regions such as India. Continued research and enhanced regulatory frameworks will be key to reducing exposure and protecting health.

## 9 Challenges and alternative solutions

EDCs at ultra-trace levels within complex combinations hamper detection and toxicity assessment, especially owing to synergistic or antagonistic interactions. Traditional analytical methods, although precise, are frequently expensive and impractical for extensive monitoring. Furthermore, EDCs induce modest but considerable biological effects among aquatic species, exhibiting high interspecies sensitivity and ambiguous long-term consequences. Regulatory frameworks are

inadequate, and public knowledge of appropriate disposal and source control is lacking. In response, many alternative methods have been suggested and are now being developed. Advanced remediation technologies, including bioremediation, photocatalysis, and engineered wetlands, provide potential methods for the degradation of EDCs. Biosensor technology and quick detection assays offer economical, field-deployable instruments to improve monitoring. Integrated methodologies that merge chemical analysis with bioassays and omics-based techniques facilitate a comprehensive knowledge of the effects of EDCs. Predictive modeling and artificial intelligence enhance the forecasting of environmental destiny and toxicity, but policy changes and public education are crucial for mitigating the release of EDCs at the source. These innovations and strategic interventions are essential for mitigating the intricate dangers presented by EDCs in aquatic ecosystems (Fig. S3).

## 10 Prospects

While BPA has been extensively studied for its transgenerational effects in fish and invertebrates, the impacts of phthalate exposure, including its influence across multiple generations, remain underexplored. It is crucial to better understand how phthalates, such as DEHP and DBP, affect fish fertility, gene expression, developmental anomalies, and epigenetic alterations over successive generations.

Although the bioaccumulation of EDCs like BPA and PAEs in aquatic organisms has been well-documented, research on their transfer from seafood to humans is limited. Many studies have shown that these chemicals accumulate in fish and shellfish, but the direct health risks posed to humans through dietary intake of contaminated aquatic organisms are poorly known. Future research should investigate the biomagnification of BPA, PAEs, and emerging analogs in aquatic food sources and assess the associated risks to human health.

NMR spectroscopy holds considerable promise as a non-invasive approach for detecting EDCs, especially in complex environmental mixtures. However, there are challenging issues related to nanoparticle dispersion and the sensitivity of NMR for trace quantities of EDCs. Future efforts should aim to refine high-resolution NMR techniques tailored specifically

for the detection of low-concentration EDCs in varied environmental matrices, thereby improving the effectiveness of NMR as a tool for environmental analysis.

Advanced sensing technologies hold great potential for monitoring EDCs in the environment. Nanomaterial-based sensors can enhance sensitivity for detecting EDCs at low dosages, improving monitoring accuracy and reliability, even in complex matrices. MIPs, aptamers, and other biomimetic materials can offer high specificity to target EDCs, reducing interference from other compounds and minimizing false positives. This is particularly crucial in industrial or agricultural environments, where the risk of EDC exposure is higher. Sensor technologies, coupled with wireless or Internet of Things (IoT) capabilities, enable remote monitoring of EDCs. Advanced methods provide real-time data to environmental authorities, allowing for prompt action to mitigate health risks. These sensor-based approaches make EDC monitoring more accessible to a broader audience, including communities and citizen scientists. Platforms designed to detect multiple EDCs simultaneously can offer a more comprehensive understanding of environmental pollution, helping stakeholders develop targeted mitigation measures to reduce exposure. Numerous emerging themes in sensor research for monitoring EDCs include fluidic integration, device downsizing, and multiplexing. The combination of sensors and microfluidics enables automated and high-throughput sample processing, reducing the time and cost associated with EDC detection. Microfluidic devices precisely regulate sample flow and reaction conditions, resulting in increased sensitivity and specificity in EDC detection. Sensor miniaturization enables the development of portable and field-deployable devices. Miniaturized sensors can reduce the number of samples and reagents required for detection, making them more economically efficient and environmentally friendly. These sensors enable in situ and real-time monitoring of EDCs in biological and environmental samples. Multiplexed sensors make it easier to identify complicated combinations of EDCs that are commonly found in environmental samples. Multi-target sensors can be developed by combining arrays of sensors with different sensing components or by using microarrays on lab-on-a-chip platforms. These advancements make it easier to develop advanced EDC detection devices that are more sensitive, specific, cost-effective, and portable than existing techniques. These sensors have

the potential to change EDC monitoring and risk evaluation, resulting in improved public health and environmental safeguards.

Future advancements to address EDC-related health and ecological risks will prioritize scalable, eco-friendly detection and removal technologies, especially in rapidly industrializing regions like the Asia-Pacific. The global endocrine disruption screening market is projected to grow from USD 141.94 million in 2025 to USD 183.86 million by 2034, reflecting a compound annual growth rate (CAGR) of 2.92% during the forecast period of 2026–2034 (<https://www.theinsightpartners.com/reports/endocrine-disruption-screening-market>). This growth emphasizes the increasing global investment in advanced and scalable EDC detection and remediation solutions.

## 11 Conclusions

EDCs are widespread pollutants in aquatic ecosystems, posing significant threats to both aquatic organisms and human health. Their release leads to contamination of surface water and sediments, with the potential for bioaccumulation and toxicity, resulting in long-term ecological risks. Their adverse effects include hormonal disruption, oxidative stress, DNA damage, and developmental anomalies, which impair immune, reproductive, and growth functions. These effects pose significant risks to human health through contaminated aquatic food sources. Advanced detection methods such as SERS and NMR are improving the identification and quantification of EDCs, and remediation strategies like hybrid activated carbon systems show promise. N-doped activated carbon shows superior field applicability due to its cost-effectiveness, scalability, and high adsorption capacity. However, its gradual efficiency loss during regeneration cycles and the ecotoxicity risks of advanced nanomaterials highlight the need for further optimization of these technologies for sustainable implementation. Despite regulatory advancements such as the EU's REACH and the US EPA's EDSP, many regions still lack comprehensive policies, highlighting the need for global harmonization and stricter enforcement. Future research should focus on understanding the transgenerational effects of phthalate exposure and investigating the biomagnification of EDCs from aquatic food sources to humans. Advances in sensor technologies, including

miniaturization and multiplexing, will further enhance monitoring capabilities, enabling real-time, cost-effective detection of EDCs in complex environmental matrices. These advancements will be crucial for improving environmental safeguards and public health protection.

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## Author contributions

Tariq DILDAR: conceptualization, visualization, and writing—original draft. Yongcheng XUE: visualization. Wenxiao CUI, Mhd IKHWANUDDIN, and Muhammad SHAFIQ: writing—review and editing. Hongyu MA: conceptualization, visualization, writing—review and editing, supervision, and funding acquisition. All authors have read and approved the final manuscript.

## Compliance with ethics guidelines

Tariq DILDAR, Yongcheng XUE, Wenxiao CUI, Mhd IKHWANUDDIN, Muhammad SHAFIQ, and Hongyu MA declare that they have no conflicts of interest.

This review does not contain any studies with human or animal subjects performed by any of the authors.

## Declaration on the use of generative AI tools

During the preparation of this work, the authors used ChatGPT to improve the language. After using this tool, the authors reviewed and edited the content as needed, and take full responsibility for the content of the publication.

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#### **Supplementary information**

Tables S1–S3; Figs. S1–S3