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REVIEW

Remediation and toxicity of endocrine disruptors: a review

Ravichandran Swathy Monisha[1] · **Ragupathy Lakshmi Mani**[1] · **Baskaran Sivaprakash**[1] · **Natarajan Rajamohan**[2] · **Dai-Viet N. Vo**[3,4]

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Abstract
Endocrine disruptors are hazardous chemicals with chronic health effects for most living organisms, inducing homeostasis, hormonal imbalances, cancer, reproductive and neurological disorders, cardiovascular diseases, vulnerability to fetus and neonates. Over 1,000 chemicals display endocrine disrupting characteristics. Endocrine disruptors are found among industrial chemicals, pharmaceuticals, heavy metals, plastic materials, fertilizers, pesticides, herbicides and fungicides. Endocrine disruptors enter human organs via ingestion, inhalation and diffusion through the skin. Here, we review the detection, toxicity, hazard identification and remediation methods of three classes of endocrine disruptors: steroid hormones, pharmaceutical and personal care products, and pesticides. Remediation methods include biological, physical, chemical, electrochemical and radiative methods. Bisphenol A was removed of 99% by biodegradation and ultraviolet with hydrogen peroxide, 98.4% by electropolymerization, 97.5% by photoelectrolysis and 80% by sand filtration. We present advanced treatment chemicals and discuss the performance of remediation using the combination of 2–3 treatment methods. In silico methods and machine learning for predicting toxicity and remediation are discussed

Keywords Endocrine · Bisphenol · Degradation · Toxicology · Hazard

Introduction

Chemical industries constitute a major sector since chemicals have entwined in human life yielding varieties of products that serve mankind, employment opportunities and economic growth. Chemicals produced are used for varied applications in industries related to food products, agricultural applications and personal care products like detergents, cosmetics, surfactants, plastics and sanitizers. However, many chemicals have immense hazardous effects when they enter the vicinity of environments that are susceptible to risks.

Among the various health issues, endocrine disruption has been identified as a high-risk class of hazards to human and environment. The term 'endocrine disruptor' was coined in the Wingspread Statement during the early 1990s and further introduced by the US Environmental Protection Agency as Endocrine Disrupting Compound in 1996 formally. The endocrine disrupting compounds were defined as exogenous agents that can manipulate the synthesis and functions of hormones in living organisms that play vital role in homeostasis, reproduction and many more functions (Yilmaz et al. 2020).

Endocrine disrupting compounds like bisphenol A, nonylphenol, 4-tert-octylphenol, and estrogen hormones like estradiol, 17α-ethinylestradiol, 17β-estradiol and azole fungicides are found to be abundant in ground and surface water. These endocrine disrupting compounds are used in the production of pesticides, pharmaceuticals, surfactants,

✉ Baskaran Sivaprakash
spshivbaskar@gmail.com

✉ Natarajan Rajamohan
RNatarajan@su.edu.om

✉ Dai-Viet N. Vo
vndviet@ntt.edu.vn

[1] Department of Chemical Engineering, Annamalai University, Annamalai Nagar, Chidambaram 608002, India

[2] Chemical Engineering Section, Faculty of Engineering, Sohar University, 311 Sohar, Oman

[3] Institute of Environmental Sciences, Nguyen Tat Thanh University, Ho Chi Minh City, Vietnam

[4] School of Chemical Engineering, Universiti Sains Malaysia, Engineering Campus, 14300 Nibong Tebal, Penang, Malaysia

wood preservatives, dyes and industrial products and by-products (Loffredo and Parlavecchia 2021; Frankowski et al. 2021).

An organochloride endocrine disrupting compound dichloro diphenyl trichloroethane, which has a composition of 1-chloro-4-[2,2,2-trichloro-1-(4-chloro-phenyl) ethyl] benzene, was largely used for its insecticidal properties after the second world war. Endocrine disrupting compounds induce reproductive problems like reduction in sperm count, elevation in hypospadias, cryptorchidism, testicular cancer, earlier puberty, and increase of endometriosis (Munier et al. 2016).

The easy entry by distinct uptakes and accumulation of endocrine disrupting compounds in all organisms is facilitated by their high lipophilic degree (Li et al. 2021). They also have the possibility of imparting ocular diseases. Investigations with occupational workers revealed that neurotoxic endocrine disrupting compounds caused color vision defects due to issues by the photosensitive retinal ganglion cells (Loffredo and Parlavecchia 2021; de Oliveria et al. 2021; Omran and Salama 2016; Rajamohan and Sivaprakash. 2010; Daghrir and Drogui 2013).

Endocrine disrupting compounds detected in lands can affect the whole ecosystem by entering into the food web through worms and plants (de Oliveria et al. 2021). Among the synthetic endocrine disrupting compounds, bisphenol is the most common one, with its global consumption increasing significantly from 2011. The bisphenols cause fatal effects like brain, behavior and prostate gland in fetuses, children and infants (de Oliveria et al. 2021; Loffredo and Parlavecchia 2021; Lu et al. 2018; Rajamohan and Sivaprakash. 2008).

Endocrine disrupting compounds such as bisphenol A, 4-nonylphenol and 4-tert-octylphenol were found to have a considerable amount of accumulation in the liver and muscle tissues of fishes. Some endocrine disrupting compounds in carboxamide fungicide, belonging to succinate dehydrogenase inhibitor, cause adverse chronic effects on humans. They are used as pesticides for vineyard protection, tomato, and apple (Errico et al. 2017).

The effects caused by azole fungicides are reported as irreversible and chronic due to high concentration, stability and high profile applications. Endocrine disrupting compounds are to be eliminated to the minimum possible level to alleviate all their health hazards. Many chemical methods, electrochemical methods, radiative methods, physical methods, advanced oxidation and biological methods have been reported for the degradation of endocrine disrupting compounds (Frankowski et al. 2021).

This report presents classification of the endocrine disrupting compounds on the context of sources of derivation and usage. The application of endocrine disrupting compounds, toxicological aspects, hazard identification, detection methods are presented. A review on the treatment methods available for treatment of endocrine disrupting compounds is made under five classes highlighting the performance efficiencies. Machine learning tools available for detection and treatment methodologies are reviewed. The outlay of the present report is presented in Fig. 1.

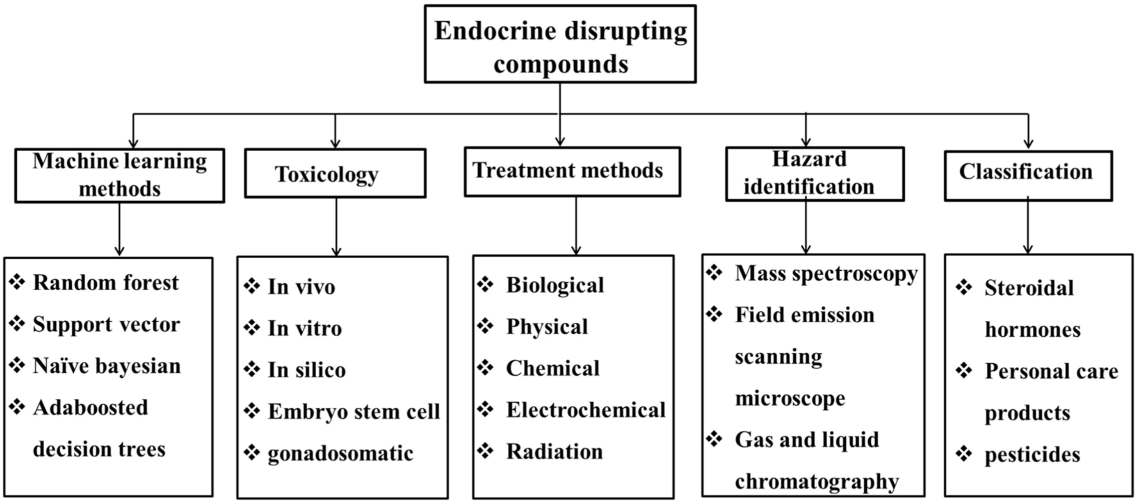

Fig. 1 Classification, hazard identification methods, treatment methods, toxicology analysis and machine learning tools for the remediation of endocrine disruptors

Classification of endocrine disrupting compounds

Endocrine chemicals can influence the endogenous peptidergic metabolism of living things (Budeli et al. 2021; Piir et al. 2021). Typical endocrine disruptive compounds cause major threats to endocrine and reproductive systems (Wee et al. 2021; Sivaprakash and Rajamohan 2011). In addition, they increase the risk of breast cancer, prostate cancer, endometriosis, metabolism disorder, obesity and thyroid-related issues (Fuhrman et al. 2015; Liu et al. 2016; Bodziach et al. 2021; Yan et al. 2018).

Increased consumption of these endocrine disrupting compounds can impersonate the endogenous hormones and can affect the production of natural hormones. Based on the source of derivation and usage, the endocrine disrupting compounds are classified into three classes namely, steroidal hormones, pharmaceutical and personal care products and pesticides. The importance of each class of compounds is very wide for human needs, and their applications have become inevitable. A detailed flowchart on classification of endocrine disrupting compounds is given in Fig. 2.

Steroidal hormones

Steroidal hormones are more hazardous due to their direct effects on endocrine system. On an average, steroids concentration above 3.5 ng/L causes major disruption to reproductive system such as reduced fertility, intersex, increased egg production and suppression of male sex characterization. Few steroidal hormones that come under this class of endocrine disrupting compounds include cortisol, 11-deoxycortisols, aldosterone, corticosterone, 11-deoxycorticosterone, androstenedione, testosterone, estrone, estradiol, estrone sulfate, progesterone and aldosterone (Lara et al. 2021; Lu et al. 2018).

17α-ethinylestradiol is a lipophilic synthetic estrogen, an active agent of many contraceptive pills which provides adverse effects in vitellogenesis, feminization and hermaphrodism (Astrahan et al. 2021). These contaminants can bioaccumulate within fat tissue of aquatic organism. Increased consumption of both natural and artificial estrogens in the form of oral contraceptive pills, cancer treatment and therapy for hormones replacement was reported (Baycan and Puma 2018).

17β-estradiol is a natural estrogen, which causes adverse effect to a living species. Even at 10 ng/L concentration in aquatic surfaces, it has potential risks to the species. This endogenous estrogen was liberated from the human excretion and wastewater treatment plant effluents. The average concentration of 17β-estradiol was reported between 4.9 and 48 ng/L in water bodies (Lara et al. 2021).

Personal care products

Other than pharmaceutical compounds, home and personal care products are also majorly consumed by human beings for many health, hygiene and cosmetic-related applications (Su et al. 2020). Few commonly used endocrine disrupting compounds in personal care products includes, triclosan, triclocarban, caffeine, alkyl phenols, paraben, phthalates, diclofenac, salicylic acid and clofibric acid (Jun et al. 2019; Kim et al. 2021a, b; Cabrera-Lafaurie et al. 2015).

Triclosan, a biphenyl ester, is one among the 10 most commonly detected endocrine disrupting compounds in wastewater, which acts as antimicrobial agent in soaps, detergents, lotions, shaving cream, sunscreens, toothpaste

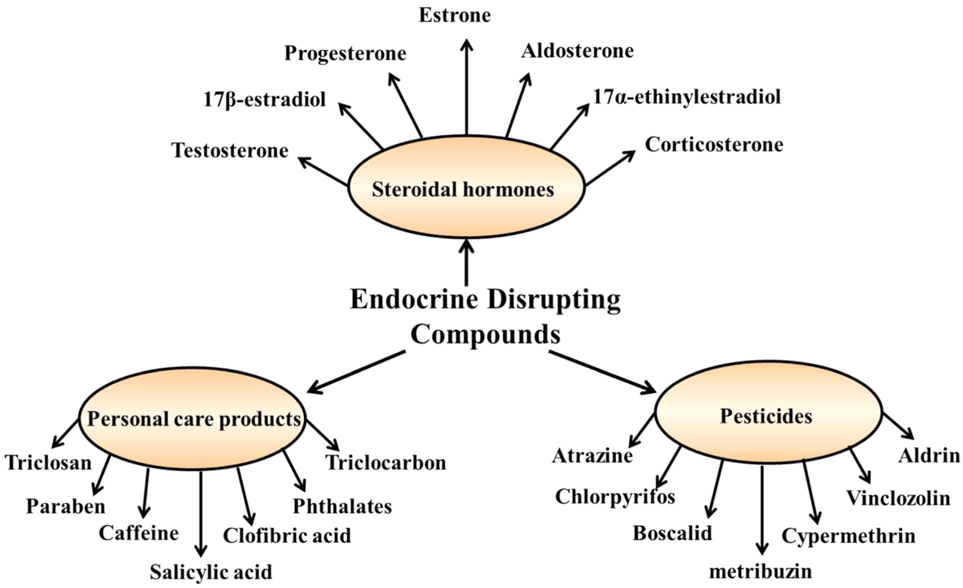

Fig. 2 Classification of major endocrine disruptors based on occurrence, usage and derivation of sources, into three categories: steroidal hormones, personal care products and pesticides

and even in plastics. Czech et al. (2020) reported that more than 50% of US streams have the presence of triclosan. In evaluating the sample of 231 personal care products collected in China and USA, the concentration of triclosan had a geometrical mean value of 3.03 ng/g (Lu et al. 2018).

Triclocarban is utilized in many household and personal care products including, sanitizing materials, which are extensively used in more than 2000 products (Torres et al. 2016). The prenatal exposure of triclocarban to pregnant women poses potential risks to fetal-mother characteristics. Other effects include, reproductive toxicity, vivo genotoxicity and human microbiome disruption (Bai et al. 2020).

Caffeine is a psychoactive compound, available in water bodies at concentration above 10,000 µg/kg. These are used in the treatment of orthostatic hypotension, bronchopulmonary dysplasia in premature infants and as a co-drug with analgesic medications. The concentration of caffeine ranged between 20 and 293 µg/L at hospital sewage effluents in Tromso, Norway (Czech et al. 2020).

Alkylphenol ethoxylates derivatives are non-ionic surfactants, widely used in personal care products such as emulsifiers, paints, cleaner and preservatives (Mallerman et al. 2019). This alkylphenol contributes about 60% of total surfactants, with an average worldwide production of 600 kilo tonnes per year. The main alkyl phenol derivatives are nonylphenol and octylphenol with prevalent usage of 85% and 15%, respectively. 4-t-octylphenol is used as a substrate in the production of phenol formaldehyde resins and non-ionic detergents (Janicki et al. 2016).

Phthalates possess application in personal care products and plasticizers (Gani and Kazmi 2020). With exclusion to these, several other compounds like diclofenac, musk ketone, musk xylene, celestolide, galaxolide and tonalide are also utilized as personal care products. (Monisha et al. 2021; Berslin et al. 2021; Petrie and Camacho-Muñoz 2021; Vlassi et al. 2020).

Pesticides

Insecticides, herbicides and fungicides are used to protect plant species from unwanted plants, weeds, worms and insects. The usage of many chemical species in the production of pesticides causes major endocrine disruptions. A brief description about few endocrine disrupting chemicals, namely, atrazine, chlorpyrifos, aldrin, cypermethrin, boscalid, vinclozolin, dichlorodiphenyl trichloroethane and metribuzin in pesticides are elaborated (Vlassi et al. 2020; Singh et al. 2018; Abdel-Razik et al. 2021; Alaa-Eldin et al. 2017).

Atrazine is a synthetic herbicide, used in cultivable land, which affects the reproductive system of amphibians, alligators and peripubertal male and female rats (Omran and Salama 2016). Atrazine occupies the second most widely utilized pesticide by contributing very large annual consumption. Atrazine possesses a long half-life of 41–231 days and contaminates the ground water sources by penetration up to 30 µg/L concentration. The permissible limit of atrazine in drinking water is prescribed as <5 µg/L (Singh et al. 2018).

Boscalid is a carboxamide fungicide used in cultivable lands of edible and ornamental plants. Dichloro diphenyl trichloroethane causes crucial disruptions in reproductive system including reduced pregnancy possibility, reduced fertility and suppressed menstrual cycle. This pesticide stimulates the formation of estrogen receptors and multiplication of androgen-sensitive cells (Munier et al. 2016).

The bisphenol derivatives have a widespread prominence in all the above-mentioned classes. Their usage in personal care products is in antibacterial soaps, nail polishes, shaving creams, anti-septic and antiperspirant products. Usage of silicones in hair conditioner, thickening of urethane medium and many *n*-polar solvents in hair cosmetics are few instances of bisphenol occurrences. The limits for detection of the bisphenol derivatives were reported as 0.2 for bisphenol A and *F* and 0.1 for bisphenol *S*, respectively (Machtinger et al. 2018). The overall concentration of bisphenol derivatives in personal care products was reported as <100 µg/g (Lu et al. 2018).

Hazard identification of endocrine disrupting compounds

Endocrine disrupting compounds are a very important class of pollutants with high environmental concern because of their toxicity and numerous negative impacts on all organisms. The wastewater treatment plant of 480,000 m^3/d capacity in Shenzhen, China, holding a population of 1.2 million was reported to have 28 types of pharmaceutical and personal care products. The endocrine disrupting compounds were identified by gas chromatography and mass spectroscopy, with concentrations of 51,357.8 ng/L, 99,136.5 ng/L, and 55,348.3 ng/L for pharmaceutical and personal care products, endocrine compounds, and odorous compounds, respectively (Chen et al. 2021).

Endocrine disrupting compounds in untreated urban and industrial wastewaters in Siberia had a significant impact on Danube river water. The presence of synthetic estrogens and alkylphenols was detected using solid phase extraction perconcentration system coupled to a triple quadrupole tandem mass spectrometer equipped with electrospray ionization. Natural and synthetic estrogen concentrations ranged from 0.1 to 64.8 ng/L in surface and wastewater and were not found in drinking water. Bisphenol A was the most abundant compound in all water types, with frequencies of detection accounting to 57% in drinking water, 70% in surface, and 84% in wastewater (Celic et al. 2020).

Endocrine disrupting compounds are found enormously in Taihu lake, Jiaozhou bay in Yellow sea, Yangtze river, Laizhou bay, and Bahe river. The detection of compounds using high-performance liquid chromatography, triple-quadrupole mass spectroscopy, liquid chromatography doped with quadrupole-orbitrap high-resolution mass spectrometry, flux analysis, gas chromatography and mass spectroscopy revealed that the concentration of bisphenol A was seen to be high in surface when compared to other stages, nonylphenol and 4-tert-octylphenol were predominant alkylphenols in the lake. Whereas tetrabromobisphenol A had high detection in suspended particulate matter in Taihu lake (Liu et al. 2016).

In coastal regions, bisphenol A was reported to have an average concentration of 449.2 ng/L in winter and 186.3 ng/L in summer. Steroidal estrogen showed 87.2 ng/L and 2.7 ng/L average concentrations in winter and summer, respectively. The equivalent concentration of all endocrine disrupting compounds was recorded as 68.87 ng/L and 1.76 ng/L in winter and summer, respectively. These concentration rates were studied using a positive matrix factorization model (Lu et al. 2020a).

In urbanized Jiaozhou bay in Yellow sea, 14 endocrine disrupting compounds and 9 household and personal care products were detected. The endocrine compounds occurrence were recorded in the range of 145–658 ng/L and 100–301 ng/L in summer and winter, respectively. The bay water concentration ranged from 56.7 to 212 ng/L (Lu et al. 2021). In Jiangsu province, 10 types of endocrine disruptive compounds were identified. Nonylphenol, 4-tert-octylphenol and (2-ethylhexyl) phthalate ranked highest having a mean concentration of 300 ng/L when compared to 4-tert-octylphenol which was found to have a high mean concentration above 100 ng/L (Fan et al. 2021).

The Yangtze river basin in Yangzhou city had the highest concentration when compared to Huai river basin followed by Xuzhou city and Suqian city, whereas in Yangtze river in Nanjing Sect. 4-tert-butylphenol, nonylphenol and bisphenol A were detected to be the dominant compounds with concentrations in the range of 225–1121 ng/L, 1.4–858 ng/L, and 1.7–563 ng/L, respectively. The mean concentration of 69 µg/g for nonylphenol and that of 51.8 µg/g for bisphenol A were witnessed, while 4-tert-octyphenol had a predominant contribution of 32.6–99.1% on surface water and suspended particulate matter (Liu et al. 2017).

The discharges in Laizhou bay have over 82% of endocrine disrupting compounds like estrone, bisphenol A and nonylphenol. Dual-isotope clarified that reclaimed water was the main reason for the presence of endocrine disrupting compounds in coastal groundwater. The endocrine disrupting compounds in costal ground water had a concentration of 35.9–52.9 ng/L, whereas seawater had 18.9–30.9 ng/L in which estradiol equivalent concentration was 3.5–7.6 ng/L and 1.4–2.3 ng/L in groundwater and seawater, respectively (Lu et al. 2020b).

On the surface of the Bahe river in China, endocrine disrupting compounds were found and their effects on wild sharpbelly (*Hemiculter leucisculus)* were studied extensively. The concentration of 4-tert-octylphenol, nonylphenol, bisphenol A, estrone, 17β-estradiol, 17α-ethinylestradiol and estriol was reported as 126.0 ng/L, 634.8 ng/L, 1573.1 ng/L, 55.9 ng/L, 23.9 ng/L, 31.5 ng/L and 5.2 ng/L in surface water. Correspondingly, 26.4 ng/L, 103.5 ng/L, 146.9 ng/L, 14.2 ng/L, 9.3 ng/L, 13.8 ng/L, and 5.2 ng/L were discovered in the muscle tissues of the fish (Wang et al. 2018).

The endocrine disrupting compounds including, hormones, pharmaceutical and pesticides were detected in the surface of Langat River in Malaysia by multi-residue analytical method of solid phase extraction and liquid chromatography-tandem mass spectrometry. Caffeine was found to have the highest concentration of 19.33 ng/L followed by bisphenol A and diclofenac with concentrate ions of 8.24 ng/L and 6.15 ng/L, respectively (Wee et al. 2019).

Bisphenol A, 4-tert-octylphenol and 4-nonylphenol were detected on the surface and at the bottom of the Gulf of Gdansk. A considerable amount of bisphenol A and 4-tert-octylphenol were dissolved in the coastal region with meltwater in spring. Bisphenol A had a concentration range of 5.0–277.9 ng dm^{-3}, 4-tert-octylphenol's concentration was in the range of 1.0–834.5 ng dm^{-3}; 4-nonylphenol had a concentration of 4.0–228.6 nm dm^{-3} (Staniszewska et al. 2015).

Oryzalin was detected using a glassy carbon electrode with chemical modification based on silver gold partial-shell bimetallic nanoparticles and chitosan. The cathodic peak current increased with the chosen endocrine disrupting compounds' concentration in the regime of 0.1–7.0 µmol/L. The limit of oryzalin detection was reported as 30 nmol/L. The sample testing was made with oryzalin mixed grape juice, and the results were validated with conventional methods of assay (Gerent and Spinelli 2019).

Reduced graphene oxide and molybdenum trioxide nanoparticles were utilized to detect bisphenol A using sensitive electrochemical bisphenol sensor. One-pot hydrothermal synthesis was carried out at lower temperature to produce the molybdenum trioxide nanocomposites, which behaves as a promising sensor for the detection of this endocrine disrupting compound. This novel nano-based molybdenum sensor was reported to reveal a high sensitivity: 13.96 µA/(log nM) cm^2, wider linear range: 0.76×10^{-9} µM-0.820 µM and the lowest limit of detection of 0.12 nM (Verma et al. 2021).

Using methylene blue indicator, the deoxyribonucleic acid damage caused by bisphenol A, 4-nonylphenol and 4-t-octylphenol was detected using electrochemical biosensor fabricated using graphene oxide-chitosan with gold nanoparticles on a glassy carbon electrode. In the differential pulse voltammetry techniques, the binding constants were reported as 2.09×10^6 M^{-1}, 1.28×10^6 M^{-1} and 9.33×10^5 M^{-1} for bisphenol A, 4-nonylphenol and 4-t-octylphenol, respectively, in the deoxyribonucleic acid of organism (Lin et al. 2015).

The phenolic and steroidal endocrine disrupting compounds, 4-t-`octylphenol, nonylphenol, bisphenol, estrone, 17*β*-estradiol, 17*α*-ethinylestradiol and estriol were investigated in the Bahe river of China using gas chromatography mass spectroscopy. The presence of these endocrine disrupting compounds on the surface water and in the muscle tissue of the sharpbelly (*Hemiculter leucisculus)* was analyzed and reported to be too high with huge hazards. The distribution of the reported endocrine disrupting compounds in the river was assayed spatially and seasonally (Wang et al. 2018). Bisphenols, parabens, and benzophenones in placenta samples were detected, and concentration of endocrine disrupting compounds ranged from 0.04 to 0.08 ng/g and relative standard deviation ranged from 4.2 to 13.4%. (Fernández et al. 2021).

Endocrine disrupting compounds and vitellogenin were detected in male crucian carp using enzyme-linked immunosorbent assay. 17*β*-estradiol, diethylstilbestrol, and hexestrol were found to have lower detection limit of 10^{-12} M. In a roasted fresh pork, estrogenic endocrine disrupting compounds were separated using thin-layer chromatography. The detection of estrogenic endocrine disrupting compounds in food showed a good estimation using an enzyme-linked immunosorbent assay (Li et al. 2021a, b, c).

A novel fluorescent aptasensor was fabricated that has high selectivity and good reproducibility in the detection of 17*β*-estradiol. The detection of 17*β*-estradiol was based on double-chain hybridization between carbon quantum dots-labeled with 17*β*-estradiol and Fe_3O_2 nanoparticles enhanced by complementary deoxyribonucleic acid. It showed a good detection of 10^{-11}– 10^{-6} M and a low detection limit of 3.48×10^{-12} M (Wei et al. 2021). Table 1 portrays the occurrence of endocrine disrupting compounds in various sources.

Toxicology of endocrine disrupting compounds

Endocrine disrupting compounds have immense toxicity which causes severe health risks in birds, mammals, aquatic organisms and human beings. It is very much essential to have assaying methods to identify the toxicity level and nature of these compounds.

The individual and combined toxicities of endocrine disrupting compounds were studied using embryonic stem cell test in human blood and urine. Three compounds, namely perfluorooctane sulfonate, perfluorooctanoic acid and bisphenol A, were detected in embryonic stem cell test, showing weak embryotoxicity. The cooperative action of perfluorooctane sulfonate and bisphenol A led to myocardial differentiation. It was concluded that perfluorooctane sulfonate was more toxic than perfluorooctanoic acid (Zhou et al. 2017).

Bisphenol A was detected utilizing 'in vitro' analysis. In stem cell toxicology, multiplicity of embryonic stem cell properties is used in toxicity analysis where bisphenol A was found to affect the proper specification of germ cells, formation of neural ectoderm and progenitor cells in the mirroring of embryonic development. In the case of the embryonic body differentiation process that mirrors in vitro embryonic development, bisphenol A changed the expression of endoderm and trophectoderm makers and caused considerable damage to neural ectoderm specification, showing evident neurotoxicity (Yin et al. 2015).

Bisphenol A toxicity was detected in fetal testes in an 'in vitro' organ assay. Post-coitus was cultured in bisphenol A for 5 days, followed by mouse fetal test for 15.5 days. Germ cells were found to get reduced when compared to steroid cells with bisphenol A treatment at a higher concentration of 100 µm. When exposed to bisphenol A, fetal Leydig cells makers such as Cyp11a1, Thbs2, Cyp17a1 and Pdgf-*α* increased when compared to the adult Leydig cell makers such as Hsd17b3, Ptgds, Sult1e1, Vcam1 and Hsd11b1 which showed decreased levels that led to steroidogenesis and hormonal imbalance (Park et al. 2021).

The metabolic pathways and genes infected by endocrine disrupting compounds using 'in silico,' 'in vivo' and 'in vitro' studies with hepatocytes and HepG2. The in vivo and in vitro tests based on gene expression data from rats and humans indicated an accuracy of greater than 90%. The rats in vivo-based analysis had an accuracy of over 75%, affirming that endocrine disrupting compounds can cause metabolic diseases (Sakhteman et al. 2021).

The toxicity of endocrine disrupting compounds of 14 different species was categorized into 4 different tropic levels by quantitative structure toxicity relationship and inter species quantitative structure. The presence of halogens, sulfur, and phosphorus greatly influenced the toxicity of endocrine disrupting compounds. This was suggested by models based on 2D atom descriptors. Hydrophilic affiliation like ester, aliphatic ethers, branching and higher oxygen content reduced the toxicity of endocrine disrupting compounds (Khan et al. 2019).

The acute toxicity of bisphenol A and lignin synthesized derived bisphenol A in aquatic organisms such as two algal species: *Chlorella pyrenoidosa* and *Scenedesmus obliquus*, a cladoceran: *Daphnia magna* and Japanese medaka: *Oryzias latipes* were evaluated. The lignin-derived bisphenol A and bisphenol A influenced the growth of *C. pyrenoidosa* at 50 mg/L of lignin-derived bisphenol with 48 h of exposure

Table 1 Occurrence of endocrine disruptors in various water bodies and detection of these compounds using analytic methods

Location	Contaminants	Concentration	Analysis method	Reference
Municipal waste water treatment plants, Shenzhen, China	Pharmaceutical and personal care products	513 ± 57.8 ng/L	Gas chromatography Mass spectrometry	Chen et al. (2021)
	Endocrine disruptive compound	991 ± 36.5 ng/L		
	Odorous compounds	553 ± 48.3 ng/L		
Thermaikos Gulf, Northern Aegean sea	Nonylphenol ethoxylate	13.3–270 ng/L	Gas chromatography coupled with ion-trap mass spectrometer	Arditsoglou and Voutsa (2012)
	Bisphenol A	10.6–52.3 ng/L		
	Tert-octylphenol	1.73–18.2 ng/L		
	Nonylphenol	22–201 ng/L		
Danube river water, Siberia	Synthetic estrogen	0.1 to 64.8 ng/L	Solid phase extraction preconcentration system coupled to a triple quadrupole tandem mass spectrometer Vantage equipped with an electrospray ionization	Čelić et al. (2020)
	Alkylphenols	1.1–78.3 ng/L, 0.1–37.3 ng/L, and 0.4–7.9 ng/L		
Coastal region, China	Bisphenol A	449.2 ng/L, 186.3 ng/L	Positive matrix factorization model	Lu et al. (2020a)
	Estrogen	87.2 ng/L, 2.7 ng/L		
	Estradiol	68.87 ng/L, 1.76 ng/L		
Jiaozhou bay in Yellow sea	14 endocrine disruptive compounds	145–658 ng/L	High-performance liquid chromatography and triple-quadrupole mass spectrometry	Lu et al. (2021)
	9 personal care products	100—301 ng/L		
Jiangsu Province, China	Nonylphenol	300 ng/L	Liquid chromatography coupled with quadrupole-orbitrap high resolution mass spectrometry	Fan et al. (2021)
	4-tert-octylphenol	100 ng/L		
Yangtze river in Nanjing section, China	4-tert-butylphenol	225–1121 ng/L	High performance liquid chromatography and triple-quadrupole mass spectrometry	Liu et al. (2017)
	Nonylphenol	1.4–858 ng/L		
	Bisphenol A	1.7–563 ng/L		
Laizhou Bay, China	Estrone	35.9–52.9 ng/L	Flux analysis	Lu et al. (2020b)
	Bisphenol A	3.5–7.6 ng/L		
	Nonylphenol	1.4–2.3 ng/L		
Bahe river, China	4-tert-octylphenol	126.0 ng/L, 26.4 ng/L	Gas chromatography and mass spectrometry	Wang et al. (2018)
	Nonylphenol	634.8 ng/L, 103.5 ng/L		
	Bisphenol A	1573.1 ng/L, 146.9 ng/L		
	Estrone	55.9 ng/L, 14.2 ng/L		
	17β-estradiol	23.9 ng/L, 9.3 ng/L		
	17α-ethinylestradiol	31.5 ng/L, 13.8 ng/L		
	Estriol	5.2 ng/L, 5.2 ng/L		
Langat river, China	Caffeine	19.33 ng/L	Solid phase extraction and liquid chromatography-tandem mass spectrometry	Wee et al. (2019)
	Bisphenol A	8.24 ng/L		
	Diclofenac	6.15 ng/L		
Gulf of Gdansk, China	bisphenol A	5.0–277.9 ng /dm^3	–	Staniszewska et al. (2015)
	4-tert-octylphenol	1.0–834.5 ng/dm^3		
	4-nonylphenol	4.0–228.6 ng/ dm^3		
Taihu Lake, China	Nonylphenol, 4-tert-octylphenol, bisphenol A	–	High-performance liquid chromatography and triple -quadrupole mass spectrometry	Liu et al. (2016)

at a low concentration. Bisphenol A promoted the growth of *C. pyrenoidosa* and hindered at high concentration after exposures of 96 and 144 h (Li et al. 2017).

The Gonadosomatic Index and Gonadal Histology stated that bisphenol A weakened the maturation of the ovary in gold fish—*Carassius auratus*. In bisphenol A introduced female fish, the hypothalamic-pituitary-gonad axis associated genes Sgnrh, fshβ and lhβ were found to be decreased. The selective exposure of bisphenol with concentration of 50 and 500 µg/L on Leydig cells and 1 µg/L on germ cells. A decline in 11-ketotestosterone levels was found in fish exposed to bisphenol A at a concentration of 50–500 µg/L. As a result of apoptosis of germ cells and Leydig cells due to bisphenol A exposure, the level of 11-ketotestosterone was reduced drastically, which further reduced the possibilities of spermatogenesis (Wang et al. 2019).

Endocrine disrupting compounds used in the production of plastic products like bisphenol A, bis(2-ethylhexyl) phthalate and nonylphenol compounds were found toxic. The chronic toxicity of these compounds was studied using Korean resident fish—*Cyprinus carpio*, crustacean—*Moina macrocopa* and green alga—*Pseudokirchneriella subcapitata*. The concentration of bis(2-ethylhexyl) phthalate was found to be 0.0012–0.1 mg/L and nonylphenol in the range of 0.00037–0.03 mg/L. The concentration of nonylphenol and bis(2-ethylhexyl) phthalate was found to be lower than no observation effect concentration to affect other freshwater species (Jung et al. 2020). Table 2 describes the various endocrine disruptor toxic effects on animals.

Major treatment technologies

The hazardous effects of endocrine disrupting compounds make the research on the treatment of wastewater with these contaminants a prospective domain in the environmental oriented investigations. Very large number of research have been carried out on global level due to the widespread nature of endocrine disrupting compounds in most of the water bodies and industrial discharge areas. The present section presents an outlook of various promising methods for the degradation under five classes, namely, biological treatment, physical treatment, chemical treatment, electrochemical treatment and radiative treatment (Fig. 3).

Biological treatment

The biodegradation of 17α-ethinylestradiol and 17β-estradiol using microalgae under anaerobic conditions was investigated. The microalgae, *Selenastrum capricornutum* and *Chlamydomonas reinhardtii* were cultured and utilized for the treatment process. The removal of 17α-ethinylestradiol

Table 2 Toxicological details of common endocrine disruptors, namely bisphenol, phthalates, progesterone and alkyl phenols, and their toxic effect on living organisms

Endocrine disruptors	Victim species	Contaminant exposure concentration	Health effects	Reference
Bisphenol A	Zebra fish larva	27.2, 29.8 and 31.4 ng/L; 6 days	Metabolic disorder	Song et al. (2014)
	Poecilia reticulata	274—549 µg/L; 21 days	Reduced sperm count	Machtinger et al. (2018); Haubruge et al. (2000)
	Pomocea lineata	1–20 mg/L; 4 days	Spawning reduction	de Andrade et al. (2017)
Alkylphenol	*Marisa cornuarietis*	1–100 µg/L; 5 and 12 months	Increased female mortality	Mallerman et al. (2019); Oehlmann et al. (2000)
	Crassostrea gigas	1 and 100 µg/L; 7–8 days	Increased incidence of hermaphroditism	Janicki et al. (2016); Nice et al. (2003)
	Clarias gariepinus	0.05, 0.08 and 0.1 mg/L; 15 days	Reduction in gonadosomatic index	Sayed et al. (2012)
Progesterone	*Pimephales promelas*	300 ng/L; 7 days	Disruption in sperm motility	Astrahan et al. (2021); Murack et al. (2011)
	Carassius auratus	5, 50 and 100 ng/L; 10–60 days	Disrupts sex ratio and gonadal development	Wang et al. (2020)
	Gambusia affinis	4, 44, 410 ng/L; 42 days	Oocyte maturation and liver damage	Hou et al. (2017)
Phthalates	*Cyprinus carpio*	1–20 mg/L	Vitellogenin induction	Gani and Kazmi. (2020); Barse et al. (2007)
	Rana rugosa	0.1—10 µm; 19–23 days	Disruption in gonadal sex differentiation	Ohtani et al. (2000)
	Ovis aries	0.05–2.81 µg/mL	Reserved body metabolism	Cases et al. (2011); Herreros et al. (2010)

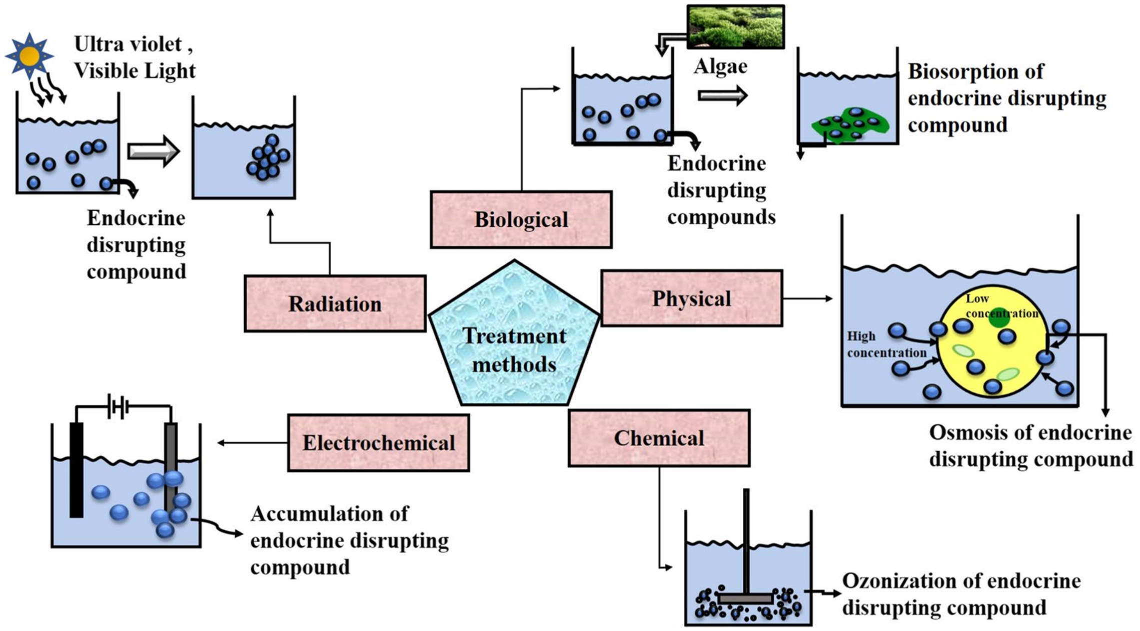

Fig. 3 Biological, chemical, physical, electrochemical and radiative remediation methods for removing endocrine disruptors

attributed by biodegradation was between 12 and 54%. For 17*β*-estradiol, the removal was between 60 and 95% (Hom-Diaz et al. 2015).

The remediation of phenolic compounds, bisphenol A and nonylphenol was tested with the intertidal macro algae species. The effect of temperature and nutrients concentration change gradually influenced the removal mechanism. The highest average removal rate accomplished for bisphenol A and nonylphenol was reported as 29.3 µg/h and 36.9 µg/h. The phytoremediation occurred in the order as green followed by brown and red algae. Of all the species investigated, *Ulva pertusa* was highly efficient showing best results even after the third cycle of regeneration (Zhang et al. 2021).

The abasement of nine endocrine active compounds whose concentration ranged between 0.2 and 7394.2 ng/L in two full scale wastewater treatment plants was evaluated. Two bacterial populations, *Novosphingobium* and *Saprospiraceae,* were responsible for biodegradation. The removal efficiency ranged between 13.7 and 98% in the secondary processing units. Notably, the wastewater treatment plant exhibited about biodegradation of 99% and 100% for bisphenol and estriol, respectively. The treated effluents were found to have less toxic endocrine active compounds comparatively (Cao et al. 2020).

The treatment of 17*α*-ethinylestradiol, bisphenol A and paracetamol utilized seaweeds, *Gracilaria*, *Ulva*, *Pyropia* species and *Hypnea musciformis*. Bromination step was added to enhance the removal efficiency. Among the four species, the macroalgae *Gracilaria* species proved to have better removal potential for 17*α*-ethinylestradiol. The technique was eminently reliant on the solubility of analytes, rate of diffusion and structure complexity of these marine macro-algae. The marine sessile organism *Gracilaria* species was observed to possess non-specific scavenging activity and hence can be considered as a potential source to degrade all phenolic compounds (Astrahan et al. 2021).

The abatement of 4-tert-octylphenol, bisphenol A, boscalid, metribuzin was carried out by adsorption and mycodegradation using wood biochar, hydrochar and spent coffee grounds. The biochar inoculated with fungus showed an adsorption potential of 80 µg/g and 62 µg/g for 4-tert octylphenol and bisphenol, respectively. The maximum removal observed for 4-tert octylphenol was around 70% and 74% by *Trametes versicolor* and *Pleurotus eryngii*, respectively. The removal percentages of 4-tert octylphenol, bisphenol, boscalid, metribuzin are 83%, 75%, 68% and 63%, respectively (Loffredo and Parlavecchia 2021).

The bisphenol A degradation under hydroponic condition using the interaction effects of *Dracaena sanderiana* bacteria species was examined. The bacterial strains *Bacillus thuringiensis* and *Pantoea dispersa* were used for inoculation. The possessed phytohormone, indole-3-acetic acid for *Pantoea dispersa* inoculated plant yielded an effective removal potential of 92.32% for bisphenol, irrespective of other inoculated and non-inoculated plant. The phytohormone indole-3-acetic acid and phytotoxicity suppression corroborated an invincible strategy for influencing removal phenomenon. However, the pristine *Bacillus thuringiensis* was better than *Pantoea dispersa* (Suyamud et al. 2018).

An exclusive field study on the phycoremediation of bisphenol A contaminated coastal area was carried out during green tide blooming. The live *Ulva prolifera* exhibited a potential to remove the pollutant level to almost 94.3%. The experimental observations revealed that the algae's potential to assimilate bisphenol A was highly dependent on the light, nutrients and temperature and did not depend on the salinity. In addition, the algae proved to be highly tolerant to the toxicity of the contaminant. Finally, the contribution of *Ulva prolifera* during the outbreak of green tide has remarkable value in the removal of endocrine disrupting compounds owing to the wide coverage of the biomass (Zhang et al. 2019).

Acetaminophen, bisphenol A, clofibric acid, caffeine, crotamiton, diclofenac, *N*-*N*-diethyl-*m*-toluamide, gemfibrozil, lincomycin, salicylic acid and sulfamethazine were investigated for their treatment from landfill leachate using a full-scale hybrid constructed wetlands system, where aeration lagoons and reed beds played a vital role. Different gene and strains resistant to sulfonamide, quinolone, aminoglycoside and tetracycline compounds were abundantly present in the raw landfill areas. The eradication procedure of the contaminants was monitored for a year, in which the overall removal efficiency reached 90% (Yi et al. 2017).

The obliteration of bisphenol A, bisphenol F, bisphenol S and 4-tert butylphenol compounds were carried out with the constructed wetland phenomenon. Two different types of constructed wetlands, namely pumice rock and activated carbon planted with common reed, were fabricated. The pumice rock-based system was found to have less bacterial population and less effective than the carbon bases system. In 8 weeks, the latter was able to result in 98 to 100% removal (Wirasnita et al. 2018).

The degradation of 17β-estradiol, 17α-ethinylestradiol and bisphenol A is carried out by three distinct methods, namely continual sterilization recharge, continual recharge and wetting and drying alternative recharge systems. The wetting and drying alternative recharge system was more effective followed by continual recharge and continual sterilization recharge. Maximum removal rate of 98%, 96% and 92% for 17β-estradiol, 17α-ethinylestradiol and bisphenol A, respectively, was obtained. The influencing factor for biodegradation was the proteobacterial population which includes betaproteobacteria and alphaproteobacteria (Ma et al. 2015).

Basidiomycetous fungi species, *Gymnopus luxurians and Hypholoma fasciculare* and *Xerocomellus chrysenteron,* were investigated for the abatement of nonylphenol polyethoxylates. The selective fungi species were capable for degrading up to concentration of 10 g/L nonylphenol polyethoxylates without the formation of any toxic metabolite intermediates. Additionally, the fermentation using *Ligustrum lucidum* substrate enhanced the removal efficacy of *Gymnopus luxurians* and *Hypholoma fascicular* up to 71.3% and 96.3%, respectively. The ligninolytic enzyme laccase and manganese peroxidase provided additional advantage to the remediation technique (Mallerman et al. 2019).

The potential of *Umbelopsis isabellina* for the reduction of hazardous effect of nonylphenol, 4-tert-octylphenol and 4-cumylphenol by biodegradation was explored with non-isomer specificity. About 90% of removal was observed, after an incubation period of 12 h. The removal of xenobiotics was accomplished with the production of hydroxylated metabolite products that have lesser harmful effects compared to parent compounds. *Artemia franciscana* and *Daphnia magna* were used as bioindicators (Janicki et al. 2016). Percentage removal of endocrine disrupting compounds using biological degradation is listed in Table 3.

Physical treatment

Cotton strips were carbonized at different temperatures at 900 °C, 1100 °C, 1300 °C and 1500 °C and utilized as carbon microtubes for the remediation of naproxen, caffeine and triclosan. The maximum adsorption capacities recorded were 69%, 89.9% and 98% for naproxen, triclosan and caffeine, respectively. The mechanism includes π–π interactions hydrophobic and electrostatic interactions, hydrogen bonds and diffusion. The adsorption kinetic data fitted for pseudo-second order, where chemisorption was determined as overall rate determining step. The carbon microtubes produced at 900 °C achieved maximum adsorption capacity for triclosan with 137 mg/g achieved by carbon microtubes produced at 900 °C (Czech et al. 2020).

Retention of bisphenol A and norfloxacin in treating drinking water was carried out using three different blended filtration systems produced from polyvinyl chloride and modified using Fe_3O_4. The initial concentration and ionic strength had meagre influence on the retention of both the compounds. Bisphenol A experienced lesser retention when the pH approached pKa, whereas norfloxacin had fluctuation in its retention with respect to pH. The retention of both the compounds improved with humic acid fouling but decreased with increasing pressure. The inference suggested that the main mechanism was adsorption and there was a heavy competition for the adsorption sites on the filtration membranes (Wu et al. 2016).

The remediation of 17α-ethinylestradiol, 17β-estradiol and estriol was tested using polyamide microplastics by adsorption. Dissolved oxygen and salinity had positive influences on the sorption process in aqueous media. The water matrix complexity played a vital role in determining the sorption rate. For 17β-estradiol, the adhesion decreased with increase in water matrix complexity and vice versa for 17α-ethinylestradiol. The hydrogen bonding and hydrophobic interaction illustrated the binding mechanism,

Table 3 Biological treatment of endocrine disruptors and removal efficiency

Treatment method	Endocrine disruptive compound	Species involved	Removal percentage %	Reference
Photodegradation	β-estradiol	*Selenastrum capricornutum*	100	Hom-Diaz et al. (2015)
Bioremediation	17α-ethinylestradiol Bisphenol A	*Gracilaria* species	80	Astrahan et al. (2021)
Bioremediation	Nonylphenol polyethoxylates	*Hypholoma fasciculare*	96.30	Mallerman et al. (2019)
Biodegradation	Bisphenol A Estriol	*Novosphingobium* and *Saprospiraceae*	99 100	Cao et al. (2020)
Biodegradation	4-n-Nonylphenol Bisphenol A 17α-ethinylestradiol	Irpex lacteus	90	Cajthaml et al. (2009)
Biodegradation	4-n-Nonylphenol Bisphenol A 17α-ethinylestradiol	*Pleurotus ostreatus*	80	Cajthaml et al. (2009)
Biotransformation	Nonylphenol 4-tert octylphenol 4-Cumylphenol	*Umbelopsis isabelline*	90	Janicki et al. (2016)
Recharge system	17β-estradiol 17α-ethinylestradiol Bisphenol A	Proteobacteria	98 96 92	Ma et al. (2015)
Primary biodegradation	Bisphenol A Bisphenol S Fluconazole	–	100	Frankowski et al. (2021)
Mycodegradation	4-tert-octylphenol Bisphenol A Boscalid Metribuzin	*Pleurotus eryngii*	83 75 68 63	Loffreda and Parlavecchia (2021)
Phytoremediation	Bisphenol	*Pantoea dispersa*	92.32	Suyamud et al. (2018)
Phytoremediation	Bisphenol A nonylphenol	*Ulva pertusa*	95.2 95 .7	Zhang et al. (2021)
Phycoremediation	Bisphenol A	*Ulva prolifera*	94	Zhang et al. (2019)
Biofilm treatment	Cypermethrin Chlorpyrifos	*Methylophilaceae* *Hyphomicrobium Bacillus Thauera*	80 68.4	Feng et al. (2014)
Constructed wetlands	Bisphenol A Bisphenol S Bisphenol F 4-tert butylphenol	–	100	Wirasnita et al. (2018)
Constructed wetlands	Bisphenol A	–	90	Yi et al. (2017)
Anaerobic membrane bioreactor	4-n-Nonylphenol	Chlorophyceae class and cyanobacteria	100	Abargues et al. (2013)
Fungal bioreactor	Endocrine disruptive compounds	*Trametes versicolor*	83.20	Cruz-Morató et al. (2014)
Membrane bioreactor	Phthalates	–	98	Cases et al. (2011)

where Freundlich isotherm best suited. On an average, the overall retention potential for 17α-ethinylestradiol and 17β-estradiol reached up to 90% (Lara et al. 2021).

The treatment of estriol, 17β-estradiol, 17α-ethinylestradiol and 4-nonylphenol using microfiltration system was examined using Thomas model. The sorption was undertaken in polyvinylidene fluoride membrane and a gel-membrane integral system. The organic fouling layer formation in microfiltration acted as an additional adsorption column that enhanced the adsorption rate, which paved way for foulant layer's hydrophobicity and thickness. The endocrine disruptive compounds' removal efficiency was about 75% by calcium alginate gel layer and 90% by calcium humate gel layer (Xue et al. 2018).

The methods of reverse osmosis and bio-degradation were introduced for the removal of 27 endocrine disrupting compounds including 1H-benzotriazole, two-tolytriazoles, 4-methyl-1H-benzotriazole and 5-methyl-1H-benzotriazole. The treatment was aided by fungal-based treatment with *Trametes versicolor*. The efficiency obtained for benzotriazole and tolytriazole reached up to 58% and 92% under sterile condition and 32% and 50% under non-sterile condition, respectively (Llorca et al. 2017).

The phenomenon of slow sand filtration method was employed for the removal of caffeine, carbamazepine, 17β-estradiol, estrone, gemfibrozil and phenazone. Complete removal of caffeine was attained, and the removal efficiency for estrone and 17β-estradiol ranged between 11 and 92%. Removal of carbamazepine, gemfibrozil and phenazone was less than 10%. Additionally, 99% removal of total coliforms and *Escherichia coli* was obtained (D'Alessio et al. 2015).

The removal of endocrine disrupting compound removal from wastewater with the molybdenum disulfide nanosheets installation onto conventional polyamide nanofiltration membranes was evaluated (Dai et al. 2021). The retention was contributed by suppression of hydrophobic interaction between membrane surface and hydrophilic endocrine disruptors. The molybdenum disulfide nanosheets intercalated membrane exhibited a simultaneous potential to enhance the water permeation and rejection of endocrine disrupting compound. The solution-diffusion theory implied that, with exception to hydrophilic surface, the selective nanochannels also explored the impeding thrust of endocrine disrupting compounds across the polyamide layer (Dai et al. 2021).

The treatment of seven endocrine disrupting compounds containing effluents by ultrafiltration and ozonation was evaluated. The effluent was cultivated with *Nannochloris* species, the green algae harvested from freshwater. In a period of 7 days, 17β-estradiol, 17α-ethinylestradiol and salicylic acid were treated to a rate of approximately 60%. However, triclosan degraded rapidly by virtue of photodegradation irrespective of algal influence. The removal rate was reported between 63 and 100% in 7 days. The maximum removal efficiency obtained was 79%, 69% and 84% for salicylic acid, bisphenol A and testosterone, respectively (Bai and Acharya 2019). Table 4 elaborates the various physical treatment and their performance levels.

Chemical treatment

The photocatalysts based on glutathione protected gold clusters for the degradation of the different endocrine disruptors was investigated. This gold cluster influenced the removal process when coupled with a non-activated Titanium dioxide acceptor, which contributed to interfacial charge separation contributed to surface redox reactions. The process of oxidation was dominated by the accumulation of photoholes on glutathione ligand was attained by the Au cluster formation of ligand to metal charge transfer. Langmuir isotherm suited for the process. The overall removal capacity of 96% was obtained even after 5 repeated cycles (Xu et al. 2017).

The eradication of bisphenol and its trace compounds by chlorination and iodine support was investigated. The observation reported that iodine promotes the transformation rate of pristine bisphenol to halogenated bisphenol, which reduces the risk of toxicity in environment. The catalytic role of iodine in combined effect of bisphenol, iodine, and chlorine provided a higher removal of bisphenol and halogenated bisphenol, than for the integrated effect of bisphenol, chlorine, bromine and bisphenol chloride (Li et al. 2021a, b, c).

The synergistic effect of photocatalytic and electrochemical processes of bisphenol A was explored. In situ zinc oxide nanoparticles generated through corrosion of sacrificial zinc anode was used as photocatalyst using visible light irradiation. In the presence of solid hydrogen peroxide and oxone, the degradation capacity got enhanced from 84% to 90.5% and 97.5%, respectively. Exclusively, the analytical studies evidenced the formation of ultrafine zinc oxide nanoparticles. The negative impact caused by inclusion of ethylic alcohol induced the formation of oxidizing radicals, which negatively influenced the degradation process (Alikarami et al. 2019).

The invention of novel fabrication on multi-walled carbon complex using titanium isopropoxide for treating dimethyl phthalate esters was reported. The titanium dioxide nanocomposites influenced photocatalytic performance, using ultraviolet irradiation. The carboxyl group present on the catalyst complex aided the formation of chemical bonding between it and the titanium dioxide nanoparticles. This yielded the synergetic effect on multi-walled carbon complex and titanium dioxide combination (Tan et al. 2018).

The removal of several endocrine disruptive compounds using photodegradation and ultrafiltration was studied. The *Nannochloris* species was tested for its influence on the removal potential. Though the removal of 17β-estradiol, 17α-ethinylestradiol and salicylic acid was reported to be influenced by the algae, triclosan got removed rapidly by photodegradation without the influence of the algae. The removal of all the compounds was accomplished in 7 days (Bai and Acharya 2019).

Table 4 Physical treatment of endocrine disruptors using adsorption, nanofiltration, ultrafiltration, microfiltration, sand filtration and microscale extraction and removal efficiency

Treatment	Endocrine disruptive compound	Mechanism	Removal percentage	Reference
Adsorption	Triclosan	Chemisorption	89.90%	Czech et al. (2020)
Adsorption	17β-estradiol 17α-ethinylestradiol	Hydrophobic interaction	90%	Lara et al. (2021)
Adsorption	Bisphenol A	Hydrophobic interaction	114.9 mg/g	Park et al. (2014)
Adsorption	Butyl benzyl phthalate	Coagulation–flocculation stage	80%	Cases et al. (2011)
Adsorption	4-tert-octylphenol Bisphenol A	Hydrophobic electrostatic interaction	91% 92%	Loffredo and Parlavecchia (2021)
Adsorption	Bisphenol Ibuprofen Clofibric acid	Chemisorption π–π interaction Hydrogen bonding	183 mg/g 72.6 mg/g 101.8 mg/g	Kittappa et al. (2020)
Adsorption	Chlorpyrifos Atrazine	Van der Waals hydrophobic interaction	270 mg/g 54 mg/g	Romero et al. (2020)
Adsorption	Estrone β-estradiol	Physisorption	22 mg/g	Elias et al. (2021)
Adsorption	Bisphenol A	π–π interaction	93%	Zbair et al. (2020)
Adsorption	Triclosan	Hydrophobicity	77.4 mg/g	Cho et al. (2021)
Ultrafiltration	Bisphenol A Norfloxacin	Humic acid fouling	–	Wu et al. (2016)
Ultrafiltration	17β-estradiol 17α-ethinylestradiol Salicylic acid	Bio-accumulation	69% 69% 79%	Bai and Acharya (2019)
Ultrafiltration	Triclosan Oxybenzone Estrone Progesterone Erythromycin	Hydrophobicity	80%	Yoon et al. (2007)
Microfiltration	Estriol 17β-estradiol 17α-ethinylestradiol 4-nonylphenol	Foulant layer's hydrophobicity	75%	Xue et al. (2018)
Nanofiltration	Mestranol Octylphenol Nonylphenol Progesterone Estrone Estriol β-estradiol	Hydrophobicity	71%	Pereira et al. (2012)
Nanofiltration	Triclosan Oxybenzone Estrone Progesterone Erythromycin	Hydrophobicity	100%	Yoon et al. (2007)
Nanofiltration	Benzylparaben	Hydrophobicity	91 .3%	Dai et al. (2021)
Nanofiltration	Estradiol Estrone	Hydrophobicity	85% 83%	Braeken and Van der Bruggen (2009)
Slow sand filtration	17β-estradiol Estrone	Microbial community	92%	D'Alesside et al. (2015)

Table 4 (continued)

Treatment	Endocrine disruptive compound	Mechanism	Removal percentage	Reference
Sand filtration	Nonylphenol Octylphenol Bisphenol A Estrone Estriol	Hydrophobicity	80%	Nakada et al. (2007)
Microscale Extraction	Dialkyl phthalate	–	95%	Trujilo-Rodríguez et al. (2021)

The treatment of genistein using ozonation and photolysis under the influence of varying pH gave interesting observations. The pH value retarded the degradation performance by ozonation, whereas opposite effect was observed with photolysis. In both the methods, pH increase led to the dissociation of genistein and yield of hydroxyl radicals. But these radicals showed competitive effect for ozone in ozonation and stimulated self-sensitized photo-oxidation with ultraviolet light. The transformation products had isoflavone structures and have the possibility of phytoestrogenic effects (Huang et al. 2020).

Under the irradiance of ultraviolet light and support provided by the titanium dioxide nanotubes, the rotation of photocatalytic reactor was utilized for the treatment of bisphenol A, 17α-ethinylestradiol and 17β-estradiol. The recombination produced by the hole scavenging effect of bisphenol was prevented by the correlation between titanium dioxide nanotubes and hexavalent chromium. Under the synergistic effect of photocatalytic reduction and oxidation, the removal of chromium interfered in removal of all compounds, which conveniently made a positive effect (Kim et al. 2015).

The method of chlorination and integrated ultraviolet with chlorination was adopted for removing benzophenone-3. The hydroxyl radicals and electrophilic aromatic halogenation attributed to prominent degradation. The bicarbonates presence, electrophilic aromatic halogenation, hydroxyl radicals influenced the degradation, whereas the humic acid suppressed the degradation. The *Vibrio fischeri's* bioluminescence inhibition upon transformation product was higher during chlorination than in ultraviolet chlorination. The degradation system followed the pseudo-first-order kinetics, and maximum degradation was achieved at pH 8 (Lee et al. 2020).

Electrochemical treatment

Steroid estrogen hormones such as estriol, 17β-estradiol, 17α-ethinylestradiol are commonly detected in aquatic environments. The concentrations of these contaminants were reported to vary from ng/L to µg/L and are less susceptible to degradation directly by conventional sewage treatment plants. Electrochemical treatments methods can aid in converting them to biodegradable compounds. Electrochemical advanced oxidation process and electrocoagulation have resulted in removal efficiency of as high as 85%, 87%, and 97% for estriol, 17β-estradiol and 17α-ethinylestradiol, respectively (Torres et al. 2021).

Steroid hormone dexamethasone detected in oligotrophic groundwater was treated by bio-electrochemical system using polyaniline-loaded activated carbon configured with three-dimensional particle electrodes, where the removal was assisted with microbial action. This resulted in a removal of 95.7%, whereas a single biological system and the two-dimensional bio-electrochemical system had only 39% and 14.1% removal efficiency, respectively. These dehalogenation genes induced the electron transfer ability by 3.7–6.1 times than that of the single biological system in the removal of dexamethasone (Guo et al. 2021).

Detection and removal of bisphenol A by electropolymerization was reported to be a prospective technology wherein the pollutant was polymerized to a non-conductive lump and layer onto the surface of a carbon felt electrode. Very high recovery of about 98.4–100% from real water samples was attained in this method. Regeneration of the electrode was accomplished using ultrasonication, and the reported methodology was found to exhibit high sensitivity and reusability in treating bisphenol A in both in situ and on-site conditions (Kim et al. 2021a, b).

A sonoelectrochemical hybrid system was devised to degrade the bisphenol A micropollutant. The hybrid system comprising ultrasound horn with a frequency of 24 kHz and two boron-doped diamond electrodes was found to have immense synergistic effects resulting in 90% removal in 30 min. This was achieved for an initial concentration of 1 mg/L with 5 V potential. For individual processes, the potential requirement was 10 V. The degradation reaction followed pseudo-first-order kinetics (Dietrich et al. 2017).

Bisphenol A removal was studied by combining electrochemical and photocatalytic processes with zinc oxide nanoparticle photocatalyst irradiated under visible light. The high synergy factor attributed by combining two process, provided a recovery about 84%. Additionally, this removal percentage hiked to 90.5 and 97.5% with hydrogen peroxide and ozone, respectively, as enhancing agents. 100% elimination of bisphenol A was obtained with the application of ultrasound for 90 min. The hybrid system was able to decrease the specific oxygen consumption inhibition of the pollutant to 18.8% from 31.3% (Alikarami et al. 2019).

Carbon nanotubes with bismuth-doped tin dioxide nanoparticles were designed and fabricated by simple vacuum filtration—electrosorption—hydrothermal process for in the removal of bisphenol A, which showed an excellent electrocatalytic activity and stability than that of pure carbon nanotube electrocatalytic membrane with the recovery of bisphenol A recorded as 65.9% in 6 h for the solution with a concentration of 30 mg/L. The intermediates formed revealed the degradation pathway, which was explored through radical scavengers that hydroxyl radical stimulated the electrolytic degradation to a greater extent (Zhao et al. 2021).

A study on the removal of nonylphenol ethoxylate 10 was undertaken by electro-oxidation process using a boron-doped diamond electron as anode with gamma irradiation. The removal efficiency attained was 100% in combined treatment with hydrogen peroxide concentration of 440 µL/L. This was possible at a pH of 2.3 ± 0.5 and various other optimum conditions of current density at 16.66 mA cm^{-2}; radiation of 40 kGy) and an operating time of 180 min. The researchers claim the proposed methodology as a long lasting and excellent technology to treat the contaminant (Barrera et al. 2021).

The nafion iron catalyst was utilized for modifying oxidation assisted by ultraviolet light for the remediation of estrone, 17*β*-estradiol, estriol and 17*α*-ethinylestradiol. The mechanism of photo-Fenton was accomplished with adherence of iron on perfluorosulfonic polymer. Nafion acted as a carrier for oxidation of pollutants by hydroxyl radicals. The sol–gel technology and nafion establishment upon silica facilitated higher surface area and active sites, respectively, which enhanced the overall efficiency of the system. All these fabrications modified the silica structure and transparency of composites, in which the photo-Fenton reaction was dominated. Additionally, 90% degradation for all the three compounds was achieved (Baycan and Puma 2018).

The comparative study on biodegradation and photo-Fenton degradation to mitigate the toxicity of selective endocrine disrupting compounds, bisphenol A, bisphenol S and fluconazole in water was investigated. The degradation of photo-Fenton process attributed to 100% of bisphenol and 90% of fluconazole removal. The formation of phenol and sulfuric acid with central cleavage of bisphenol S demonstrated the degradation process. The study also insisted that additional research is needed for the degradation of compounds of simple molecular structure (Frankowski et al. 2021).

Radiative treatment

The techniques of ultraviolet photolysis, biological treatment, hydrolysis and adsorption aided for the removal of 18 known bisphenols compounds like bisphenol AP, bisphenol C, bisphenol S, bisphenol C, bisphenol P, bisphenol M as first group followed by bisphenol B, bisphenol F, bisphenol Z, 24 bisphenol F and bisphenol E, bisphenol AF, and bisphenol A as second and third groups, respectively. The ultraviolet photolysis was reported with removal efficiency up to, 94%, 80% and 45%, for first, second and third groups, respectively. Of all these, bisphenol AF was found to be the least affected by both photolysis and biological treatment (Kovačič et al. 2019).

An advanced oxidation process using ultraviolet was used in the degradation and mineralization of bisphenol A. The oxidation process was highly supported by the ultraviolet supply. The optimum operating conditions were reported with initial concentration, hydrogen peroxide concentration and temperature ranging at 25 mg/L, 350 mg/L and 50 °C, respectively. The degradation of bisphenol A was tested under different pH conditions and it was found that pH 5.0, highest removal rate of 89.2% with 49% of mineralization was witnessed (Zorzo et al. 2021).

The photocatalytic treatment of bisphenol A was conducted using ultraviolet of (320–400 nm) irradiation with a light-emitting diode or a ultraviolet blacklight lamp and solar compound parabolic collector reactor under natural sunlight. Pseudo-first-order reaction kinetic model was found to fit the photocatalytic degradation. The bisphenol A was found to be completely degraded in 20, 30 and 120 min under ultraviolet with light-emitting diode, solar and ultraviolet with blacklight, respectively. The total organic compounds had a removal rate of 88, 67 and 33% after 90 min. In all of the cases, titanium dioxide with ultraviolet and light-emitting diode achieved great removal rate than titanium dioxide with ultraviolet and black light (Davididou et al. 2018).

Removal of 17*β*-estradiol, 17*α*-ethinylestradiol, bisphenol A and 4-tert-octylphenol was investigated using photocatalytic activity by ultraviolet–Vis radiation and N-doped bismuth oxybromide semiconductor. The mixture of four compounds chosen was subjected to treatment with ultraviolet–Vis radiation. The mixture was completely degraded with around 53.3% mineralization of the total organic compound in 240 min. The semiconductor had more stability and photocatalytic stability even after four recycles, and therefore, it would be suitable and energy efficient strategy for the removal (López-Velázquez et al. 2021).

The degradation of estrogens, 17*α*-ethinylestradiol and estrone, was conducted using nanotubes grown on titanium– 0.5 wt% alloy catalysts, and it was found to have 66% and 53.4% of degradation in 2 min. The degradation was accomplished by irradiation of ultraviolet and visible-light-assisted photoelectrocatalytic process with nanotube grown on titanium– 0.5wt% alloy catalysts. The degradation of estrogen using the visible light was around 50% with 1.8 min and 4.6 h, respectively, for 17*α*-ethinylestradiol and estrone (de Oliveira et al. 2020).

The abatement of bisphenol A using peroxodisulfate ion with ultraviolet light of 200–290 nm and hydrogen peroxide with ultraviolet light of 200–290 nm was reported. Vibrio fischeri bioassay was used to assess the toxicity and degradation products, whereas the estrogenic activity was assayed using yeast estrogen screen. Bisphenol A was found to have complete degradation with mineralization to 70% and 80% by using hydrogen peroxide with ultraviolet light of 200–290 nm and peroxodisulfate ion with ultraviolet light of 200–290 nm, respectively (Olmez-Hanci et al. 2015). Bisphenol A treatment required an extended treatment of than 20 min for complete degradation and a considerable amount of total organic compounds was retarded by 40% (Olmez-Hanci et al. 2015). Table 5 describes the electrochemical and radiative treatment of various endocrine disruptors.

Machine learning applications

The evaluation of endocrine disruption or activation potential of chemicals which are widespread in environment due to human and natural phenomenon is a major issue to be addressed. The conventional in vitro and in vivo methods are quite complex, time consuming and expensive. Utility of computational methods like ‘in silico’ models that can correlate the chemical properties, structure and several other

Table 5 Electrochemical and radiative treatment of endocrine disruptors and removal efficiency

Endocrine disruptive compound	Method	Removal efficiency %	Reference
Bisphenol A	Electropolymerization	98.4–100	Kim et al. (2021a, b)
Bisphenol A	Sonoelectrochemical	90	Dietrich et al. (2017)
Bisphenol A	Electrochemical	84	Alikarami et al. (2019)
Bisphenol A	Electrolytic degradation	65.9	Zhao et al. (2021)
Bisphenol	Photo-Fenton	100	Frankowski et al. (2021)
Bisphenol	Ultraviolet light photolysis	94	Kovačič et al. (2019)
Bisphenol A	Ultraviolet light oxidation	89.2	Zorzo et al. (2021)
Bisphenol A	Ultraviolet light–light-emitting-diode	88	Davididou et al. (2018)
Bisphenol A	Solar	67	Davididou et al. (2018)
Bisphenol A	Ultraviolet light—blacklight	33	Davididou et al. (2018)
Bisphenol A	Ultraviolet light–Vis radiation	53.3	López-Velázquez et al. (2021)
Bisphenol A	Ultraviolet light with hydrogen peroxide advanced oxidation	99	Chen et al. (2006)
Bisphenol A	Hydrogen peroxide with ultraviolet light (200–290 nm)	70	Olmez-Hanci et al. (2015)
Bisphenol A	Peroxodisulfate ion with ultraviolet light (200–290 nm)	80	Olmez-Hanci et al. (2015)
17*β*-estradiol	Electrochemical advanced oxidation and electrocoagulation	87	Torres et al. (2021)
17*α*-ethinylestradiol	Electrochemical advanced oxidation and electrocoagulation	97	Torres et al. (2021)
Estradiol	Electrochemical advanced oxidation and electrocoagulation	85	Torres et al. (2021)
17*β*-estradiol, 17*α*-ethinylestradiol, estradiol	Photo-Fenton	90	Baycan and Puma (2018)
17*β*-estradiol, 17*α*-ethinylestradiol	Ultraviolet light with hydrogen peroxide advanced oxidation	90	Rosenfeldt et al. (2007)
17*β*-estradiol, 17*α*-ethinylestradiol	Ultraviolet light–Vis radiation	53.3	López-Velázquez et al. (2021)
17*α*-ethinylestradiol, estrone	Ultraviolet radiation	66	de Oliveira et al. (2020)
17*α*-ethinylestradiol, estrone	Visible light	53.4	de Oliveira et al. (2020)
Dexamethasone	Bio-electrochemical	95.7	Guo et al. (2021)
Fluconazole	Photo-Fenton	90	Frankowski et al. (2021)
Nonylphenol ethoxylate 10	Electro-oxidation	100	Barrera et al. (2021)

factors to endocrine disruption properties are emerging as a key factor in endocrine disrupting compound oriented researches even on large scale.

The quantitative structure activity relationship machine learning technique in predicting the binding of estrogen receptor was evaluated. Inhouse cheminformatics software was employed to assess the metrics of estrogen receptors binding. The chemical features and molecular descriptors were evaluated with specific characterizations, each subjected to different algorithms pertaining to machine learning: classic machine learning like Bernoulli Naïve Bayes, AdaBoost decision tree, random forest and support vector machine and deep neural network models of distinct configurations (Russo et al. 2018).

The proprietary assay central software was evaluated to obtain the classified models for approaching the acute rat toxicity caused by endocrine disruption. This analysis was made from the informatics provided by National Toxicology Program interagency centre for evaluation of alternative toxicological methods and Environmental Protection Agency's National Centre for Computational Toxicology. The models were integrated with the machine learning methods like, random forest, k-nearest neighbors, support vector classification, naïve Bayesian and AdaBoosted decision trees and deep learning methods (Minerali et al. 2020).

The integrated molecular docking and machine learning techniques were employed to describe the effects of perfluoroalkyl and polyfluoroalkyl compounds. From the support vector machine algorithm, many chemical fingerprints like Chemistry Development Kit fingerprint, Chemistry Development Kit extended fingerprint, estate fingerprint, Molecular ACCess System fingerprint, PubChem fingerprint, substrate fingerprint, Kletota-Roth fingerprint, and 2d atom air were used as classified models to diagnose effects of endocrine disrupting compound consequences (Singam et al. 2020).

Weighted quantile sum regression was assessed to determine the effect and relationship between the effects of selective 26 endocrine disrupting compounds. Two statistical approaches, namely (1) explanatory-based approach which uses full dataset for training and testing and (2) predictive-based approach with repeated holdout validation, were used to evaluate the overall impact of endocrine disrupting compounds on neurodevelopment in children. The weighted quantile sum index was majorly contributed by the bisphenol F among the 26 endocrine disrupting compounds (Tanner et al. 2020).

The National Centre of Computational Technologies, a unit of the US Environmental Protection Agency, devised an in silico model called as Collaborative Modelling Project of Androgen Receptor Activity. This was used to identify androgen receptor with multi-variable Bernoulli naïve Bayes, a random forest and N-nearest neighbor tools. The results from these classified approaches were validated to 11 intro assays. Grisoni et al. (2019) reported that the models were more reliable, robust, and under the consent of Organisation of Economic Cooperation and Development Principles.

The evaluation of 7500 compounds including endocrine disruptors, which were pertaining to nuclear estrogen receptor activity, used 18 Toxicity Forecaster assays (ToxCast). The chemical descriptors used were extended connectivity fingerprints, functional connectivity fingerprints and molecular access system. Models for 18 assays were developed using four machine learning and two deep learning approaches. Their results were validated using appropriate methods (Ciallella et al. 2021).

The longitudinal cohort was made with 2317 women in gestational age and delivery time for evaluating the temporal interaction between 33 endocrine disrupting compounds and 14 endogenous hormones using classical machine learning aided with dynamic concentration data. Other than these, the open software for key analysis like the 'ropls' and 'stat Target' was used as multi-variate statistical analysis, 'circlize and ggalluvial' for endocrine disrupting compounds correlation, 'random forest' and 'caret' for training and plotting classification and regression models and 'treemap and ggplot2' for data visualization (Luan et al. 2021).

The hormonal imbalance resulted in malfunctioning of aromatase or cytochrome enzyme catalyzes the aromatization of androgens into estrogens. The prediction of aromatase inhibition from molecular structure used Bayesian machine learning method. The internal fivefold cross-validation statics of training data were used to compare the results obtained from multiple machine learning algorithm. The Bayesian model also includes multiple common metrics, namely receiver operator characteristic score, recall, precision, F1-score, Cohen's kappa, and Matthews' correlation coefficient for the evaluation for comparative study with training data (Zorn et al. 2020).

The usage of ternary models of machine learning technique including linear discriminant analysis, classification and regression tree and support vector machines for evaluating agonistic and antagonistic and no estrogen receptor activity was evaluated. Among all the models, the support vector machine predicted the agonistic activity with 76.6% and antagonists with 75% activity and achieved a tenfold-cross-validation with high accuracy (Zhang et al. 2017).

The proposal of machine learning pipeline to assess the endocrine disrupting compound nature of chemicals using multi-dimensional imaging data that have susceptibility to impact estrogen receptor was reported. Linear logistic regression and nonlinear random forest classifiers were used to predict the estrogenic activity of unknown compounds and to categorize them as agonists and antagonists. Along with these, feature selection, data visualization and model discrimination tools helped in classifying the endocrine disrupting compounds (Mukherjee et al. 2020).

The assessment of multiple environmental exposures including, endocrine disrupting compounds in the blood and urine samples of 229 female participants of age 12–16 during the time of menarche was made using a two-stage machine learning approach. The random forest followed by multi-variable modified Poisson regression quantified the contaminant exposure and relation of exposure with menarche timing, respectively. The result of random forest model suggested the concentration of mono-ethylhexyl phthalate was severe, followed by bisphenol A. The investigation was made using the details collected from National Health and Nutrition Examination Survey (Oskar et al. 2021).

Classified models such as multilayer perception, random forest and extreme gradient boosting models were applied to the multi-target regression for predicting the individual concentration of bisphenol A, estrone, 17-β estradiol and their mixtures. Capacitance spectra obtained from electronic tongue were the underlying base of the investigation. The extreme gradient boosting was found to provide more accurate results with individual contaminant ranging between 0.19 and 0.37 root mean square error values. The synergistic technique of machine learning and information visualization methodology was also evaluated (Christinelli et al. 2021).

The utilization of seven fingerprints and computational models for evaluating endocrine disrupting compounds associated with androgen and estrogen receptor issues was investigated. The machine learning methods includes K-nearest neighbor, C4.5 decision tree, naïve Bayes and support vector machine algorithm. The best model and best method for predicting effects of endocrine disrupting compound were reported with reliable accuracy for PubChem support vector machine and extended fingerprint—Support vector machine, respectively (Chen et al. 2014).

Conclusion

A detailed overview on the source, derivation, uses, environmental impact and health hazards of the endocrine disrupting compounds is portrayed in the review article. The production and utilization of endocrine disrupting compounds are inevitable due to their versatile applications ubiquitously. The detection of these pollutants in the environment, the nature and mechanism of the hazards posed by them to all the organisms inhabiting and their toxicological effects are presented. The major health hazards of endocrine disrupting compounds are chronic hormonal imbalances, cancer, reproductive and fertility disorders followed by ocular diseases. An outlay on the occurrences and health hazards of few endocrine disrupting compounds, namely bisphenol, triclosan, nonylphenyl, cortisol, 11-deoxycortisols, aldosterone, and corticosterone reported by various researchers, is presented. The hazard identification and toxicological analysis methods, tools and detection procedures are elaborated. The treatment methods and their performances reported are reviewed and presented under five classes, namely biological, physical, chemical, electrochemical and radiative treatment methods. Most of the research were found to apply integrative approaches to treat the endocrine disrupting compounds due to high removal efficiencies. For instance, the photocatalytic removal of 17β-estradiol, 17α-ethinylestradiol, bisphenol A, and 4-tert-octylphenol aided by doped semiconductors was able to yield 53% mineralization and 100% removal of all these four endocrine disrupting compounds. Due to structure complexities, undesirable intermediates and by-products, intricate degradation mechanisms, the identification of appropriate techniques to detect and treat endocrine disrupting compounds with in vivo and in vitro methods have a lot of limitations. Hence, the in silico methods to accomplish these tasks using advanced tools reported by investigators along with the validation methods are also described.

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Declarations

Conflict of interest There are no competing financial interests declared by the authors.

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