

Endocrine Disruptors

Subjects: Biotechnology & Applied Microbiology | Chemistry, Analytical

Contributor: Camelia Bala

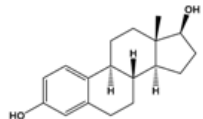
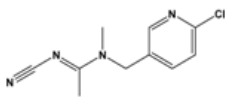
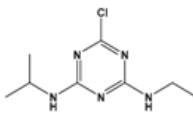
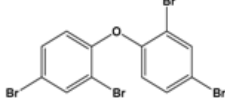
Endocrine disruptors (EDs) are contaminants that may mimic or interfere with the body's hormones, hampering the normal functions of the endocrine system in humans and animals. These substances, either natural or man-made, are involved in development, breeding, and immunity, causing a wide range of diseases and disorders. The traditional detection methods such as enzyme linked immunosorbent assay (ELISA) and chromatography are still the golden techniques for EDs detection due to their high sensitivity, robustness, and accuracy. Nevertheless, they have the disadvantage of being expensive and time-consuming, requiring bulky equipment or skilled personnel. On the other hand, early stage detection of EDs on-the-field requires portable devices fulfilling the Affordable, Sensitive, Specific, User-friendly, Rapid and Robust, Equipment free, Deliverable to end users (ASSURED) norms. Electrochemical impedance spectroscopy (EIS)-based sensors can be easily implemented in fully automated, sample-to-answer devices by integrating electrodes in microfluidic chips.

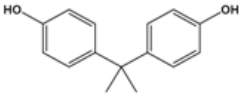
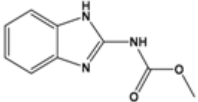
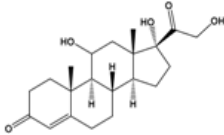
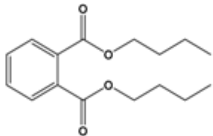
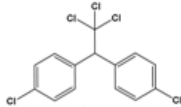
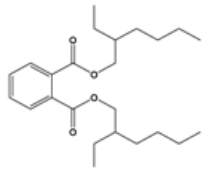
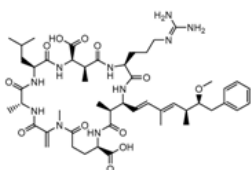
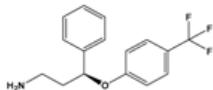
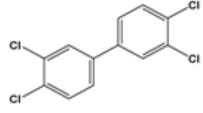
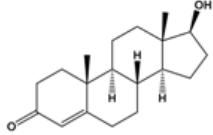
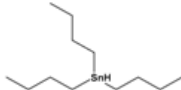
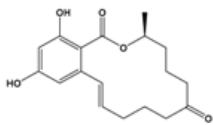
Keywords: Endocrine Disruptors ; Electrochemical Impedance Spectroscopy ; environmental contaminants

Endocrine disruptors (EDs) are environmental contaminants that disrupt the normal functioning of the endocrine system in mollusk, crustacea, fish, reptiles, birds, and mammals. For humans, these compounds may cause cancerous tumors [1][2] [3] and infertility [4]. Natural EDs originate in living organisms and can be either hormones (testosterone, estrogen, or progesterone) or mycotoxins such as zearalenone. Synthetic EDs can be found in plastic additives, industrial reagents, and waste. Some of the most common synthetic EDs are precursors in the production of rubber, pesticides and plastic additives such as atrazine, alkylphenols, bisphenol A (BPA) [5], parabens, perfluoroalkyl acids [6], phthalates and polychlorinated biphenyls (PCBs) [7]. A list of relevant EDs is given in [Table 1](#).

A variety of analytical methods have been used for the detection of EDs, including liquid chromatography coupled with mass spectrometry (LC-MS) [8], gas chromatography coupled with mass spectrometry (GS-MS) [9], high-performance liquid chromatography (HPLC) coupled with fluorescence detection [10] or with mass spectrometry [11][12]. These methods usually require laborious and time-consuming steps for sample pre-concentration, and high amounts of reagents. By comparison, electrochemical sensors and biosensors offer advantages such as low cost, portability, and do not require complex pretreatment steps. Moreover, biosensors can be used for selective, fast, and direct detection of analytes in real samples.

Table 1. List of relevant EDs compounds.

Analyte	IUPAC Name	Chemical Structure	Molecular Weight (g/mol)	Source	Ref.
17 β -estradiol (E2)	(8R,9S,13S,14S,17S)-13-Methyl-6,7,8,9,11,12,14,15,16,17-decahydrocyclopenta[a]phenanthrene-3,17-diol		272.388	endogenous hormone, medication	[13]
Acetamiprid (AAP)	N-[(6-chloro-3-pyridyl)methyl]-N'-cyano-N-methyl-acetamidine		222.678	insecticide	[14]
Atrazine (ATZ)	6-chloro-N2-ethyl-N4-(propan-2-yl)-1,3,5-triazine-2,4-diamine		215.69	herbicide for grassy weeds in crops	[15]
Pentabromodiphenyl ether (BDE-47)	2,2',4,4'-Tetrabromodiphenyl ether		485.79	flame retardant	[16]

Analyte	IUPAC Name	Chemical Structure	Molecular Weight (g/mol)	Source	Ref.
Bisphenol A (BPA)	4,4'-(propane-2,2-diyl)diphenol		228.291	precursor to polycarbonates, plastic and epoxy resins	[17]
Carbendazim (CBZ)	methyl 1H-benzimidazol-2-ylcarbamate		191.187	fungicide	[18]
Cortisol	11β,17α,21-Trihydroxypregn-4-ene-3,20-dione		362.46	endogenous hormone, medication	[19]
Dibutyl phthalate (DBP)	Dibutyl benzene-1,2-dicarboxylate		278.348	plasticizer	[20]
Dichloro-diphenyl-trichloroethane (DDT)	1-chloro-4-[2,2,2-trichloro-1-(4-chlorophenyl)ethyl]benzene		354.48	pesticide	[21]
Di(2-ethylhexyl) phthalate (DEHP)	Bis(2-ethylhexyl) benzene-1,2-dicarboxylate		390.564	plasticizer	[22]
Microcystin-LR (MC-LR)	(5R,8S,11R,12S,15S,18S,19S,22R)-15-[3-(diaminomethylideneamino)propyl]-18-[(1E,3E,5S,6S)-6-Methoxy-3,5-dimethyl-7-phenylhepta-1,3-dienyl]-1,5,12,19-tetramethyl-2-methylidene-8-(2-methylpropyl)-3,6,9,13,16,20,25-heptaoso-1,4,7,10,14,17,21-heptazacyclopentacosane-11,22-dicarboxylic acid		995.189	cyanobacteria toxin	[23]
Norfluoxetine (NorFLX)	(S)-3-Phenyl-3-[4-(trifluoromethyl)phenoxy]propan-1-amine		295.305	antidepressant	[24]
3,3',4,4'-tetrachlorobiphenyl (PCB-77)	3,3',4,4'-tetrachloro-1,1'-biphenyl		291.99	flame retardants, plasticizers, dielectric and heat transfer fluids	[25]
Testosterone	(8R,9S,10R,13S,14S,17S)-17-Hydroxy-10,13-dimethyl-1,2,6,7,8,9,11,12,14,15,16,17-dodecahydrocyclopenta[a]phenanthren-3-one		288.431	endogenous hormone, anabolic steroid	[26]
Tributyltin hydride	tributylstannane		291.06	precursor in organic synthesis	[27]
Zearalenone (ZEN)	(3S,11E)-14,16-Dihydroxy-3-methyl-3,4,5,6,9,10-hexahydro-1H-2-benzoxacyclotetradecine-1,7(8H)-dione		318.369	mycotoxin	[28]

Electrochemical impedance spectroscopy (EIS) is a sensitive technique which can be used to monitor biomolecular events occurring at the electrode surface. These events include affinity interactions involving peptides, receptors, nucleic acids, whole cells, and antibodies.

1. EIS Biosensors for the Detection of EDs

1.1. Immunosensors

Immunoassays are based on the specific interaction between an antigen and the corresponding antibody (Ab), which can be transduced into a measurable physical signal [29]. Immunosensors can be prepared using monoclonal, polyclonal or recombinant Abs. Immunosensors have been used for the detection of EDs, such as DES, estradiol, phthalates and bisphenol A [30].

1.2. Aptamer-Based Biosensors

Aptamers are oligonucleotides that bind to a specific target. Because of their in vitro selection and production, the relatively new technology of aptamers has emerged as an alternative to antibodies, as they are obtained through chemical synthesis, with high reproducibility, and their production is not dependent on living organisms. They can be easily regenerated, have a much longer shelf life, and can be stored at ambient temperature.

1.3. Estrogen Receptor-Based Biosensors

Human-estrogen receptor alpha (ER- α) is a protein that belongs to the nuclear receptor group and can bind xenoestrogens such as 17 β -estradiol. Due to its specificity and ability to be engineered, ER- α was used as bio-recognition element for the development of ED detection methods [31]. Estrogen receptor-based biosensors are not often encountered.

1.4. Enzyme-Based Biosensors

Other biorecognition elements, such as enzymes, were used to develop the ED biosensors. In the case of phenolic compounds, these biosensors are often based on the enzymatic oxidation by enzymes such as tyrosinase [32] or laccase [33]. Metal composites have been used to modify the working electrodes and to provide a large surface area for enzyme immobilization and improved surface charge transfer.

1.5. Peptide-Based Biosensors

Peptides are oligomers and polymers that can be customized with highly controlled preparation methods, due to the variety of natural and synthetic amino acids available for synthesis. Peptides have been employed in biosensing due to their specificity, better chemical and conformational stability compared to antibodies [34], low cost and facile synthesis and modification protocols that allow customization for a wide variety of applications [35].

1.6. Microbial Biosensors

Microbial biosensors use microorganisms as a sensitive biological element. Their main advantage is the fact that, unlike molecule-based biosensors, they provide information on toxicity or bioavailability [36]. The microbes are usually genetically engineered by modifying their structure to serve as bio-receptors for the target molecule [37].

References

1. Soto, A.M.; Sonnenschein, C. Environmental causes of cancer: Endocrine disruptors as carcinogens. *Nat. Rev. Endocrinol.* 2010, 6, 363–370.
2. Bedia, C.; Dalmau, N.; Jaumot, J.; Tauler, R. Phenotypic malignant changes and untargeted lipidomic analysis of long-term exposed prostate cancer cells to endocrine disruptors. *Environ. Res.* 2015, 140, 18–31.
3. Troisi, R.; Hatch, E.E.; Palmer, J.R.; Titus, L.; Sampson, J.N.; Xu, X.; Hoover, R.N. Estrogen Metabolism in Postmenopausal Women Exposed In Utero to Diethylstilbestrol. *Cancer Epidemiol. Biomark. Prev.* 2018, 27, 1208–1213.
4. Giulivo, M.; Lopez de Alda, M.; Capri, E.; Barcelo, D. Human exposure to endocrine disrupting compounds: Their role in reproductive systems, metabolic syndrome and breast cancer. A review. *Environ. Res.* 2016, 151, 251–264.
5. Ohore, O.E.; Zhang, S. Endocrine disrupting effects of bisphenol A exposure and recent advances on its removal by water treatment systems. A review. *Sci. Afr.* 2019, 5, e00135.
6. White, S.S.; Fenton, S.E.; Hines, E.P. Endocrine disrupting properties of perfluorooctanoic acid. *J. Steroid Biochem. Mol. Biol.* 2011, 127, 16–26.

7. Metzler, M.; Pfeiffer, E. Chemistry of Natural and Anthropogenic Endocrine Active Compounds. In *Endocrine Disruptors —Part I*; Metzler, M., Ed.; Springer: Berlin/Heidelberg, Germany, 2001; pp. 63–80.
8. Benigni, P.; Thompson, C.J.; Ridgeway, M.E.; Park, M.A.; Fernandez-Lima, F. Targeted High-Resolution Ion Mobility Separation Coupled to Ultrahigh-Resolution Mass Spectrometry of Endocrine Disruptors in Complex Mixtures. *Anal. Chem.* 2015, 87, 4321–4325.
9. Pintado-Herrera, M.G.; González-Mazo, E.; Lara-Martín, P.A. In-cell clean-up pressurized liquid extraction and gas chromatography–tandem mass spectrometry determination of hydrophobic persistent and emerging organic pollutants in coastal sediments. *J. Chromatogr. A* 2016, 1429, 107–118.
10. Pérez, R.L.; Escandar, G.M. Multivariate calibration-assisted high-performance liquid chromatography with dual UV and fluorimetric detection for the analysis of natural and synthetic sex hormones in environmental waters and sediments. *Environ. Pollut.* 2016, 209, 114–122.
11. Barreca, S.; Busetto, M.; Colzani, L.; Clerici, L.; Daverio, D.; Dellavedova, P.; Balzamo, S.; Calabretta, E.; Ubaldi, V. Determination of estrogenic endocrine disruptors in water at sub-ng L⁻¹ levels in compliance with Decision 2015/495/EU using offline-online solid phase extraction concentration coupled with high performance liquid chromatography-tandem mass spectrometry. *Microchem. J.* 2019, 147, 1186–1191.
12. Myridakis, A.; Balaska, E.; Gkaitatzi, C.; Kouvarakis, A.; Stephanou, E.G. Determination and separation of bisphenol A, phthalate metabolites and structural isomers of parabens in human urine with conventional high-pressure liquid chromatography combined with electrospray ionisation tandem mass spectrometry. *Anal. Bioanal. Chem.* 2015, 407, 2509–2518.
13. Stanczyk, F.Z.; Archer, D.F.; Bhavnani, B.R. Ethinyl estradiol and 17 β -estradiol in combined oral contraceptives: Pharmacokinetics, pharmacodynamics and risk assessment. *Contraception* 2013, 87, 706–727.
14. Kong, D.; Zhang, J.; Hou, X.; Zhang, S.; Tan, J.; Chen, Y.; Yang, W.; Zeng, J.; Han, Y.; Liu, X.; et al. Acetamiprid inhibits testosterone synthesis by affecting the mitochondrial function and cytoplasmic adenosine triphosphate production in rat Leydig cells. *Biol. Reprod.* 2016, 96, 254–265.
15. Silveyra, G.R.; Canosa, I.S.; Zanitti, M.; Rodríguez, E.M.; Medesani, D.A. Interference of an atrazine commercial formulation with the endocrine control of ovarian growth exerted by the eyestalks. *Environ. Sci. Pollut. Res.* 2020, 27, 965–973.
16. Sheikh, I.A. Endocrine-disrupting potential of polybrominated diphenyl ethers (PBDEs) on androgen receptor signaling: A structural insight. *Struct. Chem.* 2020.
17. Loffredo, L.F.; Coden, M.E.; Berdnikovs, S. Endocrine Disruptor Bisphenol A (BPA) Triggers Systemic Para-Inflammation and is Sufficient to Induce Airway Allergic Sensitization in Mice. *Nutrients* 2020, 12, 343.
18. Yan, S.; Wang, M.; Zha, J.; Zhu, L.; Li, W.; Luo, Q.; Sun, J.; Wang, Z. Environmentally Relevant Concentrations of Carbamazepine Caused Endocrine-Disrupting Effects on Nontarget Organisms, Chinese Rare Minnows (*Gobiocypris rarus*). *Environ. Sci. Technol.* 2018, 52, 886–894.
19. Oray, M.; Abu Samra, K.; Ebrahimiadib, N.; Meese, H.; Foster, C.S. Long-term side effects of glucocorticoids. *Expert Opin. Drug. Saf.* 2016, 15, 457–465.
20. Xie, F.; Chen, X.; Weng, S.; Xia, T.; Sun, X.; Luo, T.; Li, P. Effects of two environmental endocrine disruptors di-n-butyl phthalate (DBP) and mono-n-butyl phthalate (MBP) on human sperm functions in vitro. *Reprod. Toxicol.* 2019, 83, 1–7.
21. Soto, A.M.; Sonnenschein, C. Endocrine disruptors: DDT, endocrine disruption and breast cancer. *Nat. Rev. Endocrinol.* 2015, 11, 507–508.
22. Rowdhwal, S.S.S.; Chen, J. Toxic Effects of Di-2-ethylhexyl Phthalate: An Overview. *BioMed Res. Int.* 2018, 2018, 1750368.
23. Mallia, V.; Ivanova, L.; Eriksen, G.S.; Harper, E.; Connolly, L.; Uhlig, S. Investigation of In Vitro Endocrine Activities of Microcystis and Planktothrix Cyanobacterial Strains. *Toxins* 2020, 12, 228.
24. Hudon Thibeault, A.-A.; Laurent, L.; Vo Duy, S.; Sauvé, S.; Caron, P.; Guillemette, C.; Sanderson, J.T.; Vaillancourt, C. Fluoxetine and its active metabolite norfluoxetine disrupt estrogen synthesis in a co-culture model of the feto-placental unit. *Mol. Cell. Endocrinol.* 2017, 442, 32–39.
25. Bell, M.R. Endocrine-disrupting actions of PCBs on brain development and social and reproductive behaviors. *Curr. Opin. Pharmacol.* 2014, 19, 134–144.
26. Lo, E.M.; Rodriguez, K.M.; Pastuszak, A.W.; Khera, M. Alternatives to Testosterone Therapy: A Review. *Sex. Med. Rev.* 2018, 6, 106–113.

27. Mitra, S.; Srivastava, A.; Khandelwal, S. Long term impact of the endocrine disruptor tributyltin on male fertility following a single acute exposure. *Environ. Toxicol.* 2017, 32, 2295–2304.
28. Kowalska, K.; Habrowska-Górczyńska, D.E.; Piastowska-Ciesielska, A.W. Zearalenone as an endocrine disruptor in humans. *Environ. Toxicol. Pharmacol.* 2016, 48, 141–149.
29. Duffy, G.F.; Moore, E.J. Electrochemical Immunosensors for Food Analysis: A Review of Recent Developments. *Anal. Lett.* 2017, 50, 1–32.
30. Li, X.; Huang, Y.; Chen, M.; Tong, Y.; Zhang, C. A label-free electrochemical bisphenol A immunosensor based on chlorogenic acid as a redox probe. *Anal. Methods* 2017, 9, 2183–2188.
31. La Spina, R.; Ferrero, V.E.V.; Aiello, V.; Pedotti, M.; Varani, L.; Lettieri, T.; Calzolari, L.; Haasnoot, W.; Colpo, P. Label-Free Biosensor Detection of Endocrine Disrupting Compounds Using Engineered Estrogen Receptors. *Biosensors* 2017, 8, 1.
32. Ba, S.; Vinoth Kumar, V. Recent developments in the use of tyrosinase and laccase in environmental applications. *Crit. Rev. Biotechnol.* 2017, 37, 819–832.
33. Asadgol, Z.; Forootanfar, H.; Rezaei, S.; Mahvi, A.H.; Faramarzi, M.A. Removal of phenol and bisphenol-A catalyzed by laccase in aqueous solution. *J. Environ. Health Sci. Eng.* 2014, 12, 93.
34. Liu, Q.; Wang, J.; Boyd, B.J. Peptide-based biosensors. *Talanta* 2015, 136, 114–127.
35. Pavan, S.; Berti, F. Short peptides as biosensor transducers. *Anal. Bioanal. Chem.* 2012, 402, 3055–3070.
36. Melamed, S.; Elad, T.; Belkin, S. Microbial sensor cell arrays. *Curr. Opin. Biotechnol.* 2012, 23, 2–8.
37. Gawrys, M.D.; Hartman, I.; Landweber, L.F.; Wood, D.W. Use of engineered *Escherichia coli* cells to detect estrogenicity in everyday consumer products. *J. Chem. Technol. Biot.* 2009, 84, 1834–1840.

Retrieved from <https://encyclopedia.pub/entry/history/show/9857>