

Environmental and Medicinal Impact of Endocrine Disrupting Compounds: A Comprehensive Review

**Santhi Raju Pilli^{*1}, Sowjanya Motana², Hemachandran Jeldi³,
Mallela Bharath Kumar ^{**4}, Sabina Paul Dhawale⁵,
Saravanan Kumar Nanjan⁴, Bhuvanesh Babu Mondey Ganesan⁴,
Shiraz Ahmed Maniyar⁶, Fazeela Tunnisa⁷**

¹*Department of Chemical Engineering Technology, College of Applied Industrial
Technology (CAIT), Jazan University, Jazan, Kingdom of Saudi Arabia,*

²*Centre of Nanotechnology, Indian Institute of Technology Roorkee,
Roorkee 247 667, India*

³*Faculty of Medicine, Department of Human Physiology, Jazan University, Jazan,
45971, Kingdom of Saudi Arabia*

⁴*Physical Therapy Department, College of Nursing & Health Sciences, Jazan University,
P.O. Box 114, Jazan 45142, Saudi Arabia*

⁵*Department of Physics, College of Science, Jazan University, Jazan 45142,
Saudi Arabia*

⁶*Department of Public Health, College of Nursing & Health Sciences,
Jazan University, Saudi Arabia*

⁷*Department of Computer Science, College of Engineering & Computer Science,
Jazan University, Saudi Arabia*

Abstract

Over many decades, there has been a proportionate rise in novel chemicals in the interior of buildings, and quick development of new drugs, construction materials, furniture, cosmetics, and consumer goods. Most of these chemicals and products contain Endocrine-disrupting chemicals (EDCs, these are chemicals that mimic, block, or interfere with hormones in the body's endocrine system. EDCs have been connected with a distinct array of health issues. EDCs are absorbed by humans through food and drinking water, dermal contact, and inhalation. In this article, an attempt was made to study the EDCs such as bisphenol A, phthalates, PCP and DDT, endosulfan, polychlorinated biphenyls, dioxins, and their main source of exposure, severe health effects were reviewed with recent literature. To predict the impacts on populations and communities based on a comprehension of the effects on individuals, methodologies must be established to know the exposure and risk factors of people resulting from EDCs as well as the treatments for these. A comprehensive inclusion of the mechanisms of action and consequences of exposure to EDCs necessitates several difficulties been thoroughly reviewed in this article.

Keywords: *Endocrine-disrupting chemicals, Environment, Medicine, Human, Wild-life*

Corresponding Author*: spilli@jazanu.edu.sa, ssanthirajup@gmail.com

Co-corresponding Author**: mallelabharath.m@gmail.com mkumar@jazanu.edu.sa

1. Introduction

Endocrine hormones have a vital part in influencing temperament, development, metabolism, reproductive system, and the function of human organs. The quantity of each hormone released is operated by the endocrine system. [1, 2] (Chou, 2014, EDSP, 2024). The pituitary gland, which is situated beneath the brain, is the master gland of the endocrine system. In general, no larger than a pea, the gland regularizes various other endocrine glands' functions. Hormones are relinquished into the bloodstream by endocrine glands. Hormones can now reach cells in many areas of the body.

1.1 Endocrine disruptors: what are they?

An external substance or combination of chemicals that modifies one or more endocrine system functions and subsequently has a negative impact on the health of an intact organism or its progeny is categorized as an endocrine disruptive chemical (EDC) by the World Health Organization [3 Di Pietro et al., 2023]. Endocrine-disrupting substances and the most common ingredients in these products such as pentachlorophenol (PCP), dichlorodiphenyltrichloroethane (DDT), endosulfan (ES), phthalic acid (PA), esters of phthalic acid (PAEs), bisphenol A (BPA), triclosan, benzophenones, parabens, and phthalates, and other chemicals frequently present in cosmetics and personal care products used in daily life [4,5 Pilli et al., 2012, Peinado et al., 2020]. These can mimic hormones that are normally generated or block hormone receptors, which cause aberrant hormone synthesis. These may have an impact on the risk of endometriosis because the endometrium is estrogenic-dependent. Figure 1 depicts the most popular personal care product in the United States by category by December 2023.

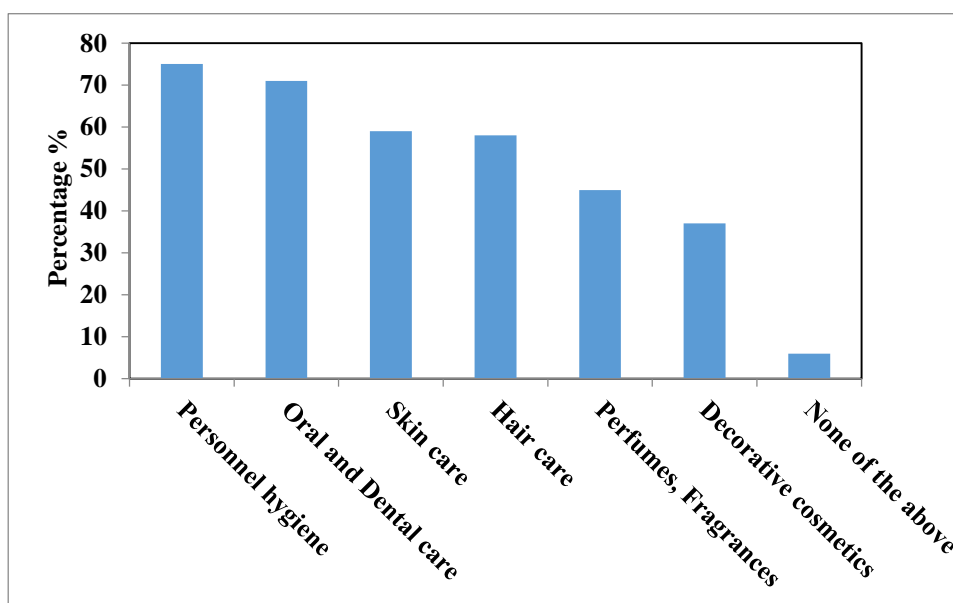
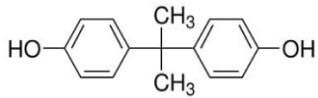
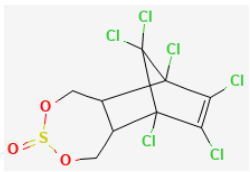
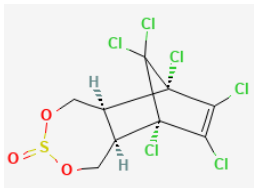


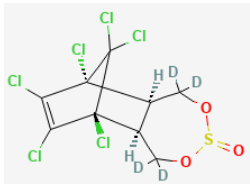
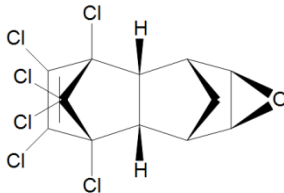
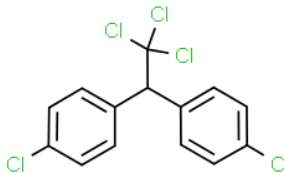
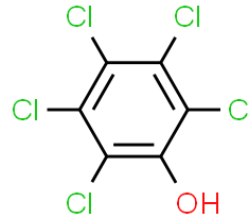
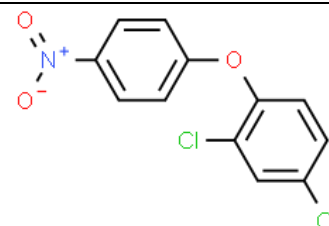
Figure 1. As of December 2023, the most popular personal care product in the United States by category [adopted and re-drawn from the data of ref. 6 Statista, 2024].

Because of their toxicity and dioxin contamination, PCP and DDT are among the hazardous compounds that pollute the environment. PCP can be observed in two forms: as a sodium salt, which is created by chlorinating phenol with a catalyst. PA and PAEs, are substances that pollute the environment due to their toxicity and dioxin contamination. ES is an organochlorine insecticide that is off patent that is used to eradicate mites and insects. One of the many chemical compounds known as Persistent Organic Pollutants (POPs) is endosulfan.

Endocrine difficulties can arise from different sources, including hormone instabilities, tumors, and genetic factors. The endocrine system, which is made up of all the hormones in the body, controls every biological function in the body, from birth to adulthood and old age. These processes include blood sugar levels, metabolism, brain and nervous system development, and the growth and operation of the reproductive system [2 EDSP, 2024]. Table 1 describes the names, structures, molecular formulas, molecular weights, and applications of a few EDC compounds.

Table 1: Some of the EDC compound names, structures, molecular formula, molecular weight, and their uses.

S. No.	Name	Molecular Structure/ IUPAC Name	Molecular Formula	M.Wt. (g.mol ⁻¹)	Uses
1	Bisphenol-A (BPA)		C ₁₅ H ₁₆ O ₂	228.29	-Used in making baby feeding bottles - Beverage containers, toys, epoxy resins
2	Endosulfan		C ₉ H ₆ Cl ₆ O ₃ S	406.9	- Employed in pesticides to effectively kill leafhoppers, beetles, and fruit worms
3	Endosulfan (alpha)		C ₉ H ₆ Cl ₆ O ₃ S	406.9	- Applied to crops as a pesticide, like tobacco, teas, grains, cotton, fruit, and vegetables

4	Endosulfan (Beta)		$C_9H_6Cl_6O_3S$	410.9	- Used as a wood preservative in the US to protect wood from insect damage and deterioration.
5	Endrin		$C_{12}H_8Cl_6O$	380.91	- To keep birds, rodents, and insects under control, it was applied as a pesticide. - Since 1991, it has not been manufactured or utilized within the USA.
6	DDT (dichloro-diphenyl-trichloroethane)		$C_{14}H_9Cl$	354.486	- Pesticide applied to crops - Utilized to control pests in buildings
7	PCP (pentachlorophenol)		C_6HCl_5O	266.336	- Used as a wood preservative - As a wood preservative in the US to protect wood from insect damage and deterioration.
8	Nitrofen		$C_{12}H_7Cl_2NO_3$	284.09	- treating insomnia, - used as a herbicide

2. What are the sources and roots of exposure to EDCs?

Recent literature described that EDCs have been associated with changes in both male and female reproductive function, increased chances of cancer, including breast cancer [7 Zuccarello et al., 2018], altered transcription of miRNAs, obesity, type II diabetes, delays in children's neurodevelopment, atypical development patterns, and abnormal immunological function [8 Monneret, 2017]. EDCs are ingested by humans through food and water, direct skin contact, and inhalation [Zuccarello et al., 2018]. It is important to remember that EDCs can travel through the placenta from pregnant women to developing embryos and from mother to baby through breast milk. Moreover, it is thought that pregnant women and children are the most vulnerable to EDCs [Zuccarello et al., 2018]. The carcinogenicity status of EDCs has been disclosed by the International Agency for Research on Cancer (IARC) [9 IARC, 2024]. Figure 2 illustrates the model of the human hormone system that alters hormones targeted by endocrine-disrupting chemicals and EDCs-mediated activation of aryl hydrocarbon receptors and oxidative stress.

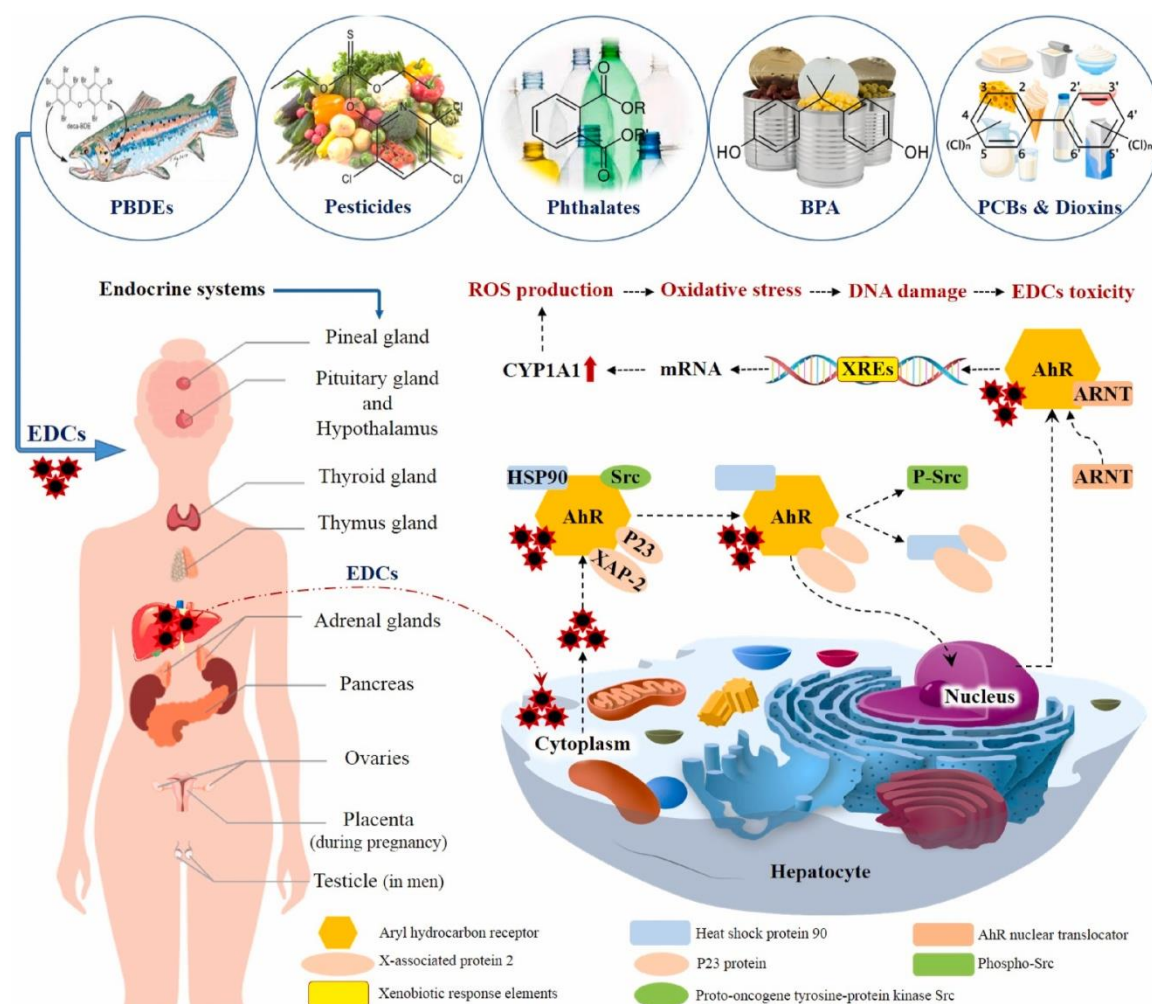


Figure 2: Model of the hormone systems that alter hormones targeted by endocrine disrupting chemicals and EDCs-mediated activation of aryl hydrocarbon receptors and oxidative stress [adapted from ref. Peivasteh-Roudsari et al., 2023 10]

The four main endocrine disorders and their classifications as diabetes, hypothyroidism, hyperthyroidism, and adrenal are as follows:

Diabetes Mellitus [11-14 Howard, 2018, Predieri, 2020, Tuculina, 2022, Yan, et al., 2022]:

Type I diabetes: an autoimmune illness that causes insulin insufficiency by destroying the pancreatic beta cells that release insulin.

Type II diabetes: This type of diabetes, which is often associated with obesity, inactivity, and poor food, occurs when the body grows resistant to insulin or produces inadequate quantities of it.

Gestational diabetes: This kind of diabetes generally appears in the second or third month of pregnancy and leaves away after the birth of the baby.

Hypothyroidism (a glandular disorder) [15-19 Brück, 1983, Boas, 2011, Calsolar., 2017, Das and Das, 2021, Pearce, 2023]:

Primary hypothyroidism: The thyroid gland's failure to produce enough thyroid hormones (T3 and T4) is the root of the issue. This is frequently brought on by autoimmune diseases like iodine insufficiency or Hashimoto's thyroiditis.

Secondary hypothyroidism: The disorder results from minimal thyroid hormone production caused by the pituitary gland's failure to produce enough thyroid-stimulating hormone (TSH).

Tertiary hypothyroidism: This kind of disorder is brought on by a malfunction in the hypothalamus, which results in inadequate thyrotropin-discharging hormone (TRH), which lowers the synthesis of thyroid hormone and TSH.

Hyperthyroidism [16,19 Boas, 2011, Pearce, 2023]:

Graves' disease: The most predominant cause of thyrotoxicosis is Graves' disease, an autoimmune condition in which the thyroid gland produces excessive thyroid hormones because of immune system responses.

Toxic nodular goitre: Thyroid gland nodules or lumps that become hyperactive and create an excess of thyroid hormones are known as toxic nodular goitre (also known as Plummer's disease).

Thyroiditis: inflammation of the thyroid that can result in hyperthyroidism or an excess of thyroid hormones.

Adrenal disorders [20-23 Hinson and Raven, 2006, Lauretta et al., 2019, Egalini et al., 2022, Pötzl et al., 2023]:

Addison's disease (hypoadrenalism): a medical condition when the adrenal glands are unable to generate enough cortisol and aldosterone, resulting in symptoms such as low blood pressure, tiredness, and weight loss.

Cushing's Syndrome (hyperadrenalism): A disorder brought on by continuous exposure to excessive levels of cortisol, either as a result of the adrenal glands producing an excess of it or as a result of using corticosteroid drugs. A round face, increased blood pressure, and obesity are some of the symptoms.

Pheochromocytoma: An uncommon tumor of the adrenal glands that results in an excess of catecholamines, such as noradrenaline and adrenaline, which can produce symptoms like headaches, sweating, and hypertension. The adrenal gland secretes insufficient amounts of cortisol and occasionally aldosterone.

For many years, there has been a commensurate increase in novel chemicals in the interior of buildings due to the quick development of new construction materials, furniture, and consumer goods [24 Weschler, 2008]. Indoor concentrations are mainly unknown, although they may have grown over time as more chemicals are used and building air exchange rates are lowered to boost energy efficiency.

A comprehensive inclusion of the mechanisms of action and consequences of exposure to extracellular dyes (EDCs) necessitates several difficulties. These have already been thoroughly examined elsewhere [25 Gore, and Crews, 2009].

3. Pharmaceuticals with Endocrine Disrupting Properties

EDC can interfere with the endocrine (hormonal) system, potentially contributing to negative health effects. These substances can interact with hormone receptors, alter hormone synthesis, or imitate or block the body's natural hormones, which can result in several health problems, such as immunological, metabolic, developmental, and reproductive abnormalities [26-27 Benotti et al., 2008, Chabchoubi et al., 2021].

In the view of medicine and drugs, selected pharmaceutical compounds and chemicals can act as endocrine disruptors. These may impact the normal function of the endocrine system in patients, either during medical treatment or via environmental exposure. It was also reported that EDCs not only impact endocrine glands in patients but also on Bone Development and Health. Figure 3 depicts the facts on EDCs' impact on bone development and health.

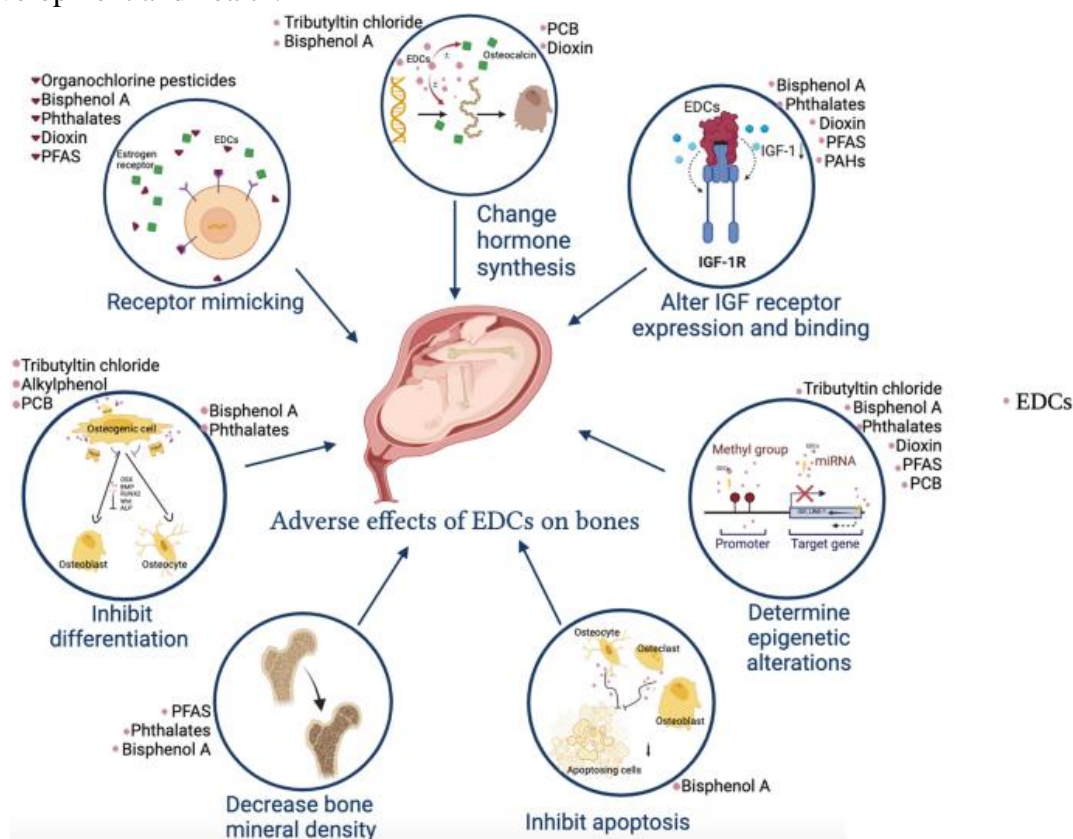


Figure 3. The current collection of facts on EDCs' Impact on Bone Development and Health [adopted from 28 Shulhai et al., 2023]

Below are some examples of EDCs discovered in medications and drugs, prescribed by medical practitioners in general:

Hormonal medications and HRT: Oral contraceptives like synthetic estrogen and progestin used in birth control tablets can simulate natural hormones, disrupting the endocrine balance in the human body. The extensive use of these hormonal drugs can also contribute to environmental contamination (e.g., via urine excretion) that alters wildlife [29-30 Chou, 2023, Kokotović et al., 2023]. HRT better known as hormone replacement therapy drugs containing synthetic or bioidentical hormones (like estrogen and progesterone) used to treat menopausal symptoms can have endocrine-disrupting effects, particularly if taken inappropriately or over a long period.

Thyroid medications (levothyroxine, methimazole): These medications used to treat thyroid dysfunctions can affect the usual regulation of thyroid hormones and may change feedback loops or hormone metabolism if not taken appropriately [31 Street et al., 2018], Figure 4 represents the effect of EDCs' on human, metabolism, fertility, obesity, and other epigenetic alterations.

EDCs: BPA is used in making plastic containers, and baby feeding bottles and as a stabilizer in certain medications (some forms of oral contraceptives), BPA is a known endocrine disruptor that can mimic estrogen. While not often used as an active ingredient in medicine, its presence in packaging or certain drugs raises alarms. Phthalates used as plasticizers in some drug formulations and pill coatings have been shown to act as endocrine disruptors. They may interfere with androgen (testosterone) action and affect reproductive development [32-34 Panigrahi et al., 2013, Pilli et al., 2014, Pilli et al., 2023].

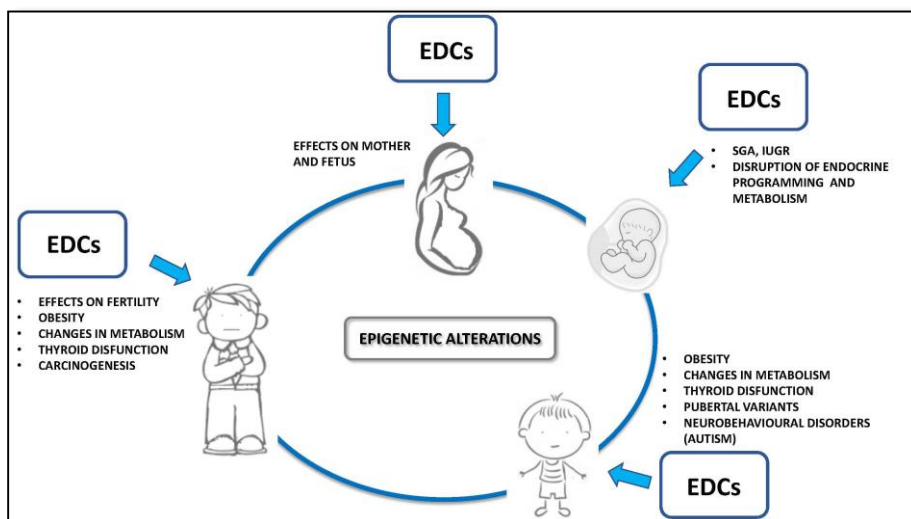


Figure 4. Effect of EDCs' on human, metabolism, fertility, obesity, and other epigenetic alterations. [adopted from 31 Street et al., 2018]

It was proved that the antibiotic triclosan, which is present in various medications and topical treatments (such as antibacterial soaps), interacts with thyroid and estrogen receptors to interfere with hormone regulation. Dioxins are environmental pollutants that can be detected in some medications, especially those that have been produced using chemicals that contain chlorine. It has been demonstrated that dioxins impact reproductive health and thyroid function [35 Kabir et al., 2015].

Antipsychotic Drugs (e.g., Haloperidol, Olanzapine): Some antipsychotic drugs can affect the hypothalamic-pituitary-gonadal (HPG) axis, resulting in changes in reproductive hormones [Smith, 2003, Ilgin 2020, Vidarsdóttir, 2024]. For example, **dopamine antagonists** (such as haloperidol) can increase prolactin secretion, leading to potential issues like lactation or menstrual irregularities in women and reduced libido in both sexes [26, 36-38 Benotti et al., 2008, Smith, 2003, Ilgin 2020, Vidarsdóttir, 2024].

Chemotherapeutic Agents (e.g., Cyclophosphamide) [39-41 Casals-Casas and Desvergne, 2011, Lymperi and Giwercman 2018, Stiefel and Stintzing, 2023]:

Some chemotherapy drugs can disrupt endocrine function by affecting ovarian and testicular function, leading to fertility issues. For example, cyclophosphamide is known to cause ovarian failure in women and testicular damage in men, often leading to infertility. These drugs can also alter the balance of estrogen and testosterone in the body. Figure 4 evaluates the potential impacts of different EDC groups on female reproduction [42 Grindler et al., 2015].

EDCs in cosmetics [41-45 Stiefel and Stintzing, 2023, Nicolopoulou-Stamati, 2018, Martín-Pozo et al., 2021, Kalofiri et al., 2023].

Cosmetics and personal care products (PCPs) have become essential parts of our everyday lives. A common cause of EDs is cosmetic products, which include makeup and a wide range of personal care and fairness and beauty items for the skin and hair. They are made by the cosmetics industry and are intended to protect, wash, and exfoliate our skin and hair in order to promote good health and wellness. Among these products are soaps, gels, shampoos, cosmetics, and nail paint. They are usually complex formulations that include a range of chemicals based on their intended application, including solvents, colorants, fixatives, perfumes, UV filters, and preservatives. Chemicals from cosmetics can be absorbed through the skin, which is the primary exposure route, this exposure can occur by ingesting and inhalation. Concerns over the existence of EDs in these items have been generated by their extensive use. Table 2 shows some of the EDCs that are mostly used for personal hygiene and cosmetic commodities.

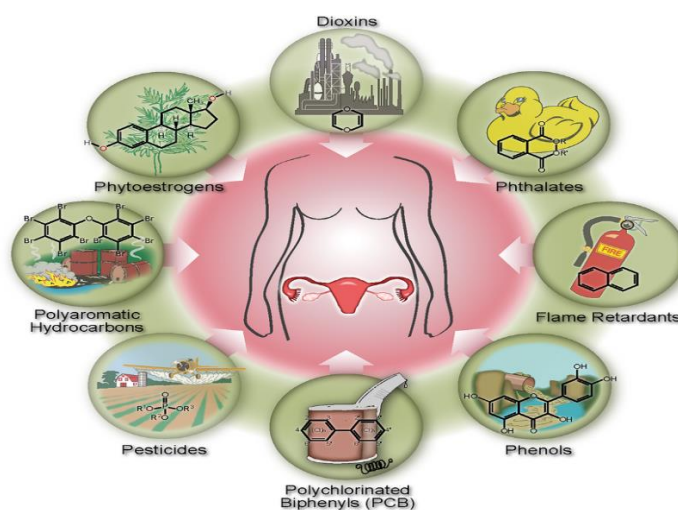


Figure 4. Assessing the possible effects of various EDCs groupings on female reproductive [Adopted from 42 Grindler et al., 2015].

Table 2. The most used personal hygiene and cosmetic commodities [adopted and re-edited, added extra information from the ref. 46 Peinado et al., 2020].

Product use	Type of Product
Baby care products	Infant creams, lotions, oils, and shampoos, talcum powder
Eye	Lash mascara, eyeliner, eyebrow kits, eye pencils, eye shadows, and makeup-up-remover
Skin Care, Skin lightener	Exfoliator to remove dead skin cells from your skin's surface and improve its texture. Toner-immediately after cleansing, but before applying any serums or moisturizers. Serums are applied first, then moisturizer. Anti-Aging Nighttime Lotions Sunscreen, cleanser, moisturizer, and masks every week
Lips	Lipstick, lip gloss, lip balm, lip liners
Hygiene	Soap, oil, lotions, shampoos, cleaning wipes, powders and bathing salts
Deodorants and antiperspirants	Deodorants and antiperspirants
Hair	Dry shampoos and moisture shampoos, Shampoos for color care, deep conditioner, volumizing shampoo, and shampoo conditioner that soothes hair, Hair serums and oils, Pomade /hair wax, Spray heat protector, Hair gel, and Curl Enhancing Creams.
Nails	Nail polishes, nail polish removers, glitter, acrylic, gel, dip powders, softeners, and base coats
Shaving	Shaving creams, soap/foams, shave balm, lotions, and shave gels
Mouth	Mouthwash and toothpaste
Tanning/UV protection	Creams, oils, sunscreens, and suntan lotions
Hair removers	Depilatories- cream, lotion, or gel, oils and waxes
Skin lightening	Lightening creams, and
Feminine hygiene	Tampons, panty liners, sanitary napkins, period panties, sponges, cloth menstrual pads, and menstrual cups

4. EDCs in Plastics and Microplastics

The pervasive and necessary character of plastics in day-to-day life, along with their long-term negative effects on living things, makes them a contemporary ecological and socioeconomic problem. As the world's population grows, plastic consumption will also increase. When plastic breaks down, microplastics (less than 5 mm) and nanoplastics (less than 1 nm) can reach the terrestrial ecosystem by a variety of techniques [47 Ullah et al., 2023].

Moreover, certain plastics have substances that influence hormones. Phthalates are present in flexible vinyl (PVC #3) and bisphenol-A, or BPA, may be present in one common shatter-proof plastic (PC #7). They are referred to as EDCs. EDCs that leach from plastics and pose a health risk to people include BPA and related chemicals, flame retardants,

phthalates, per- and poly-fluoroalkyl substances (PFAS), dioxins, UV stabilizers, and dangerous metals including lead and cadmium [47 Ullah et al., 2023].

Microplastics tainted with phthalate esters [PAEs] accumulate in the testes, changing testicular weight and sperm physiology by decreasing the quantity and vibrancy of sperm [48 Gangolli, 1982]. The sperm morphological variation caused by Microplastics includes tailless sperm, acephalia sperm without a head, cephalic sperm with a tiny head, and sperm losing their acrosome [49 Jin, et al. 2022]. The seminiferous tubules' germ cells shriveled and the density of sperm dropped as a result of embryonic exposure to these plastic particles [50 Huang, et al. 2022]. A detailed review of mammals' endocrine disruption caused by micro and nano plastics and the compounds that are linked to EDCs is given by Ullah et al., and Huang, et al. [47,50 Ullah et al., 2023, Huang, et al., 2022]

The following are the most important characteristics of EDC exposure [51-52 Anway and Skinner, 2006, Peinado and Iribarne-Durán, 2020]:

- ✓ EDCs have no safe dosage. The fact that they work at low doses and in concert with endogenous hormones makes it challenging to determine the point at which they have no effect.
- ✓ Exposure to EDCs throughout a person's most vulnerable developmental stages—puberty, nursing, and pregnancy—causes harm that negatively impacts the person's life as well as the lives of their offspring.
- ✓ The exposure dosages to EDCs that have a negative impact are related to nonlinear curves. Not every time does the response rise in direct proportion to the exposure dose.
- ✓ People are often exposed to a variety of EDCs rather than just one kind. Because chemical residues may function in an antagonistic, additive, or synergistic manner, it is challenging to forecast the effects.
- ✓ Due to either genomic involvement or epigenetic pathways, the effects of exposure to EDCs in a particular individual can be shown in successive generations. Since the effects that are seen after exposure may take a long time to manifest, it is extremely difficult to establish a causal relationship.

5. Available techniques for removing EDCs

Traditionally, EDCS has been removed by physico-chemical techniques such as solvent extraction and micro-extraction, sorption, photolytic and photodegradation, magnetic nanomaterials, composite membranes augmented with surfactants, ultrasonication, and improved catalytic oxidation processes. The lowest amounts of removal in the literature were achieved via coagulation, sedimentation, and filtration. Aerobic and biological degradation are two more noteworthy techniques [4, 53 Pilli et al., 2012, Weber, and Coble, 1968]. Table 3 illustrates several examples of EDC exposure routes and their origin in humans.

Table 3. Examples of origin, and exposure routes of EDCs in humans [Adopted and re-written from ref. 52 Andrea et al., 2014].

S. No.	Human exposure to EDCs	The origin of the EDCs	Example EDCs
1	Ingestion of contaminated food or water by mouth	Soil and groundwater contamination due to pesticides or industrial waste	DDT, perfluorinated compounds, dioxins, and PCBs
2	eating or drinking contaminated food or water	Chemicals leaching off food or beverage containers; pesticide residues in food or drink,	DDT, BPA, phthalates, and chlorpyrifos
3	Make contact with skin and/ or inhalation	Flame-retardant treatments for household furniture	brominated flame retardant (BFRs)
4	Make contact with skin and/ or Breathing.	Pesticides used for residential, agricultural, or public health vector control	DDT, perfluorinated compounds, and PCBs, chlorpyrifos, vinclozolin, pyrethroids
5	Intravenous (IV)	Intravenous tubing	Phthalates
6	Dermal Application	Certain drugs, antibacterials, sunscreens, personal hygiene items, and cosmetics	Phthalates, insect repellents, parabens, and triclosan
7	Biological transfer from the placenta	Maternal body burden as a result of past or present exposures	The placenta is permeable to many EDCs.
8	biological transmission by breast milk	Maternal body burden as a result of past or present exposures	Numerous EDCs are detected in milk

6. Summary

Endocrine disruptors are substances that interfere with the endocrine system's normal functioning. The endocrine system is in charge of controlling the body's hormones. In the view of medicine and drugs, selected pharmaceutical compounds and chemicals can act as endocrine disruptors. Numerous possible health issues may result from these drugs' ability to mimic, block, or change the body's natural hormones. Changes can have far-extensive consequences since the endocrine system regulates several essential processes, including growth, metabolism, reproduction, and mood regulation. EDCs are ingested by humans through food and water, direct skin contact, and inhalation. In this article, an attempt was made to study the EDCs such as bisphenol A, phthalates, PCP and DDT, endosulfan, triclosan, benzophenones, parabens, polychlorinated biphenyls, dioxins, flame retardants, and their main source of exposure, severe health effects were reviewed with recent literature. The carcinogenicity status of EDCs has been disclosed by citing recent studies.

Although research on endocrine disruptors is still in progress, the data points to the necessity for minimizing exposure, especially for children, pregnant women, and vulnerable groups, in order to protect long-term health.

In order to make the world a safer place for everyone, one can take action right now to limit exposure to some of the EDCs that are present everywhere. Reduce your intake of processed food, as well as your use of medications and cosmetics. Foods in cans or plastic packaging are not to be stored in heated places, such as in a car on a sunny day in the summer. Additionally, don't heat or microwave food in plastic containers. EDCs may seep into the food and body from the container. Minimize the use of pesticides in agriculture. Finally, care must be taken to develop robust technology to treat the effluents containing EDCs.

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