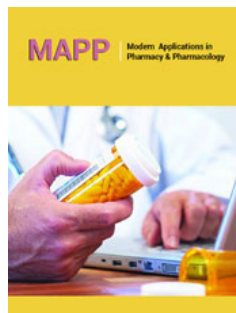


Chemicals that Disrupt the Endocrine System and their Effects on Human Health

ISSN: 2637-7756



***Corresponding author:** Yousaf Khan,
Department of Chemistry, BUITEMS,
Airport Road, Quetta, Pakistan

Submission:  October 28, 2022

Published:  March 21, 2023

Volume 3 - Issue 2

How to cite this article: Yousaf Khan*,
Hakeemullah, Madeeha Bibi and Zia Ur
Rehman Panizai. Chemicals that Disrupt
the Endocrine System and their Effects
on Human Health. *Mod Appl Pharm
Pharmacol.* 3(2). MAPP.000557. 2023.
DOI: [10.31031/MAPP.2023.03.000557](https://doi.org/10.31031/MAPP.2023.03.000557)

Copyright@ Yousaf Khan, This article is
distributed under the terms of the Creative
Commons Attribution 4.0 International
License, which permits unrestricted use
and redistribution provided that the
original author and source are credited.

Yousaf Khan^{1*}, Hakeemullah¹, Madeeha Bibi² and Zia Ur Rehman Panizai³

¹Department of Chemistry, BUITEMS, Airport Road, Pakistan

²Department of Chemistry, Hazara University Mansehra, Pakistan

³Department of Environmental Sciences, BUITEMS, Pakistan

Abstract

Endocrine glands are the important glands of human that performs certain functions and has specific characteristics. The main function of these glands is that they regulate the whole system by producing hormones which they produce indigenously and pours them directly in the blood for a targeted action and all their functions are involuntary. They are specifically ductless glands, and their course of action is regulated by a pea size Pituitary gland or sometimes referred as the Master Gland. Until now, very less has been known about these glands that their actions or functions are being interrupted or disturbed by chemicals or other environmental actions. There are certain chemicals which include chlorpyrifos, DDT, insecticides, pesticides, fungicides and other daily use items such as plastics, paints, furniture, perfumes, toys polishes, electronic gadgets, items of food packaging are reported to have disturbed the normal hormonal functions in humans that are leading to numerous diseases due to either lack of production of specific hormone or increased production of a specific hormone by the action of these chemicals. The diseases that are commonly reported due to the action of the above chemicals and daily use items includes neurological disorders, behavioral disorders, metabolic dysfunction leading to obesity or weakness, thyroid dysfunction, reproductive disturbances and several others that can prove fatal and lead to cancer as well.

Definition of Endocrine Disruptors

There has been universal recognition of the WHO and IPC's 2002 definition and explanation of EDs. To paraphrase the definition given by these researchers, an Endocrine Disruptor (ED) is "an exogenous chemical or combination that interrupts the function(s) of the endocrine system and, as a consequence, causes detrimental health implications in an intact organism or its offspring" [1]. There have been a number of in-depth scientific publications written since the beginning of this century that discuss the topic of the steep increase of endocrine disruption. These works are now available in print. World Health Organization and United Nations Environment Programme's (UNEP) joint definition of EDs for the Chemical Safety conference, which was addressed by individuals from all around the world [2]. In a study entitled "Endocrine Disruptors and Child Health," the World Health Organization (WHO) highlighted the predicament of pregnant women and children as particularly susceptible populations [3]. Furthermore, in 2015, a report was published by the Endocrine Society that examined endocrine disruption from a variety of perspectives [4]. Almost 1300 citations were included in the original manuscript. In 2016, UNEP unveiled plans to publish three distinct studies on a worldwide penalty for chemical pollution [5-7].

Relevant knowledge from endocrinology

Hormone act at very low doses within three main endocrine axes: While interrupting with the system connected to reproduction may possibly change the time period of puberty

and aggrandize the chances of cancers of various types. The EDs which influence the production of thyroid hormones, can affect the development and smooth function of the brain too. Therefore, it is thyroid disruption which leads to numerous neurodevelopmental diseases and diseases such as thyroid cancer and other than neurodevelopmental are also considered to be the cause of thyroid disruption [8,9]. Nuclear receptor which through hormones act, have a direct control over gene expression. Human beings have a bunch of 48 nuclear hormones such as those which control sexual thyroid harmonic activities. These have been highly in the focus of ED research but it is also in our understanding that several receptors such as the peroxide proliferate activated receptors involved in metabolism, targeted by ED [10].

Non-linear responses are seen for endogenous responses and in endocrine disruption: The commonly key characteristic of Endogenous hormone response and ED action, is the inability of displaying or showcasing monotonic responses. Both of them vary up and down as noticed in the thyroid hormonal level during pregnancy. Whereas the effect or influence of ED is concerned, it has a more intense psychological impact at lower ED doses. Desensitization and internalization of receptors create a breeding ground for non-monotonic responses in case of exogenous hormones. Whereas, EDs are concerned, the factors are observed entering the play. It is thanks to the distinctions in the sensitivity of tissues and responses conveyed to ED affecting different tissues at various doses [11]. Secondly, identical tissues can be activated at various doses by applying unlike receptors. In pancreas different dose responses are noticed to Bisphenol A in accordance with activated receptors [12].

The endocrine system plays essential roles from conception to aging: To tackle any stage of organogenesis (the development of body organs) from earlier to later, endocrine signals are utilized. Apart from this growth, placental functions, post-natal life of child and adolescents go through the same process. Reproduction and adulthood function such chemical reactions in body, regulation of temperature and the function of brain and aging use endocrine signaling [13].

Fine scale evidence that exogenous substances can interfere with the endocrine system

It has been made evident that EDs interrupt Endogenous endocrine signaling at both cellular and molecular levels. In myriad of cases, this lets to comprehend the action mechanism of ED.

Interference with the oestrogen or androgen binding to their receptors: There are multiple EDs observed availing the proficiency to interrupt with oestrogens binding to oestrogen receptor. It provides the tools with a couple of oestrogen receptors to EDs [14]. Tools identical to cell based have been given development for the sake of receptor like Androgen [15]. In the body of human cells and model organisms, countless screening tests have been devised for several other nuclear receptors. In contrast, for such screening tests thyroid is not fit to be used owing to its high specification in ligands domains [16].

EDs affecting aromatase action: There are innumerable number of EDs which interrupt aromatase enzyme in order to convert androgen to 17 β -oestradiol (an oestrogen) by the process of demethylation. Aromatase, which is of key importance for functions such as in placenta, bone mineralization, the function of brain and ovarian follicle, is cytochrome enzyme P450 [17]. Its other prolific function is in post-natal masculinity of various domains of brain. It is strongly collaborated with reproduction and behaviour of brain including neurodevelopmental and disorders of behaviour. Disrupters such as oestrogen and androgen have been improved to scrutinize disruption of aromatase [18].

ED Interference with thyroid hormone distribution in the blood: Hormones which are produced in their specific sites and carried to their functional cells through bloodstream, function as messengers to convey messages from one site to another. Thyroid hormones are transferred by three distributor proteins where they become exposed to the EDs targets. Certain pesticides, flame retardants and perfluorinated compounds are the supposed EDs that change the equilibrium between thyroid hormone and distributor protein [19].

Interference with iodine uptake by the thyroid gland: Thyroid gland requires iodine to yield thyroid hormone. The inadequacy of both iodine and thyroid hormone leads to the impairment of brain, causes loss of IQ and enhances the chances of neuro developmental diseases. Maternal thyroid hormone can be modulated and promulgated as exposed perchlorate during pregnancy. In amniotic fluid has reported the contamination of perchlorate. In various parts of Europe, paucity of Mild iodine [20].

Evidence available at the scale of organisms and populations

while moving to higher level of organism from molecular or cellular level, there is no paucity or dearth of evidence that limpidly exhibits the EDs interruption in psychological systems even if the doses are kept very trifle.

Compounds affecting brain development through alteration of the endocrine system: While conducting studies both on epidemiological and experimental levels, it emerged replete with evidence that the loss of IQ or an enhanced risk of neurodevelopmental diseases are caused when parental exposures are made to many EDs. The function of several EDs is dependent on the alternation of thyroid signaling, whereas other EDs influencing androgen and estrogen signaling are found workable during neurodevelopmental disturbance, especially in the times of sexual distinction of hypothalamus [21].

Compounds altering diabetes risk and other metabolic disorders through alteration of the endocrine system: Bisphenol A has been considered by a French health agency (ANSES) to enhance disruption in metabolic functions which will terminally lead to diabetes of type 2. In accordance with another systematic study, that impacts were notice when a body weighted 50 μ g/kg is exposed to it. Moreover, EDs is implicated in the enhancement of

obesity and in case of tributyltin (TBT, a banned compound used as in anti-fouling paints) when study was conducted on mouse exhibiting first generation and trans generation being influenced badly. Besides, experiment on different other models resulted in triclosan and benzo A pyrene in disturbance of metabolic functions [22].

Compounds inducing reproductive disorders through alteration of the endocrine system: Apart from cancer inflicted to reproductive organs such as testis, prostate or breast, there have been identified EDs implicated in various anomalies of reproduction of in both Male and female genders. This disturbance in reproduction may be in the form of infertility and fecundity or magnified ovarian cycles, fibroids and endometriosis. Male reproduction such as testicular dysgenesis and infertility has always been in focus through animal experiments and epidemiology with investing an handsome amount of 15 billion euros per year in Europe [23].

Implication of oestrogen-like compounds in breast cancer: Since 1970s, There has been promulgated practicable data making oestrogens workable during breast cancer. The probability of breast cancer leads to having limited number of progenies, reduced time period of breastfeeding, a prompt menarche and awaiting menopause, which limpidly exhibits that the naturally secreted hormones during menstrual cycles promote the enhancing chances of breast cancer. The feasibly rising factor for breast cancer is Bisphenol A while connecting with other receptors as Oestrogen that solidifies or fortifies the grow and upbringing of mammary cells. It has been confirmed in an elucidated study through chemical industry that insecticide DDT when exposed to intrauterine causes the emergence of breast cancer. Innumerable potential EDs have been observed affecting other kinds of cancer during their implantation. Chlordecone which is a chlorinated pesticide, enhances the risk of cancer and is the reason of influence dotted above. Bisphenol A is too experimentally noticed influencing prostate cancer, clearing vagina's adenocarcinoma cell and DES [24].

Some populations are more vulnerable to EDs

The initial days of pregnancy and the period after childbirth are considered to be entirely susceptible to sensitivity for ED exposure. The organs of the body develop simultaneously despite the immaturity of endocrine scheme and system. Notwithstanding with the above statement, there is still dearth of satiated information amalgamated that can widen the area of reckoning childhood and adolescence dependency on the mechanism of endocrine. In contrast, there has been attempts made on animal models so as to get documentation and to know dubious impacts of ED in epidemiological understanding [25].

Conclusion

Hormones coordinate harmonious development and function of all organs and act at minute concentrations (part per trillion to per billion range). Given the essential role of the endocrine system during development, ED exposure during vulnerable

periods can induce long-lasting changes, with adverse effects in the short and long terms; some of these effects are expected at very low doses. Non-monotonic dose responses can be observed. Hundreds of man-made and some natural chemicals can disrupt the function of the endocrine system. Certain of them have been demonstrated to induce adverse effects as a consequence of this disruption. Although multifactorial, many chronic health disorders have been clearly linked by animal experiments and epidemiology to EDs. These disorders include obesity and metabolic disorders, reproductive disorders, reproductive cancers, thyroid disorders, neurodevelopmental disease and IQ loss.

EDs are present in food, food contact materials, cosmetics, consumer goods (including furnishings, cleaning products), toys, as well as drinking water. Consequently, the EU population is widely exposed to known and suspected EDs. This fact is confirmed by biomonitoring studies, including on susceptible subgroups such as pregnant women and children. Annual costs related to ED exposure were estimated to be €163 billion (above €22 billion with a 95% probability and above €196 billion with a 25% probability). Multiple exposures result in cumulative effects, a situation expected for compounds acting via similar pathways, and that is also likely for compounds acting on similar health outcomes via different pathways. Synergistic effects can also be observed. Currently, EU chemical regulations do not generally consider these cumulative effects, notably for ED exposures.

References

1. WHO/IPCS (2002) Global assessment of the state-of-the-science of endocrine disruptors.
2. Bergman A, Heindel JJ, Jobling S, Kidd KA, Zoeller RT (2012) State of the science of endocrine disrupting chemicals.
3. Toppari J, (2002) Endocrine disrupters and child health - Possible developmental early effects of endocrine disrupters on child health, Switzerland.
4. Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, et al. (2015) EDC-2: The endocrine society's second scientific statement on endocrine-disrupting chemicals. *Endocr Rev* 36(6): E1-E150.
5. UNEP/IPCP (2017) Overview report I: Worldwide initiatives to identify Endocrine Disrupting Chemicals (EDCs) and potential EDCs.
6. UNEP/IPCP (2017) Overview Report II: An overview of current scientific knowledge on the life cycles, environmental exposures, and environmental effects of select Endocrine Disrupting Chemicals (EDCs) and Potential EDCs.
7. UNEP/IPCP (2017) Overview Report III: Existing national, regional, and global regulatory frameworks addressing Endocrine Disrupting Chemicals (EDCs).
8. Kohrle J (2008) Environment and endocrinology: The case of thyroidology. *Ann Endocrinol (Paris)* 69(2): 116-122.
9. Perdichizzi S, Mascolo MG, Silingardi P, Morandi E, Rotondo F, et al. (2014) Cancer-related genes transcriptionally induced by the fungicide penconazole. *Toxicol In Vitro* 28(1): 125-130.
10. Evans RM, Mangelsdorf DJ (2014) Nuclear receptors, RXR, and the big bang. *Cell* 157(1): 255-266.
11. Ropero AB, Magdalena PA, García EG, Ripoll C, Fuentes E, et al. (2008) Bisphenol-A disruption of the endocrine pancreas and blood glucose homeostasis. *Int J Androl* 31(2): 194-200.
12. Soriano S, Magdalena PA, Arévalo MG, Novials A, Muhammed SJ, et al. (2012) Rapid insulinotropic action of low doses of bisphenol-A on

- mouse and human islets of Langerhans: Role of estrogen receptor beta. *PLoS ONE* 7(2): e31109.
13. Bowers J, Terrien J, Froidevaux MS, Gothié JD, Rozing MP, et al. (2013) Thyroid hormone signaling and homeostasis during aging. *Endocr Rev* 34(4): 556-589.
 14. Judson RS, Houck KA, Watt ED, Thomas RS (2017) On selecting a minimal set of in vitro assays to reliably determine estrogen agonist activity. *Regul Toxicol Pharmacol* 91: 39-49.
 15. Bhattacharjee GB, Paul SM (2014) In vitro reporter assays for screening of chemicals that disrupt androgen signaling. *J Toxicol* 2014: 701752.
 16. Mughal BB, Fini JB, Demeneix BA (2018) Thyroid-disrupting chemicals and brain development: An update. *Endocr Connect* 7(4): R160-R186.
 17. Patel S (2017) Disruption of aromatase homeostasis as the cause of a multiplicity of ailments: A comprehensive review. *J Steroid Biochem Mol Biol* 168: 19-25.
 18. Chen S, Hsieh JH, Huang R, Sakamuru S, Hsin LY, et al. (2015) Cell-based high-throughput screening for aromatase inhibitors in the Tox21 10K library. *Toxicol Sci* 147(2): 446-457.
 19. ENVA.3/FRA/2014/0029, F.c., (2017) Supporting the organisation of a workshop on thyroid disruption-Final Report.
 20. Steinmaus C, Pearl M, Kharrazi M, Blount BC, Miller MD, et al. (2016) Thyroid hormones and moderate exposure to perchlorate during pregnancy in women in southern california. *Environ Health Perspect* 124(6): 861-867.
 21. Dickerson SM, Cunningham SL, Patisaul HB, Woller MJ, Gore AC (2011) Endocrine disruption of brain sexual differentiation by developmental PCB exposure. *Endocrinology* 152(2): 581-594.
 22. Regnault C, Usal M, Veyrenc S, Couturier K, Batandier C, et al. (2018) Unexpected metabolic disorders induced by endocrine disruptors in *Xenopus tropicalis* provide new lead for understanding amphibian decline. *Proc Natl Acad Sci USA* 115(19): E4416-E4425.
 23. Hauser R, Skakkebaek NE, Hass U, Toppari J, Juul A, et al. (2015) Male reproductive disorders, diseases, and costs of exposure to endocrine-disrupting chemicals in the European Union. *J Clin Endocrinol Metab* 100(4): 1267-1277.
 24. Herbst AL, Ulfelder H, Poskanzer DC (1971) Adenocarcinoma of the vagina. Association of maternal stilbestrol therapy with tumor appearance in young women. *N Engl J Med* 284(15): 878-881.
 25. Sergeev O, Burns JS, Williams PL, Korricks SA, Lee MM, et al. (2017) The association of peripubertal serum concentrations of organochlorine chemicals and blood lead with growth and pubertal development in a longitudinal cohort of boys: A review of published results from the Russian Children's study. *Rev Environ Health* 32(1-2): 83-92.