Review Article: A Short Review on Effects of Bisphenol A and Its Analogues on Endocrine System

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ABSTRACT

Bisphenols A and its analogues are among the most common endocrine-disrupting chemicals (EDCs) and have been a particular focus of environmental concern for decades due to their pervasiveness and severe hazard to organism health. Because of greater regulatory action and scientific and public concern about bisphenols adverse health effects, it is increasingly being used in a wide range of consumer and industrial products. According to an increasing amount of studies, bisphenol and analogues have a deleterious impact on various neuroendocrine functions in living organisms. It has the potential to produce neurotoxicity and behavioral impairment in addition to reproductive damage.

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Content

1. Introduction

The environment has been impacted greatly from industrial activities over the last few decades. Chemicals that are hazardous to plants and animal are becoming more prevalent. Chemicals known as "plant killers" have the potential to destroy animal cells, but they differ substantially in how they affect the organisms. Some chemicals produce malignant tumors on their own or in combination with other chemicals, while others are general poisons, strong metabolism-stimulants [1, 2] that can elevate body temperature to deadly levels, and some attack the genetic composition of a race by causing gene mutations. Today, every human is exposed to toxic substances from the time of conception until death. Synthetic chemical substances are present in all environmental compartments since they have been so widely distributed over the past few decades in both the living and inanimate worlds. Endocrine-disrupting chemicals (EDCs) are environmental neurotoxins that have drawn a lot of attention recently because of their widespread use in consumer products, high production volume, and pervasive presence in the environment, high potential for bioaccumulation, and potential for harm to organisms, including humans. EDCs are described as chemicals or mixtures that unintentionally disrupt the endocrine system's regular operations, including hormone production, secretion, transport, binding, biodegradation, and excretion. These disruptions might have a negative impact on the health of an organism, its offspring, or communities. A wide range of anthropogenic chemicals, such as those that act as agonists and antagonists of the estrogen receptors (ERs), androgen receptor, thyroid hormone receptor, and other receptors, are referred to as endocrine disrupting compounds (EDCs). Estrogenic substances (ECs), which include some organochloride pesticides, polychlorinated biphenyls, plasticizers like phthalates and BPA [3], alkylphenolic compounds, and natural and synthetic estrogens, can interact with the estrogen receptor or change estrogen metabolism, mimicking the effects of the natural steroid 17-estradiol (E2).

Bisphenol A (BPA) in particular has received a lot of attention because of its detrimental effects on both organisms and the environment [1]. Bisphenol A [2, 2-*bis*(4-hydroxyphenyl)propane; BPA] is the most commonly used and well-studied of the seventeen bisphenolic compounds. BPA has been identified as an endocrine disrupting substance that could harm both wildlife and human health [3]. BPA was initially produced in 1891 by Aleksandr Dianin, but it was in 1936 that its estrogenic properties were recognized. It is one of the first synthetic substances known to have endocrine activity, despite the fact that diethylstilbestrol (DES) has more strong estrogenic activity. In the 1950s, it was discovered that BPA could be polymerized to generate polycarbonate plastic [4], an economical material that is light, transparent, colorable, impervious to shock, heat, and chemicals, unalterable over time, and simple to shape and thermoform. BPA swiftly became one of the most commonly produced and used chemical in the world despite being a known synthetic estrogen. BPA is a phenolic organic synthetic compound used as an additive or monomer in the production of hard plastic and epoxy resins, which are then used as dental sealants, coatings, food cans, toys, water bottles, water pipes, thermal paper receipts, adhesives, digital media (CDs and DVDs), and polycarbonate plastics (**Figure 1**). Polycarbonates are used in a wide range of common products such as optical, media, automotive, electrical and electronics, housewares and appliances, construction, medical. The chemical bisphenol A (BPA), which has been linked to a number of health problems including heart disease, male erectile dysfunction, mammary and prostate cancers, diabetes, and early sexual maturation, has been outlawed in many developed countries [5].

BPA have analogues with toxicities that are at par with or higher than those of BPA [7, 8]. The effects of BPB, BPF, and BPS on the activities of the estrogen and androgen receptors have also been examined in numerous laboratory

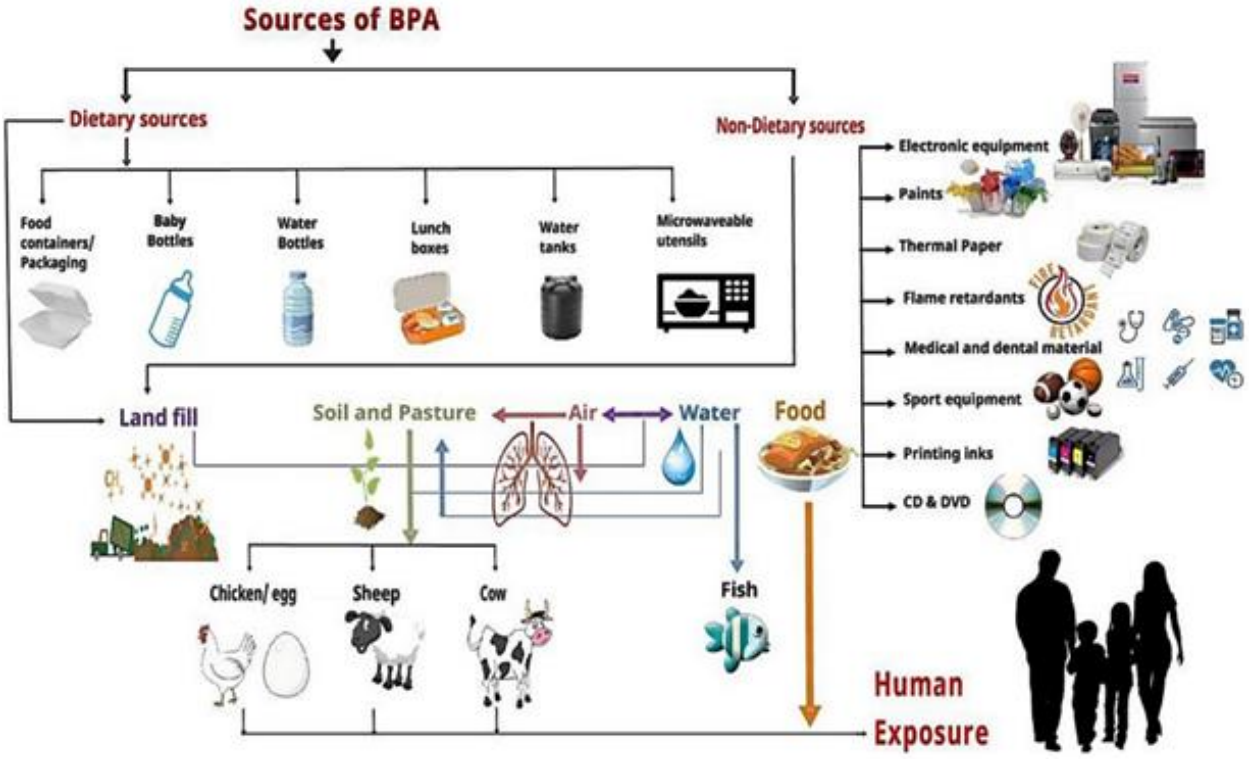

Figure 1. Humans are exposed to BPA from various sources, including exposed roots. There are dietary and non-dietary sources [6]

experiments [9, 10], and it was discovered that most analogues had the similar ability to influence endocrinological processes as BPA. The effects of these compounds on neurotoxicity, acute toxicity, and reproductive toxicity have been further identified by these investigations. Moreover, it was demonstrated that urine BPA interacts with the hormones c-reaction protein (CRP) in postmenopausal women and follicle-stimulating hormone (FSH) in men to cause immunological and endocrine disruption. It was shown that BPA promotes oxidative stress by either creating reactive oxygen species (ROS) or by changing anti-oxidant defenses in numerous animals' *in vitro* laboratory investigations. BPA, BPS, BPF, and BPAF can also worsen the effects of oxidative stress on biomacromolecules [11], which are its main targets. Because urinary BPs appeared to be related to malondialdehyde (MDA) and 8-hydroxy-2′-deoxyguanosine (8-OHdG), which are byproducts of lipid per-oxidation and DNA oxidative damage brought on by oxidative stress and frequently used as biomarkers of oxidative stress, analyses of the effects of pollutants on humans suggested that BPs might cause oxidative stress. Numerous studies in epidemiology have examined how BPs affect several diseases, including diabetes, obesity, and cancer in humans [12, 13].

2. Chemical Composition and Synthesis of BPA and Analogues

There is mounting evidence that organic compounds with various industrial uses and varied chemical structures interact with living things and interfere with their endocrine systems. Two phenolic rings are connected by a bridging carbon in the chemical structure of one class of endocrine disruptors that mimic estrogens. These diphenylalkanes are known as bisphenols, specifically bisphenol F (BPF), bisphenol A (BPA), and bisphenol AF (BPA with perfluorinated methyl groups), depending on whether the bridging carbon has a substituent or not. The manufacturing of polycarbonates, epoxy resins, phenolic resins, polyesters, and polyacrylates all start with BPA, which is today one of the most important compounds in plastics [14, 15]. Due to their widespread use, significant amounts of bisphenols are released into various aquatic and terrestrial habitats. As a result, it is important to pay great attention to how they behave in the environment. The synthesis of BPA and its analogues is accomplished using a condensation reaction involving phenol and the proper solvent and catalyst. Phenol with acetone, hexafluoroacetone, formaldehyde, sulfur trioxide, and other chemicals can be combined to create BPA, BPAF, BPF, and BPS, respectively. BPA is classified as a high-volume production (HVP) chemical by the U.S. Environmental Protection Agency due to its extensive use. The first phenolic plastic, often known as Bakelite, was patented by L.H. Baekeland in 1909. This substance was created by a phenol and formaldehyde reaction that results in BPF. By copolymerizing formaldehyde and simple phenols or bisphenols, phenolic resins are created. For instance, perfluorinated BPA and formaldehyde are used to make polyformal II. A number of compounds, including bisphenol S (BPS), bisphenol F (BPF), bisphenol B (BPB), bisphenol P (BPP), fluorine-9-bisphenol (BPFL, also known as BHPF), bisphenol AF (BPAF), 4,4′-thiodiphenol (TDP), and 4,4′-dihydroxy-benzophenone (DHBP), are as BPA analogues [14-16], as depicted in **Figure 2**.

3. The Endocrine System Affected by BPs, BPA, and Analogues Mimics

Endocrine disrupting chemicals (EDCs) are a broad category of environmental substances that obstruct any part of hormone action. EDCs influence a variety of biological processes through both nuclear hormone receptors and membrane-initiated fast signaling events, which can either imitate or antagonize the actions of native hormones. Bisphenol A (BPA) is a typical EDC. BPA is an estrogenic EDC and a synthetic compound used in the production of polycarbonate plastics and epoxy resins. BPA exposure is common among humans and has been associated with a number of harmful health outcomes. BPA is almost always present in the environment. Bisphenols are present freshwater, surface water, air, river water, and soil, in rather significant proportions. Due to

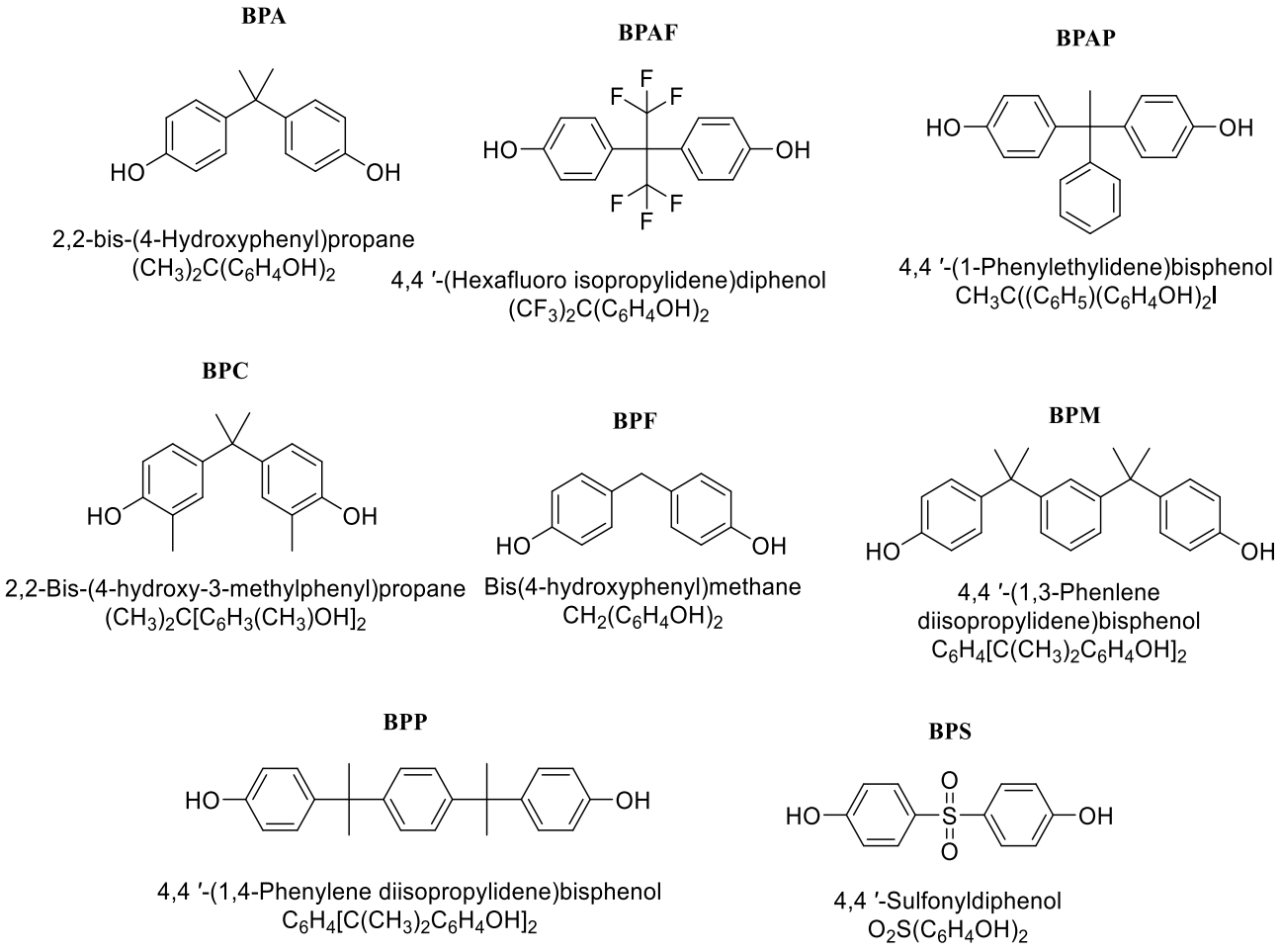

Figure 2. Molecular structures and formulas of bisphenols

the effects these substances have on human health, research into EDCs has become a top concern. Since EDCs are common and easily detected in the environment, such as in the air, river water, and the general population of different age groups, public awareness of EDCs, such as bisphenol A and analogues, has substantially increased over the past few decades [17, 18]. Among other products, bisphenol A and analogues are frequently used in household goods and food packaging. Exposure can happen through skin contact, ingestion, or inhalation. EDCs make up a large portion of the thousands of anthropogenic chemicals that are currently being released into the environment. Exogenous chemicals or chemical combinations that have a detrimental influence on the structure or operation of the endocrine system are what are referred to as these. Embryonic development, gonadal formation, sex differentiation, growth, and digestion are among the developmental, metabolic, and reproductive processes that are regulated by endocrine systems. These processes may be impacted by endocrine-disrupting substances that bind to or block hormone receptors, causing or preventing hormonal response. Biocides, industrial substances, surfactants, and plasticizers like bisphenol A (BPA) are among the chemicals linked to endocrine disruption. Due to its use in a wide range of items, such as food and beverage packaging, flame retardants, adhesives, building materials, electronic components, and paper coatings, bisphenol A has become pervasive in the environment during the last 80 years. BPA is therefore widely dispersed in the air, water, and soil

habitats due to widespread waste disposal. It is currently preserved in human tissues as a result of human contact and absorption. However, BPA is losing ground to its equivalents in terms of prevalence as they take its place [19]. These include [20, 21] bisphenol S (BPS), bisphenol F (BPF), and bisphenol AF (BPAF).

BPA is replaced by the chemicals bisphenol S (BPS) and bisphenol F (BPF). BPF and BPS [22] found in Baby bottles [23], food (such as dairy goods, meat and meat products, vegetables, canned foods, and cereals), beverage containers, paper products, personal care products (such as body wash, hair care products, makeup [24], lotions, and toothpaste) [25], and food packaging items (such as beverage containers). These alternatives have also recently become the subject of health concerns. Asthma, hay fever [26], and depressed symptoms [27, 28] were all linked to higher levels of BPS and BPF. Exposure to BPS or BPF is linked to a higher risk of cardiovascular disease (CVD) in people because they have endocrine-disrupting effects comparable to those of BPA. BPS and BPF are not secure BPA substitutes, despite the fact that BPA, BPS, and BPF have comparable chemical properties. The effects of BPS, BPF, and BPA on testosterone secretion were studied in a study [29], and it was discovered that BPS inhibited testosterone synthesis even more than BPA did [18, 30, 31]. Compared to BPA and BPF exposure, BPS exposure significantly affected the metabolism of liver lipids and glucose [32]. According to researches, obesity and abnormal thyroid signaling pathways are caused by exposure to high concentrations of BPS and BPF [33, 43]. BPA, BPF, and BPS all have comparable chemical structures and operate in the body in similar ways [21, 35, 36]. However, BPS is just as harmful to biological systems as BPA, if not more so. Mice that had been prenatally exposed to BPS had a considerably higher incidence of spontaneous epithelium lesions and inflammation than did BPA-exposed mice [37, 38]. It has been suggested that BPS exposure among humans is increasing, with dietary consumption, inhalation, and skin contact being the main routes of exposure.

It was discovered experimentally that BPS exposure changes the endocrine functions of the human adrenocortical carcinoma (H295R) cells and causes cell damage. The synthesis of steroid hormones is decreased because of BPS, and the transcripts of genes that produce steroid hormones are also down regulated [39]. According to reports, BPS has the potential to be harmful and estrogenic *in vivo*. Acute toxicity from BPS exposure was observed in *Daphnia magna* [40], and postnatal exposure to BPS caused rats' uteruses to enlarge [42]. BPS exposure has been linked to lower gonadal weight, egg production [42], and hatchability in zebra fish, according to recent studies [43-45]. BPS exposure increased hatching time, decreased sperm count, and caused abnormalities in the developing fetus [46]. Similarly, exposure to BPS raises plasma estrogen levels, lowers testosterone levels, and decreases the production of GnRH transcripts in the hypothalamus [47, 48]. BPS exposure in humans has been documented in the past and is rising as more BPS is used. Human urine [49] samples have been observed to exhibit various concentrations. By employing rats as an animal model, the potential consequences of BPS exposure were observed on the mammalian reproductive system [50]. BPA and analogues have also been found in different human biological tissues and fluids, including breast milk, urine [49], blood [51], and adipose tissue, indicating long-term environmental exposure [43] and inadvertent absorption of these compounds, as shown in **Figure 3**.

3.1 Prenatal, postnatal, and concurrent exposure behavioral outcomes to bisphenols

Studies on the behavioral and social-emotional growth of boys discovered that prenatal exposure to bisphenol A may be linked to externalizing and internalizing issues, anxiety and sadness, and somatizing tendencies. On the other hand, it was noted that externalizing issues in females were significantly linked to prenatal bisphenol A exposure. The social domain of Developmental Quotient (DQ) and social impairment were also linked to prenatal bisphenol A exposure. Girls' increasing inability to exercise inhibitory self-control was linked to

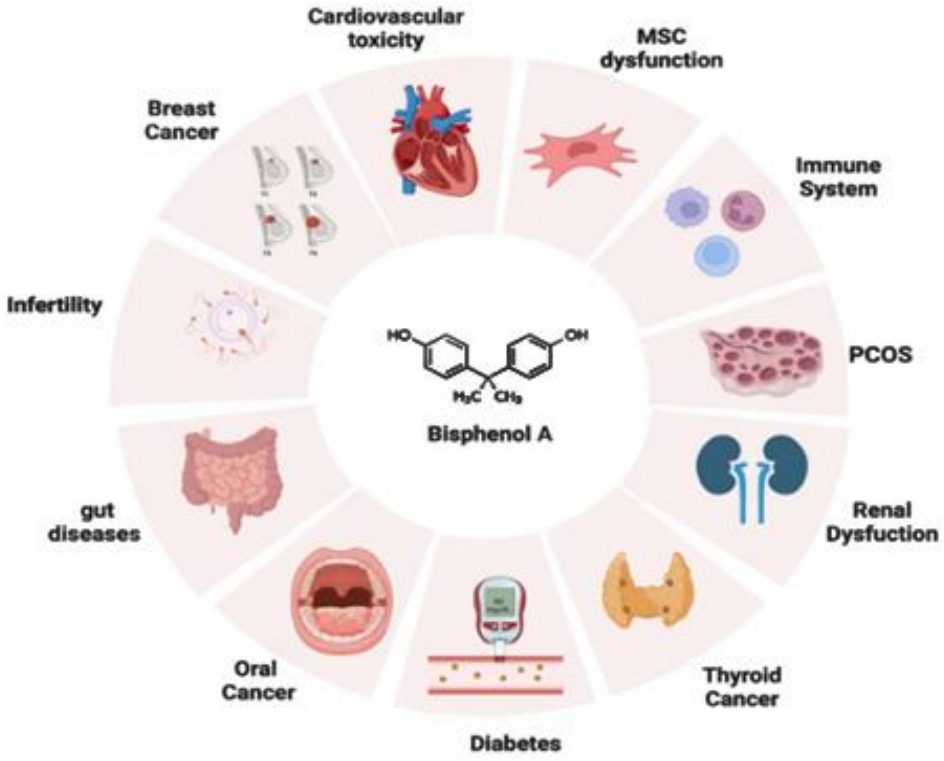

Figure 3. BPs and BPA mimics' effects on endocrine system [52]

exposure to l-bisphenol A both during pregnancy and after [53-55]. According to these researches, exposure to bisphenol A during and after pregnancy may have sex-specific effects [56, 57] on a child's behavioral results. Children of school age were shown to have both negative and behavioral impacts when exposed to bisphenol A concurrently, according to studies.

3.2 Fetal exposure and cognitive development and psychomotor development

Studies looking at the emergence of cognitive and communicative abilities, such as language and intelligence quotient (IQ), have produced mixed results. According to studies, prenatal bisphenol A exposure had no effect on cognitive growth up to the age of four and on visual-spatial skills at the age of eight. Only in boys did prenatal bisphenol A exposure lead to lower full-scale IQ, verbal comprehension, and vocabulary scores. In contrast, only in girls did prenatal bisphenol A exposure lead to negative effects on full-scale IQ, perceptual reasoning, and working memory [51, 58-60]. Recent research has linked prenatal exposure to lower Full Intelligence Quotient (FIQ) scores and semester-specific exposure to lower mental development index (MDI) scores in young children. Overall, it has been hypothesized that prenatal bisphenol A exposure may have negative impacts on cognitive and communication development. However, more research is required to clarify this link because these studies only offered limited association in terms of sex and child age [61-64].

In case-control, cross-sectional, and longitudinal investigations, it was hypothesized that attention deficit hyperactivity disorder (ADHD) symptoms, particularly in boys, were related to both prenatal and postnatal exposure to bisphenol A. However, a recent case-control research found no discernible difference in children's urine bisphenol A levels between ADHD cases and controls [65, 66]. Studies comparing case-control subjects to controls revealed that those with diagnosed Autism Spectrum Disorder (ASD) had greater levels of bisphenol A in their urine [49, 67].

3.3 Effects of bisphenol A on thyroid hormones

During pregnancy and childhood, thyroid hormones are essential for neural migration, synaptogenesis, and myelination [51]. Biosynthesis, biotransport, biotransformation, and metabolism are all mechanisms through which bisphenol A might affect thyroid hormones. Di-2-ethylhexyl phthalate (DEHP) can also affect thyroid hormones by disruption of the hypothalamus-pituitary-thyroid axis, activation of the Ras-Akt-thyrotropin pathway, release of hormone receptors, and induction of hepatic enzymes [66]. According to the current literature, DEHP may also alter thyroid-specific transcription factor (TTF)-1, Paired Box 8 (PAX8), sodium iodide symporter (NIS), thyroperoxidase (TPO), and the deiodinase protein family, damage thyroid follicles, and impair T4 production [68, 69].

Male mice exposed to bisphenol A during pregnancy [51] show decreased synaptogenesis and synaptic proteins, altered synaptic structure, altered behavior, and impaired learning-memory. The morphology and postnatal gene expression of sexually dimorphic areas in the rat brain are influenced by prenatal and postnatal bisphenol A exposure. Hippocampal dendrites have been reported to change. In animal research, prenatal exposure to bisphenol A diminishes spine density, branching, and spine synapses in hippocampal CA1 neurons [70-72]. Although some of these effects are sex-specific, an exposure can influence tyrosine hydroxylase immunoreactive neurons, lowering expression in the substantia nigra, locus coeruleus, periventricular preoptic hypothalamus, and midbrain areas [73]. Tyrosine hydroxylase, the homeostasis of calcium-dependent neurotransmitters, the dopamine receptor D2, and dopamine release could all be affected by bisphenol A. In human cell lines, bisphenol A metabolites impair calcium signaling linked with nicotinic acetylcholine receptors (nAChRs), and nicotinic acetylcholine receptors-mediated calcium channels in the brain and peripheral nervous system are crucial for various neurodevelopment processes. In addition, investigations on animals have revealed that exposure to bisphenol A causes morphological and functional changes in the hippocampus neurons as well as their death [74-77]. The blood of rodent offspring exposed to bisphenol A during pregnancy shows altered DNA methylation and gene expression, which is controlled by an underlying genetic profile. According to growing data, exposure to types of bisphenol may have significant epigenetic impacts. The placental epigenetic effects of maternal bisphenol A exposure, including genomic imprinting, DNA methylation, and the expression of non-coding RNAs, were discussed in a recent review studies. According to a recent study, bisphenol A exposure may have sex-specific impacts on placental epigenetic alterations. Previous researches have also revealed that leptin plays a function in the formation of behavior. Leptin production by the placenta, which is epigenetically controlled by promoter DNA methylation and newborn neurodevelopment, was further studied. According to this study, enhanced placental leptin DNA methylation may be important for the neurodevelopment of newborn humans, notably for the way in which they respond sex-specifically to varied stimuli.

4. Conclusion

Due to its extensive use and serious hazard to both human and animal health, bisphenol A (BPA), one of the most prevalent EDCs, has been a special focus of environmental concern for decades. BPA has been replaced with a number of structurally similar, but less well-known alternative chemicals as a result of increased regulatory actions, scientific research, and public concern regarding the harmful health effects of BPA. The primary BPA alternatives that are increasingly being employed in a variety of consumer and industrial items are analogues to bisphenol A. Although it was thought to be a secure BPA substitute, accumulating data indicates that BPA analogues have negative impacts on various neuroendocrine systems in animals. Recent experimental work suggests that BPS has a significant potential to cause neurotoxicity and behavioral impairment in addition to its toxicity to reproduction.

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References

[1]. T. Colborn, S. Frederick vom Saal, A.M. Soto, Developmental effects of endocrine-disrupting chemicals in wildlife and humans, *Environmental health Perspectives*, **1993**, *101*, 378–384. [Crossref], [Google Scholar], [Publisher]

[2]. A. Ballesteros-Gómez, F.J. Ruiz, S. Rubio, D. Pérez-Bendito, Determination of bisphenols A and F and their diglycidyl ethers in wastewater and river water by coacervative extraction and liquid chromatography-fluorimetry, *Analytica Chimica Acta*, **2007**, *603*, 51–59. [Crossref], [Google Scholar], [Publisher]

[3]. a) M. Sendra, M. Štampar, K. Fras, B. Novoa, A. Figueras, B. Žegura, Adverse (geno)toxic effects of bisphenol A and its analogues in hepatic 3D cell model, *Environment international*, **2023**, *171*, 107721. [Crossref], [Google Scholar], [Publisher] b) S. Mohamed Saleh Omar Korbag, I. Mohamed Saleh Omar Korbag, A new study biological role of hpv infection, oral contraceptive use, sex hormones and bisphenol A and increase rate cancer of cervical in libya. *Journal of Medicinal and Chemical Sciences*, **2020**, *3*, 354-362. [Crossref], [Google Scholar], [Publisher]

[4]. E.C. Dodds, W. Lawson, Synthetic oestrogenic agents without the phenanthrene nucleus, *Nature*, **1936**, *137*, 996-996. [Crossref], [Google Scholar], [Publisher]

[5]. S. Korbag, I. Korbag, A new study biological role of HPV infection, oral contraceptive use, sex hormones and bisphenol A and increase rate cancer of cervical in Libya, *Journal of Medicinal and Chemical Sciences*, **2020**, *3*, 354-62. [Crossref], [Google Scholar], [Publisher]

[6]. M.F. Manzoor, T. Tariq, B. Fatima, A. Sahar, F. Tariq, S. Munir, S. Khan, M.M.A. Nawaz Ranjha, A. Sameen, X.A. Zeng, S.A. Ibrahim, An insight into bisphenol A, food exposure and its adverse effects on health: A review, *Frontiers in Nutrition*, **2022**, 9, 1047827. [Crossref], [Google Scholar], [Publisher]

[7]. M. Huang, S. Liu, L. Fu, X. Jiang, M. Yang, Bisphenol A and its analogues bisphenol S, bisphenol F and bisphenol AF induce oxidative stress and biomacromolecular damage in human granulosa KGN cells, *Chemosphere*, **2020**, *253*, 126707. [Crossref], [Google Scholar], [Publisher]

[8]. P. Alonso-Magdalena, S. Morimoto, C. Ripoll, E. Fuentes, A. Nadal, The estrogenic effect of bisphenol A disrupts pancreatic β-cell function in vivo and induces insulin resistance, *Environmental Health Perspectives*, **2006**, *114*, 106-112. [Crossref], [Google Scholar], [Publisher]

[9]. S. Mahalingaiah, J.D. Meeker, K.R. Pearson, A.M. Calafat, X. Ye, J. Petrozza, R. Hauser, Temporal variability and predictors of urinary bisphenol A concentrations in men and women, *Environmental health perspectives*, **2008**, *116*, 173-178. [Crossref], [Google Scholar], [Publisher]

[10]. N. Seltenrich, Bisphenol exposure and type 2 diabetes: New evidence for a potential risk factor, *Environmental Health Perspectives*, **2020**, *128*, 074006. [Crossref], [Google Scholar], [Publisher]

[11]. K. Hercog, S. Maisanaba, M. Filipič, M. Sollner-Dolenc, L. Kač, B. Žegura, Genotoxic activity of bisphenol A and its analogues bisphenol S, bisphenol F and bisphenol AF and their mixtures in human hepatocellular carcinoma (HepG2) cells, *Science of The Total Environment*, **2019**, *687*, 267–276. [Crossref], [Google Scholar], [Publisher]

[12]. A. Shankar, S. Teppala, C. Sabanayagam, Urinary bisphenol a levels and measures of obesity: results from the national health and

nutrition examination survey 2003–2008, *International Scholarly Research Notices*, **2012**, *2012*, 965243. [Crossref], [Google Scholar], [Publisher]

[13]. M.M. Stojanoska, N. Milosevic, N. Milic, L. Abenavoli, The influence of phthalates and bisphenol A on the obesity development and glucose metabolism disorders, *Endocrine*, **2017**, *55*, 666–681. [Crossref], [Google Scholar], [Publisher]

[14]. A. Mendy, P.M. Salo, J. Wilkerson, L. Feinstein, K.K. Ferguson, M.B. Fessler, P.S. Thorne, D.C. Zeldin, Association of urinary levels of bisphenols F and S used as bisphenol A substitutes with asthma and hay fever outcomes, *Environmental Research*, **2020**, *183*, 108944. [Crossref], [Google Scholar], [Publisher]

[15]. P. Loganathan, S. Vigneswaran, J. Kandasamy, T.V. Nguyen, A. Katarzyna Cuprys, H. Ratnaweera, Bisphenols in water: Occurrence, effects, and mitigation strategies, *Chemosphere*, **2023**, *328*, 138560. [Crossref], [Google Scholar], [Publisher]

[16]. E. Danzl, K. Sei, S. Soda, M. Ike, M. Fujita, Biodegradation of bisphenol A, bisphenol F and bisphenol S in seawater, *International journal of environmental research and public health*, **2009**, *6*, 1472–1484. [Crossref], [Google Scholar], [Publisher]

[17]. K. Czarny, B. Krawczyk, D. Szczukocki, Toxic effects of bisphenol A and its analogues on cyanobacteria Anabaena variabilis and Microcystis aeruginosa, *Chemosphere*, **2021**, *263*, 128299. [Crossref], [Google Scholar], [Publisher]

[18]. G. Russo, F. Barbato, D.G. Mita, L. Grumetto, Occurrence of bisphenol A and its analogues in some foodstuff marketed in Europe, *Food and Chemical Toxicology*, **2019**, *131*, 110575. [Crossref], [Google Scholar], [Publisher]

[19]. A. Ullah, M. Pirzada, S. Jahan, H. Ullah, N. Turi, W. Ullah, M.F. Siddiqui, M. Zakria, K.Z. Lodhi, M.M. Khan, Impact of low-dose chronic exposure to bisphenol A and its analogue bisphenol B, bisphenol F and bisphenol S on hypothalamo-pituitary-testicular activities in adult rats: A focus on the possible hormonal mode of action, *Food and Chemical Toxicology*, **2018**, *121*, 24-36. [Crossref], [Google Scholar], [Publisher]

[20]. X. Zhu, G. Wu, Y. Xing, C. Wang, X. Yuan, B. Li, Evaluation of single and combined toxicity of bisphenol A and its analogues using a highly-sensitive micro-biosensor, *Journal of hazardous materials*, **2020**, *381*, 120908. [Crossref], [Google Scholar], [Publisher]

[21]. A. Usman, M. Ahmad, From BPA to its analogues: Is it a safe journey?, *Chemosphere*, **2016**, *158*, 131–142. [Crossref], [Google Scholar], [Publisher]

[22]. J.R. Rochester, A.L. Bolden, Bisphenol S and F: A systematic review and comparison of the hormonal activity of bisphenol A substitutes, *Environmental Health Perspectives,* **2015**, *123*, 643–650. [Crossref], [Google Scholar], [Publisher]

[23]. C. Simoneau, S. Valzacchi, V. Morkunas, L. Van den Eede, Comparison of migration from polyethersulphone and polycarbonate baby bottles, *Food additives & contaminants. Part A*, **2011**, *28*, 1763–1768. [Crossref], [Google Scholar], [Publisher]

[24]. S.M. Korbag, I.M. Korbag, A.B. Iqrin, Risks of cosmetics and level of awareness of both genders in Libya, *Nigerian Journal of Technology*, **2022**, *41*, 114-122. [Crossref], [Google Scholar], [Publisher]

[25]. C. Liao, K. Kannan, A survey of alkylphenols, bisphenols, and triclosan in personal care products from China and the United States, *Archives of Environmental Contamination and Toxicology*, **2014**, *67*, 50–59. [Crossref], [Google Scholar], [Publisher]

[26]. K. Hao, J. Luo, J. Sun, H. Ge, Z. Wang, Associations of urinary bisphenol A and its alternatives bisphenol S and F concentrations with depressive symptoms among adults, *Chemosphere*, **2021**, *279*, 130573. [Crossref], [Google Scholar], [Publisher]

[27]. R. Kuruto-Niwa, R. Nozawa, T. Miyakoshi, T. Shiozawa, Y. Terao, Estrogenic activity of alkylphenols, bisphenol S, and their chlorinated derivatives using a GFP expression system, *Environmental Toxicology and Pharmacology*, **2005**, *19*, 121–130. [Crossref], [Google Scholar], [Publisher]

[28]. X. Fu, J. Xu, R. Zhang, J. Yu, The association between environmental endocrine disruptors and cardiovascular diseases: A systematic review and meta-analysis, *Environmental Research*, **2020**, *187*, 109464. [Crossref], [Google Scholar], [Publisher]

[29]. J. Zhou, X.H. Chen, S.D. Pan, J.L. Wang, Y.B. Zheng, J.J. Xu, Y.G. Zhao, Z.X. Cai, M.C. Jin, Contamination status of bisphenol A and its analogues (bisphenol S, F and B) in foodstuffs and the implications for dietary exposure on adult residents in Zhejiang Province, *Food Chemistry*, **2019**, *294*, 160–170. [Crossref], [Google Scholar], [Publisher]

[30]. S. Eladak, T. Grisin, D. Moison, M.J. Guerquin, T. N'Tumba-Byn, S. Pozzi-Gaudin, A. Benachi, G. Livera, V. Rouiller-Fabre, R. Habert, A new chapter in the bisphenol A story: bisphenol S and bisphenol F are not safe alternatives to this compound, *Fertility and Sterility*, **2015**, *103*, 11–21. [Crossref], [Google Scholar], [Publisher]

[31]. Z. Meng, D. Wang, S. Yan, R. Li, J. Yan, M. Teng, Z. Zhou, W. Zhu, Effects of perinatal exposure to BPA and its alternatives (BPS, BPF and BPAF) on hepatic lipid and glucose homeostasis in female mice adolescent offspring, *Chemosphere*, **2018**, *212*, 297–306. [Crossref], [Google Scholar], [Publisher]

[32]. S. Lee, C. Kim, H. Shin, Y. Kho, K. Choi, Comparison of thyroid hormone disruption potentials by bisphenols A, S, F, and Z in embryo-larval zebrafish, *Chemosphere*, **2019**, *221*, 115–123. [Crossref], [Google Scholar], [Publisher]

[33]. Y. Zhang, M. Huang, P. Zhuang, J. Jiao, X. Chen, J. Wang, Y. Wu, Exposure to acrylamide and the risk of cardiovascular diseases in the national health and nutrition examination survey 2003-2006, *Environment International*, **2018**, *117*, 154–163. [Crossref], [Google Scholar], [Publisher]

[34]. M. Audebert, L. Dolo, E. Perdu, J.P. Cravedi, D. Zalko, Use of the γH2AX assay for assessing the genotoxicity of bisphenol A and bisphenol F in human cell lines, *Archives of Toxicology*, **2011**, *85*, 1463–1473. [Crossref], [Google Scholar], [Publisher]

[35]. W. Qiu, H. Shao, P. Lei, C. Zheng, C. Qiu, M. Yang, Y. Zheng, Immunotoxicity of bisphenol S and F are similar to that of bisphenol A during zebrafish early development, *Chemosphere*, **2018**, *194*, 1–8. [Crossref], [Google Scholar], [Publisher]

[36]. W. Qiu, M. Yang, S. Liu, P. Lei, L. Hu, B. Chen, M. Wu, K.J. Wang, Toxic effects of bisphenol S showing immunomodulation in fish macrophages, *Environmental Science & Technology*, **2018**, *52*, 831–838. [Crossref], [Google Scholar], [Publisher]

[37]. D.K. Tucker, Hayes S. Bouknight, S.S. Brar, G.E. Kissling, S.E. Fenton, Evaluation of prenatal exposure to bisphenol analogues on development and long-term health of the mammary gland in female mice, *Environmental Health Perspectives*, **2018**, *126*, 087003. [Crossref], [Google Scholar], [Publisher]

[38]. Y. Feng, Z. Jiao, J. Shi, M. Li, Q. Guo, B. Shao, Effects of bisphenol analogues on steroidogenic gene expression and hormone synthesis in H295R cells, *Chemosphere*, **2016**, *147*, 9–19. [Crossref], [Google Scholar], [Publisher]

[39]. M.Y. Chen, M. Ike, M. Fujita, Acute toxicity, mutagenicity, and estrogenicity of bisphenol-A and other bisphenols. *Environmental Toxicology*, **2002**, *17*, 80–86. [Crossref], [Google Scholar], [Publisher]

[40]. K. Yamasaki, S. Noda, N. Imatanaka, Y. Yakabe, Comparative study of the uterotrophic potency of 14 chemicals in a uterotrophic assay and their receptor-binding affinity, *Toxicology Letters*, **2004**, *146*, 111–120. [Crossref], [Google Scholar], [Publisher]

[41]. K. Ji, S. Hong, Y. Kho, K. Choi, Effects of bisphenol s exposure on endocrine functions and reproduction of zebrafish, *Environmental*

Science & Technology, **2013**, *47*, 8793–8800. [Crossref], [Google Scholar], [Publisher]

[42]. Z. Xiao, R. Wang, D. Suo, T. Li, X. Su, Trace analysis of bisphenol A and its analogues in eggs by ultra-performance liquid chromatography-tandem mass spectrometry, *Food Chemistry*, **2020**, *327*, 126882. [Crossref], [Google Scholar], [Publisher]

[43]. a) X. Li, Y. Liu, Y. Chen, X. Song, X. Chen, N. Zhang, H. Li, Y. Guo, Z. Wang, Z. Dong, Long-term exposure to bisphenol A and its analogues alters the behavior of marine medaka (Oryzias melastigma) and causes hepatic injury, *Science of The Total Environment*, **2020**, *841*, 156590. [Crossref], [Google Scholar], [Publisher] b) M. Khalil, S. Noor, Z. Ahmad, F. Ahmad, Fate of Pakistani exported mango due to its toxicity (Heavy metals, pesticides, and other toxic organic components), *Journal of Applied Organometallic Chemistry*, **2023**, *3*, 86-107. [Crossref], [Publisher]

[44]. K. Ji, S. Hong, Y. Kho, K. Choi, Effects of bisphenol s exposure on endocrine functions and reproduction of zebrafish, *Environmental Science & Technology*, **2013**, *47*, 8793–8800. [Crossref], [Google Scholar], [Publisher]

[45]. Y.M. Wong, R. Li, C.K.F. Lee, H.T. Wan, C.K.C. Wong, The measurement of bisphenol A and its analogues, perfluorinated compounds in twenty species of freshwater and marine fishes, a time-trend comparison and human health based assessment, *Marine Pollution Bulletin*, **2017**, *124*, 743–752. [Crossref], [Google Scholar], [Publisher]

[46]. M. Naderi, M.Y. Wong, F. Gholami, Developmental exposure of zebrafish (*Danio rerio*) to bisphenol-S impairs subsequent reproduction potential and hormonal balance in adults, *Aquatic Toxicology*, **2014**, *148*, 195–203. [Crossref], [Google Scholar], [Publisher]

[47]. a) H. Kojima, S. Takeuchi, S. Sanoh, K. Okuda, S. Kitamura, N. Uramaru, K. Sugihara, K. Yoshinari, Profiling of bisphenol A and eight its analogues on transcriptional activity via human nuclear receptors, *Toxicology*, **2019**, *413*, 48–55. [Crossref], [Google Scholar], [Publisher] b) R.S. Nabila, N. Darsini, A. Agustinus, Evaluation of the protective role of marigold leaf extract ethanol on FSH levels in male laboratory mice exposed to cigarette smoke, *Journal of Medicinal and Chemical Sciences*, **2023**, *6*, 3036-3043. [Crossref], [[Publisher]

[48]. E. Clark, Sulfolane and sulfones, Kirk-Othmer encyclopedia of chemical technology, John Wiley & Sons, New York, **2000**. [Crossref], [Google Scholar], [Publisher]

[49]. a) H. Wang, Z.H. Liu, J. Zhang, R.P. Huang, H. Yin, Z. Dang, Human exposure of bisphenol A and its analogues: understandings from human urinary excretion data and wastewater-based epidemiology, *Environmental Science and Pollution Research*, **2020**, *27*, 3247–3256. [Crossref], [Google Scholar], [Publisher] b) R. Sha'Ato, A.U. Itodo, A.A. Ugbedeojo, Chemical screening for codeine and tramadol in urine of anonymous students attending university sick bays. *Journal of Medicinal and Chemical Sciences*, **2020**, *3*, 208-218. [Crossref], [Google Scholar], [Publisher]

[50]. Y. Della Rocca, E.M. Traini, F. Diomede, L. Fonticoli, O. Trubiani, A. Paganelli, J. Pizzicannella, G.D. Marconi, Current evidence on bisphenol A exposure and the molecular mechanism involved in related pathological conditions, *Pharmaceutics*, **2023**, 15, 908. [Crossref], [Google Scholar], [Publisher]

[51]. Y.H. Neggers, Increasing prevalence, changes in diagnostic criteria, and nutritional risk factors for autism spectrum disorders, *International Scholarly Research Notices*, **2014**, *2014*, 514026. [Crossref], [Google Scholar], [Publisher]

[52]. S. Kang, B.H. Shin, J.A. Kwon, C.W. Lee, E.K. Park, E.Y. Park, B. Kim, Urinary bisphenol A and its analogues and haemato-biochemical alterations of pregnant women in Korea, *Environmental Research*, **2020**, *182*, 109104. [Crossref], [Google Scholar], [Publisher]

[53]. D.C. Bellinger, Prenatal exposures to environmental chemicals and children's neurodevelopment: An update, *Safety and Health at Work*, **2013**, *4*, 1–11. [Crossref], [Google Scholar], [Publisher]

[54]. J. Jurewicz, K. Polańska, W. Hanke, Exposure to widespread environmental toxicants and children's cognitive development and behavioral problems, *International Journal of Occupational Medicine and Environmental Health*, **2013**, *26*, 185–204. [Crossref], [Google Scholar], [Publisher]

[55]. T.E. Arbuckle, K. Davis, K. Boylan, M. Fisher, J. Fu, Bisphenol A, phthalates and lead and learning and behavioral problems in Canadian children 6–11 years of age: CHMS 2007–2009, *Neuro Toxicology*, **2016**, *54*, 89-98. [Crossref], [Google Scholar], [Publisher]

[56]. Y. Li, H. Zhang, H. Kuang, R. Fan, C. Cha, G. Li, Z. Luo, Q. Pang, Relationship between bisphenol A exposure and attention-deficit/ hyperactivity disorder: A case-control study for primary school children in Guangzhou, China, *Environmental Pollution*, **2018**, *235*, 141–149. [Crossref], [Google Scholar], [Publisher]

[57]. S.L. Stacy, G.D. Papandonatos, A.M. Calafat, A. Chen, K. Yolton, B.P. Lanphear, J.M. Braun, Early life bisphenol A exposure and neurobehavior at 8 years of age: identifying windows of heightened vulnerability, *Environment International*, **2017**, *107*, 258-265. [Crossref], [Google Scholar], [Publisher]

[58]. C.C. Lin, C.J. Chien, M.S. Tsai, C.J. Hsieh, W.S. Hsieh, P.C. Chen, Prenatal phenolic compounds exposure and neurobehavioral development at 2 and 7 years of age, *Science of The Total Environment*, **2017**, *605-606*, 801–810. [Crossref], [Google Scholar], [Publisher]

[59]. R. Pan, C. Wang, R. Shi, Y. Zhang, Y. Wang, C. Cai, Y. Gao, Prenatal bisphenol A exposure and early childhood neurodevelopment in Shandong, China, *International Journal of Hygiene and Environmental Health*, **2019**, *222*, 896-902. [Crossref], [Google Scholar], [Publisher]

[60]. S. Tewar, P. Auinger, J.M. Braun, B. Lanphear, K. Yolton, J.N. Epstein, S. Ehrlich, T.E. Froehlich, Association of bisphenol A exposure and attention-deficit/hyperactivity disorder in a national sample of U.S. children, *Environmental Research*, **2016**, *150*, 112–118. [Crossref], [Google Scholar], [Publisher]

[61]. Braun, J. M., Yolton, K., Stacy, S. L., Erar, B., Papandonatos, G. D., Bellinger, D. C., Lanphear, B. P., Chen, A., Prenatal environmental chemical exposures and longitudinal patterns of child neurobehavior, *Neuro Toxicology*, **2017**, *62*, 192–199. [Crossref], [Google Scholar], [Publisher]

[62]. R. Perez-Lobato, V. Mustieles, I. Calvente, I. Jimenez-Diaz, R. Ramos, N. Caballero-Casero, M.F. Fernandez, Exposure to bisphenol A and behavior in school-age children, *Neuro Toxicology*, *53*, 12-19. [Crossref], [Google Scholar], [Publisher]

[63]. J.D. Meeker, Exposure to environmental endocrine disruptors and child development, *Archives of Pediatrics & Adolescent Medicine*, **2012**, *166*, 952-958. [Crossref], [Google Scholar], [Publisher]

[64]. L. Peyre, P. Rouimi, G. de Sousa, C. Héliès-Toussaint, B. Carré, S. Barcellini, M.C. Chagnon, R. Rahmani, Comparative study of bisphenol A and its analogue bisphenol S on human hepatic cells: a focus on their potential involvement in nonalcoholic fatty liver disease. *Food and Chemical Toxicology*, **2014**, *70*, 9–18. [Crossref], [Google Scholar], [Publisher]

[65]. M. Minatoya, S. Sasaki, A. Araki, C. Miyashita, T. Ikeno, T. Nakajima, R. Kishi, Effects of prenatal phthalate exposure on thyroid hormone levels, mental and psychomotor development of infants: The Hokkaido Study on Environment and Children's Health, *Science of The Total Environment*, **2016**, *565*, 1037-1043. [Crossref], [Google Scholar], [Publisher]

[66]. C.G. Bornehag, C. Lindh, A. Reichenberg, S. Wikström, M. Unenge Hallerback, S.F. Evans, S. Sathyanarayana, E.S. Barrett, R.H.N. Nguyen, N.R. Bush, S.H. Swan, Association of prenatal phthalate exposure with language development in early childhood, *JAMA Pediatrics*, **2018**, *172*, 1169–1176. [Crossref], [Google Scholar], [Publisher]

[67]. X. Qian, J. Li, S. Xu, Y. Wan, Y. Li, Y. Jiang, W. Xia, Prenatal exposure to phthalates and neurocognitive development in children at two years of age, *Environment International*, **2019**,

131, 105023. [Crossref], [Google Scholar], [Publisher]

[68]. X. Xu, L. Xie, X. Hong, Q. Ruan, H. Lu, Q. Zhang, X. Liu, Perinatal exposure to bisphenol-A inhibits synaptogenesis and affects the synaptic morphological development in offspring male mice, *Chemosphere*, **2013**, *91*, 1073-1081. [Crossref], [Google Scholar], [Publisher]

[69]. J. Cao, J.A. Mickens, K.A. McCaffrey, S.M. Leyrer, H.B. Patisaul, Neonatal bisphenol A exposure alters sexually dimorphic gene expression in the postnatal rat hypothalamus, *Neuro Toxicology*, 33, 23–36. [Crossref], [Google Scholar], [Publisher]

[70]. J.D. Elsworth, J.D. Jentsch, C.A. Vandevoort, R.H. Roth, D.E. Redmond, C. Leranth, Prenatal exposure to bisphenol A impacts midbrain dopamine neurons and hippocampal spine synapses in non-human primates, *Neuro Toxicology*, **2013**, *35*, 113–120. [Crossref], [Google Scholar], [Publisher]

[71]. B.S. Rubin, J.R. Lenkowski, C.M. Schaeberle, L.N. Vandenberg, P.M. Ronsheim, A.M. Soto, Evidence of altered brain sexual differentiation in mice exposed perinatally to low, environmentally relevant levels of bisphenol A, *Endocrinology*, **2006**, *147*, 3681–3691. [Crossref], [Google Scholar], [Publisher]

[72]. S. Tando, K. Itoh, T. Yaoi, H. Ogi, S. Goto, M. Mori, S. Fushiki, Bisphenol A exposure disrupts the development of the locus coeruleus-noradrenergic system in mice, *Neuropathology*, **2014**, *34*, 527–534. [Crossref], [Google Scholar], [Publisher]

[73]. T. Chen, W. Yang, Y. Li, X. Chen, S. Xu, Mono-(2-ethylhexyl) phthalate impairs neurodevelopment: inhibition of proliferation and promotion of differentiation in PC12 cells, *Toxicology Letters*, **2011**, *201*, 34–41. [Crossref], [Google Scholar], [Publisher]

[74]. R. Wang, X. Xu, Q. Zhu, Pubertal exposure to di-(2-ethylhexyl) phthalate influences social behavior and dopamine receptor D2 of adult female mice, *Chemosphere*, **2016**, *144*, 1771–1779. [Crossref], [Google Scholar], [Publisher]

[75]. M. Tohmé, S.M. Prud'homme, A. Boulahtouf, E. Samarut, F. Brunet, L. Bernard, W. Bourguet, Y. Gibert, P. Balaguer, V. Laudet, Estrogen-related receptor γ is an in vivo receptor of bisphenol A, *The FASEB Journal*, **2014**, *28*, 3124–3133. [Crossref], [Google Scholar], [Publisher]

[76]. G.G. Kuiper, J.G. Lemmen, B. Carlsson, J.C. Corton, S.H. Safe, P.T. van der Saag, B. van der Burg, J.A. Gustafsson, Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta, *Endocrinology*, **1998**, *139*, 4252–4263. [Crossref], [Google Scholar], [Publisher]

[77]. H.J. Lee, S. Chattopadhyay, E.Y. Gong, R.S. Ahn, K. Lee, Antiandrogenic effects of bisphenol A and nonylphenol on the function of androgen receptor, *Toxicological Sciences*, **2003**, *75*, 40–46. [Crossref], [Google Scholar], [Publisher]