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A Chemical Invasion on Waters and Aquatic Organisms: Bisphenol A

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ABSTRACT

The main reason for the intense discharge of chemical pollutants into nature is the increase in the world population. These pollutants disrupt the natural balance in soil, water and air. However, this effect is most prominent in the aquatic ecosystem. These pollutants are considered to be predominantly endocrine disruptors (EDCs) and which well-known EDC is bisphenol A (BPA). BPA is a chemical used in making polycarbonate plastics and epoxy resins. Also, it is one of the most produced chemicals worldwide and it cause serious problems to health of aquatic population. The most common problems are increased abnormalities of reproductive systems, deformities in developing embryos, deformation in behavioral activities This review provides information about the discharge routes of BPA, its effects in the aquatic system and its mechanisms of action.

Sularda ve Akuatik Canlılarda Kimyasal Bir İstila: Bisfenol A

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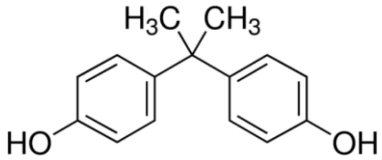
ÖZET

Kimyasal kirleticilerin doğaya yoğun bir şekilde atılmasının temel nedeni dünya nüfusunun artmasıdır. Bu kirleticiler toprak, su ve havadaki doğal dengeyi bozar. Bununla birlikte, bu etki en çok su ekosisteminde belirgindir. Bu kirleticilerin ağırlıklı olarak endokrin bozucu kimyasallar (EBK) olduğu ve iyi bilinen EBK'nın Bisfenol A (BPA) olduğu bildirilmektedir. BPA polikarbonat plastiklerin ve epoksi reçinelerin yapımında kullanılan bir kimyasaldır. Ayrıca dünya çapında en çok üretilen kimyasallardan biridir ve sucul popülasyonun sağlığında ciddi sorunlara neden olur. En yaygın problemler üreme sistemlerindeki anormallikler, gelişen embriyolardaki deformiteler, davranışsal aktivitelerdeki deformasyonlardır. Bu derleme, BPA'nın deşarj yolları, su sistemindeki etkileri ve etki mekanizmaları hakkında bilgi vermektedir.

1. Introduction

Synthetic chemicals that may simulation or intruded with the body's hormones are referred as EDCs. These substances have an effect on production, release, transmission, destruction and elimination of hormones in the body (Uğuz et al., 2009). Some of EDCs are 4-nonylphenol (NP), bisphenol A (BPA), bisphenol S (BPS), octylphenol (OP), vinclozolin and diethylstilbestrol (DES). BPA which was observed mostly in the nature among these EDCs is a colorless solid, classified in phenol group. BPA (4,4'-dihydroxy-2,2-diphenylpropane) is a colorless solid, classified in phenol group, synthesized by condensing acetone with two moles of phenol, solute in organic solvents but poorly solute in water (Minaz et al., 2022a) The physicochemical properties of BPA are shown in Table 1.

Table 1. The physicochemical properties of BPA (Umar et al., 2013; Wirasnita et al., 2014)

Properties	**Bisphenol A**
Molecular structure	
Molecular weight (g/mol)	228,29
Decomposition point (°C)	220
Melting point (°C)	150-155
Boiling point (°C)	220
Solubility, in water (25°C; mg/L)	120 – 300
Dissolution, (28°C; g/kg)	Ethanol, ether, benzene
Density (25°C; g/cm^3)	1,195

BPA is robust enough to substitute steel and transparent enough to substitute glass. Therefore, its usage areas are expanding day by day. BPA is used in the manufacture of plastic and industrial products such as food and beverage packaging, adhesives, electronic parts, safety equipment (Namat et al., 2021).

Numerous taxonomic groups have been studied for fresh and marine water, worms, mollusks, sponges, amphibians, insects, fish, crustaceans, algae, and hydra to identify the toxicity of BPA on aquatic animals (Mihaich et al., 2009; Staples et al., 1998, 2002, 2008; Minaz et al., 2022a,b; Diler et al., 2022; Faheem and Lone, 2018).

2. Production, Distribution and Degradation pathways of BPA

BPA is an organic pollutant, primarily produced from phenol and acetone, usually used as a basic monomer in a variety of plastics (epoxy resins, polyethersulphones, polycarbonates, polyesters etc.). BPA is produced by acid catalyzed condensation reaction of two moles of phenol and one mole of acetone. In the production of BPA, the reaction of phenol and acetone is carried out in the presence of a strong acid such as hydrochloric acid. Polycarbonates, epoxy resins, polyethersulphones, polyesters are produced from BPA released as a result of this reaction (Parkinson, 2001). It is shown in Figure 1 (Liguori et al., 2020). BPA has the strength and transparency to replace steel and glass (Vogel, 2009). BPA is commonly used in the production of polycarbonate (74% of production) and epoxy resin (20% of production) (Konieczna et al., 2015). Polycarbonates is used food and beverage containers, medical devices, protective equipment, greenhouses, disks and lighting fittings. Epoxy resins are mainly used for the production of industrial coatings, paints and adhesives (Nane et al., 2021).

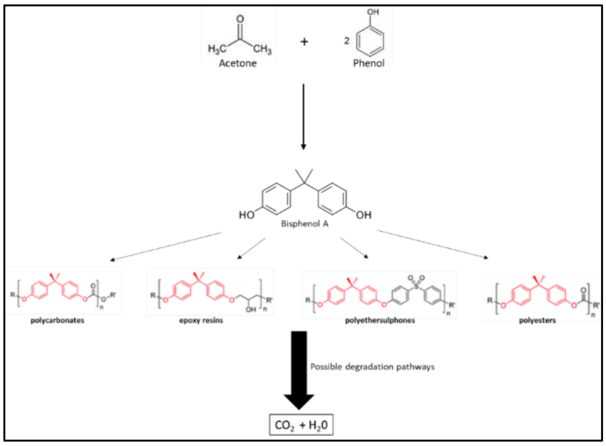


Figure 1. Synthesis of BPA and BPA-based products (Chruściel et al., 2019; Garg et al., 2019; Liguori et al., 2020).

Polycarbonates, epoxy resins, polyethersulfones, polyesters are encountered every day in our daily life. These plastics input the seas, rivers and lakes in different ways such as via wastewater treatment plants, leaching from landfills, and the biodegradation of plastics in the environment (Sidhu et al., 2005; Kinney et al., 2006; Crain et al., 2007; Kang et al., 2007; Anonymous, 2010).

Both detection and treatment studies for BPA in aquatic environment are reported to continue in parallel (Chen et al., 2016; Zhang et al., 2019; Wang et al., 2020). The water-octanol partition coefficient Kow for BPA in the aquatic environs is reported as 3.47±0.08. This situation indicates moderate bioaccumulation of BPA in matrices such water, air and sediment (Borrirukwisitsak et al., 2012).

BPA in the aquatic environment can be exposed to photodegradation (Neamţu and Frimmel 2006; Lu et al., 2013; Kong et al., 2020), photoelectrocatalytic oxidation (Brugnera et al., 2010; Wang et al., 2019; Zhang et al., 2019), oxidation (Deborde et al., 2008; Burgos-Castillo et al., 2018; Wang et al., 2019), and biodegradation (Kang et al., 2006; Xiong et al., 2017; Tong et al., 2021) by microorganisms, plant activities and aquatic organisms. Biodegradation is a method used to remove chemicals from water (Zhang et al., 2013). BPA in aquatic ambient is decomposed with microorganisms (Dorn et al.,1987; Staples et al., 1998). Microorganism strains belonging to degradation are isolated from soil, clay, river, sea water, agricultural soil and even food samples (Kang et al., 2006; Melcer and Klečka 2011; Kamaraj et al., 2018). Bacteria are shown separately as gram positive and gram negative in Table 2 and Table 3.

Table 2. Recommended gram-negative strains for BPA

Gram-negative strains	Studies
***Sphingomonas* sp.**	(Gao et al., 2022; Jia et al., 2020; Kolvenbach et al., 2007; Matsumura et al., 2009; Oshiman et al., 2007; Sakai et al., 2007; Yamanaka et al., 2008)
***Pseudomonas* sp.**	(Eltoukhy et al., 2020; Him, Zainuddin, and Basha 2017; Kang and Kondo 2002; Kučić Grgić et al., 2019; Noszczyńska et al., 2021; Fischer et al., 2010; Zhang et al., 2007)
***Achromobacter* sp.**	(Fischer et al., 2010; Zhang et al., 2007)
***Nitrosomonas* sp.**	(Roh et al., 2009)
***Croceicoccus bisphenolivorans* sp.**	(Li et al., 2021)
***Bacillus megaterium* sp.**	(Suyamud et al., 2018)
***Pandoraea* sp.**	(Matsumura et al., 2009)
***Cupriavidus* sp.**	(Fischer et al., 2010; Zhang et al., 2007; Zühlke et al., 2017)
***Acinetobacter* sp.**	(Noszczyńska et al., 2021)
***Virgibacillus* sp.**	(Kamaraj et al., 2018)

Table 3. Recommended gram-pozitive strains for Bisphenol A

Gram-pozitive strains	Studies
***Streptomyces* sp.**	(Das et al., 2018; Kamaraj et al., 2014; Kang et al., 2004; Kučić Grgić et al., 2019; Matsumura et al., 2009; Saiyood et al., 2010)
***Bacillus* sp.**	(Das et al., 2018; Kamaraj et al., 2014; Matsumura et al., 2009; Saiyood et al., 2010)

BPA-degrading bacteria communities differ greatly with strain specificity. In addition, physicochemical properties (temperature, pH, oxygen, salinity etc.) of water affect degradation (Zhang et al., 2013). BPA is rapidly degraded in the with half-lives in water and soil of nearly five days. The rate of degradation in air is even shorter, with a relatively short time of about one day (Cousins et al., 2002). However, it is quite common in biota (Oehlmann et al., 2009). The size of bacterial population in BPA degradation, aerobic and anaerobic conditions; river, lake or sea water has different effects. These conditions affect complete degradation and mineralization (Kleĉka et al., 2001; Sajiki and Yonekubo 2002, 2003; Kang and Kondo 2005; Zhang et al., 2007). For example, while BPA is easily degraded by bacteria in fresh water as degrades in sea water in about 40 days (Kang and Kondo 2005; Danzl et al., 2009). BPA is a carbon source for the bacterial environment and bacteria can easily use it. It is converted into metabolites unless the bacteria cannot fully use BPA (Gao et al., 2022).

3. Bioaccumulation of BPA

Bioaccumulation is run of a chemical entering into the organism from water, sediment, soil, air, or diet. It is explained by the bioaccumulation factor (BAF). However, bioaccumulation in water is expressed by measuring it as a bioconcentration factor (BCF) (Anonymous 1999a; Anonymous 1999b; Goulet et al., 2011). The United States Environmental Protection Agency (USEPA) has reported that bioconcentration factor (BCF) of BPA is less than 1000, the concern threshold. So, they would classify BPA as “not a bioaccumulate chemical of concern” (Staples et al., 1998). Bioaccumulation is generally thought to occur at high BPA concentrations. It is believed to be biodegradable or metabolized at low concentrations. In a study on this subject, trout were exposed to 100 µg/BPA L for 2 hours. Then the bioaccumulation factor was calculated and values of approximately 3.5-5.5 BCF were found (Lindholst et al., 2001).

4. Metabolic destiny of BPA

The mechanism of action of all chemicals is different. After any chemical is taken into the organism, it determines different metabolic pathways. So that comprehend the chemical mechanism of the effects of BPA in a body, it is very important to know the metabolic pathway of in the organisms. The main pathway of exposure BPA in aquatic animals is through the gills and skin (Kang et al., 2007). In aquatic organisms, BPA can be taken into the body in several ways (gill, skin or mouth). BPA that chooses one of these must pass across the gastrointestinal system and liver before achieving target tissues. It is possible to enlighten the fate of the compound by watching it pass through these paths step by step. Once the compound reaches the target tissue, it begins to break down into metabolites. While xenobiotics break down into their metabolites in tissues, they encounter protective barriers to reduce their potential harmful effects. These barriers are known as the hepatointestinal pathway. The hepatointestinal tract consists of 3 parts (Bock, 2014). In the first category, it consists of P450 (CYP), which is one of the primary phases I type detoxification enzymes found in continental or aquatic animals. Xenoestrogen or xenobiotic type drugs are separated into their metabolites by CYPs (Nelson et al., 1993; Snyder, 2000). The second category is the class of those called phase II enzymes. Phase II enzymes break down BPA into its metabolites by glucuronidation (Figure 2). Glucuronidation; it is the main route of biotransformation of endogenous compounds and takes place in the liver (Mackenzie et al., 1997; MacKenzie et al., 2003; Di Pietro et al., 2010). The third category consists of drug carriers, which are proteins responsible for drug uptake and excretion (Hediger et al., 2004; Iwano et al., 2018).

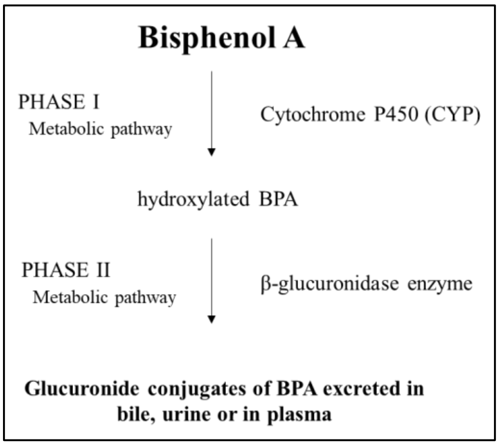


Figure 2. Metabolism and elimination of bisphenol A, fish and rat (van den Berg et al., 2003; Iwano et al., 2018)

Metabolic destiny of BPA exposure had been first identified in the rats (Knaak and Sullivan, 1966). The rats were fed orally with BPA for 8 days and at the end of the period, urine and fecal matters were sampled. The results show that BPA is initially discharged as the glucuronide. In another, rainbow trout was exposed to BPA and its metabolites were examined in muscle, liver, and plasma samples. Glucuronitated degradation products were found in the blood plasma of fish groups exposed intraperitoneally and in water. According to the results obtained from the present experiment; glucuronidated products are reported to be a xenoestrogen more susceptible than BPA (Lindholst et al., 2001).

BPA contains two phenol rings as its molecular structure. Therefore, metabolites produced from BPA are expected to be sulfonated and glucuronidated as degradation products. However, Atkinson and Roy (1995), had suggested a different degradation pathway. This method BPA is turned into DNA-binding metabolites in liver, by the cytochrome P450 path. Alongside the phase II metabolites produced from BPA, quinines are formed by the addition of hydroxyl to the main molecule.

5. Estrogenic Effects of BPA

BPA can cause feminization on aquatic organisms (Idowu et al., 2022). Increasing information about BPA's properties that mimic estrogen and its possible toxic effects is evidence that this chemical may have negative consequences on the fertility of aquatic organisms. It has been reported in trials on estrogen receptors that BPA changes the suite of genes as the dose increases, which explains the impact at low doses, or at doses in between, can't be forecasted from high-dose tests (Vom Saal and Myers, 2008).

In recent years, researchers show that various reproductive dysfunction in humans, birds, mammals or aquatic organisms are closely related with BPA (Manzetti et al., 2014). There are different effects inside and outside the reproductive system in aquatic organisms. It can cause morphological anomalies such as gonadal size, oogenesis and behavior, immunity and metabolism (Susiarjo et al., 2007; Chen et al., 2015; Fang et al., 2016; Santangeli et al., 2016; Molina et al., 2018).

Ongoing research about BPA's properties that mimic estrogen receptors and its possible toxic effects have reported this chemical may have negative consequences on the fertility of aquatic organisms.The estrogen receptors are responsible for capturing and holding estrogens such as estradiol (female hormone) in the body (Frenzilli et al., 2021).

Xenoestrogens share some structures found in estrogens. This situation makes it easier for them to bond to the estrogen receptor. BPA chemical structure is like estradiol so in binding to the estrogen receptor, BPA can disorder the animals endocrine or hormone system (Vom Saal et al., 2007). BPA has affinity for estrogen receptors subtypes (ERα/Erβ). But this affinity is far less than 17β-estradiol, the body's most active estrogen (Calafat et al., 2009; Bolli et al., 2010;). It has been declared in trials on estrogen receptors that BPA changes the suite of genes as the dose increases, which explains the impact at low doses, or at doses in between, can't be forecasted from high-dose tests (Vom Saal and Myers, 2008). In a study on zebrafish; exposure to BPA delayed the individual's development at the level of sex differentiation or sex development. This effect of BPA exposes that it can influence the process whereby the gonad transformation into an ovary or testis (Song et al., 2020).

Labeo bata was treated with BPA (2 and 4 μM/L) and the data were consistent with the induction of vitellogene, which was used as a biomarker for fish and egg vertebrates to examine estrogen exposure. Again, in the same experiment, BPA modified the gene expression of estrogen receptors subtypes (ERα/ERβ) (Mukherjee et al., 2020). Many works have declared that gonadal development is affected opposite in aquatic microorganisms (Luo et al., 2017; Wang et al., 2019; Forner-Piquer et al., 2020).

6. Carcinogenic effects

Recent studies for the endocrine disruptor BPA in human from birth defects to reproductive disorders, from tissue damage to obesity, its negative effects have been tried to be clarified. However, there are still many unexplained questions and problems. Arguments from in vivo and in vitro surveys has suggested an association between increased ratio of cancer and BPA exposure at dose measures (Wang et al., 2017).

Endocrine disrupting chemicals are known to often mimic sex steroids. Therefore, the breeding system is thought to be especially sensible to this chemical., Most study in the discipline of endocrine disruption has centered on breeding modification (Ankley et al., 2001; Gray Jr et al., 2002; Parrott and Wood 2002; Van der Oost et al., 2003; Kloas et al., 2009). Carcinogenic effects are also related to whether there is a health problem transmitted from generation to generation (Al-Sakran et al., 2016). Other researchers guided research to examine the transgenerational abnormalities and health problems of

BPA and 17a-ethinylestradiol (EE2) in medaka. In the trial established by exposure to three generations of BPA and EE2; first embryo (F0) and the fry medaka (F1) produced from this embryo did not reason any significant phenotypic anomalies. However, after two generations, fry (F2) led to an expressive reduce in fertilization ratio and after three generations, embryo survival in offspring (F3) was reduced (Bhandari et al., 2015).

7. BPA-Based Histopathological Changes in Aquatic Organisms

Fish accumulate all the toxic substances they take into their bodies in the aquatic environment. It is accepted as an indicator of environmental pollution. Histopathological examination of fish tissues enables early warning signs of possible diseases. Many histopathological studies have been done on the kidney, liver, gill, and gonad tissues of aquatic animals. Chemical exposure in fish occurs through the gills (Kang et al., 2007). Mosquito fish and guppy fish tissues were examined in research to evaluate the histopathological effect of BPA exposure in gill tissues. All of samples were exposed to 50µg/L BPA, for short and long term. In gills from fish treated with BPA were observed necrosis and desquamation, edema. (Elshaer et al., 2013). Damage to gill tissues has been reported in other studies on BPA exposure (Chitra and Sajitha, 2014; Faheem et al., 2016). Liver has biomarkers that ensure whether living things have been exposed to environmental stress factors before. In addition, this organ is important in terms of uptake of contaminants and ensuring biotransformation (Belfroid et al., 2002; Hatice and Şişman, 2017). In the studies carried out, degeneration, necrosis, vacuolization (Faheem et al., 2016; Li et al., 2017; Minaz et al., 2022a), central vein congestion, inflammation, edema (Faheem et al., 2016; Li et al., 2017); lipid accumulation in hepatocytes (Pathiraja and Rajapaksa, 2019) were observed. The kidneys are responsible for homeostasis, waste removal and selective reabsorption in the body lesions in this organ allow histological determinations as signs of environmental pollution (Karlsson 1983). Fish muscles are the tissue that is usually determined for the biological accumulation of toxic substances and the pathological changes caused by it. The kidney and tissue of tilapia were examined exposed to BPA for 28 days. Severe lesions in the kidney tissue, hyperplasia and necrosis of the tubular epithelium were observed. In muscle tissue, degeneration in muscle bundles, shortened muscle bundles and various degeneration were observed (Vasu et al., 2019).

8. Antioxidant Enzyme Activity Effects

Antioxidant enzyme systems that catalyze reactions to counterbalance free radicals and reactive oxygen species include superoxide dismutase (SOD), catalase (CAT), malondialdehyde (MDA), Glutathione Reductase (GR) and Glutathione S-Transferase (GST), Glutathione-peroxidase (GSH-Px) (Nazeer et al., 2012) .These form the body's endogenous defense mechanisms to help guard against free radical-induced cell damage. In a study, Antioxidant activity was determined for liver and gill tissues of O. mykiss, while there is no change in SOD and CAT values, GSH-Px values for both tissues showed a significantly lower effect (Minaz et al., 2022b). In a chronic toxicity study with Aristichthys nobilis, no difference was observed in SOD and CAT values in tissues exposed to BPA compared to the control group for 30 days (Akram et al., 2021). Crayfish, a benthic animal, has been exposed to BPA for 5 and 20 days. Antioxidant enzyme activity (SOD, GST, GR) was examined for both tests and the results were compared. The results of the experiments was considerably lower than in the control group for 5 days. In this study is claimed that A. leptodactylus had high tolerance to BPA (Diler et al., 2022)

9. Conclusion

This review of literature clearly shows that BPA is moderately toxic in the aquatic medium (Staples et al., 1998). However, this chemical not only bioaccumulates in organisms but also even the sub-lethal dosage of this chemical exerts estrogenic effects that disrupt the endocrine system. Laboratory studies have revealed that BPA causes developmental, reproductive and hormonal disorders on aquatic species. The damage caused by BPA in all species in the aquatic environment differs depending on the dose-response relationship (Canesi and Fabbri, 2015).

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Conflict of Interest

No potential conflict of interest was reported by the author(s).

Authors' Contributions

The authors declare that they have contributed equally to the article.

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