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# **Role of Fungi in Biodegradation of Bisphenol A: A Review**

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#### **SUBMITTED: 7 April 2023; REVISED: 27 June 2023; ACCEPTED: 30 June 2023**

**ABSTRACT:** Bisphenol A (BPA) is recognized as an endocrine disruptor, capable of interfering with the normal functioning of hormones within the body by mimicking the effects of estrogen. Drinking water is one of the most common pathways of exposure to BPA as it can permeate plastic products and other materials, entering water sources. This article presents a comprehensive overview of BPA, including its incidence, origins, environmental fate, its impact on human health, and the role of fungi in the biodegradation of BPA. Fungi are natural decomposers, capable of breaking down organic compounds, including BPA, under suitable conditions. Studies have demonstrated that specific species of fungi can effectively biodegrade BPA. Some fungi utilize ligninolytic enzymes, such as laccases and peroxidases, to break down the phenolic rings of BPA. Other fungi employ non-ligninolytic enzymes, such as esterases and hydrolases, to cleave the ester linkages in BPA. Furthermore, some fungi can break down BPA via cometabolic pathways, whereby the chemical is degraded as a side reaction to the degradation of another substrate. The use of immobilized enzymes for BPA degradation has also demonstrated potential. Immobilized enzymes are those that are attached to a solid support, such as a polymer or matrix, allowing them to be used multiple times and enhance their stability and catalytic activity.

**KEYWORDS:** Endocrine disruptor; ligninolytic enzymes; immobilized enzymes; cometabolic pathways.

## **1. Introduction**

Bisphenol A (BPA) is a chemical compound that is commonly used in the production of plastics and resins. It has been detected in various environmental media, including air, water, soil, and sediments. Bisphenol A (BPA) is a synthetic organic compound with the chemical formula  $(CH<sub>3</sub>)<sub>2</sub>C(C<sub>6</sub>H<sub>4</sub>OH)<sub>2</sub>$ . It is a colorless, crystalline solid that is soluble in organic solvents but poorly soluble in water [1]. BPA is classified as a phenolic compound, meaning it contains a phenol group (-OH) attached to a benzene ring. It is also classified as a diphenylmethane, meaning it contains two phenyl groups  $(-C_6H_5)$  connected by a methane group  $(-CH_2)$ . BPA is known to undergo various chemical reactions, including hydrolysis, oxidation, and esterification. It can also form complexes with certain metals, such as copper and iron. One of the key chemical characteristics of BPA is its ability to mimic the effects of estrogen in the body. This is due to its structural similarity to the hormone, which allows it to bind to estrogen receptors in the body and interfere with normal hormonal signaling pathways. This is why BPA is classified as an endocrine disruptor and is a cause for concern in terms of human health and environmental impacts [2]. Bisphenol A (BPA) is commonly used in the production of polycarbonate plastics and epoxy resins, which are widely used in the manufacturing of food and beverage containers, medical equipment, electronics, and other consumer goods [3]. However, BPA is known to leach out of these products and can enter the environment through various pathways. One of the main ways that BPA enters the environment is through the disposal of plastic products in landfills. As plastic products break down over time, BPA and other chemicals can be released into the surrounding soil and groundwater. From there, it can potentially enter nearby waterways and other ecosystems, where it can have negative impacts on wildlife and other organisms [4]. In addition to leaching out of plastic products in landfills, BPA can also be released into the environment during the manufacturing process. When plastics containing BPA are produced, the chemical can be released into the air or wastewater. This can lead to contamination of nearby waterways and soil, and can also potentially expose workers in manufacturing facilities to harmful levels of BPA. Once BPA enters the environment, it can persist for long periods of time and can potentially bioaccumulate in organisms, meaning that it can accumulate in the tissues of living organisms over time. This can have negative impacts on the health of wildlife, as well as potentially impacting human health through the consumption of contaminated food or water [5].

Studies have shown that Bisphenol A (BPA) is present in the environment at low levels, but even these low levels of exposure are a cause for concern because of the potential health effects associated with this chemical. BPA is known to be an endocrine disruptor, meaning that it can interfere with the normal function of hormones in the body. One of the key ways that BPA exerts its effects on the body is by mimicking the effects of estrogen. BPA has a similar chemical structure to estrogen, allowing it to bind to estrogen receptors in the body and disrupt normal hormonal signaling pathways. This can lead to a range of negative health effects, particularly in vulnerable populations such as developing fetuses, infants, and young children [6, 7]. Exposure to BPA has been linked to a range of health problems, including reproductive disorders, developmental delays, and cancer. For example, studies have found that exposure to BPA during pregnancy may increase the risk of miscarriage and fetal developmental abnormalities. Exposure to BPA has also been associated with hormonal imbalances, which can impact fertility and increase the risk of certain types of cancer, such as breast and prostate cancer [7, 8]. In addition to its effects on human health, BPA has also been shown to have negative impacts on wildlife and ecosystems. BPA can interfere with the reproduction and development of aquatic organisms, and has been detected in a wide range of aquatic environments. Efforts are being made to reduce exposure to BPA, particularly in vulnerable populations. Many countries have banned the use of BPA in certain products, and many companies have voluntarily phased out the use of BPA in their products [3]. However, continued research and regulatory efforts are needed to fully understand the potential health impacts of BPA and to address its presence in the environment. This article summarizes an overview of BPA including their occurrence, source, environmental fate, their impacts on human health, and the role of fungi in the degradation of BPA.

#### **2. Occurrence of bisphenol A in the environment**

#### *2.1. Water.*

One of the most common routes of exposure to BPA is through drinking water, as the chemical can leach out of plastic products and other materials into water sources. Studies have shown that BPA is present in water at low levels, but even these low levels of exposure can have negative health effects. BPA has been linked to a range of health problems, including reproductive disorders, developmental delays, and cancer. This is particularly concerning in vulnerable populations such as pregnant women, infants, and young children, who may be more susceptible to the effects of BPA exposure. BPA can enter water sources through various pathways [9]. BPA enters water through various pathways, and one of the most common ones is through the disposal of plastic products that contain BPA. As these products degrade over time, BPA can be released into the soil and groundwater, eventually entering nearby water sources. The manufacturing process can also lead to BPA entering water sources, as the chemical can be emitted into the air or wastewater [5]. Once BPA is present in water sources, it can persist for extended periods, and its accumulation in aquatic organisms is a matter of concern. BPA has the potential to bioaccumulate, meaning that it can build up in the tissues of living organisms over time, leading to toxic effects. Bioaccumulation occurs because BPA has a long half-life, which is the time it takes for half of the chemical to break down or be excreted from the body. BPA's long half-life enables it to accumulate in the tissues of organisms, leading to potential harm to both aquatic and terrestrial organisms. Additionally, the accumulation of BPA in aquatic organisms can pose a risk to humans if these organisms are consumed as a part of the food chain. This can have negative impacts on the health of wildlife, as well as potentially impacting human health through the consumption of contaminated fish or seafood [10].

Microplastic contamination in water bodies is a growing concern worldwide. Studies have revealed the presence of microplastics in various locations, shedding light on the extent of this issue. In the United States, BPA has been detected in various water sources, including drinking water, groundwater and surface water [11]. In South Africa, surface water samples from Capetown contained microplastic concentrations ranging from 3,310 to 15,700 nanograms per liter (ng/l) [12]. Along the coast of Aveiro in Portugal, a coastal lagoon showed microplastic concentrations ranging from 1.1 to 17 ng/l [13]. The Thermaikos Gulf in Greece, a sea water body, exhibited microplastic concentrations ranging from 10.6 to 52.3 ng/l [14]. In Germany, the Elbe River and the North Sea had microplastic concentrations ranging from 17 to 776 ng/l in both river and sea water [15]. The Yangtse River in China showed microplastic concentrations ranging from 0.98 to 43.7 ng/l in its river water [16]. The Danube River in Serbia had a microplastic concentration of 6.8 ng/l in its river water [17]. In Korea, tap water in some major cities was found to contain microplastic concentrations as high as 140 μg/l [18]. These findings underscore the widespread presence of microplastics in different water bodies globally. The varying concentrations highlight the diverse sources and levels of contamination in different regions. Understanding the extent and distribution of microplastics in various environments is essential for devising effective strategies to mitigate their impact on ecosystems and human health. Occurrence of BPA in water sample in some countries in Table 1.



#### **Table 1.** Occurrence of BPA in water sample in some countries.

#### *2.2. Soil.*

One of the primary sources of BPA contamination in soil is the disposal of BPA-containing products in landfills. Landfills contain a variety of waste products, including plastics that contain BPA. Over time, BPA can leach out of these products and into the surrounding soil. In Croatia, sediment samples collected from the Adriatic Sea revealed microplastic concentrations ranging from 1.05 to 46.31 µg/kg [19]. In Kenya, soil samples from Nairobi exhibited microplastic concentrations ranging from 490 to 154,820 μg/g [20]. South Africa's Cape Town had microplastic concentrations in sludge ranging from 0.17 to 2.28  $\mu$ g/g [21]. In Nigeria, sediment samples from Lagos had microplastic concentrations at or below 0.0004 μg/g [22]. In Mexico's Tula Valley, soil samples displayed microplastic concentrations ranging from 1.6 to 30.2 μg/kg [23]. Zhejiang province in China showed soil microplastic concentrations below 150 μg/kg [24]. Caxias do Sul in Brazil exhibited microplastic concentrations of 21.30 μg/kg in its soil [25]. These findings illustrate the presence of microplastics in various environmental compartments, including sediment, soil, and sludge. The concentrations vary across different locations, reflecting the diverse sources and levels of microplastic contamination is shown in Table 2.



China Zhejiang Soil <150 μg kg [24] Brazil Caxias do Sul Soil 21.30 μg/kg [25]

**Table 2.** Occurrence of BPA in soil and sediment sample in some countries.

#### *2.3. Food.*

BPA in food can come from a variety of sources, including food packaging, storage containers, and equipment used in food processing. BPA is commonly used in the production of polycarbonate plastics, which are often used in food and beverage containers. BPA can also be found in epoxy resins, which are used to line metal cans and containers. The pathway for BPA to enter food products is through leaching. When food products are in contact with BPA-

containing materials, BPA can leach into the food. This can occur during the manufacturing process, transportation, storage, or even during the cooking process. In addition, BPA can also be released into the environment and contaminate soil and water sources, leading to potential exposure through food [26, 27]. Studies have shown that BPA is present in a wide range of food products, including canned foods and even culinary aromatic herbs and spices. The levels of BPA in food products can vary widely, depending on the type of product, the packaging, and the processing methods used. The potential health effects of BPA in food are a concern because BPA is an endocrine disruptor. BPA can mimic the effects of estrogen in the body, leading to potential hormonal imbalances and other health problems [26-34]. Exposure to BPA has been linked to a range of health problems, including reproductive disorders, developmental delays, and cancer [35]. In response to concerns about BPA in food, some countries have taken measures to limit the use of BPA in food packaging and storage containers. For example, the European Union banned the use of BPA in baby bottles in 2011 and in all food contact materials in 2018 [36, 37]. In the United States, the Food and Drug Administration (FDA) has banned the use of BPA in baby bottles and sippy cups, but has not banned the use of BPA in other food packaging [38].

<b>rapic 5.</b> Occurrence of Dr A in 1000 sample in some countries.			
Country	<b>Sample</b>	<b>Concentration</b>	<b>Reference</b>
Tunisia	Culinary aromatic herbs and	$1 < 3013$ ng/g	[26]
	spices		
Nigeria	Sachet/package material	$<$ 1.2nM-0.224 ng/l	[27]
Egypt	Corned beef (Can)	$74.56 - 255.78$ ng/g	[28]
Korea	Canned meat and meat products	$\leq$ 98.3 µg/kg	[29]
China	Canned meat and meat products	$< 0.01 - 3.14 \mu$ g/kg	[30]
USA.	Canned meat and meat products	$< 0.01 - 8.78 \mu$ g/kg	$\lceil 31 \rceil$
Japan	Canned meat and meat products	$4-20 \mu g/kg$	$[32]$
Canada	Canned meat and meat products	$1.2 - 35 \mu g/kg$	$[33]$
New Zealand	Canned meat and meat products	$<$ 20-98 µg/kg	[34]

**Table 3.** Occurrence of BPA in food sample in some countries.

#### *2.4. Air.*

The sources of BPA in air are diverse and can vary depending on the location. One significant source of BPA in air is the release of BPA-containing products into the environment. For example, dust particles containing BPA can be released from plastic products through wear and tear or heating. In addition, BPA can be released into the air during the production and disposal of BPA-containing products. Another potential source of BPA in air is the use of BPAcontaining products indoors. For example, cooking with BPA-containing cookware or using products such as air fresheners and cleaning agents that contain BPA can result in the release of BPA into the air. Once BPA is released into the air, it can be transported through the atmosphere over long distances. BPA can also be deposited onto surfaces, including plants and soils, where it can accumulate. The pathways for BPA to enter the body through air exposure are not well understood. However, studies have suggested that inhalation is a potential pathway for BPA to enter the body. Once in the body, BPA can mimic the effects of estrogen, leading to potential hormonal imbalances and other health problems [39]. Previous study assessed the emissions from polypropylene manufacturing plants located in Colombia and Brazil. The researchers specifically examined the gaseous compounds released during the manufacturing process and identified the presence of BPA and four different types of biphenyls (BPs). The total concentrations of these BPs, represented as the sum of all the detected types, ranged from 92 to 1565 ng/g [40]. From July 2019 to November 2020, a study was conducted in Shanghai

to measure the presence of bisphenol A (BPA) in outdoor PM2.5 samples. BPA was frequently detected in 88% of the samples, with concentrations ranging from 0.051 to 7.52 ng/m<sup>3</sup>, and average and median concentrations of 2.75 ng/m<sup>3</sup> and 2.40 ng/m<sup>3</sup>, respectively. The study also evaluated the potential health effects associated with the inhalation of BPs by different age groups. Based on the estimated daily intakes (EDIs) and hazard quotients (HQs) data, it was found that children were more susceptible to health effects related to the inhalation of BPs compared to adults [41].

### **3. Exposure, biotransformation and toxic effects in humans**

Exposure to bisphenol A (BPA) can occur through various routes, including ingestion of contaminated food and water, inhalation of air contaminated with BPA, and dermal contact with products containing BPA. Once BPA enters the body, it undergoes biotransformation and can have toxic effects on human health. Ingestion of contaminated food and water is considered to be the primary route of BPA exposure for humans. BPA can leach into food and drinks from containers made with BPA-containing materials, such as plastic bottles and cans. BPA can also contaminate food through the use of BPA-based food packaging materials, such as plastic wraps and containers. In addition, BPA has been found in drinking water sources, including groundwater and surface water. Once ingested, BPA can be absorbed through the intestines and enter the bloodstream. Inhalation of air contaminated with BPA is another route of exposure, although it is considered to be a minor source. BPA can be released into the air during the production and use of BPA-containing products, such as plastic manufacturing and waste incineration. Once inhaled, BPA can be absorbed into the bloodstream through the lungs. Dermal contact with products containing BPA is considered to be a minor route of exposure. BPA can be found in some personal care products, such as sunscreen and lotions, as well as in certain types of thermal paper, such as receipts. Although the amount of BPA that can be absorbed through the skin is low, it can still contribute to overall exposure [41, 42].

BPA is primarily metabolized in the liver through a process known as conjugation, wherein it binds to another molecule, such as glucuronic acid or sulfate. This results in the formation of BPA-glucuronide and BPA-sulfate, which are less toxic than the parent compound and can be excreted from the body through urine or feces. However, during biotransformation, some BPA may be transformed into more reactive forms, such as quinones, which can damage cellular DNA and proteins, leading to various health problems, including cancer and developmental disorders. Various factors, such as age, sex, and genetic variations, can affect the biotransformation of BPA. For example, infants and young children have higher levels of BPA-glucuronide compared to adults, indicating that they may have a slower rate of biotransformation. Genetic variations in enzymes involved in BPA metabolism can also impact the biotransformation of BPA and its toxic effects. Although biotransformation is an important mechanism for reducing BPA toxicity, the formation of reactive metabolites such as quinones can still cause damage to cellular DNA and proteins [43]. Therefore, it is crucial to minimize BPA exposure in the first place by avoiding products that contain BPA and reducing exposure to contaminated food, water, and air. Additionally, studies on the effect of genetic variations on the biotransformation of BPA can help identify individuals who may be more vulnerable to the toxic effects of BPA and inform personalized prevention and intervention strategies [44].

BPA's toxic effects on human health are still a subject of ongoing research. BPA has estrogenic effects, meaning that it can bind to estrogen receptors in the body and imitate the effects of the hormone. This can disrupt the body's natural hormonal balance, which may result in a range of health problems, including reproductive disorders, developmental delays, and cancer. BPA exposure has also been linked to metabolic disorders, such as obesity and type 2 diabetes. One theory is that BPA may interfere with the body's insulin signaling pathways, leading to insulin resistance and impaired glucose metabolism [42–44].

#### **4. Biodegradation by Fungi**

Fungi are natural decomposers that are capable of breaking down a range of organic compounds, including BPA. Studies have shown that certain species of fungi can effectively biodegrade BPA under the right conditions. This is an attractive solution to the problem of BPA contamination, as it is a natural process that does not require the use of harmful chemicals or energy-intensive processes. White-rot fungi are a group of fungi that are known for their ability to degrade a wide range of pollutants, including organic compounds such as Bisphenol A (BPA). BPA is a common environmental contaminant that has been shown to have negative impacts on human health and the environment. The use of white-rot fungi to biodegrade BPA is an attractive solution to this problem, as it is a natural and sustainable process that does not require the use of harmful chemicals. Several studies have demonstrated the capability of certain species of white-rot fungi to effectively biodegrade Bisphenol A (BPA). For instance, one study investigated the biodegradation of BPA by the white-rot fungus *Stereum hirsutum and Heterobasidium*. The researchers examined the estrogenic activity of the degradation products using MCF-7 cell proliferation assays and analyzed pS2 mRNA expression in the MCF-7 cells. Both *S. hirsutum* and *H. insulare* demonstrated high resistance to BPA at a concentration of 100 ppm. Their mycelial growth was completed within 8 days of incubation at 30 °C. It took between 7 and 14 days for the fungi to achieve complete degradation of BPA, reaching approximately 99% [45]. Another study showed that BPA was subjected to treatment using manganese peroxidase (MnP) and laccase obtained from lignin-degrading fungi. While BPA disappeared completely from the reaction mixture after a 1-hour treatment with MnP, their estrogenic activities remained at 40%, respectively. Extending the treatment time to 12 hours resulted in the complete removal of estrogenic activities. Laccase exhibited lower efficiency in removing these activities compared to MnP; however, when combined with HBT, the laccase-HBT system successfully eliminated the activities within 6 hours. Even after 48 hours of enzymatic treatment, the estrogenic activities did not reappear, indicating that the ligninolytic enzymes effectively remove the estrogenic activities of BPA [46].

The use of white-rot fungi for the biodegradation of BPA has several advantages over other methods of remediation. Firstly, it is a natural process that does not require the use of harmful chemicals or energy-intensive processes. Secondly, it is a sustainable approach that can be applied in situ, meaning that the fungi can be applied directly to the contaminated soil or water without the need for excavation or removal of the contaminated material. However, there are also some limitations to the use of white-rot fungi for BPA biodegradation. For example, the effectiveness of the process may be influenced by factors such as pH, temperature, and the presence of other contaminants in the environment. Furthermore, the cost and time required for the cultivation of the fungi may be a barrier to its widespread use [47]. White rot fungi are known to be effective in biotransforming a wide range of organic compounds, including bisphenol A (BPA). When white rot fungi are exposed to BPA, they can use different enzymes to transform it into simpler and less harmful compounds. One of the main mechanisms

by which white rot fungi degrade BPA is through the production of ligninolytic enzymes such as lignin peroxidase (LiP), manganese peroxidase (MnP), and laccase. LiP is a heme-containing enzyme that can oxidize and cleave the aromatic rings of BPA, leading to the formation of benzoquinones and other intermediates. MnP, on the other hand, can oxidize BPA to form BPA-quinones, which can then be further degraded by other enzymes such as hydrolases. Laccase can also oxidize BPA to form BPA-quinones, which can then undergo further reactions with other enzymes [48]. Previous research revealed that *Trametes hirsuta* was capable of biotransforming BPA into several metabolites. The biotransformation of bisphenol A (BPA) involves the action of both extracellular and intracellular enzymes, such as laccase and cytochrome P-450 monooxygenase. Various enzymatic processes, including polymerization, hydroxylation, dehydration, bond cleavage, dehydrogenation, and carboxylation, are believed to contribute to the transformation of BPA. The results indicate that the fungus T. hirsuta La-7 has significant potential for bioremediation applications, as the intermediate products generated during the process are either harmless or less hazardous [49].



**Figure 1.** Removal of BPA by white-rot fungi.

#### **4. Biodegradation by immobilized enzyme**

One approach that has shown promise is the use of immobilized enzymes for BPA degradation. Immobilized enzymes are enzymes that are bound to a solid support, such as a polymer or a matrix, which allows them to be reused multiple times and can improve their stability and catalytic activity. The immobilization process involves attaching the enzyme molecules to the support matrix, which can be achieved through a variety of techniques, such as covalent bonding, adsorption, encapsulation, and crosslinking. covalent bond is formed between the enzyme and the support material. This method is known for providing strong and stable immobilization, which is particularly useful for applications requiring high stability, but it can be a time-consuming and expensive process [50]. Another method for enzyme immobilization is adsorption, which involves the attachment of the enzyme to the support material through weak electrostatic or hydrophobic interactions. This method is simple and easy to use, but it can result in unstable immobilization and low activity due to the weak attachment between the enzyme and the support material [51]. Encapsulation is another method for immobilizing enzymes, where the enzyme is trapped within a microsphere or capsule. This method provides a protective barrier for the enzyme, which can increase stability and prevent degradation by external factors. However, encapsulation can also result in low activity due to the limited substrate diffusion through the microsphere or capsule [50].

Previous study showed the the stability and reusability of laccase enzymes pose significant challenges in industrial and environmental biotechnology. The laccase enzyme was immobilized onto SiO<sub>2</sub> supports through covalent binding and exhibited superior stability and durability compared to the free form. Even after 30 continuous reaction cycles, the relative activity remained above 80%. Furthermore, the immobilized laccase demonstrated enhanced efficiency in degrading BPA, especially in the presence of TX-100. Complete degradation of BPA was achieved within 5 hours of incubation. These findings highlight the feasibility of enzyme immobilization as a means to improve the stability, reusability, and efficacy of laccase for various applications [52]. Another study showed that *Trametes versicolor* laccase immobilized on Ba-alginate beads effectively degraded bisphenol A (BPA) under optimal conditions: 40 °C, 2 mg/L BPA concentration, and 50 minutes. Both Box-Behnken design (BBD) and artificial neural network (ANN) accurately predicted the degradation efficiency, with BBD achieving 83.48% and ANN achieving 84.33%. Statistical analysis confirmed the reliability of both models  $(R^2: 0.98$  for BBD, 0.97 for ANN; MSE: 9.88 for BBD, 38.25 for ANN). Immobilized laccase exhibited superior storage stability, retaining 68.64% and 44.62% activity compared to free laccase [53].

## **5. Conclusion**

Bisphenol A (BPA) is a harmful industrial chemical that is widely used in the manufacturing of plastics, resins, and coatings. It has been shown to have negative effects on human health and the environment, which has led to increased efforts to find effective and sustainable methods for its removal from the environment. One approach that has shown promise is the use of fungi for the biodegradation of BPA. Fungi are known for their ability to degrade a wide range of organic compounds, including pollutants and toxic chemicals. They use a variety of enzymes and metabolic pathways to break down these compounds, which can result in their complete mineralization to harmless end-products. Several studies have reported the ability of fungi to biodegrade BPA, making them a promising tool for environmental remediation. Fungi can degrade BPA through different mechanisms, depending on the fungal species and the environmental conditions. Some fungi use ligninolytic enzymes, such as laccases and peroxidases, to break down the phenolic rings of BPA. Other fungi use non-ligninolytic enzymes, such as esterases and hydrolases, to cleave the ester linkages in BPA. In addition, some fungi can degrade BPA through cometabolic pathways, where the chemical is degraded as a side reaction to the degradation of another substrate. The use of immobilized enzymes for BPA degradation has also shown promise. Immobilized enzymes are enzymes that are bound to a solid support, such as a polymer or a matrix, which allows them to be reused multiple times and can improve their stability and catalytic activity. Immobilization can improve enzyme stability and activity, as it protects the enzyme from degradation, proteolysis, and thermal denaturation. The choice of support material is a critical factor in the successful immobilization of enzymes.

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## **Conflicts of Interest**

The authors declare no conflict of interest.

# **References**

- [1] Della Rocca, Y.; Traini, E.M.; Diomede, F.; Fonticoli, L.; Trubiani, O.; Paganelli, A.; Pizzicannella, J.; Marconi, G.D. (2023). Current Evidence on Bisphenol A Exposure and the Molecular Mechanism Involved in Related Pathological Conditions. *Pharmaceutics, 15*, 908. [https://doi.org/10.3390/pharmaceutics15030908.](https://doi.org/10.3390/pharmaceutics15030908)
- [2] Besaratinia, A. (2023). The State of Research and Weight of Evidence on the Epigenetic Effects of Bisphenol A. *International Journal of Molecular Sciences, 24*, 7951. [https://doi.org/10.3390/ijms24097951.](https://doi.org/10.3390/ijms24097951)
- [3] Ni, L.; Zhong, J.; Chi, H.; Lin, N.; Liu, Z. (2023). Recent Advances in Sources, Migration, Public Health, and Surveillance of Bisphenol A and Its Structural Analogs in Canned Foods. *Foods, 12*, 1989. [https://doi.org/10.3390/foods12101989.](https://doi.org/10.3390/foods12101989)
- [4] Cheng, Z.; Lin, X.; Wu, M.; Lu, G.; Hao, Y.; Mo, C.; Li, Q.; Wu, J.; Wu, J.; Hu, B.X. (2023). Combined Effects of Polyamide Microplastics and Hydrochemical Factors on the Transport of Bisphenol A in Groundwater. *Separations, 10,* 123[. https://doi.org/10.3390/separations10020123.](https://doi.org/10.3390/separations10020123)
- [5] Campanale, C.; Massarelli, C.; Savino, I.; Locaputo, V.; Uricchio, V.F. (2020). A Detailed Review Study on Potential Effects of Microplastics and Additives of Concern on Human Health. *International Journal of Environmental Research and Public Health, 17*, 1212. [https://doi.org/10.3390/ijerph17041212.](https://doi.org/10.3390/ijerph17041212)
- [6] Pérez-Bermejo, M.; Mas-Pérez, I.; Murillo-Llorente, M.T. (2021). The Role of Bisphenol A in Diabetes and Obesity. *Biomedicines, 9,* 666[. https://doi.org/10.3390/biomedicines9060666.](https://doi.org/10.3390/biomedicines9060666)
- [7] Liu, J.; Qi, Y.; Fonseca, M.I.; Lorigo, M.; Cairrao, E. (2022). Endocrine-Disrupting Effects of Bisphenol A on the Cardiovascular System: A Review. *Journal of Xenobiotics*, 12, 181–213. [https://doi.org/10.3390/jox12030015.](https://doi.org/10.3390/jox12030015)
- [8] Zahra, A.; Kerslake, R.; Kyrou, I.; Randeva, H.S.; Sisu, C.; Karteris, E. (2022). Impact of Environmentally Relevant Concentrations of Bisphenol A (BPA) on the Gene Expression Profile in an In Vitro Model of the Normal Human Ovary. *International Journal of Molecular Sciences, 23*, 5334. [https://doi.org/10.3390/ijms23105334.](https://doi.org/10.3390/ijms23105334)
- [9] Repossi, A.; Farabegoli, F.; Gazzotti, T.; Zironi, E.; Pagliuca, G. (2016). Bisphenol A in Edible Part of Seafood. *Italian Journal of Food Safety, 5*, 5666. [https://doi.org/10.4081/ijfs.2016.5666.](https://doi.org/10.4081/ijfs.2016.5666)
- [10] Arnold, S.M.; Clark, K.E.; Staples, C.A.; Klecka, G.M.; Dimond, S.S.; Caspers, N.; Hentges, S.G. (2013). Relevance of drinking water as a source of human exposure to bisphenol A. *Journal of Exposure Science and Environmental Epidemiology, 23*, 137‒144. [https://doi.org/10.1038/jes.2012.66.](https://doi.org/10.1038/jes.2012.66)
- [11] Chevrier, J.; Gunier, R.B.; Bradman, A.; Holland, N.T.; Calafat, A.M.; Eskenazi, B.; Harley, K.G. (2013). Maternal urinary bisphenol A during pregnancy and maternal and neonatal thyroid function in the CHAMACOS study. *Environmental Health Perspectives*, 121, 138–144. [http://doi.org/10.1289/ehp.1205092.](http://doi.org/10.1289/ehp.1205092)
- [12] Olatunji, O.S.; Fatoki, O.S.; Opeolu, B.O.; Ximba, B.J.; Chitongo, R. (2017). Determination of selected steroid hormones in some surface water around animal farms in Cape Town using HPLC-DAD. *Environmental Monitoring and Assessment, 189*, 363. [https://doi.org/10.1007/s10661-017-](https://doi.org/10.1007/s10661-017-6070-8) [6070-8.](https://doi.org/10.1007/s10661-017-6070-8)
- [13] Jonkers, N.; Sousa, A.; Galante-Oliveira, S.; Barroso, C.M.; Kohler, H.-P.E.; Giger, W. (2009). Occurrence and sources of selected phenolic endocrine disruptors in Ria de Aveiro, Portugal. *Environmental Science and Pollution Research, 17,* 834‒843. [https://doi.org/10.1007/s11356-009-](https://doi.org/10.1007/s11356-009-0275-5) [0275-5.](https://doi.org/10.1007/s11356-009-0275-5)
- [14] Arditsoglou, A.; Voutsa, D. (2012). Occurrence and partitioning of endocrine-disrupting compounds in the marine environment of Thermaikos Gulf, Northern Aegean Sea, Greece. *Marine Pollution Bulletin, 64*, 2443‒2452. [https://doi.org/10.1016/j.marpolbul.2012.07.048.](https://doi.org/10.1016/j.marpolbul.2012.07.048)
- [15] Heemken, O.; Reincke, H.; Stachel, B.; Theobald, N. (2001). The occurrence of xenoestrogens in the Elbe river and the North Sea. *Chemosphere*, 45, 245–259. [https://doi.org/10.1016/s0045-](https://doi.org/10.1016/s0045-6535(00)00570-1) [6535\(00\)00570-1.](https://doi.org/10.1016/s0045-6535(00)00570-1)
- [16] Shi, J.; Liu, X.; Chen, Q.; Zhang, H. (2014). Spatial and seasonal distributions of estrogens and bisphenol A in the Yangtze River Estuary and the adjacent East China Sea. *Chemosphere, 111*, 336‒343. [https://doi.org/10.1016/j.chemosphere.2014.04.046.](https://doi.org/10.1016/j.chemosphere.2014.04.046)
- [17] Čelić, M.; Škrbić, B.D.; Insa, S.; Živančev, J.; Gros, M.; Petrović, M. (2020). Occurrence and assessment of environmental risks of endocrine disrupting compounds in drinking, surface and wastewaters in Serbia. *Environmental Pollution, 262*, 114344. [https://doi.org/10.1016/j.envpol.2020.114344.](https://doi.org/10.1016/j.envpol.2020.114344)
- [18] Lee, S.; Jeong, W.; Kannan, K.; Moon, H.-B. (2016). Occurrence and exposure assessment of organophosphate flame retardants (OPFRs) through the consumption of drinking water in Korea. *Water Research, 103, 182-188. [https://doi.org/10.1016/j.watres.2016.07.034.](https://doi.org/10.1016/j.watres.2016.07.034)*
- [19] Anđelić, I.; Roje-Busatto, R.; Ujević, I.; Vuletić, N.; Matijević, S. (2020). Distribution of Bisphenol A in Sediment and Suspended Matter and Its Possible Impact on Marine Life in Kaštela Bay, Adriatic Sea, Croatia. *Journal of Marine Science and Engineering, 8,* 480. [https://doi.org/10.3390/jmse8070480.](https://doi.org/10.3390/jmse8070480)
- [20] Odera, P.A. (2019). Determination of Bisphenol A (BPA) in Thermal Papers, Selected Soil Samples and the Effect of Temperature and Humidity on Its Concentration. Master Thesis, University of Nairobi, Nairobi, Kenya.
- [21] Olujimi, O.; Fatoki, O.; Daso, A.; Akinsoji, O.; Oputu, O.; Oluwafemi, O., et al. (2013). Levels of Nonylphenol and Bisphenol A in wastewater treatment plant effluent, sewage sludge, and leachates around Cape Town, South Africa. In Handbook of Wastewater Treatment; Valdez, C.J., Maradona, E.M., Eds.; Nova Science: New York, USA; pp. 305–315.
- [22] Oketola, A.A.; Fagbemigun, T.K. (2013). Determination of nonylphenol, octylphenol and bisphenol-A in water and sediments of two major rivers in Lagos, Nigeria. *Journal of Environmental Protection, 4,* 38‒45. [http://doi.org/10.4236/jep.2013.47A005.](http://doi.org/10.4236/jep.2013.47A005)
- [23] Gibson, R.; Duran-Alvarez, J.C.; Estrada, K.L.; Chavez, A.; Jimenez Cisneros, B. (2010). Accumulation and leaching potential of some pharmaceuticals and potential endocrine disruptors in soils irrigated with wastewater in the Tula Valley, Mexico. *Chemosphere, 81*, 1437–1445. [https://doi.org/10.1016/j.chemosphere.2010.09.006.](https://doi.org/10.1016/j.chemosphere.2010.09.006)
- [24] Song, S.; Ruan, T.; Wang, T.; Liu, R.; Jiang, G. (2012). Distribution and preliminary exposure assessment of bisphenol AF (BPAF) in various environmental matrices around a manufacturing

plant in China. *Environmental Science & Technology*, 46, 13136–13143. [https://doi.org/10.1021/es303960k.](https://doi.org/10.1021/es303960k)

- [25] Vieceli, N.; Baldasso, R.; Filho, I.; Manfredini, K. (2014). Occurrence of Bisphenol A in soil and leachate of a municipal landfill: effect of the sample acidification. *Scientia cum Industria*, 2, 10– 14. [http://dx.doi.org/10.18226/23185279.v2iss1p10.](http://dx.doi.org/10.18226/23185279.v2iss1p10)
- [26] Di Bella, G.; Ben Mansour, H.; Ben Tekaya, A.; Beltifa, A.; Potortì, A.G.; Saiya, E., et al. (2018). Plasticizers and BPA residues in Tunisian and Italian culinary herbs and spices. *Journal of Food Science, 83*, 1769‒1774. [https://doi.org/10.1111/1750-3841.14171.](https://doi.org/10.1111/1750-3841.14171)
- [27] Omoruyi, I.M.; Ahamioje, D.; Pohjanvirta, R. (2014). Dietary exposure of Nigerians to mutagens and estrogen-like chemicals. *International Journal of Environmental Research and Public Health, 11*, 8347‒8367. [https://doi.org/10.3390/ijerph110808347.](https://doi.org/10.3390/ijerph110808347)
- [28] Osman, M.A.; Mahmoud, G.I.; Elgammal, M.H.; Hasan, R.S. (2018). Studying of bisphenol A levels in some canned food, feed and baby bottles in Egyptian markets. *Fresenius Environmental Bulletin, 27*, 9374‒9381.
- [29] Lim, D.S.; Kwack, S.J.; Kim, K.-B.; Kim, H.S.; Lee, B.M. (2009). Risk Assessment of Bisphenol A Migrated from Canned Foods in Korea. *Journal of Toxicology and Environmental Health Part A: Current Issues, 72*, 1327‒1335. [https://doi.org/10.1080/15287390903212444.](https://doi.org/10.1080/15287390903212444)
- [30] Liao, C.Y.; Kannan, K. (2014). A survey of bisphenol A and other bisphenol analogues in foodstuffs from nine cities in China. *Food Additives & Contaminants: Part A, 31,* 319‒329. [https://doi.org/10.1080/19440049.2013.868611.](https://doi.org/10.1080/19440049.2013.868611)
- [31] Liao, C.Y.; Kannan, K. (2013). Concentrations and Profiles of Bisphenol A and Other Bisphenol Analogues in Foodstuffs from the United States and Their Implications for Human Exposure. Journal of Agricultural and Food Chemistry, 61, 4655–4662. [https://doi.org/10.1021/jf400445n.](https://doi.org/10.1021/jf400445n)
- [32] Sajiki, J.; Miyamoto, F.; Fukata, H.; Mori, C.; Yonekubo, J.; Hayakawa, K. (2007). Bisphenol A (BPA) and its source in foods in Japanese markets. *Food Additives & Contaminants: Part A, 24*, 103‒112. [https://doi.org/10.1080/02652030600936383.](https://doi.org/10.1080/02652030600936383)
- [33] Cao, X.L.; Kosarac, I.; Popovic, S.; Zhou, S.; Smith, D.; Dabeka, R. (2019). LC-MS/MS analysis of bisphenol S and five other bisphenols in total diet food samples. *Food Additives & Contaminants: Part A, 36,* 1740‒1747. [https://doi.org/10.1080/19440049.2019.1643042.](https://doi.org/10.1080/19440049.2019.1643042)
- [34] Thomson, B.M.; Grounds, P.R. (2005). Bisphenol A in canned foods in New Zealand: An exposure assessment. *Food Additives & Contaminants*, 22, 65–72. [https://doi.org/10.1080/02652030400027920.](https://doi.org/10.1080/02652030400027920)
- [35] Khan, N.G.; Correia, J.; Adiga, D.; Rai, P.S.; Dsouza, H.S.; Chakrabarty, S.; Kabekkodu, S.P. (2021). A comprehensive review on the carcinogenic potential of bisphenol A: clues and evidence. *Environmental Science and Pollution Research International, 28*, 19643‒19663. [https://doi.org/10.1007/s11356-021-13071-w.](https://doi.org/10.1007/s11356-021-13071-w)
- [36] Siddique, M.A.; Harrison, S.M.; Monahan, F.J.; Cummins, E.; Brunton, N.P. (2021). Bisphenol A and Metabolites in Meat and Meat Products: Occurrence, Toxicity, and Recent Development in Analytical Methods. *Foods, 10*, 714. [https://doi.org/10.3390/foods10040714.](https://doi.org/10.3390/foods10040714)
- [37] Krivohlavek, A.; Mikulec, N.; Budeč, M.; Barušić, L.; Bošnir, J.; Šikić, S.; Jakasa, I.; Begović, T.; Janda, R.; Vitale, K. (2023). Migration of BPA from Food Packaging and Household Products on the Croatian Market*. International Journal of Environmental Research and Public Health, 20,* 2877. [https://doi.org/10.3390/ijerph20042877.](https://doi.org/10.3390/ijerph20042877)
- [38] Robles-Aguilera, V.; Gálvez-Ontiveros, Y.; Rodrigo, L.; Salcedo-Bellido, I.; Aguilera, M.; Zafra-Gómez, A.; Monteagudo, C.; Rivas, A. (2021). Factors Associated with Exposure to Dietary Bisphenols in Adolescents. *Nutrients, 13,* 1553. [https://doi.org/10.3390/nu13051553.](https://doi.org/10.3390/nu13051553)
- [39] Adegoke, E.O.; Rahman, M.S.; Park, Y.-J.; Kim, Y.J.; Pang, M.-G. (2021). Endocrine-Disrupting Chemicals and Infectious Diseases: From Endocrine Disruption to Immunosuppression. *International Journal of Molecular Sciences, 22*, 3939. [https://doi.org/10.3390/ijms22083939.](https://doi.org/10.3390/ijms22083939)
- [40] Fernández, J.H.; Guerra, Y.; Cano, H. (2022). Detection of Bisphenol A and Four Analogues in Atmospheric Emissions in Petrochemical Complexes Producing Polypropylene in South America. *Molecules, 27*, 4832. [https://doi.org/10.3390/molecules27154832.](https://doi.org/10.3390/molecules27154832)
- [41] Ribeiro, E.; Ladeira, C.; Viegas, S. (2017). Occupational Exposure to Bisphenol A (BPA): A Reality That Still Needs to Be Unveiled. *Toxics, 5*, 22. [https://doi.org/10.3390/toxics5030022.](https://doi.org/10.3390/toxics5030022)
- [42] Della Rocca, Y.; Traini, E.M.; Diomede, F.; Fonticoli, L.; Trubiani, O.; Paganelli, A.; Pizzicannella, J.; Marconi, G.D. (2023). Current Evidence on Bisphenol A Exposure and the Molecular Mechanism Involved in Related Pathological Conditions. *Pharmaceutics, 15*, 908. [https://doi.org/10.3390/pharmaceutics15030908.](https://doi.org/10.3390/pharmaceutics15030908)
- [43] Mączka, W.; Grabarczyk, M.; Wińska, K. (2022). Can Antioxidants Reduce the Toxicity of Bisphenol? *Antioxidants, 11*, 413. [https://doi.org/10.3390%2Fantiox11020413.](https://doi.org/10.3390%2Fantiox11020413)
- [44] Cimmino, I.; Fiory, F.; Perruolo, G.; Miele, C.; Beguinot, F.; Formisano, P.; Oriente, F. (2020). Potential Mechanisms of Bisphenol A (BPA) Contributing to Human Disease. *International Journal of Molecular Sciences, 21*, 5761. [https://doi.org/10.3390/ijms21165761.](https://doi.org/10.3390/ijms21165761)
- [45] Lee, S.M., Koo, B.W., Choi, J.W., Choi, D.H., An, B.S., Jeung, E.B., Choi, I.G. (2005). Degradation of bisphenol A by white rot fungi, Stereum hirsutum and Heterobasidium insulare, and reduction of its estrogenic activity. *Biological and Pharmaceutical Bulletin, 28, 201–207*. [https://doi.org/10.1248/bpb.28.201.](https://doi.org/10.1248/bpb.28.201)
- [46] Tsutsumi, Y., Haneda, T., Nishida, T. (2001). Removal of estrogenic activities of bisphenol A and nonylphenol by oxidative enzymes from lignin-degrading basidiomycetes. *Chemosphere, 42*, 271– 276. [https://doi.org/10.1016/s0045-6535\(00\)00081-3.](https://doi.org/10.1016/s0045-6535(00)00081-3)
- [47] Li, S.; Tian, K.; Qiu, Q.; Yu, Y.; Li, H.; Chang, M.; Sun, X.; Gu, J.; Zhang, F.; Wang, Y.; et al. (2023). Study on Genomics of the Bisphenol A-Degrading Bacterium *Pseudomonas* sp. P1. *Water, 15*, 830. [https://doi.org/10.3390/w15040830.](https://doi.org/10.3390/w15040830)
- [48] Lee, H., Jang, Y., Choi, Y.S., Kim, M.J., Lee, J., Lee, H., Hong, J.H., Lee, Y.M., Kim, G.H., Kim, J.J. (2014). Biotechnological procedures to select white rot fungi for the degradation of PAHs. *Journal of Microbiological Methods, 97,* 56‒62. [https://doi.org/10.1016/j.mimet.2013.12.007.](https://doi.org/10.1016/j.mimet.2013.12.007)
- [49] Liu, J., Sun, K., Zhu, R., Wang, X., Gatheru Waigi, M., Li, S. (2023). Biotransformation of bisphenol A in vivo and in vitro by laccase-producing *Trametes hirsuta* La-7: Kinetics, products, and mechanisms. *Environmental Pollution, 321*, 121155. [https://doi.org/10.1016/j.envpol.2023.121155.](https://doi.org/10.1016/j.envpol.2023.121155)
- [50] Zdarta, J., Meyer, A.S., Jesionowski, T., Pinelo, M. (2018). A General Overview of Support Materials for Enzyme Immobilization: Characteristics, Properties, Practical Utility. *Catalysts, 8,* 92. [https://doi.org/10.3390/catal8020092.](https://doi.org/10.3390/catal8020092)
- [51] Dong, M., Wu, Z., Lu, M., Wang, Z., Li, Z. (2012). Combining the Physical Adsorption Approach and the Covalent Attachment Method to Prepare a Bifunctional Bioreactor. *International Journal of Molecular Sciences, 13*, 11443‒11454. [https://doi.org/10.3390/ijms130911443.](https://doi.org/10.3390/ijms130911443)
- [52] Chang, K.-L., Teng, T.-C., Fu, C.-K., Liu, C.-H. (2019). Improving biodegradation of Bisphenol A by immobilization and inducer. *Process Safety and Environmental Protection, 128,* 128‒134. [https://doi.org/10.1016/j.psep.2019.05.038.](https://doi.org/10.1016/j.psep.2019.05.038)
- [53] Abdul Latif, A., Maqbool, A., Zhou, R., Arsalan, M., Sun, K., Si, Y. (2022). Optimized degradation of bisphenol A by immobilized laccase from Trametes versicolor using Box-Behnken design (BBD) and artificial neural network (ANN). *Journal of Environmental Chemical Engineering, 10*, 107331. [https://doi.org/10.1016/j.jece.2022.107331.](https://doi.org/10.1016/j.jece.2022.107331)



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