Risk of Brominated Flame Retardants for Aquatic Organisms

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Abstract. Nowadays, many experiments have detected the residues of halogenated flame retardants in organisms and even human bodies, among which the amount and type of brominated flame retardants (BFRs) are the most. Therefore, research on biological toxicity and possible harms of BFRs need to be studied to adjust the use and disposal of these chemicals to prevent irreversible consequences on the human body. This article mainly introduced the harm of BFRs to aquatic organisms and the solutions to reduce the concentration of BFRs in water. The harm of BFRs to aquatic organisms is mainly reflected in reproductive toxicity and thyroid hormone toxicity. BFRs, as toxic substances, are bio enriched and can enter the human body along the food chain, causing hormonal disorders and other problems. There are three main ways to reduce the concentration of BFRs in the environment including by using simple and easily degradable BFRs at the source, adjusting the light source conditions to enhance the photochemical degradation rate, and developing new adsorption materials.

Keywords: Brominated flame retardants, aquatic organism, human health, toxicity, photochemical degradation.

1. Introduction

Halogenated flame retardants (HFRs) are widely used in various industries because of their better fire resistance, while brominated flame retardants (BFRs) are the most commonly used. It has been found that HFRs widely exist in the ocean and can be migrated over long distances and enriched in organisms [1]. Most HFRs enter the water body through surface runoff along with the discharge of factory wastewater or the leachate from landfills, and eventually flow into the ocean to be absorbed by sediments or absorbed and enriched by aquatic organisms, and then enter the human body along the food chain [2]. Thus, in this process, marine water bodies and marine organisms will be directly affected by the toxic hazards of HFRs. It was claimed that several traditional BFRs, including hexabromocyclododecane (HBCD) and polybrominated diphenyl ethers (PBDEs), were regulated persistent organic pollutants (POPs) according to Stockholm Convention, because of their greater toxicity and ecological risks [3]. Studies have found that PBDEs are the main HFRs in organisms, possibly due to the strong absorption and bio enrichment of 4-6 brominated diphenyl ethers in organisms [4]. Therefore, the research on the harm of halogenated flame retardants to aquatic organisms and even the human body should start with BFRs.

BFRs as a class of synthetic organic compounds with excellent flame-retardant properties, are mainly composed of aliphatic, alicyclic, aromatic, and aromatic-aliphatic bromine compounds, including polybrominated biphenyl (PBB), polybrominated diphenyl ethers and hexabromocyclododecane. BFRs can be cleaved to form less active bromine radicals under the condition of heat, thus slowing down or stopping the combustion reaction. At the same time, the HBr generated by the reaction is a dense and non-flammable gas, which can dilute oxygen in the air and play a flame-retardant role on the surface of the material [5]. Studies show that BFRs have toxic effects on the endocrine system, nervous system, and reproductive development of organisms. BFRs often have a similar structure to pre-existing signaling substances or receptors in organisms, which can lead to misidentification and misbinding of responses. This in turn disrupts normal hormone levels or causes the organism to respond incorrectly [6].

To fill the vacancy of traditional BFRs, humans have developed novel brominated flame retardants (NBFRs) as a substitute for it, the main types are hex bromobenzene (HBB), tetra bromobutane (TBB), tetrabromophthalate diester (TBPH), 1, 2, 5, 6-tetrabromocyclooctane (TBCO), Tri (2, 3-

dibromopropyl) isothiocyanate (TBC) [7]. Like traditional BFRs, NBFRs have also been found to have strong "PBT properties" (environmental persistence, bioaccumulation, toxicity), while the ecological risks of NBFRs are still unknown due to a lack of relevant research [8].

This paper will analyze the possible impact and extent of NBFRs on aquatic organisms, and put forward solutions to reduce the content of NBFRs in water bodies.

2. Risk of Brominated Flame Retardants

2.1. Reproductive Toxicity of NBFRs

Reproductive toxicity is related to the growth of individual organisms and the continuation of the population, so the study of reproductive toxicity is helpful to determine whether pollutants will cause harm to the existence and continuation of species, and then affect the stability of the water ecological environment food chain and ecosystem.

The effects of NBFRs on aquatic organisms are mainly reflected in sex differentiation and gonad development. By affecting the synthesis of sex hormones or related receptors, the population sex ratio of aquatic organisms is unbalanced, and the gonadal development of aquatic organisms is inhibited, especially in female fish, which has a certain adverse effect on the reproduction and continuation of the population. However, when the concentration of NBFRs is low, the effect intensity of NBFRs is not high, and whether the degree of its impact is serious enough to affect the safety of the population needs to be further studied.

Xie et al. [9] studied the reproductive toxicity of NBFRs to aquatic organisms. Xie et al. took three types of NBFRs, TBCO, TBPH, and TBB as the main research objects, and determined the effects of NBFRs on gonad development of zebrafish by observing the male and female differentiation, sex hormone levels, and yolk protein raw water equality after adulthood. Observing the phenomenon of sex differentiation in zebrafish, Xie found that different types of NBFRs with the same concentration had different influence directions on the gonad development of zebrafish. BCO and TBB of 1μM significantly increased the proportion of female and male zebrafish, respectively. For the same NBFRs, the effect of the concentration is also different. As for TBB, the proportion of male zebrafish in the low concentration group (0.01μM and 0.1μM) was significantly increased, while the proportion of female zebrafish in the high concentration group (1μM) was significantly increased. By observing levels of sex hormones, study shows that these phenomena are the results of the promotion of NBFRs to the expression of genes related to estrogen or androgen synthesis. At the same time, the study also found that with the increase in TBCO exposure concentration, the proportion of mature germ cells in Zebrafish in high-concentration groups was less than those in control groups. The radius of late vitellogenic oocytes in female zebrafish was only 85.8% of that in the control group. Also, the expression of genes related to gonad maturation was downregulated, which would also lead to delayed gonad development. In contrast to TBCO, TBPH exposure significantly upregulated genes that promote gonad development and maturation, thus promoting the development of female oocytes.

Tu et al. [10] studied the reproductive toxicity of NBFRs from the molecular mechanism of its anti-estrogenic activity. It has been found that NBFRs can produce hydrogen bonds with the Ligand Binding Domain (LBD) of the estrogen receptor, thereby hindering the formation of the estrogen receptor and preventing it from selectively binding with estrogens and affecting normal estrogen signaling. The yellow dashed lines in Fig. 1 are the double hydrogen bonds of 2,3,4,5-etrabromobenzoic acid (TBBA), a kind of NBFRs, to the estrogen receptor ERα, with bond lengths of 2.9 Å and 3.3 Å, respectively. Eventually, the sex ratio of the population is unbalanced, or the fertility of female fish is reduced and the gonad development is delayed.

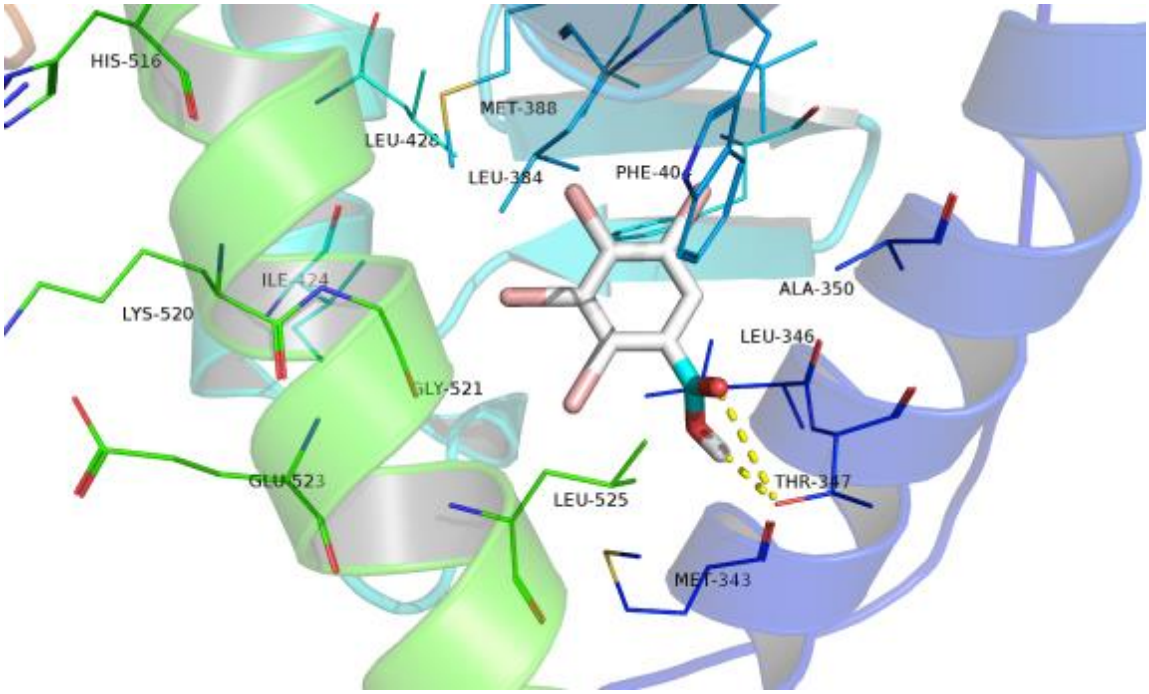


Figure 1. Schematic diagram of the interaction of TBBA with the estrogen receptor ERα [10].

2.2. Thyrotoxicity of NBFRs

NBFRs have a certain effect on the homeostasis of thyroxine in fish, which promotes the secretion and synthesis of thyroid hormone in fish. The mechanism is that NBFRs can inhibit or promote the content of triiodothyronine (T3), tetraiodothyronine (T4), free triiodothyronine (FT3) and free tetraiodothyronine (FT4) amino acids by binding with transport proteins, and then affect the abnormal synthesis and secretion of thyroxine in organisms, which may destroy the stability of thyroid feedback regulation mechanism [11].

Guo et al. [12] studied the effects of FM550 on thyroid hormone in fish, which were analyzed by measuring the contents of TSH and various amino acids required for synthesis. The serum T3 content of tilapia gradually decreased with the increase of FM550 exposure concentration, while T4 decreased first and then increased. In the experimental group of low, medium and three concentrations, the contents of T3 and T4 in the first two groups were reduced, while the inhibition rate of T3 in the high concentration group was up to 45.96%, and the promotion rate of T4 was up to 20.91%. For FT3 and FT4, the changing trend of these two free amino acids with the change of FM550 concentration corresponded to T3 and T4, respectively. Among them, the promotion rate of high-concentration FM550 on FT4 was up to 77.98%. However, the effect of FM550 exposure on thyroid-stimulating hormone (TSH) levels was not significant. It can be seen that FM550 will promote the secretion and synthesis of thyroid hormone in tilapia to a certain extent, and then affect the homeostasis of thyroid hormone in fish.

Ma et al. [13] using 3, 5, 3', 5'-tetrabromo-4, 4'-dihydroxydiphenyl sulfone (TBS) as the experimental object, the binding of BFRs to thyroxine carrier protein was studied by non-denaturating electrospray mass spectrometry and molecular docking simulation. Studies have shown that TBS and Transthyretin (TTR) proteins can form stable stoichiometric ratios of 1:1 complex. This binding interferes with the transport and normal physiological function of TTR proteins for T4 and T3 in the blood, resulting in toxic effects.

2.3. Bioenrichment of NBFRs

NBFRs are bioaccumulative, which can also be harmful to human health. He et al. [14] detected TBPH in the serum samples of residents from the production source area of HFRs located on the south bank of Laizhou Bay in northeast China, with an average concentration of 260 ng·g-1 fat weight,

which is the first report on TBPH found in the human body. A growing number of subsequent studies have detected residues of NBFRs in human serum, especially in residents close to factories that use NBFRs. In addition, Hoffman K, et al. [15] recruited a group of volunteers and tested their urine and serum. Among the volunteers, TBBA was detected in the urine of both mother and their children, at 70% and 27% respectively, and the concentration of TBBA in the urine of their children was higher. Zhou et al. [16] tested the serum and breast milk samples of 102 lactating women, and TBB was detected in more than 55% of the serum and breast milk samples. It can be seen that NBFRs will not only enter the human body with the food chain, but also may be passed from mother to child, and this transmission process continues to enrich NBFRs.

Similar to the way they affect fish, NBFRs also affect the homeostasis of the body's hormone system by affecting the expression of genes relating to hormone synthesis in humans. According to a study by Z. Dong et al. [17], exposure to NBFRs can affect the mRNA expression of genes encoding deiodinases. Also, some kinds of NBFRs like DBDPE can affect the production and metabolism of THs by inhibiting relative enzyme activity. The unusual expression of hormones can be the cause of hyperthyroidism or hypothyroidism. Also, L. Dong et al. [18] have shown that NBFRs have a direct toxic effect on nerve cells, which can lead to neurotoxicity. Studies on mouse exposed to different concentrations of TBC have shown that after exposure to NBFRs, two major enzymes in the antioxidant system, oxidative and anti-oxidative enzymes, reduced significantly in SH-SY5Y cells, which means they are unable to cope with the oxidative stress induced by NBFRs. The antioxidant system plays an important role in converting reactive oxygen species (ROS) into harmless metabolites. If it cannot be cleaned, it will attack cells and tissues, and even cause apoptosis.

3. Reduction of the Concentration of NBFRs in Water

To prevent more NBFRs from further spreading into the ecosystem and the human body, scientists are looking for ways to reduce the content of NBFRs from the aspects of their structure, degradation and adsorption.

3.1. Usage of NBFRs with Simple Structure

When choosing brominated flame retardants, NBFRs with simple structure and degradation products that will not cause secondary pollution should be selected as far as possible. Zhang et al. showed [19] that for the allyl-2,4,6-tribromophenoxy ether (ATE), 2-bromoallyl-2,4,6-tribromophenoxy ether (BATE) and 2,3-dibromopropyl-2,4, 6-tribromophenoxyl ether (DPTE), which have only one benzene ring and one branch chain, the apparent photolysis rate constant (k_{obs}) was respectively 0.262±0.021, 0.244±0.009, 0.139±0.003 in hexyl hydride. According to Fig. 1, it can be seen that k_{obs} decrease with the increase of the number of atoms on the branch chain. Relative light absorption (A_r) of these three NBFRs was calculated to be 2.75×10^{-2}, 2.14×10^{-2}, and 2.02×10^{-2} in hexyl hydride, respectively, which means the photochemical conversion rate also decreases and NBFRs are more difficult to degrade. The results also showed that bromophenol was found in the degradation products of 1, 2-bis (2,4, 6-tribromophenoxy) ethane (BTBPE), which can enhance the potential environmental risk (Fig 2).

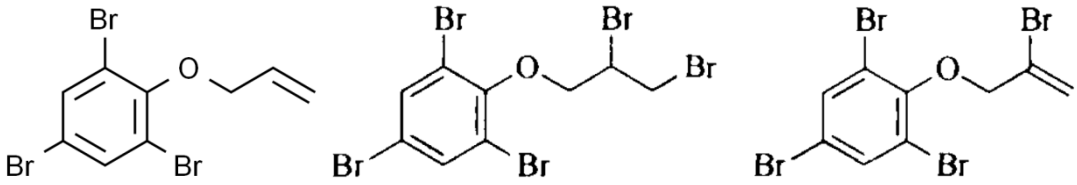


Figure 2. Structure of ATE, BATE and DPTE [19].

3.2. Photochemical Degradation

The photochemical degradation of BFRs can be improved by adjusting the light source. Studies [20] show that organic solvents, high-intensity irradiation and UV-B light sources are conducive to the rapid degradation of BFRs. By comparing the photochemical degradation rate and potential products of tri (2, 3-dibromopropyl) isocyanurate (TDBP-TAZTO) and decabromodiphenyl ethane (DBDPE) under different conditions, Zhou et al. [20, 21] found that increasing the light intensity could promote the degradation of these two types of NBFRs, and the use of UV-B could also promote their degradation. The experimental data showed that the half-lives (t1/2) of DBDPE in low-intensity light sources (UV-A-L, UV-B-L) and high-intensity light sources (UV-A-H, UV-B-H) were 53.7 min, 20.0 min, 6.1 min and 0.9 min, respectively. The half-lives (t1/2) of TDBP-TAZTO were 3466 min, 770 min, 315 min and 227 min, respectively. The higher the intensity of the light source, the shorter the half-lives (t1/2) of NBFRs, which means the higher the degradation rate. For the same intensity light source, the corresponding half-lives (t1/2) of UV-B groups are always smaller than that of UV-A.

In addition, the half-lives (t1/2) of TDBP-TAZTO and DBDPE in organic solvents were significantly lower than those in the solvent-free state, especially those of tetrahydrofuran (THF). The degradation rates of DBDPE exposed to UV-B were 100%, 79.5% and 38.2% in tetrahydropyran, methanol and solvo-free media, respectively. While those of TDBP-TAZTO were 100%, 51.3%, and 25.6%, respectively. Therefore, the discharged NBFRs can be transferred to an organic solvent, and the NBFRs can be pretreated before entering the environment by adjusting the light intensity and wavelength of the light source, and the degraded part can be further disposed of.

3.3. Adsorption with New Material

The adsorbents with large surface area and strong force with Br atoms can better eliminate BFRs in the environment. To reduce the cost of water treatment and efficiently remove NBFRs from water bodies, Duan et al. [22] found that the Azo polycyclic polymer (AzO-POP) can be used as a high-efficiency adsorbent to adsorb added BFRs, pentabromotoluene (PBT), by π-π interaction and hydrophobic interaction. Its adsorption equilibrium time is 10 min and the saturated adsorption capacity can reach 10.71 $mg \cdot mg^{-1}$. Besides, the raw material treatment cost of AzO-POP is 0.43 yuan per ton of water, which is economically feasible for water treatment projects.

4. Summary

With brominated flame retardants (BFRs) widely used worldwide, the study of their biotoxicity hazards and mechanisms is helpful for people to adjust the use and disposal of BFRs. Also, it can provide a theoretical basis for the research and treatment of related diseases. The aquatic organisms that are most directly affected by BFRs are used as the object of study. The specific biological toxicity of BFRs and how to reduce the concentration of BFRs in the environment are discussed as two main contents of the paper.

The harm caused by BFRs to aquatic organisms is mainly reflected in their reproductive toxicity and endocrine toxicity. The specific manifestations of reproductive toxicity are hindering the normal reproductive development of fish and interfering with the sex differentiation of juvenile fish, which will result in the imbalance of sex ratio. Endocrine toxicity, especially thyrotoxicity, reflects in destroying the homeostasis of the thyroid hormone feedback mechanism, which can affect the growth and development of aquatic organisms. These impacts threaten the health of individuals and the reproduction of populations and are not conducive to maintaining the stability of aquatic ecosystems. At the same time, several studies have shown that due to the biological enrichment of BFRs, their toxicity will continue to accumulate along the food chain and eventually enter the human body causing harm, like disturbing the homeostasis of the human body's hormone system. To reduce the risk of BFRs to aquatic organisms and the human body, the concentration of BFRs in water can be

reduced by adjusting the types of BFRs used in production, strengthening the photochemical degradation rate, and developing new adsorption materials.

At present, the problem of high residual concentration of BFRs in the environment and great biological harm is still serious and prominent. Human beings should continue to study the toxicity mechanism of BFRs, and control the amount of BFRs entering the environment from the two aspects of source prevention and pollution treatment.

References

[1] Jia Hongliang, Sun Yeqing, Liu Xianjie, et al. Concentration and bioaccumulation of dechlorane compounds in coastal environment of northern China. Environmental Science and Technology, 2011, 45 (7): 2613 - 2618.

[2] Streets S S, Henderson S A, Sroner A D, et al. Partitioning and bioaccumulation of PBDEs and PCBs in Lake Michigan. Environmental Science and Technology, 2006, 40 (23): 7263 - 7269.

[3] Sharkey M, Harrad S, Abou-Elwafa Abdallah M, et al. Phasing-out of legacy brominated flame retardants: The UNEP Stockholm Convention and other legislative action worldwide. Environment International, 2020, 144106041.

[4] Orn U, Klasson-Wehler E. Metabolism of 2, 2, 4, 4-tetrabromodiphenyl ether in rat and mouse. Xenobiotica, 1998, 28: 199 - 211.

[5] Zhang Yushan, Gao Chunjuan, Cai Ronghua, et al. Application research and development trend of brominated flame retardants. Chemical Industry and Engineering, 2009, 26 (5): 460 - 466.

[6] Cao Yan, Hu Shuangqing, Shen Genxiang, et al. An analysis of research situation on ecological environment and health risks of brominated flame retardants based on bibliometric analysis. Journal of Ecotoxicology, 2022, 17 (02): 381 - 391.

[7] Xiong Ping, Yan Xueting, Zhu Qingqing, et al. A review of environmental occurrence, fate, and toxicity of novel brominated flame retardants. Environmental Science & Technology, 2019.

[8] Wang Qin, Li Chenguang, Yin Shiqi, et al. Research progress on ecotoxic effects of novel brominated flame retardants (NBFRs). Chinese Journal of EcoToxicology, 2019, 18 (02): 212 - 223.

[9] Xie Xianyi. Effects of novel brominated flame retardants on gonad development and endocrine disrupting mechanism of zebrafish. Nanjing University, 2020.

[10] Tu Wenqing, Zhou Binbin, Wu Yongming, et al. Molecular mechanism of antiestrogenic activity of novel brominated flame retardants metabolites TBBA and TBMEHP. Jiangxi Science, 2015, 33 (06): 804 - 806.

[11] Zou Yilong, WU Yongming, Deng Mi et al. Research progress on ecotoxicology of new brominated flame retardants TBB and TBPH. Chinese Journal of Ecotoxicology, 2019, 16 (02): 72 - 85.

[12] Guo Zhen, Tao Yonggang, Chen Mianbiao, et al. Effects of new brominated flame retardants TBB and TBPH mixture on thyroid hormone and physiological and biochemical indices of tilapia. Journal of Ecotoxicology, 2019, 14 (05): 219 - 226.

[13] Ma Jieyao, Li Yawen, Mei Nan, et al. Study on interaction between brominated flame retardants and thyroxine carrier protein by electrospray mass spectrometry. Journal of Analysis and Testing, 2018, 37 (05): 525 - 531.

[14] He Songjie, Li Mingyuan, Jin Jun, et al. Concentrations and trends of halogenated flame retardants in the pooled serum of residents of Laizhou Bay, China. Environmental Toxicology and Chemistry, 2013, 32 (6): 1242 - 1247.

[15] Butt C M, Congleton J, Hoffman K, et al. Metabolites of organophosphate flame retardants and 2-ethylhexyl tetra bromobenzoate in urine from paired mothers and toddlers. Environmental Science & Technology, 2014, 48 (17): 10432 - 10438.

[16] Zhou S N, Buchar A, Siddique S, et al. Measurements of selected brominated flame retardants in nursing women: Implications for human exposure. Environmental Science & Technology, 2014, 48 (15): 8873 - 8880.

[17] Dong Zhaoju, Hu Zhengping, Zhu Haibo, et al. Tris-(2,3-Dibromopropyl) isocyanurate induces depression-like behaviors and neurotoxicity by oxidative damage and cell apoptosis in vitro and in vivo. The Journal of Toxicological Sciences, 2015: 701 – 709.

[18] Dong, Liying, et al. new understanding of novel brominated flame retardants (NBFRs): Neuro (Endocrine) Toxicity. Ecotoxicology and Environmental Safety, 2021.

[19] Zhang Yanan. Environmental photochemical transformation of hydroxyl halogenated diphenyl ethers and novel brominated flame retardants in water. Dalian University of Technology, 2016.

[20] Zhou Daming. Study on the photodegradation of novel brominated flame retardants and phthalates. Jinan University, 2020.

[21] Zhou Daming, Zheng Xiaoshi, Liu Xiaotu, et al. Photodegradation of 1, 3, 5-Tris- (2, 3-dibromopropyl) -1, 3, 5-triazine-2, 4, 6-trione and decabromodiphenyl ethane flame retardants: kinetics, main products, and environmental implications. Journal of Hazardous Materials, 2020.

[22] Duan Shu Chang. Study on preparation of polycyclic polymer and adsorption efficiency of brominated flame retardants in water. Beijing Forestry University, 2020.