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Bioaccumulation patterns, trophic transfer characteristics and dietary exposure potential of tetrabromobisphenol A analogs in a coral reef food web of the Xisha Islands, South China Sea

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Abstract

As a typical class of novel organic pollutants, tetrabromobisphenol A (TBBPA) analogs have been widely detected in various environmental matrices. Several toxicological studies have highlighted that the accumulation of pollutants is the basis for assessing their ecological effects and potential risks. However, the bioaccumulation and trophic transfer of TBBPA analogs in marine food webs are not fully understood. This study selected the most important coral reef islands in the South China Sea as the study area to investigate the bioaccumulation patterns

and trophic transfer characteristics of TBBPA analogs within the tropical marine food web. TBBPA, tetrabromobisphenol S (TBBPS), TBBPA bis(2-hydroxyethyl ether) (TBBPA-BHEE), and TBBPA bis(glycidyl ether) (TBBPA-BGE) are prevalent in water, sediment, and organisms around the Xisha Islands. The concentrations of these compounds varied significantly among species ($P < 0.05$), with notably higher concentrations of ∑TBBPA analogs observed in invertebrates than in fish. Moreover, the Log *BAFs* of TBBPA, TBBPS, and TBBPA-BHEE were all lower than 3.30, whereas TBBPA-BGE exhibited high bioaccumulation potential in some species. The concentrations of TBBPA, TBBPS, TBBPA-BHEE, and TBBPA-BGE in organisms were significantly negatively correlated with trophic level ($P < 0.05$), indicating pronounced trophic dilution effects throughout the food web. In addition, hydrophobicity and metabolism were found to be important factors affecting the bioaccumulation of TBBPA analogs. The results revealed that dietary exposure to seafood poses no significant health risks to the local population.

Keywords: Tetrabromobisphenol A analogs, bioaccumulation, trophic transfer, aquatic food web, dietary exposure

INTRODUCTION

Brominated flame retardants (BFRs) are extensively used in various materials, including electronic products, electrical equipment, plastic products, textiles, and building materials, owing to their cost-effectiveness and excellent flame-retardant properties[1-3]. Currently, more than 75 different aliphatic, aromatic, and polymer-based compounds are marketed as BFRs[4], making them among the most widely produced and used chemical additives worldwide. Traditional BFRs primarily include hexabromocyclododecane, polybrominated diphenyl ethers, polybrominated biphenyls, and tetrabromobisphenol A (TBBPA). Owing to its superior flame retardancy and excellent heat resistance, TBBPA is widely used in electronic devices, printed circuit boards, plastic products, and textiles. As a result, TBBPA has become the most extensively produced and utilized BFR, accounting for approximately 60% of the global BFR market[5]. However, due to its persistence and potential toxicity to living organisms, the production and use of TBBPA are increasingly subject to restrictions[6]. Therefore, the production and consumption of TBBPA analogs, such as tetrabromobisphenol S (TBBPS), tetrabromobisphenol A diallyl ether (TBBPA-DAE), tetrabromobisphenol A bis (glycidyl ether) (TBBPA-BGE), tetrabromobisphenol A bis (2-hydroxyethyl ether) (TBBPA-BHEE), and tetrabromobisphenol A bis (2,3-dibromopropyl ether) (TBBPA-BDBPE), have been increasing steadily in recent years. Among them, TBBPS is used mainly as a reactive BFR in the production of polycarbonate and epoxy resins[7]; TBBPA-DAE is used as an additive BFR in expanded polystyrene and polystyrene foams as well as a reactive BFR in polystyrene foams[2]; TBBPA-BHEE is used as an additive BFR in engineering polymers, epoxy resins, and polyurethanes[8]; TBBPA-BDBPE is used as an additive BFR in polyolefin resins and polystyrene[9]; and TBBPA-BGE is used as a reactive BFR in thermoset resin-based housings for commercial mechanical and electrical/electronic components[8]. The widespread use of TBBPA analogs globally has led to their inevitable release into the environment during production, application, and disposal processes. These compounds have been detected in various environmental matrices, such as the atmosphere[10,11], water[12,13], soil, and sediment[14,15], as well as in organisms (including humans)[16-20]. Studies have demonstrated their toxic effects, such as reproductive/developmental toxicity in aquatic animals[21], neurotoxicity[22], liver toxicity[23] and endocrine-disrupting effects[24,25], garnering significant global attention.

The concentration and toxicity of pollutants within organisms are key determinants of their ecological risk[26], and understanding their bioaccumulation patterns and trophic transfer characteristics is essential for assessing their ecological risk[2,27,28]. Hydrophobic organic pollutants can accumulate in aquatic organisms through various mechanisms[29], and studies have revealed that ingestion via food, rather than direct absorption from water, is the primary pathway for the accumulation of these compounds in fish[30,31]. Although the toxicokinetics of TBBPA have been investigated across different aquatic species[32], field

studies have shown that its bioaccumulation and biomagnification patterns are influenced by species and habitat characteristics within aquatic food webs[33-35]. However, due to the limited research available, little is known about the bioaccumulation patterns of TBBPA analogs in aquatic ecosystems. Considering the differences in the physicochemical properties of the TBBPA analogs, it can be reasonably assumed that these analogs may exhibit different enrichment and trophic transfer behaviors in aquatic ecosystems than TBBPA.

The coral reef system in the South China Sea is a unique aquatic environment with abundant biological resources. It serves as a vital habitat for tropical ecosystems such as islands, mangroves, and seagrass beds, making it the most significant area for these ecosystems in China. However, chemical pollution has transformed it into a potential reservoir for persistent organic pollutants from China and Southeast Asia, contributing to the degradation of coral reef ecosystems in the region. Understanding the occurrence of TBBPA analogs in environmental matrices and marine food webs is therefore crucial for conducting accurate risk assessments. Despite this urgency, the bioaccumulation patterns and trophic transfer characteristics of TBBPA analogs within the South China Sea food web remain poorly understood. This study focuses on the occurrence of TBBPA analogs in water, sediment, and organisms from the coral reef system of the Xisha Islands in the South China Sea. The bioaccumulation patterns, trophic transfer characteristics, and dietary exposure potentials of these emerging pollutants within a typical tropical marine food web were examined. The findings provide critical insights into the bioavailability and toxicity of TBBPA analogs, offering essential data for accurately evaluating the ecological and health risks associated with these emerging pollutants.

MATERIALS AND METHODS

Chemicals and reagents

Five widely reported TBBPA analogs were selected for this study [Supplementary Table 1]. Chemical standards (purity ≥ 96%) were purchased from Macklin Biochemical (Shanghai, China), SHANGHAI ZZBIO (Shanghai, China), and Accustandard Inc. (New Haven, CT, U.S.A.). The isotope-labeled internal standard (IS) TBBPA-d_{10} was obtained from SHANGHAI ZZBIO (Shanghai, China). High-performance liquid chromatography (HPLC)-grade methanol, dichloromethane, n-hexane, and formic acid were purchased from Merck (Darmstadt, Germany) and Aladdin Biochemical Technology Co., Ltd. (Shanghai, China). Oasis HLB cartridges (200 mg/6 mL) were purchased from Waters Corporation (Milford, MA, U.S.A.).

Sample collection

Surface water (n = 8), sediments (n = 8), and 29 species of marine food web organisms (n = 108) were sampled using Agassiz trawl and macroplankton trawl from 8 sampling sites in the coral reef waters of the Xisha Islands, South China Sea, in October and November 2020 [Figure 1]. The biological samples included 5 species of shells (*Trochus sacellum*, n = 4; *Turbo chrysostomus*, n = 6; *Nerita striata*,n = 3; *Strombus lentiginosus*, n = 5; *Haliotis diversicolor*, n = 3), 3 species of sea cucumber (*Bohadschia marmorata*, n = 4; *Holothuria hilla*, n = 3; *Thelenota ananas*, n = 3), 3 species of crabs (*Etisus dentatus*, n = 5; *Clibanatius corallines*, n = 6; *Calcinus laevimanus*, n = 4), and 18 species of fish (*Upeneus sulphureus*, n = 6; *Parupeneus trifasciatus*, n = 6; *Parupeneus barberinus*, n = 3; *Epinephelus fasciatus*, n = 3; *Variola louti*, n = 4; *Cephalopholis argus*, n = 3; *Epinephelus merra*, n = 3; *Siganus puellus*, n = 3; *Siganus argenteus*, n = 3; *Siganus punctatissimus*, n = 3; *Scarus tricolore*, n = 3; *Scarus schlegeli*, n = 3; *Scarus sordidus*, n = 4; *Cheilinus trilobatus*, n = 3; *Hemigymnus melapterus*, n = 3; *Plectorhynchus orientalis*, n = 3; *Cantherhines dumerilii*, n = 3; *Lethrimus rubrioperculatus*, n = 3). 5 L of surface water samples were randomly collected, 2 mL of 4 mol/L H_2SO_4 and 250 mL of methanol were added, and the mixture was stored in darkness. Approximately 5 cm of surface sediments were collected via stainless-steel grabs and stored at -20 °C. All the biological samples were cleaned with Milli-Q water for species identification, and their body lengths and weights were

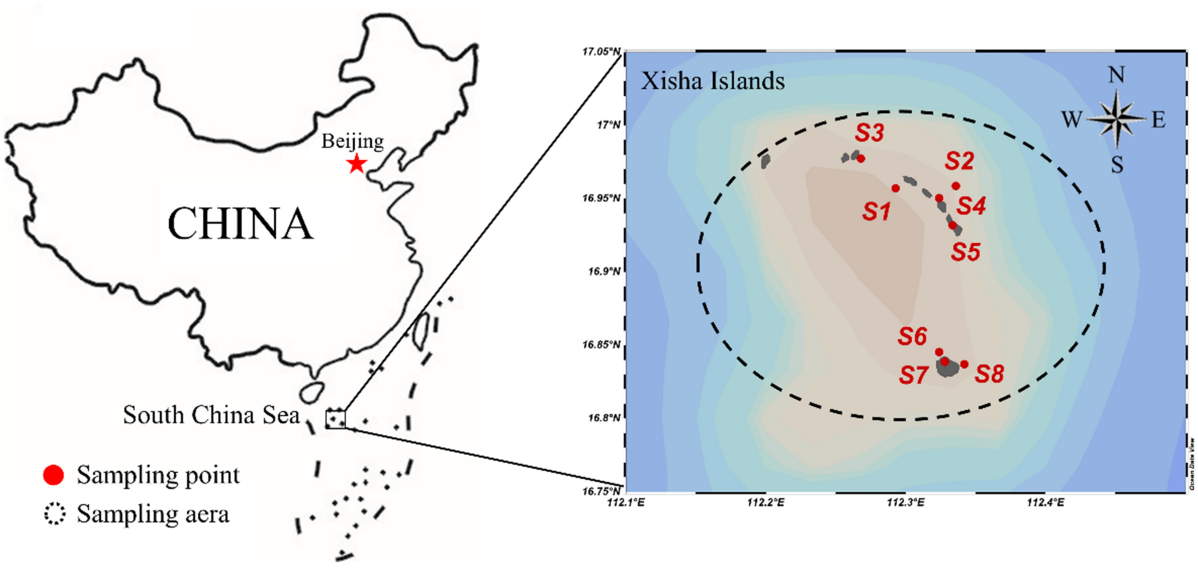

Figure 1. Schematic diagram of sampling point distribution.

recorded. The samples were frozen at -20 °C until pretreatment. The species classification, names, numbers, and physiological parameters are shown in Supplementary Table 2.

Sample preparation and instrumental analysis

A solid-phase extraction (SPE) method using Oasis HLB cartridges was performed for the pretreatment of TBBPA analogs from 1 L of water samples[36]. The freeze-dried sediment samples were extracted with dichloromethane/n-hexane (1:1, v/v) and methanol and cleaned with copper to remove any sulfur residues[2,37]. The extraction and purification procedures for the biological samples followed our previously established methods[2,38]. A detailed description of the collected samples is provided in Supplementary Text 1 .

An Agilent 1290 Infinity ultra-high-performance liquid chromatograph coupled to an Agilent 6470 triple quadrupole mass spectrometer with negative electrospray ionization was used for the analysis of the TBBPA analogs. Chromatographic separation was conducted via a ZORBAX RRHD Eclipse Plus 95 Å C18 column (2.1 mm × 50 mm, 1.8 μm, Agilent Technologies, U.S.A.) and a corresponding protective column (2.1 mm × 5 mm, 1.8 μm, Agilent Technologies, U.S.A.). Ultrapure water (A) and methanol (B) were used as the mobile phases, the column temperature was 30 °C, the flow rate was controlled at 0.3 mL/min, and the injection volume was 5 μL. The gradient elution conditions were as follows: 0-1 min, phase A 60%, phase B 40%; 5 min, phase A 15%, phase B 85%; 7 min, phase A 5%, phase B 95%; 10-12 min, phase A 60%, phase B 40%. The mass spectrometry conditions were as follows: gas temperature, 325 °C; gas flow rate, 8 L/min; nebulizer pressure, 45 psi; sheath gas temperature, 340 °C; sheath gas flow rate, 12 L/min; capillary voltage, 3,500 V; and nozzle voltage, 1,500 V. The detailed information of the target compound and recovery indicator is shown in Supplementary Table 3.

Quality assurance and quality control

The solvent blank, procedural blank, matrix effects, and quality control measures were evaluated to minimize interference from target compounds during sample processing. The method detection limit (MDL) and method quantitation limit (MQL) were established as 3 and 10 times the signal-to-noise ratio, respectively. The concentrations of the TBBPA analogs in both solvent and method blanks were below the

MDL. The intraday variation of the target compounds ranged from 3.09% to 15.8%. The recovery rates of TBBPA-d_{10} were 88.7%-93.4% for water, 81.8%-89.5% for sediments, and 71.2%-86.5% for biological samples. Absolute recovery rates for the target compounds were 79.5%-112% in water samples, 67.2%-87.0% in sediment samples, and 66.7%-99.1% in biological samples, satisfying analytical requirements. For further details on quality assurance (QA) and quality control (QC), refer to Supplementary Table 4.

Data processing

Trophic level (*TL*) represents the position of organisms within the food chain, reflecting their predation relationships. It is calculated as follows:

$$TL_{sample} = \frac{\delta^{15}N_{sample} - \delta^{15}N_{reference}}{\Delta\sigma^{15}N} + \lambda \quad (1)$$

where TL_{sample} denotes the trophic level of each aquatic organism, $\delta^{15}N_{sample}$ and $\delta^{15}N_{reference}$ represent the stable nitrogen isotope ratios of the sample and the reference organism, respectively. λ indicates the *TL* of the reference organism, and $\Delta\sigma^{15}N$ refers to the nitrogen isotope enrichment factor during trophic transfer. Based on the report by Zheng *et al.*, planktonic animals were selected as reference organisms in this study, with λ set to 2.0 and $\Delta\sigma^{15}N$ set to 3.8[39,40].

The bioaccumulation factor (*BAF*) measures the extent of chemical accumulation in organisms and is calculated as:

$$BAF = \frac{C_{biota,ww}}{C_{water}} \quad (2)$$

where $C_{biota,ww}$ is the concentration of TBBPA analogs in organisms (ng/kg, wet weight), and C_{water} is the concentration of TBBPA analogs in water (ng/L).

The biota sediment accumulation factor (*BSAF*) assesses the accumulation of chemicals between organisms and sediment, providing a reference for evaluating the ecological risks of specific chemicals. It is calculated using the following formula:

$$BSAF = \frac{C_{biota,lw}}{C_{sediment,TOC}} \quad (3)$$

where $C_{biota,lw}$ is the concentration of TBBPA analogs in organism (ng/g, lipid weight), and $C_{sediment}$ is the TOC-normalized concentration of TBBPA analogs in sediment (ng/g).

The trophic magnification factor (*TMF*) quantifies the biomagnification of chemicals within the food web and is determined using the following equations:

$$\mathrm{Log}\, C_{biota,lw} = a \times TL_{biota} + b \quad (4)$$

$$TMF = 10^{a} \quad (5)$$

where Log $C_{biota,lw}$ is the logarithm of TBBPA analog concentrations normalized by lipids in biological samples, a is the slope of the linear regression equation, and b is the intercept. The *TMF* is considered valid only if a is statistically significant.

To assess the human health risks from TBBPA analogs via seafood consumption, the estimated daily intake (EDI) was calculated as follows:

$$EDI = \frac{C \times DC}{BW} \quad (6)$$

where *C* is the TBBPA analog concentration in marine organisms (ng/g, ww), *DC* represents the daily consumption amount of seafood [82.4 g/(person·day)[41]], and *BW* represents the average body weight for adults (70 kg[42]).

Data analysis

The geographical locations of sampling points were plotted using Ocean Data View 5.5.2, while data analysis and visualization were carried out using Origin 2021 and SPSS 25. The results are expressed as the mean ± standard deviation. One-way analysis of variance (ANOVA) was performed to assess the significance between groups, and univariate correlation analysis (Spearman correlation coefficients) was conducted to evaluate the impact of parameters on the accumulation of TBBPA analogs. Statistical significance level was defined at a level of 0.05, with $P < 0.05$ indicating statistical significance.

RESULTS AND DISCUSSION

Trophic level construction for the coral reef food web in the South China Sea

In recent years, the analysis of stable carbon ($\delta^{13}C$) and nitrogen ($\delta^{15}N$) isotopes in organisms has emerged as an effective tool for reconstructing dietary relationships, characterizing nutritional structures, elucidating resource allocation patterns, and constructing food webs[43]. Stable isotope analysis leverages predictable biochemical fractionation processes[44]. Briefly, the $\delta^{13}C$ isotope ratio reflects the carbon source utilized by organisms; however, the difference in $\delta^{13}C$ between predators and prey is relatively small, with an enrichment coefficient ranging from 0‰-1‰, which makes it particularly useful for food source analysis[45,46]. In contrast, $\delta^{15}N$ has a trophic level-dependent fractionation effect, with enrichment coefficients of approximately 3‰-4‰ between consecutive trophic levels, making it a valuable tool for determining the trophic levels of organisms[47].

In this study, the $\delta^{13}C$ and $\delta^{15}N$ values were measured for muscle tissues of marine organisms in the coral reef food web of the Xisha Islands. The results are presented in Supplementary Figure 1A, and the $\delta^{13}C$ values ranged from -26.2‰ (masked rabbitfish) to -12.0‰ (prickly red sea cucumber), with a mean value of -19.2‰ ± 3.17‰ and a total range of 14.2‰. These values varied significantly ($P < 0.05$), reflecting the complex diet and diverse food sources within the coral reef food web. Shells had the lowest average $\delta^{13}C$ value of -20.8‰, with a maximum difference of 2.80‰. Fish exhibited the broadest $\delta^{13}C$ range, from -26.2‰ (masked rabbitfish) to -16.1‰ (dash-and-dot goatfish), with an average of -20.0‰, indicating a more varied diet, which is consistent with findings from Du *et al.*[48]. The $\delta^{15}N$ values ranged from 2.00‰ (hermit crab) to 10.2‰ (redfin emperor), spanning a total of 8.20‰, with significant differences observed between species (shell < sea cucumber < crab < fish, $P < 0.05$). Overall, the $\delta^{15}N$ values were lower than those reported in other estuarine or coral reef ecosystems[49,50], likely due to the area's relative isolation from human activities[51,52].

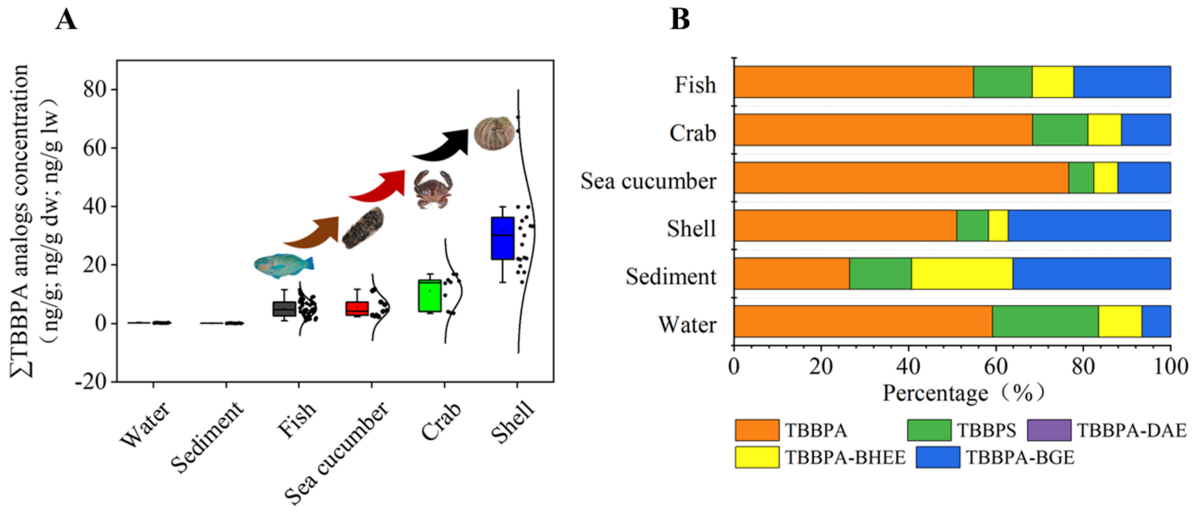

Figure 2. Concentration (A) and composition (B) of TBBPA analogs. TBBPA: Tetrabromobisphenol A.

Planktonic animals were used as reference organisms to calculate the *TL*s of the primary consumers in the coral reef food web [Supplementary Figure 1B]. The *TL*s of the 29 marine organisms surveyed ranged from 2.00 (hermit crab) to 4.14 (redfin emperor), with a food chain length of 2.14. Significant differences were observed in the *TL*s across groups, with shells, sea cucumbers, crabs, and fish showing *TL*s ranging from 2.22-2.90, 2.18-2.80, 2.00-2.92, and 3.21-4.14, respectively. Previous research has shown that overfishing, environmental changes, and habitat degradation can alter species composition and community structure[53], ultimately affecting the trophic composition of food webs. Li *et al.* reported *TL*s of marine organisms from the South China Sea coral reef ecosystem in 2016, with levels ranging from 1.26 (sea cucumber) to 4.25 (black parrotfish) and a food chain length of 2.99[54]. Between 2016 and 2020, disturbances in the South China Sea coral reef system, possibly driven by human activities, climate change, or the asynchrony of trophic organisms, led to decreased species diversity and disrupted consumer community stability[53]. In general, the organisms collected in this study span multiple *TL*s within the South China Sea coral reef food web, providing representative samples for analyzing the bioaccumulation patterns and trophic transfer characteristics of TBBPA analogs in this ecosystem.

Bioaccumulation patterns of the TBBPA analogs

The concentrations of TBBPA analogs in organisms within the coral reef food web are shown in Figure 2A and Table 1. Except for TBBPA-DAE (which was not detected, ND), the detection rates of TBBPA, TBBPS, TBBPA-BHEE, and TBBPA-BGE in 99 biological samples were 100%, 84.8%, 75.8%, and 90.9%, respectively. The average concentration (ng/g lw) ranges of TBBPA, TBBPS, TBBPA-BHEE, and TBBPA-BGE in the 29 organisms were 0.842-24.2, ND-4.66, ND-2.34, and ND-24.3, respectively, with significant differences observed among species ($P < 0.05$). The order of ∑TBBPA analog concentrations (ng/g lw) in organisms from lowest to highest was as follows: fish (5.11 ± 2.81) < sea cucumber (5.55 ± 3.32) < crab (11.2 ± 5.21) < shell (31.6 ± 14.7). Overall, the concentration of ∑TBBPA analogs in invertebrates was significantly greater than that in fish ($P < 0.01$), which is consistent with previous findings from the Bohai Sea of China[55]. It can be concluded that the accumulation of TBBPA analogs in organisms is influenced by species, perhaps due to differences in metabolism and exposure routes[56-58]. The concentrations of TBBPA analogs in the organisms were considerably lower than those observed in aquatic organisms from the Bohai Sea (ND-2782.8 ng/g lw)[55] and Qingdao, China (ND-4.2 μg/g dw)[59], aligning with concentrations of TBBPA-DAE and TBBPA-BDBPE detected in herring eggs from the Great Lakes[60] and TBBPA-BDBPE found in biological samples

Table 1. Concentrations of TBBPA analogs in biota samples

Classifications	Abbreviations	Water content (%)	Protein content (%)	Lipid content (%)	Concentrations of TBBPA analogs (ng/g lw[a])					
					TBBPA	TBBPS	TBBPA-DAE	TBBPA-BHEE	TBBPA-BGE	∑TBBPA analogs
Shell (n[b] = 5)	JKRL	73.9	11.6 ± 0.56	2.41 ± 0.57	17.6 ± 8.84	2.07 ± 0.588	ND	1.37 ± 0.332	4.30 ± 1.89	25.3 ± 8.57
	TYL	74.4	14.8 ± 0.97	1.50 ± 0.19	13.6 ± 3.38	2.08 ± 0.446	ND	1.49 ± 0.210	14.4 ± 1.85	31.6 ± 3.39
	ZSB	78.9	11.5 ± 0.78	1.43 ± 0.14	24.2 ± 6.29	4.66 ± 2.18	ND	2.34 ± 0.378	24.3 ± 11.5	55.5 ± 18.1
	ZTMT	75.3	15.2 ± 1.43	2.16 ± 0.87	16.8 ± 6.25	1.84 ± 0.418	ND	1.18 ± 0.188	12.5 ± 4.01	32.3 ± 7.68
	BFL	77.6	14.2 ± 0.79	2.33 ± 0.02	11.1 ± 1.76	1.58 ± 0.296	ND	1.10 ± 0.208	8.09 ± 4.66	21.9 ± 6.46
Sea cucumber (n = 3)	TWBN	90.2	4.40 ± 0.22	2.76 ± 0.11	2.35 ± 0.215	ND[c]	ND	ND	< 0.558	2.63 ± 0.215
	HYHS	90.9	3.77 ± 0.29	2.69 ± 0.15	7.26 ± 2.19	1.06 ± 0.273	ND	0.615 ± 0.085	1.09 ± 0.482	10.0 ± 1.97
	JMHS	91.5	4.69 ± 0.20	2.88 ± 0.34	3.77 ± 0.697	ND	ND	0.409 ± 0.111	0.777 ± 0.268	4.96 ± 1.07
Crab (n = 3)	CHMX	85.6	6.43 ± 0.44	1.46 ± 0.32	9.16 ± 1.08	2.24 ± 0.673	ND	0.986 ± 0.119	1.87 ± 1.02	14.3 ± 0.455
	TYDQ	81.1	5.77 ± 0.34	2.16 ± 1.02	10.4 ± 2.15	1.34 ± 0.487	ND	1.00 ± 0.241	1.73 ± 0.527	14.4 ± 2.92
	SHXA	88.7	7.86 ± 0.86	2.78 ± 0.32	2.5 ± 0.226	0.676 ± 0.145	ND	0.564 ± 0.128	ND	3.74 ± 0.230
Fish (n = 18)	SS	78.7	7.08 ± 0.23	2.92 ± 0.18	3.41 ± 0.811	0.740 ± 0.102	ND	0.807 ± 0.382	0.618 ± 0.185	5.58 ± 1.39
	WS	78.5	7.50 ± 0.81	2.31 ± 0.40	4.58 ± 0.782	1.60 ± 0.687	ND	0.986 ± 0.160	1.78 ± 0.437	8.94 ± 1.52
	XS	76.7	6.61 ± 0.36	2.68 ± 0.36	4.45 ± 0.875	0.94 ± 0.117	ND	0.945 ± 0.037	2.98 ± 1.50	9.32 ± 1.16
	YD	77.9	8.58 ± 0.79	3.12 ± 0.31	4.60 ± 1.61	1.00 ± 0.293	ND	0.861 ± 0.111	1.47 ± 0.358	7.93 ± 2.17
	YL	77.6	10.4 ± 1.46	3.21 ± 0.37	3.95 ± 0.618	1.08 ± 0.136	ND	0.764 ± 0.114	2.07 ± 1.12	7.86 ± 0.721
	BD	81.4	7.66 ± 0.71	4.35 ± 0.44	1.75 ± 0.225	< 0.327[d]	ND	ND	1.67 ± 0.665	3.59 ± 0.702
	CC	79.3	6.44 ± 0.43	3.96 ± 0.30	2.51 ± 0.069	0.616 ± 0.063	ND	0.461 ± 0.044	< 0.558	3.86 ± 0.050
	CY	81.7	6.58 ± 0.16	6.12 ± 0.06	1.35 ± 0.567	< 0.327	ND	ND	ND	1.51 ± 0.567
	DF	78	10.5 ± 1.68	4.31 ± 0.39	2.88 ± 0.47	0.670 ± 0.117	ND	0.747 ± 0.093	1.12 ± 0.422	5.42 ± 1.06
	FC	77	9.14 ± 1.26	9.28 ± 0.44	1.33 ± 0.013	ND	ND	ND	ND	1.33 ± 0.013
	HB	76.5	6.55 ± 0.56	8.88 ± 0.21	1.44 ± 0.314	ND	ND	ND	0.622 ± 0.217	2.06 ± 0.483
	HD	78.5	8.20 ± 0.86	6.45 ± 0.69	1.46 ± 0.545	< 0.327	ND	ND	0.777 ± 0.422	2.40 ± 0.600
	HL	77.2	9.60 ± 0.60	5.25 ± 0.61	3.51 ± 1.07	1.05 ± 0.350	ND	0.587 ± 0.208	0.942 ± 0.297	6.09 ± 1.64
	HS	78.3	11.9 ± 1.23	4.46 ± 0.54	2.62 ± 1.01	0.923 ± 0.051	ND	0.701 ± 0.184	0.823 ± 0.248	5.06 ± 1.13
	JW	77.3	7.32 ± 0.32	3.39 ± 0.29	3.87 ± 1.49	1.01 ± 0.207	ND	0.890 ± 0.357	2.02 ± 0.771	7.78 ± 2.45
	SD	77.2	7.67 ± 0.87	5.31 ± 0.12	3.14 ± 1.13	0.848 ± 0.477	ND	0.548 ± 0.155	1.00 ± 0.515	5.54 ± 1.76
	SY	79.3	8.10 ± 1.05	4.28 ± 0.30	2.56 ± 1.00	1.18 ± 0.185	ND	0.492 ± 0.055	1.37 ± 0.159	5.60 ± 0.726
	TB	79.1	7.33 ± 0.97	6.47 ± 0.70	0.842 ± 0.076	ND	ND	ND	0.778 ± 0.177	1.62 ± 0.252

lw[a]: Lipid weight; *n*[b]: the number of samples; ND[c]: not detected; < 0.327[d]: below the MQL. TBBPA: Tetrabromobisphenol A; TBBPS: tetrabromobisphenol S; TBBPA-DAE: tetrabromobisphenol A diallyl ether; TBBPA-BHEE: tetrabromobisphenol A bis (2-hydroxyethyl ether); TBBPA-BGE: tetrabromobisphenol A bis (glycidyl ether) MQL: method quantitation limit.

from the Xisha Islands[38].

The compositions of TBBPA analogs in water, sediment, and organisms are depicted in Figure 2B. Composition analysis revealed that TBBPA was the dominant component in water, accounting for 59.2% of ∑TBBPA analogs, followed by TBBPS at 24.2%. In sediments, TBBPA-BGE was the predominant component, accounting for 36.1% of the ∑TBBPA analogs, with TBBPA and TBBPA-BHEE accounting for 26.5% and 23.3%, respectively. In organisms, TBBPA was the most abundant compound, comprising 62.7% ± 10.3% of the total analogs, while TBBPA-BHEE had the lowest average proportion at 6.82% ± 1.93%. Among the shells, fish, and sea cucumbers, TBBPA-BGE was the second most abundant analog, making up 37.2%, 22.2%, and 12.1% of ∑TBBPA analogs, respectively. In crabs, TBBPS and TBBPA-BGE were present in similar proportions, at 12.6% and 11.2%, respectively. These results indicate that the accumulation of TBBPA in organisms is substantially greater than that of its analogs, likely due to the relatively lower production and use of these analogs. Additionally, TBBPA derivatives may undergo metabolic transformation within organisms, as TBBPA itself has been detected as a metabolite[61,62]. Hydrophobicity also plays a key role in the partitioning of TBBPA analogs across these marine organisms ($P < 0.05$, Figure 3A). Furthermore, according to the method reported by Kim *et al.*, this study compared the fugacity ratios of TBBPA analogs in water and biological samples [Figure 3B][63]. The results indicated that the Log $f_{organism}/f_{water}$ values in all biological samples were negative, suggesting that thermodynamic equilibrium between the biological and water phases had not been reached. Moreover, TBBPA and TBBPA-BGE were significantly negatively correlated between Log $f_{organism}/f_{water}$ and Log K_{OW} (Figure 3C, $P < 0.05$), suggesting that kinetic limitations were present for hydrophobic compounds.

The *BAF* values of TBBPA analogs in the coral reef food web are summarized in Table 2. The Log *BAF* values of TBBPA, TBBPS, TBBPA-BHEE, and TBBPA-BGE ranged from 2.05-2.90, 1.56-2.47, 2.15-2.61, and 2.16-3.75, respectively. Notably, the Log *BAF* value of TBBPA-BGE in organisms was consistently greater than that of TBBPA, TBBPS, and TBBPA-BHEE, indicating a greater bioaccumulation potential of TBBPA-BGE. Interestingly, the Log *BAF* values for TBBPA, TBBPS, and TBBPA-BHEE were all less than 3.30 across the organisms, suggesting that these compounds have limited bioaccumulation potential in this food web. TBBPA-BGE, however, exhibited bioaccumulation effects (Log *BAF* > 3.30) in certain species and even showed super bioaccumulation effects (Log *BAF* > 3.70) in ear shell (*Haliotis diversicolor*). Field-based *BAF* values for the TBBPA analogs were found to be higher (Log *BAF* > 3.10) than those measured under laboratory conditions. For example, Harrad *et al.* reported a Log *BAF* value of 0.62 for TBBPA in fish[64], Zhao *et al.* found bioconcentration factor (*BCF*) values ranging from 12.0-266 for TBBPA-DAE in carp under laboratory conditions[65], and our previous study reported *BCF* values of 5.68 and 1.04 for TBBPS and TBBPA-DAE in invertebrates and zebrafish, respectively[2]. We speculated that the observed differences in *BAF* values could be attributed to the complex interactions among environmental conditions[66], species differences, and exposure durations[67].

The *BSAF* values of TBBPA, TBBPS, TBBPA-BHEE, and TBBPA-BGE ranged from 0.052-1.49, 0.019-0.537, 0.032-0.184, and 0.012-1.10, respectively [Table 2]. Unlike the Log *BAF* values, TBBPA exhibited higher *BSAF* values compared to the other three analogs. In addition, the *BSAF* values of TBBPA analogs were

Table 2. The estimated Log *BAF*, *BASF* and *TMF* for TBBPA analogs

Factors	Categories	TBBPA	TBBPS	TBBPA-DAE	TBBPA-BHEE	TBBPA-BGE
Log *BAF* (ww)	Shell	2.79 ± 0.171	2.31 ± 0.158	ND	2.52 ± 0.103	3.53 ± 0.256
	Sea cucumber	2.33 ± 0.213	2.14 ± 0.110	ND	2.23 ± 0.119	2.45 ± 0.277
	Crab	2.44 ± 0.219	2.11 ± 0.155	ND	2.32 ± 0.121	2.74 ± 0.218
	Fish	2.35 ± 0.176	2.12 ± 0.276	ND	2.50 ± 0.133	2.91 ± 0.248
BASF	Shell	0.995 ± 0.444	0.265 ± 0.163	ND	0.113 ± 0.039	0.533 ± 0.386
	Sea cucumber	0.262 ± 0.149	0.122 ± 0.031	ND	0.040 ± 0.011	0.030 ± 0.021
	Crab	0.471 ± 0.229	0.162 ± 0.090	ND	0.068 ± 0.021	0.081 ± 0.035
	Fish	0.173 ± 0.090	0.093 ± 0.058	ND	0.057 ± 0.020	0.057 ± 0.039
TMF[a]	-	0.397	0.452	-	0.773	0.395
TMF[b]	-	0.410	0.460	-	0.790	0.420
Standard deviation	-	0.260	0.300	-	0.640	0.230
95% confidence interval	-	0.120-0.710	0.180-0.820	-	0.510-1.11	0.130-0.890
$f < 1$	-	99.8%	99.6%	-	91.7%	98.8%

TMF[a]: Calculated trophic magnification factors; *TMF*[b]: Monte Carlo simulated trophic transfer factors. BAF: Bioaccumulation factor; BASF: biota sediment accumulation factor; TBBPA: tetrabromobisphenol A; TBBPS: tetrabromobisphenol S; TBBPA-DAE: tetrabromobisphenol A diallyl ether; TBBPA-BHEE: tetrabromobisphenol A bis (2-hydroxyethyl ether); TBBPA-BGE: tetrabromobisphenol A bis (glycidyl ether); ND: not detected.

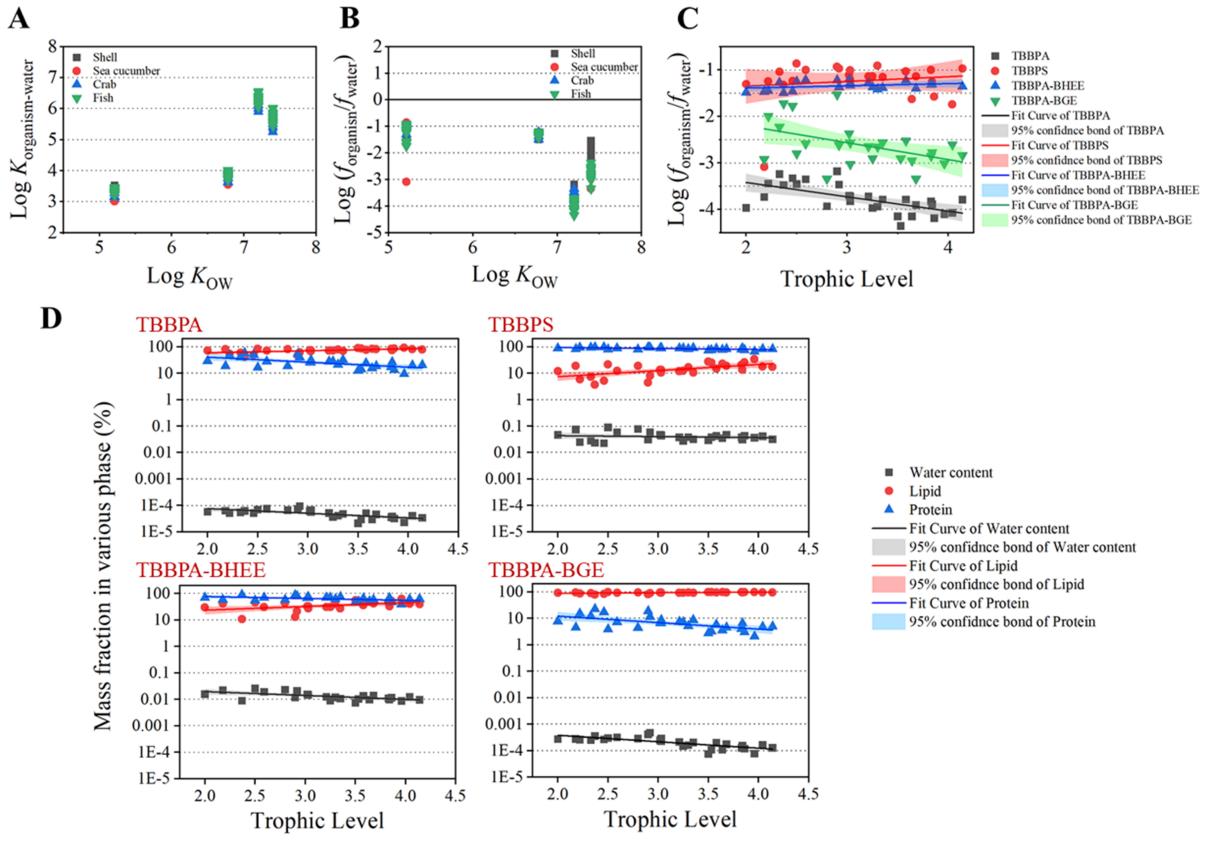

Figure 3. The Log $K_{organism\text{-}water}$ (A) and Log ($f_{organism}/f_{water}$) (B) values of TBBPA analogs related to Log K_{OW}, the relationships between Log ($f_{organism}/f_{water}$) values of TBBPA analogs and *TL*s (C), and the mass fraction of TBBPA analogs in various phases within the samples related to *TL*s (D). TBBPA: Tetrabromobisphenol A.

greater in shells than in sea cucumbers, crabs, and fish, which aligns with findings by Gu *et al.* in aquatic organisms from southern South Korea[68]. The distribution of pollutants between organisms and sediments has been shown to be habitat-dependent. For example, the *BSAF* value for TBBPA in organisms near the South China electronic waste disposal area was 0.02[69], whereas the range of *BSAF* values for TBBPA in mangrove organisms measured by Li *et al.* was 1.13-3.18[33]. Overall, the *BSAF* values for TBBPA analogs in this food web were generally less than 1, indicating that these compounds tend to accumulate more in sediments than in marine biota.

Trophic transfer characteristics of TBBPA analogs

Studies have demonstrated that TBBPA analogs in aquatic organisms originate not only from water and sediments but also from trophic transfer within the food chain[38]. This study aimed to calculate the *TMF* of TBBPA analogs in the coral reef food web [Figure 4]. A significant negative correlation was observed between the concentrations of TBBPA analogs and their *TL*s ($P < 0.05$). The *TMF* values calculated for TBBPA, TBBPS, TBBPA-BHEE, and TBBPA-BGE were 0.397, 0.452, 0.773, and 0.395, respectively. To verify the reliability of these results, Monte Carlo simulations were employed to assess the *TMF* values and probability distributions of these analogs in the food web [Table 2 and Supplementary Figure 2]. The simulations revealed that the *TMF* values for TBBPA, TBBPS, TBBPA-BHEE, and TBBPA-BGE were 0.410, 0.460, 0.790, and 0.420, respectively, with the probabilities of *TMF*s < 1 being 99.8%, 99.6%, 91.7%, and 98.8%, respectively. These findings suggest a high likelihood that TBBPA analogs have undergone trophic dilution in the food webs of coral reefs in the South China Sea. This study represents the first report on the trophic transfer behavior of TBBPA analogs in a tropical marine food web. However, it is important to note that different ecosystems may yield varied conclusions regarding the *TMF* of TBBPA analogs. For example, Liu *et al.* reported that TBBPA and TBBPS in the food web of the Bohai Sea, China, exhibited trophic dilution tendencies (with *TMF* values ranging from 0.31 to 0.55)[55]. In South Korea, the *TMF* value of TBBPA in the food web was found to be less than 1[35], whereas in the mangrove wetlands of southern China, the *TMF* values ranged from 1.22 to 2.17[33].

Several studies have suggested that water, protein, and lipid contents can influence the trophic transfer characteristics of chemicals[33,70,71]. In this study, the fractional masses of TBBPA analogs in biological phases were calculated to identify the most relevant sorption phase to the trophic transfer efficiency[72] [Figure 3D]. The results showed that the lipids were key biological phases for the mass distribution of TBBPA and TBBPA-BGE, possibly because of their relatively high Log K_{OW} values [Supplementary Table 1]; however, for TBBPS and TBBPA-BHEE, proteins were more important for their mass distribution. Additionally, correlation analysis was used to analyze the relationships between biological phases and *TL*s. Interestingly, the mass fraction of lipids was significantly positively correlated with *TL*s for all TBBPA analogs ($P < 0.05$). Furthermore, the correlation between *TL*s and the mass distribution of protein was significantly negatively correlated ($P < 0.05$). No strong correlation with *TL*s was observed for the mass fraction of TBBPS in the water phase. Previous studies have shown a significant correlation between TBBPA concentrations and lipid content in organisms[71], whereas Hou *et al.* reported no significant correlation between TBBPA-BDBPE concentrations and lipid content[38]. Similarly, Li *et al.* reported that the body length and weight of organisms in mangrove ecosystems did not significantly affect TBBPA accumulation[33]. These discrepancies suggest that the bioaccumulation of TBBPA analogs is a complex process, warranting further investigation into the combined effects of multiple factors.

Hydrophobicity and metabolic transformation are known to be key factors influencing the enrichment of organic compounds in aquatic food webs[2,38]. This study also evaluated the impacts of Log K_{OW} and metabolic rate (Log K_M) on the Log *BAF* [Supplementary Figure 3]. The results revealed a significant positive correlation between Log *BAF* and Log K_{OW} values of TBBPA analogs in shells, crabs, and fish ($P < 0.01$). Moreover, we calculated the organism-water partition coefficient ($K_{organism\text{-}water}$), which is likely to

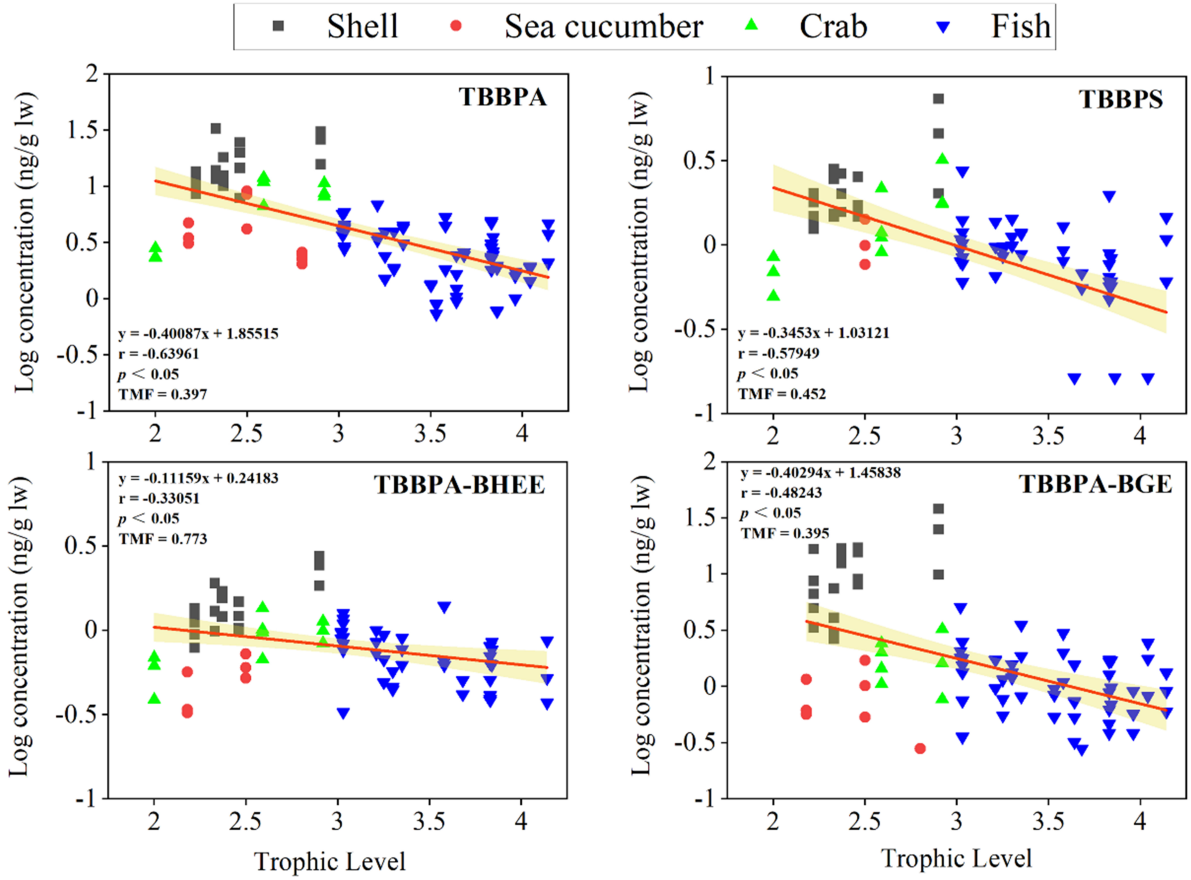

Figure 4. Relationships between concentrations of TBBPA analogs and trophic levels in biota. TBBPA: Tetrabromobisphenol A.

provide a more accurate prediction of the bioaccumulation potential of chemicals[73,74]. Figure 3A shows that the $K_{organism\text{-}water}$ values were also significantly correlated with Log K_{OW} for these samples ($P < 0.05$). In contrast, a significant negative correlation was observed between Log *BAF* and Log K_M in shells and fish ($P < 0.01$). These findings indicate that both hydrophobicity and metabolic transformation significantly influence the bioaccumulation of TBBPA analogs. Specifically, TBBPA-BGE demonstrated increased bioaccumulation potential within the coral reef food web of the South China Sea. However, it is important to note that the Log K_M values used in this study are predictive, and real-world factors such as species specificity and environmental conditions should be considered. Future studies should focus on the metabolic transformation of TBBPA analogs *in vivo* or *in vitro* to more accurately assess the impact of metabolic processes on bioaccumulation.

Human dietary exposure and health risk assessment

The toxic effects of TBBPA analogs on humans have not been thoroughly investigated[75]. However, studies have reported that TBBPA analogs can elicit comparable adverse effects in rodents and humans, with primary health concerns including endocrine disruption, metabolic disturbances, developmental toxicity, and genotoxicity[76-80]. Previous studies have shown that fish consumption is a significant route for human exposure to organic pollutants from aquatic environments, especially BFRs with high accumulation potentials in fish[81-83]. To comprehensively evaluate the risks of exposure to TBBPA analogs through fish consumption, the potential noncarcinogenic risk was estimated using the hazard quotient (HQ), which is the ratio of the EDI value to the reference oral dose (RfD). Considering a worst-case scenario of exposure,

the maximum investigated concentrations of TBBPA analogs in the food web samples were used to calculate the EDI. Among the 5 TBBPA analogs, only TBBPA has undergone a comprehensive evaluation for human noncarcinogenic risk, with an RfD for TBBPA estimated at 600 μg/(kg·day)[84,85]. For the other analogs, deriving a health-based guidance value was deemed inappropriate because of significant gaps in the toxicological data[75,80]. Therefore, the RfDs for TBBPA were adapted as a substitute for the ∑TBBPA analog in this study. Even under a worst-case exposure scenario, the maximum HQ of ∑TBBPA analog concentrations in seafood was found to be in the range of no risk (≤ 0.001) for the general population across southern China. However, the adoption of the RfD of TBBPA for its analogs may introduce uncertainty due to potential differences in toxicological profiles and variability in seafood consumption patterns, which may lead to an underestimation of risks. Addressing these limitations requires targeted toxicological evaluations and dynamic risk models that account for analog-specific properties, environmental trends, and consumption variability.

CONCLUSION

This study investigated the occurrence of TBBPA analogs in coral reef water, sediments, and organisms in the South China Sea. The results revealed that TBBPA analogs are widely distributed in environmental matrices and organisms in the region. Most of the TBBPA analogs had Log *BAF* values less than 3.7 and *BSAF* values less than 1, indicating weak bioaccumulation potential. Additionally, all the detected TBBPA analogs had *TMF* values less than 1, suggesting significant trophic dilution within this food web. This study also highlighted the critical role of hydrophobicity and metabolic transformation as influential factors in the bioaccumulation of TBBPA analogs in organisms. While TBBPA analogs are widely present in the environment, this study concluded that seafood consumption does not currently pose a significant health risk to local populations. However, future research is needed to explore the detailed bioaccumulation and trophic transfer mechanisms of TBBPA analogs in other food webs and assess their human toxicological effects more comprehensively to better define their ecological and health risks.

DECLARATIONS

Authors' contributions

Investigation, data curation, formal analysis, visualization, writing - original draft: Sun, C.
Data curation, formal analysis, visualization, and writing - review and editing: Zhang, S.
Writing - review and editing: Yan, S.; Zheng, X.; Huang, Q.
Conceptualization and methodology, project administration, reviewing and editing: Hou, R.
Resources and supervision: Xu, X.

Availability of data and materials

The data supporting the findings of this study are available within this article and its Supplementary Materials. Further data are available from the corresponding authors upon reasonable request.

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Conflicts of interest

Hou, R. and Xu, X. are Editorial Board members of *Journal of Environmental Exposure Assessment*. Yan, S. is a Junior Editorial Board member of *Journal of Environmental Exposure Assessment*. They are not involved in any steps of editorial processing, notably including reviewer selection, manuscript handling, and decision making. The other authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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