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Review article

Environmental levels, toxicity and human exposure to tributyltin (TBT)-contaminated marine environment. A review

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Abstract

Tributyltin (TBT) is a toxic chemical used for various industrial purposes such as slime control in paper mills, disinfection of circulating industrial cooling waters, antifouling agents, and the preservation of wood. Due to its widespread use as an antifouling agent in boat paints, TBT is a common contaminant of marine and freshwater ecosystems exceeding acute and chronic toxicity levels. TBT is the most significant pesticide in marine and freshwaters in Europe and consequently its environmental level, fate, toxicity and human exposure are of current concern. Thus, the European Union has decided to specifically include TBT compounds in its list of priority compounds in water in order to control its fate in natural systems, due to their toxic, persistent, bioaccumulative and endocrine disruptive characteristics. Additionally, the International Maritime Organization has called for a global treaty that bans the application of TBT-based paints starting 1 of January 2003, and total prohibition by 1 of January 2008. This paper reviews the state of the science regarding TBT, with special attention paid to the environmental levels, toxicity, and human exposure. TBT compounds have been detected in a number of environmental samples. In humans, organotin compounds have been detected in blood and in the liver. As for other persistent organic pollutants, dietary intake is most probably the main route of exposure to TBT compounds for the general population. However, data concerning TBT levels in foodstuffs are scarce. It is concluded that investigations on experimental toxicity, dietary intake, potential human health effects and development of new sustainable technologies to remove TBT compounds are clearly necessary.

Keywords: TBT; Environmental levels; Toxicity; Human exposure; Environmental fate; Review; Sediment

Contents

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1. Introduction

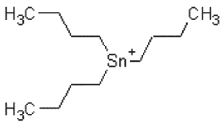
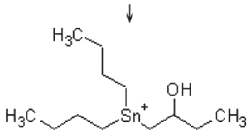
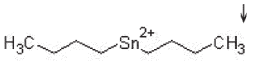
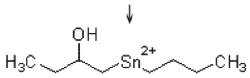
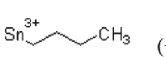
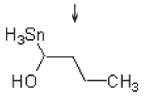
Due to its widespread use as an antifouling agent in boat paints, tributyltin (TBT) is a common contaminant of marine and freshwater ecosystems. TBT studies became of broad interest when antifouling paints were related to the worldwide decline of marine molluscs in costal areas. The first hints date from the early 1970s when the phenomenon of imposex was reported for *Nucella lapillus* in the UK (Blaber, 1970). Imposex occurs when male sex characteristics are superimposed on normal female gastropods. In studies with inter-tidal mud snails, the imposex condition was linked to pollution in marinas and mainly to TBT (Smith, 1981). This is because gastropods bioaccumulate TBT and its endocrine disruptive effects result in elevated testosterone levels giving rise to imposex (Horiguchi et al., 1997; Matthiessen and Gibbs, 1998).

In awareness of the undesired impacts of TBT, efforts have been undertaken in order to find a global solution to this problem and legal requirements have been enforced to protect the aquatic environment. Thus, the use of TBT in small boats was prohibited in many countries since the mid-1980s (Konstantinou and Albanis, 2004). France was the first country to ban the use of organotin-based antifouling paints on boats less than 25 m long in 1982 (Alzieu et al., 1986). Comparable regulations came into effect a few years later in North America, UK, Australia, New Zealand, Hong Kong and most European countries after 1988 (Alzieu et al., 1989; Champ, 2000, 2003; De Mora et al., 1995; Dowson et al., 1993). The International Maritime Organization (IMO) called for a global treaty that bans the application of TBT-based paints starting 1 January 2003, and total prohibition by 1 January 2008 (CD, 2002; IMO, 2001). In Europe, the current Water Framework Directive is the major Community instrument for the control of point and diffuse discharges of dangerous substances. Decision no. 2455/2001/EC of 20 November 2001 of the European Commission Parliament, amending water policy directive 2000/60/EC defines 11 priority hazardous substances, including TBT compounds, subject to cessation of emissions, discharges and losses into water. Additionally, decision no. 415/2004/EC of 5 March 2004 of the European Commission Parliament, amending Regulation 2099/2002 adopted the Regulation 782/2003 of 14 April 2003 on the prohibition of organotin compounds on ships. In the case of the Spanish regulation, the Royal Decree 995/2000 established that the sum of organotin species in waste discharges to continental surface waters must be lower than 20 ng l^{-1}, but no legislation for seawater samples has been yet approved. In America, the United States enacted the Organotin Antifouling Paint Control Act in 1988, where the restriction to a leaching rate of 4 μg cm^{-2} d^{-1} was introduced to the Federal level (US, 1988). The Occupational Safety and Health Administration American federal agency and the National Institute for Occupational Safety and Health American federal agency have established workplace exposure limits of 0.1 mg m^{-3}. The Food and Drug Administration American federal agency has set limits for the use of tin as an additive for food (ATSDR, 2005). Additionally, the water quality criterion of the US Environmental Protection Agency is that aquatic life and their uses should not be affected unacceptably if the one-hour average concentration of TBT does not exceed 460 ng l^{-1} and 420 ng l^{-1} in freshwater and saltwater aquatic live, respectively, more than once every three years on the average (acute criterion) and if the four-day average concentration of TBT does not exceed 72 ng l^{-1} and 7.4 ng l^{-1} in freshwater and saltwater aquatic live respectively more than once every three years on the average (chronic criterion) (EPA, 2002). A wide and detailed review of worldwide organotin regulatory strategies can be obtained from Champ (2000).

Present and future restrictions will unfortunately not immediately remove TBT and its degradation products from the marine environment, since these compounds are retained in the sediments where they persist. Additionally, while the use of antifouling paints containing TBT has been banned in countries that join the IMO, it is likely that organotin compounds will continue to be produced and used as effective biocides, especially in developing countries and those countries that do not join the IMO. Also they continue to be used in material and wood preservatives.

Once released from an antifouling coating, TBT is rapidly absorbed by organic materials such as bacteria and algae or adsorbed onto suspended particles in the water (Burton et al., 2004; Gadd, 2000; Luan et al., 2006). Subsequently it is readily incorporated into the tissues of filter-feeding zooplankton, grazing invertebrates, and, eventually, higher organisms such as fish, water birds, and mammals where it accumulates (Berge et al., 2004; Borghi and Porte, 2002; Harino et al., 2000; Ohji et al., 2007b). TBT may under favourable conditions degrade through successive dealkylation to produce dibutyltin (DBT), monobutyltin (MBT), and ultimately inorganic tin, becoming progressively less toxic in the process (Table 1) (Dubey and Roy, 2003). This mechanism of degradation is accelerated by UV radiation, increasing temperature, and biological activity, with the latter of greatest importance (Barug, 1981). Nevertheless, information on the mechanisms of TBT degradation mediated by microorganisms both in soil, fresh water, marine and estuarine environments, on the tolerance mechanisms of microbes and their relative significance, and also information on the role of anionic radicals in the degradation process is still limited (Dubey and Roy, 2003; Gadd, 2000). In freshwaters, half-life estimates for TBT range from around 6 weeks to 5 months, but degradation may be much slower in sediments, particularly under anaerobic conditions with persistence estimated at tens of decades (Dowson et al., 1996; Gadd, 2000). Wide distribution, high hydrophobicity, and persistence of organotin compounds have raised concern about their bioaccumulation, their potential biomagnification in the food webs, and their adverse effects to the human health and environment (Galloway, 2006; Nakanishi, 2007; Takahashi et al., 1999; Veltman et al., 2006). In recent years many reviews have reported on TBT environmental levels (Bayona and Albaiges, 2006; Diez et al., 2005; Nhan et al., 2005; Voulvoulis, 2006) and TBT toxicity (Cooke, 2006; Konstantinou and Albanis, 2004), and most recent reviews focuses on possible endocrine disrupting effects of organotin compounds (Lagadic et al., 2007; Nakanishi, 2007; Oehlmann et al., 2007; Sumpter, 2005). Nevertheless, a review on the human exposure to TBT — contaminated marine environment has not been yet published.

Table 1
Degradation of TBT via successive dealkylation

Compound	Chemical structure	Enzyme	Formula	Molecular weight
Tributyltin, TBT			$C_{12}H_{27}Sn^{+}$	290.06
β-hydroxybutyl-dibutyltin		TBT dioxygenase	$C_{12}H_{27}OSn^{+}$	306.06
Dibutyltin, DBT	 (+ Methyl ethyl ketone)	DBT dioxygenase	$C_8H_{18}Sn^{2+}$	232.94
β-hydroxybutyl-butyltin			$C_8H_{18}OSn^{2+}$	248.94
Monobutyltin, MBT	 (+ Methyl ethyl ketone)	MBT dioxygenase	$C_4H_9Sn^{3+}$	175.83
β-hydroxybutyl			$C_4H_{12}OSn^{3+}$	194.85
	Sn (+ Methyl ethyl ketone)		Sn^{4+}	118.71

Adapted from "Biocatalysis/Biodegradation Database" University of Minnesota; http://umbbd.msi.umn.edu/ last updated 16 April 2007.

Thus, the aim of this work is to provide the current state of the science regarding TBT and related compounds in the marine environment (water, sediment and biological materials), environmental levels, toxicity and then overview the current knowledge of human exposure to organotin compounds, with special emphasis on TBT due to its widespread use as an antifouling agent in boat paints and toxicity.

2. Properties, production and use

TBT compounds are organic derivatives of tin (Sn^{4+}) characterized by the presence of covalent bonds between three carbon atoms and a tin atom (Table 1). They conform to the following general formula $(n\text{-}C_4H_9)_3Sn\text{-}X$, where X is an anion or a group linked covalently through a hetero-atom. The nature of X influences the physicochemical properties, notably the relative solubility in water and non-polar solvents and the vapour pressure. Generally, the toxicity of the organotin is influenced more by the alkyl substitutes than the anionic substitutes. Progressive introduction of organic groups to the tin atom in any number of the R_nSnX_{4-n} series produces maximal biological activity against all species, when $n=3$ (Blunden et al., 1984; Dubey and Roy, 2003). Tributyltin oxide (TBTO) and tributyltin chloride have been normally used in laboratory experiments to investigate organotin toxicity.

In the aquatic environment, TBT is quickly removed from the water column and adheres to bed sediments because TBT has a high specific gravity near 1.2 kg l^{-1} at 20 °C (Landmeyer et al., 2004), low solubility less than 10 mg l^{-1} at 20 °C and pH 7.0 (Fent, 1996), and log K_{ow} values near 4.4 at pH 8 (Meador, 2000). Additionally, TBT is ionisable and exhibits a pK_a acidity constant of 6.25 (Meador, 2002). TBT sorption/desorption with natural sediment can be strongly influenced by changes in the pH and salinity, which may be explained by considering the contrasting sorptive behaviour of the neutral and ionic species at given pH and salinity conditions (Arnold et al., 1998, 1997; Burton et al., 2004; Hoch et al., 2003; Meador, 2000), similarly to what has been reported for other ionisable hydrophobic organic contaminants in sandy sediments (Antizar-Ladislao and Galil, 2004). Because the adsorption of TBT to sediments is reversible, contaminated sediments can act as a long-term source of dissolved-phase contamination to the overlying water column (Unger et al., 1988). Additionally, aging may be an important component of the fate of TBT in contaminated sediments, particularly in samples with high contents in organic carbon (3–5% w/w) (Burton et al., 2006). The affinity of organotins for adsorption to sediments is positively correlated to the extent of organo-substitution on the tin, such that increasing adsorption is seen for monobutyltin (MBT)<dibutyltin (DBT)<TBT (Landmeyer et al., 2004).

TBT was originally designed for use on the hulls of large ships to reduce the build-up of barnacles and to improve on speed and economic efficiency. However, an aggressive marketing program in the 1960s saw its fashionable use worldwide on much smaller craft both, in the oceans and within inland waterways (Sayer et al., 2006). World production of organotin compounds was estimated at about 40,000 ton/year in 1985 (Alzieu, 1998), increasing to 50,000 ton/year in 1996 (OECD, 2001). TBT compounds are the main active ingredients in biocides used to control a broad spectrum of organisms. Uses include wood preservation, antifouling of boats (in marine paints), antifungal action in textiles and industrial water systems, such as cooling tower and refrigeration water systems, wood pulp and paper mill systems, and breweries (Fent, 2006;

Fent and Muller, 1991; Hoch, 2001). MBT and DBT are mainly used as heat and light stabilizers for PVC materials. DBT is also increasingly used as binder in water-based varnishes (NCI, 2000). Thus, the various applications of TBT and derivates may result in a direct and indirect input into the environment.

3. Chemical analysis

An accurate characterization of environmental levels of TBT and derivates requires sample preparation and chemical analysis, which generally consist of several steps and depends on the physicochemical characteristics of the chemical compounds to be determined, of the matrix to be analyzed (water, sediment and biological materials), and of the chosen analytic technique. Each analytical step needed in such determinations (e.g. derivatization, extraction, separation and detection) can affect the accuracy and precision of the final quantitative speciation results (Adams and Slaets, 2000; Dietz et al., 2007; Morabito et al., 2000).

TBT compounds are present in seawater at ng l^{-1} levels, therefore their quantification requires highly sensitive techniques, and/or the collection of large sample volumes together with the application of pre-concentration methods. The high salt content of seawater may cause difficulties in the determination step, and the complete validation of organotin analysis in seawater samples is still far from being achieved, mainly because reproducibility problems (Brunori et al., 2005). Generally the applied extraction methods for organotin analysis in seawater are: (i) direct derivatization with organoborates or hydride in an acidic medium followed by liquid-liquid extraction (LLE), solid-phase extraction (SPE) or solid-phase micro-extraction (SPME) of the derivatized compounds; and (ii) LLE with non-polar solvents (toluene, dichloromethane) alone or in mixture and in the presence or not of acidic conditions and subsequent derivatization (Brunori et al., 2005). Additionally, the extraction of organotins from the aqueous to organic phase is enhanced by the addition of a complexing agent such as tropolone or carbamates (Brunori et al., 2005; Dietz et al., 2007; Pellegrino et al., 2000).

LLE is currently the less preferred solvent extraction technique because the procedures are normally quite time consuming and the pre-concentration factors achieved are very low. Nevertheless, LLE is relatively robust and can directly be applied to non-filtered samples, and allow transfer of analytes into an organic solvent (e.g., hexane, toluene) for subsequent analysis. SPE involves passing the liquid sample through a solid adsorbent that retains the analytes by mechanisms of retention that include adsorption, chelation, ion-exchange or ion pair; and subsequent recovery upon elution with an appropriate solvent. The main advantages of SPE are the possible integration of columns and cartridges in on-line flow injection systems, less solvent consumption, ease of use and possible application as species storage device for field sampling. Additionally, SPE is quite robust, fast and sensitive. SPME is based on the partition equilibrium of target analytes between a polymeric stationary phase attached onto a fibre and the sample matrix, combining analyte extraction and pre-concentration in a single step. The analyte is then desorbed from the fibre at high temperature into an appropriate separation and detection system. Currently, most SPME applications consist in analyte ethylation and headspace extraction, followed by gas chromatography separation. Thus, SPE and SPME meet modern requirements for analysis following point sampling.

Speciation of organotin compounds in sediments and biota may present difficulties during extraction, such as the process of isolating the target chemical compounds from complex cell structures and bio-molecules, and the number of possible errors is much higher. Generally the applied extraction methods for organotin analysis in solid samples are soxhlet, mechanical shaking, use of a sonication probe or ultrasonic bath, microwave and pressured liquid extraction (PLE) (Dietz et al., 2007). The most frequently adopted methods for organotin extraction from sediment are leaching with acids (acetic or hydrochloric acid) or acid-polar solvent (methanol) mixtures (Abalos et al., 1997).

The use of soxhlet extraction is time consuming and requires large amounts of solvent, and mechanical shaking may not provide adequate extraction efficiencies. Therefore there is a tendency to use faster, more efficient extraction methods with lower volume of solvent requirements. The use of ultrasonic radiation is easy to implement, fast and efficient. Acoustic cavitation, which is provoked by bubbles formed by the sound wave in a liquid that continuously compresses and decompresses, results in extreme local temperatures and pressures and facilitates solute extraction. Microwave extraction can be employed to accelerate leaching of organometallic species without affecting carbon-metal bonds while working at atmospheric pressure. Nevertheless in order to avoid species losses or transformation, parameters such as extraction medium, applied microwave power and exposure time have to be carefully optimised. PLE is based in applying increased temperatures, accelerating the extraction kinetics, and elevated pressure, keeping the solvent below the boiling point, thus enabling safe and rapid extractions. PLE is an analyte- and matrix-independent technique which provides cleaner extracts than other classical extraction procedures.

Developments within the last years concerned to the extraction and pre-concentration steps include the use of alternative energies (microwaves, PLE and ultra-sound) which have favoured extraction efficiency and time, and the use of SPME which has improved the pre-concentration step. Furthermore, the possibility of using isotope dilution techniques for tracing possible degradation and inter-conversion of organotin compounds during sample treatment has became available (García Alonso et al., 2002; Kumar et al., 2004).

Following extraction, methods for the determination of organotin compounds should provide sufficient sensitivity and selectivity. Most reported methods so far combine a separation technique such as gas chromatography (GC), coupled to element-specific detection systems, including atomic absorption spectrometry (AAS) (Donard et al., 1995; Sanz-Medel, 1998), flame photometric detection (FPD) (Lalère et al., 1995; Tao et al., 1999), pulsed flame photometric detection (PFPD) (Bravo et al., 2005) or inductively coupled plasma mass spectrometry (ICP-MS) (Encinar et al., 2000; Moens et al., 1997; Montes Bayón et al., 1999). In the case of GC, a derivatization step is

necessary prior to separation, due to the low volatility of the target compounds. The conversion of ionic alkyl-tins into species that can be analyzed by gas chromatography can be divided into two categories, those based on in situ hybridisation (with sodium borohydride, $NaBH_4$) or alkylation (with sodium tetraethylborate, $NaBEt_4$) (Brunori et al., 2005).

The ongoing development, optimization and validation of sample preparation and chemical analysis has provided a considerable amount of data indicative of organotin environmental levels around the world. Nevertheless, proper validation of the sample treatment step for speciation purposes is one of the main remaining problems basically due to the lack of matrix matched Certified Reference Materials (CRM) for a variety of biological and environmental samples. Currently, there are six CRM for tin species. One for fresh water sediment (BCR-CRM 646), certified for MBT, DBT, TBT, monophenyltin (MPhT) and diphenyltin (DPhT), triphenyltin (TPhT), one for a coastal sediment (BCR 462) certified for DBT and TPhT, one for harbour sediment (NRCC-PACS-2) certified for MBT, DBT and TBT as Sn, on for marine sediment (NIST-SRM 1941b) certified for MBT, DBT and TBT, one for fish tissue (NIES-CRM-11) certified for TBT and TPhT, and one for mussel tissue (BCR-CRM 477) certified for MBT, DBT and TBT (Dietz et al., 2007; IAEA, 2003). Additionally, it has been indicated that in order to assess long-term and diffuse contamination new sampling approaches would be required to provide large scale time weighed average data on tin species distribution (Dietz et al., 2007). A wide and detailed information on organotin sample preparation and analyses can be obtained from Brunori et al. (2005), Dietz et al. (2007) and Nemanic et al. (2007).

4. Environmental levels

A relatively large number of studies have involved surveys of TBT distribution in the water column, sediments, and biota. Tables 2–4 summarize organotin concentrations in water, sediment and biological tissue reported in several countries around the world. Given its strong affinity for suspended particulates and sediments, benthic sediments are regarded as the major sink for TBT in the environment (Batley, 1996; Clark et al., 1988; Hoch, 2001).

Measurements taken prior to restrictions on TBT use in antifouling paints have shown levels higher than 500 ng l^{-1} in North American and European marinas. For example one year before the UK ban (1986), TBT concentrations in Wroxham Broad and at a nearby River Bure boatyard were 898 ng l^{-1} and 1540 ng l^{-1}, respectively (Waite et al., 1989).

In recent investigations, it has been reported that TBT concentrations in water, sediment and biota have generally declined (Champ, 2000; Diez et al., 2006; Sayer et al., 2006), and maximum concentrations in marine water rarely exceed 100 ng l^{-1} (Bhosle et al., 2004). This reflects the fact that past measures against pollution caused by organotin compounds have been at least partly successful (EU-SCOOP, 2006). For example, it has been reported that TBT concentrations in surface marine waters have declined in France (Alzieu et al., 1986), in the UK (Dowson et al., 1996; Waite et al., 1989), in US (Espourteille et al., 1993; Valkirs et al., 1991), in the Gulf of Mexico (Wade et al., 1991) and Australia (Batley et al., 1992). Nevertheless, this decline might be argued. For example, one study in the UK covers all national shoreline during a period from early 1990s up to 2003, but the results cannot be used to assess a temporal trend since different areas were sampled in different years (OSPAR, 2005). A more systematic study in Norway covering nine stations from 1997 to 2003 did not show a statistical significant trend, while a Danish study covering 25 stations from 1998 to 2003 did show a statistical significant decrease in three stations (OSPAR, 2005).

Exceptions to this general decline of TBT in bottom sediments have been reported as hot spots associated with ship channels, ports, harbours, and marinas in Galveston Bay, US (Wade et al., 1991), Hong Kong (Ko et al., 1995), the Netherlands (Ritsema et al., 1998), Iceland (Svavarsson and Skarphedinsdottir, 1995), Israel (Rilov et al., 2000) and Japan (Harino et al., 2007). For example, Harino et al. (2007) recently reported TBT concentrations in sediments as high as 14,000 ng g^{-1}. These values were relatively higher than those reported in other coastal areas around the world (Table 3). Other exceptions to this general decline of

Table 2
Butyltin compounds in seawater (ng Sn l^{-1}) reported for several regions in the world

Sampling		Levels of organotin compounds			Reference
Location	Year	MBT	DBT	TBT	
American harbours and marinas					
West and east coast, Canada	1995	<d.l.–460	<d.l.–270	<d.l.–500	Chau et al. (1997)
Asian an Oceanian harbour and marinas					
Coast, Korea	1997–1998	<d.l.–13.4	<d.l.–22.3	<d.l.–4.5	Shim et al. (2005)
North coast of Kyoto, Japan	2003	2.5–23	2.1–13	3.9–27	Ohji et al. (2007a)
European harbours and marinas					
South west coast, Spain	1993	<d.l–51	6.8–20	9.1–79	Gomez-Ariza et al. (1998)
South east coast, France	1998	–	–	<0.015–0.12	Michel and Averty (1999)
Coastal waters, Greece	1998–1999	<d.l.–19	<d.l.–159	<d.l.–70	Thomaidis et al. (2007)
North west coast, Spain	Not provided	0.8–11.6	0.3–33.7	0.4–196.6	Rodriguez-Gonzalez et al. (2006)

MBT: monobutyltin; DBT: dibutyltin; TBT: tributyltin; <d.l.: below detection limit.

Table 3
Butyltin compounds in sediments (ng Sn (g dw)$^{-1}$ unless indicated otherwise) reported for several regions in the world

Sampling		Levels of organotin compounds			Reference
Location	Year	MBT	DBT	TBT	
American harbours and marinas					
West and east coast, Canada	1995	<d.l.–330	<d.l.–1100	<d.l.–5100	Chau et al. (1997)
Crystal Lake, US	2001–2003	21.3–320 [a]	59–350 [a]	1.5–14,000 [a]	Landmeyer et al. (2004)
Asian an Oceanian harbour and marinas					
Port of Osaka, Japan	1995–1996	<d.l.	<d.l.	10–2100	Harino et al. (1998)
Coast, Malaysia	1997–1998	5.0–360 [a, b]	3.8–310 [a, b]	2.8–1100 [a, b]	Sudaryanto et al. (2004)
Great Barrier Reef World Heritage Area, Australia	1999	<d.l.–161	<d.l.–71	<d.l.–1275	Haynes and Loong (2002)
Alexandria harbour, Egypt	1999	<0.1–186 [c]	<0.1–379 [c]	1–2076 [c]	Barakat et al. (2001)
Kochi harbour, India	2000–2001	<d.l.–470 [b]	n.a.	16.4–16,816 [b]	Bhosle et al. (2006)
Mumbai harbour, India	2000–2001	<d.l.–131 [b]	n.a.	4.5–1193 [b]	Bhosle et al. (2006)
Fishing harbours, Taiwan	2001–2004	n.a.	n.a.	2.4–8548 [b]	Lee et al. (2006)
West coast, India	2002–2003	n.a.	<d.l.–469	5–2384 [b]	Bhosle et al. (2004)
North coast of Kyoto, Japan	2003	4.3–22	2.3–23	1.2–19	Ohji et al. (2007a)
Coast, Vietnam	2003	3.9–30	8.1–42.7	8.3–51	Nhan et al. (2005)
Sanricu coast, Japan	2005	<d.l.–3300	<d.l.–3400	2–14,000	Harino et al. (2007)
European harbours and marinas					
West coast, France	1993	25–74	9–29	7–30	Ruiz et al. (1997)
River Thames, UK	1994	12–172	12–219	1–60	Scrimshaw et al. (2005)
South west coast, Spain	1998	2.5–95	2.1–284	1.2–130	Gomez-Ariza et al. (1998)
Tagus Estuary, Portugal	1998–1999	n.a.	n.a.	5.4–35 [b]	Nogueira et al. (2003)
Danish harbours and marinas, Denmark	1998–1999	n.a.	n.a.	100–5000 [b]	Jacobsen (2000)
North west Sicilian coast, Italy	1999–2000	<d.l.	<d.l.	3–27	Chiavarini et al. (2003)
North east coast, Spain	1995–2000	5–1131	47–3519	51–7673	Diez et al. (2002)
Coast, Portugal	1999–2000	<5.2–78	<5.3–65	<3.8–12.4	Diez et al. (2005)
North coast, Spain	2000	860–2870 [a]	150–710 [a]	50–5480 [a]	Arambarri et al. (2003)
South west, France	2001	1.0–125	<d.l.–87	<d.l.–89	Bancon-Montigny et al. (2004)
Barcelona harbour, Spain	2002	35–440	67–2607	98–4702	Diez et al. (2006)
North west coast, Spain	2005	0.7–3.8	0.5–357	0.6–303	Üveges et al. (2007)

MBT: monobutyltin; DBT: dibutyltin; TBT: tributyltin; <d.l.: below detection limit; n.a.: no data available.
[a] Wet weight.
[b] ng organotin instead of Sn.
[c] It is not specificied whether concentration is given on basis of dry or wet weight.

TBT pollution have been observed in newly industrialising countries. Many Eastern European countries implemented measures against pollution caused by organotin compounds later and additionally, old neglected deposits of toxic waste may be found at higher number in those areas, the latter with the intrinsic risk of releasing high amounts of pollutants in accidental events (UNEP, 2006). Additionally, exceptions may also occur in countries were no regulations have been adopted, such as in Bahrain where concentrations of TBT ranged from 2.29–17.9 μg l^{-1} in seawater and 128–1930 ng g^{-1} in sediments in samples collected from four coastal stations (Hasan and Juma, 1992).

The occurrence of organotin compounds in estuarine superficial sediments has been associated to their historical use, mainly related to fishing activities in the contaminated regions (Arambarri et al., 2003; Nogueira et al., 2003). The presence of organotin compounds in deep bed sediments cannot be ignored, particularly in those regions likely to be reworked by anthropogenic activities or also storm events (Scrimshaw et al., 2005).

Even though there is a great concern for the toxic effects of organotin in various aquatic organisms, more data about the accumulation and eco-toxicological implications of organotins along the food chain is needed. The most obvious routes of organotin exposure to biota and consequently to the food chain is through the diet and accumulation from surroundings (Lee et al., 2006, Strand and Jacobsen, 2005). Thus, the main route of the higher trophic levels like birds and mammals is through the diet; in invertebrates and fish direct uptake of organic contaminants from the surroundings, e.g., water and sediment, by skin or ventilator organs like gills are also important; and in a carnivore gastropod, it has been estimated that about half of the accumulated amount of organotin comes from the diet and the other half is accumulated from the surroundings (Bryan et al., 1989).

The accumulation and eco-toxicological implications of organotins along the food chain requires a complete characterisation of organotin levels in biological tissue of organisms of lower and higher trophic levels. Findings from Japan and Europe report that concentrations in fish have decreased significantly following restrictions in the use of TBT as an antifouling agent (de Brito et al., 2002; Harino et al., 2000; Rüdel et al., 2007) as it would have been expected. The average concentrations of the three butyltins (TBT, DBT, MBT) species normally monitored in marine food range from 100 to 1500 ng g^{-1} with highest concentrations present in cultured fish and molluscs in Asian and Oceanian countries (Kannan et al., 1995). For example, concentrations of TBT in zebra mussels in freshwater docks, up to 1440 ng g^{-1} wet weight have been

Table 4
Butyltin compounds in biological tissues (ng Sn (g dw)$^{-1}$ unless indicated otherwise)

Sampling		Biological sample	Levels of organotin compounds			Reference
Location	Date		MBT	DBT	TBT	
American harbours and marinas						
Coast, Canada	1995	Mussel	<d.l.–708	<d.l.–1062	20–1198	Chau et al. (1997)
Saint Lawrence river, Canada	1996	Mussel			<1440 [a, b]	Regoli et al. (1999)
Asian an Oceanian harbour and marinas						
Japan sea, Japan	1991	Walleye pollock	<3 [a]	<2.5 [a]	2.2–6.4 [a]	de Brito et al. (2002)
Bangladesh	1994	Fish	<5.6–170 [a, b]	<0.36–15 [a, b]	0.47–3 [a, b]	Kannan et al. (1995)
Aomori, Japan	1996	Fish	<d.l.–20 [a, b]	<d.l.–50 [a, b]	<d.l.–240 [a, b]	Ueno et al. (1999)
Coast, Korea	1997–1998	Vivalves	<d.l.–461	23–699	16–1610	Shim et al. (2005)
Coast, Korea	1997–1998	Starfish	51–2860	8–139	7–323	Shim et al. (2005)
Coast, Malaysia	1998	Fish	2.3–7.4 [a, b]	<1.3–13 [a, b]	2.4–190 [a, b]	Sudaryanto et al. (2004)
Aquaculture area, Taiwan	2002	Oyster	<3.3–407 [a, b]	<3.9–281 [a, b]	<3.8–417 [a, b]	Hsia and Liu (2003)
North coast of Kyoto, Japan	2003	Mussel	0.8–2.9 [a]	0.8–3.1 [a]	0.8–11 [a]	Ohji et al. (2007a)
Coast, Vietnam	2003	Clam	2.8–18	4.4–27	3.8–15	Nhan et al. (2005)
Coastline of Hong Kong, China	2004	*T. clavigera*	<d.l.–336	<d.l.–197	<d.l.–18	Leung et al. (2006)
Coastline of Hong Kong, China	2004	*T. luteostoma*	<d.l.–51	<d.l.–85	3.8–170	Leung et al. (2006)
Sanricu coast, Japan	2005	Mussel	4–32	3–92	3–287	Harino et al. (2007)
European harbours and marinas						
Northwestern Mediterranean, Spain	1996	Deep sea fish	<d.l.–54 [a]	4.0–67 [a]	1.0–52 [a]	Borghi and Porte (2002)
River Elbe and North Sea	1993	Fish	<d.l.–89 [a, b]	<d.l.–55 [a, b]	66–490 [a, b]	Shawky and Emons (1998)
The Netherlands	1993	Fish	23–41 [a, b]	13–183 [a, b]	9.2–67 [a, b]	Stab et al. (1996)
South west coast, Spain	1993–1994	Oyster	28.1±12.6	59.3±21.3	269±96	Gomez-Ariza et al. (1997)
Strait between Denmark and Sweden	1997	Vivalve	2.5–15 [b]	–	200–300 [b]	Strand et al. (2003)
Baltic Sea, Polland	1998	Mussel	<1.4–4.7 [a]	<1.4–24 [a]	2.2–39 [a]	Albalat et al. (2002)
South west coast, Spain	1999	*H. trunculus*	63	85	48	Gomez-Ariza et al. (2006)
Coast, Portugal	1999–2000	Mussel	<7.9–41	<2.5–18	<5.7–489	Diez et al. (2005)
North-Western Sicilian coasts, Italy	1999–2000	*H. trunculus*	<d.l.–167	<d.l.–316	<d.l.–91	Chiavarini et al. (2003)
West coast, Portugal	2000	Mussel	<10–605	<10–345	11–789	Barroso et al. (2004)
Aegean Sea, Greece	2001–2003	Bivalves	<d.l.–151	<d.l.–366	<d.l.–109	Chandrinou et al. (2006)
North west coast, Spain	2005	Oyster	0.4–12.9	7.6–441	74–193	Üveges et al. (2007)
North west coast, Spain	2005	Mussel	52.8–96.1	20.2–25.7	52.8–96	Üveges et al. (2007)

MBT: monobutyltin; DBT: dibutyltin; TBT: tributyltin; <d.l.: below detection limit; n.a.: no data available.
[a] Wet weight.
[b] ng organotin instead of Sn.

reported (Regoli et al., 1999). The presence of organotin compounds in marine plants and animals [eelgrass (*Zostera marina*), bladder wrack (*Fucus vesiculosus*), blue mussel (*Mytilus edulis*), black clam (*Arctica islandica*), common whelk (*Buccinum undatum*), spider crab (*Hyas araneus*), flounder (*Platichthys flesus*), cod (*Gadus morrhua*), herring (*Clupea harengus*), sculpin (*Myoxocephalus scorpius*), mute swan (*Cygnus olor*), eider duck (*Somateria mollissima*), common scoter (*Melanitta nigra*), great black-backed gull (*Larus marinus*), great cormorant (*Phalacrocorax carbo*), harbour seal (*Phoca vitulina*) and harbour porpoise (*Phocoena phocoena*)], all sampled in Danish coastal waters, was characterised, and all the analysed samples contained organotin compounds (Strand and Jacobsen, 2005). The highest hepatic concentrations of butyltins were found in flounder (60–259 ng Sn g^{-1} wet weight), eider duck (12–202 ng Sn g^{-1} wet weight) and maximum values were found in harbour porpoise (134–2283 ng Sn g^{-1} wet weight), which are higher than those reported by Kannan et al. (1995). Additionally, the lowest concentrations were found in seaweed and a plant-feeding bird (Strand and Jacobsen, 2005).

It has been observed that TBT tends to accumulate more in organs where more lipid exists, where the order of bioconcentration factors (BCF) is muscle < gill < viscera (Hongxia et al., 1998). The rates of uptake and elimination of TBT appear to control whole body tissue concentrations (Meador, 2000). For TBT, it appears that kinetics determine tissue residues and that body lipid regulates the toxic response, not the amount bioaccumulated (Meador, 2000). Controversially, it has been reported that there is evidence of organotin compounds accumulation at higher levels in liver than in most other organs, and it seems that organotins have a higher affinity to proteins than to lipids (Strand and Jacobsen, 2005). Therefore, further investigation is required to elucidate whether organotins present a higher affinity to proteins or to lipids, and what factors may affect either.

In summary, higher levels of organotin compounds have been found in coastal waters (up to 500 ng Sn l^{-1}) and sediments in harbours and shipping lanes or "hot spots" (up to 16,800 ng Sn g^{-1}), than in biological tissues (up to 790 ng Sn g^{-1}) (Tables 2–4). It has been reported that organisms of higher trophic levels present higher organotin levels than organisms of lower trophic levels, and higher than those expected to result through accumulation from water only. These observations have corroborated that uptake via food may be an important accumulation route (Rouleau et al., 1999). Nevertheless, clams, whelks and sediments collected in 2002 in Northwest Greenland presented organotins concentrations

at levels of 4 ng g^{-1} MBT, 4.4 ng g^{-1} DBT and 6.6 ng g^{-1} TBT in clams, *Chlamys islandica*, 3.1 ng g^{-1} DBT and MBT, TBT below the detection limit in whelks, *Buccinum finmarkianum*, and bellow the detection limit in sediments (Strand et al., 2006). Additionally, the occurrence of imposex was observed to occur in *B. Finmarkianum*. These results gave evidences of a widespread contamination of TBTs, and probably that the development of imposex in *B. Finmarkianum* is a more sensitive biomarker of TBT than the detection limit of analytical methods currently available (Strand et al., 2006).

5. Toxicity

The toxic potentials of organotins to various organisms are well documented (Fent, 1996). Research undertaken since the early 1970s has shown that TBT is very toxic to a large number of aquatic organisms (Blaber, 1970; Smith, 1981). TBT presents the highest toxicity, by disturbing the function of mitochondria, DBT is less toxic and its toxicity action is by blocking the absorption of oxygen in the mitochondria, whereas MBT has no obvious toxic effect on mammals (Hongxia et al., 1998; Selwyn, 1989). Thus, most studies dealing with organotin toxicity focus on TBT. TBT has been demonstrated to cause impairments in growth, development, reproduction and survival of many marine species (Beaumont and Budd, 1984; Haggera et al., 2005). Of particular concern has been the decline of marine molluscs in costal areas due to imposex (Gibbs and Bryan, 1996).

The embryonic and larval stages of marine invertebrates are less tolerant to toxicants than adults, and have been used for assessing the biological quality of marine water and sediments. In fact, it has been observed that TBT is likely to be absorbed into the eggs of fish, and a BCF of 107 (wet wt.) for TBT in minnow embryos *Phoxinus phoxinus* has been reported (Fent, 1991). Fish larvae are very sensitive to TBT and often exhibit effects in the 0.05 ng ml^{-1} range (Fent, 1996). Extreme toxicity of TBT to aquatic organisms in early life stages has been observed, although it is not yet clear if the increased sensitivity in juveniles is due to TBT-induced alterations in the uptake and elimination kinetics or differences in the tissue concentration (Meador and Rice, 2001). For example, the 48 h and 72 h lethal concentrations (LC50, lowest concentration to cause 50% lethality in the test population) for the estuarine zooplankter *Eurytemora affinis* were 2200 and 600 ng l^{-1} TBT, respectively (Hall et al., 1988). TBT concentrations of 100 ng l^{-1} significantly reduced the survival of neonates (young) of *Eurytemora affinis* after 6 d of exposure in a 13 d chronic experiment, however significant adverse effects were not reported at TBT concentrations ranging from 12.5 to 100 ng l^{-1} in another 13 d chronic test, but at 200 ng l^{-1} (Hall et al., 1988). Additionally, a TBT concentration of 6550–9250 ng l^{-1} TBT caused 100% mortality in larvae of minnows *Phoxinus phoxinus* in 96 h (Fent, 1991), which was within a concentration range found to affect other fish larvae and subadults/adults, 2000–23,400 ng l^{-1} (Bushong et al., 1988). Hatched veligers exposed to nominal TBT-Sn concentrations of 0.9, 1.4, 1.9, 2.8, 3.8, 4.7 and 5.6 μg l^{-1} for up to 96 h, under static conditions (17±1 °C and 33±1 psu) indicated a highly significant effect on larvae survival ($p<0.001$) for all times of exposure, except for the first hour, and LC50 decreased from 4.87 μg l^{-1} at 24 h to 1.78 μg l^{-1} at 96 h (Sousa et al., 2005). Another stage-related acute toxicity of TBT has been reported for the seabream *Sparus aurata*, L. fertilized eggs and larvae providing a 24 h LC50 of 28.3 μg l^{-1} and 38.6 μg l^{-1} respectively (Dimitriou et al., 2003). The sensitivity difference between the egg and the larval LC50 values was possibly due to an increased sensitivity of the earlier egg developmental phases to toxic substances (Weis et al., 1987). Additionally, the investigation of embryogenesis success from fertilized to normal larvae in *Paracentrotus lividus* (Echinodermata, Euechinoidea; 48 h incubation at 20 °C), *Ciona intestinalis* (Chordata, Ascidiacea; 24 h incubation at 20 °C), and larval mortality at 24 and 48 h in *Maja squinado* and *Palaemon serratus* (Arthropoda, Crustacea) provided an EC50 of 0.309 μg l^{-1} for *P. lividus* and 7.1 μg l^{-1} for *C. intestinalis*, and an LC50 of 22.30 μg l^{-1} (24 h) and 17.52 μg l^{-1} (48 h) for *P. serratus* (Bellas et al., 2005a,b). TBT has also proven to be extremely toxic to aquatic organisms in the adult life stages (Haggera et al., 2005). For example, one 96 h acute and two bioconcentration tests (500 ng l^{-1} of TBT for 50 days) with the test fish Tilapia indicated that TBT has a very high toxicity to Tilapia, with a 96 h LC50 value of 3800 ng l^{-1} (Hongxia et al., 1998). Interesting observations indicated that Tilapia can degrade TBT to less toxic DBT and a very small amount of MBT (Hongxia et al., 1998).

Several endpoints have been considered to evaluate TBT toxicity. For example, acute toxicity tests of TBT on the larvae of the rock shell, *Thais clavigera*, the disk abalone, *Haliotis discus discus* and the giant abalone, *Haliotis madaka* indicated that for the rock shell larvae, the LC50 values (based on the nominal concentrations) were 8400 ng l^{-1} (24 h) and 5600 ng l^{-1} (48 h), for the disk abalone larvae, the 48 h LC50 value was 5400 ng l^{-1}, and for the giant abalone larvae, the LC50 values were 3900 ng l^{-1} (24 h) and 1200 ng l^{-1} (48 h) (Horiguchi et al., 1998). Some effects on swimming behaviour and irregular movement of cilia due to atrophy of velum compared to that in the control, as well as stripping out of the larvae from the shell were observed even at lower concentrations than the LC50 values. In fact, it has been observed that growth impairment is a much more sensitive response to TBT exposure than mortality (Meador and Rice, 2001).

Other studies investigated the effect of TBT toxicity on several marine organisms, and compared different toxic effects in different species and gender. In general, it has been observed that species with a high rate of uptake or a low rate of metabolic conversion and elimination presents relatively high bioaccumulation ratios (Meador and Rice, 2001). The investigation of the LC50, BCF, lethal tissue residue (LR50), uptake clearance constant and elimination rate constant for TBT in four marine invertebrate and one marine fish species indicated that the toxic response and BCFs were vastly different among the species when exposed to the dissolved compound (Meador, 1997). The gammaridean amphipod *Rhepoxynius abronius* presented the fastest elimination rate constant when exposed to TBT concentration of 14.3±3.8 ng ml^{-1}, and also produced increasing concentrations of DBT and MBT during elimination

experiments, which gave evidences of metabolism of TBT (Meador, 1997). Further tests for the acute toxicity of TBT on amphipod crustaceans (five species of caprellids and three species of gammarids) collected from Otsuchi Bay (Japan) provided 48 h LC50 values of 1.2–6.6 μg l^{-1} for the caprellids, which were significantly lower than those of the gammarids (17.8–23.1 μg l^{-1}) (Ohji et al., 2002). These results suggested that caprellids are more sensitive to TBT than gammarids. Furthermore, the proportions of TBT and its derivatives, DBT and MBT, were measured in the amphipods collected from Otsuchi Bay. In the caprellids, TBT was the predominant compound, accounting for 72% of the total butyltin which reflected the butyltin ratio in seawater, while in the gammarids, TBT's breakdown products (DBT and MBT) predominated, accounting for 75% of the total butyltin. This difference suggested that caprellids may have lower metabolic capacity to degrade TBT than gammarids (Ohji et al., 2002). Further studies have reported 96 h LC50 values for copecode *Nitocra spinipes* of 13 μg l^{-1} (Karlsson et al., 2006), which are in accordance with other crustacean species, but higher and thus less sensitive than for the copecode *Tigriopus japonicus* (0.149 μg l^{-1}) (Kwok and Leung, 2005). Thus, it has been suggested that the difference in sensitivity to TBT among the amphipods is related to the species-specific capacity to metabolize TBT (Lee et al., 2006). Thus, differences in the uptake and elimination kinetics between species have been observed. Additionally, some species may need approximately 75 d for tissue concentration to reach steady-state conditions, which indicates that many mortality responses reported in the literature may underestimate the true response (Meador, 2000).

Although there is a wide amount of information available on acute toxicity of TBT, information on chronic toxicity of TBT is still relatively scarce. Recent toxicity studies have used the midge *Chironomus riparius* as a benthic model invertebrate to investigate effects of TBT at a sublethal, environmentally relevant concentration on development and reproduction over eleven generations (Vogt et al., 2007). A high variation in several life-cycle parameters during the study both in the exposed and the control population was observed. Adult male dry body weight was the only parameter showing a constant TBT effect over time, where male weights were higher in the TBT treatment in all generations compared to the control. Evidence for genetic adaptation of the TBT-exposed group over time to the stressful (TBT concentrations of 2–200 μg Sn l^{-1}) monitored as changes in reproductive outputs was also observed (Vogt et al., 2007). An alteration of evolutionary processes at low chronic exposure occurred and thus, an endangerment of natural populations could not be excluded (Vogt et al., 2007). Furthermore, it has been observed that with increases in TBT concentration, the proportion of females increased to 55.6% at 10 ng l^{-1} and 85.7% at 100 ng l^{-1} (Ohji et al., 2005). These results supported the hypothesis that males may have a higher sensitivity to TBT than females do resulting in high mortality of males, and thus, the difference in sensitivity to TBT among species may also be gender related.

Until relatively recently, most studies focused on the evaluation of biocide concentration on toxicity to various aquatic organisms at given environmental conditions. Acute effects for saltwater species for concentrations exceeding 420 ng l^{-1}, and lowest acute effects for a freshwater species for TBT concentrations of 1110 ng l^{-1} have been reported (Hall et al., 2000). The acute 10th percentiles for 43 saltwater species and 23 freshwater species were 320 and 103 ng l^{-1}, respectively (Hall et al., 2000). The order of sensitivity from most to least sensitive for saltwater trophic groups and corresponding acute 10th percentiles were as follows: zooplankton (5 ng l^{-1}), phytoplankton (124 ng l^{-1}), benthos (312 ng l^{-1}) and fish (1009 ng l^{-1}). For freshwater species, the order of sensitivity from most to least sensitive trophic groups and corresponding acute 10th percentiles were: benthos (44 ng l^{-1}), zooplankton (400 ng l^{-1}), and fish (849 ng l^{-1}). Additionally, differences between chronic effects for both saltwater and freshwater species have been observed, where the saltwater and freshwater chronic 10th percentiles were 5 and 102 ng l^{-1}, respectively (Hall et al., 2000). Mesocosm and microcosm studies in saltwater suggest that TBT concentrations less than 50 ng l^{-1} do not impact the structure and function of biological communities (Hall et al., 2000). Further studies to investigate acute toxicity of TBT (11.6–116.5 ng l^{-1}) in saltwater species *Artemia salina*, provided a 24 h LC50 value of 41.41 ng l^{-1} (Panagoula et al., 2002). Recently, chronic toxicity, growth and reproduction in the freshwater gastropod *Lymnaea stagnalis* exposed to waterborne TBTO over a range of four concentrations in the range of 0–10 μg l^{-1} has been investigated (Leung et al., 2007). It was observed that egg development was completely inhibited at 10 μg l^{-1}, whilst abnormal embryonic development occurred at 1000 ng l^{-1}. Survivorship of hatchlings was significantly reduced by TBT at 1000 ng l^{-1} while inhibition of shell growth of *L. stagnalis* was also observed at this concentration. Comparing these results with those reported in the literature, Leung et al. (2007) indicated that saltwater species are more susceptible to TBT than their freshwater counterparts. Higher toxicity of TBT in saltwater may be due to a "salting out effect". The solubility and thus chemical activity of lipophilic compounds, such as TBT, can differ between saltwaters and freshwaters because of strong ionic interactions between water molecules and major seawater ions, resulting in reduced solubility in salt waters. At levels below saturation, the effective concentration of the substance is therefore higher, leading to increased activity and greater bioavailability in saltwater conditions (Wheeler et al., 2002). This explains the existence of saltwater quality guidelines for TBT about one order of magnitude lower than freshwater quality guidelines (EPA, 2002).

Furthermore, a need to evaluate the combined effect of TBT concentration and environmental parameters was raised. Thus, the effect of temperature and salinity on the acute toxicity of the copepod *Tigriopus japonicus* against TBT was investigated (Kwok and Leung, 2005). 96 h LC50 of TBT was 149 ng l^{-1} at 25 °C and 34.5‰ salinity. Rising the temperature by 10 °C resulted in a significant toxicity increase of TBT, which could be attributed to the increase of the metabolic rate at higher temperatures and a consequent faster depletion of energy reserves resulting in an increase of susceptibility to TBT. The effect of temperature seemed to be greater than the effect of salinity due to a "salting out effect". A combined effect of TBT

concentration, temperature and salinity was suggested, where mortality increased with temperature but decreased with elevated salinity. Nevertheless, further investigations to understand the complex effect of salinity on TBT toxicity is still needed (Kwok and Leung, 2005).

In sediments, clams had disappeared in areas where TBT concentrations were approximately 800 ng g^{-1} dry wt. (Fent and Hunn, 1995), the polychaete *Armandia brevis* presented moderated to severe reduction in growth for sediment TBT concentration in the range 100–1000 ng g^{-1} dry wt. (Meador and Rice, 2001), and the bivalves *Macoma balthica* and *Scrobicularia plana* disappeared in sediment TBT concentrations over 700 ng g^{-1} dry wt. (Bryan and Langston, 1992; Langston and Burt, 1991). Additionally, in sediments the effect of total organic carbon (TOC) has been investigated and a strong influence of TOC on bioaccumulation and toxicity of TBT was suggested, where tissue residues and toxicity decreases when TOC levels increase in the sediment (Meador et al., 1997).

In an effort to understand mechanisms of TBT toxicity to aquatic organisms, toxicity and accumulation experiments in the gill tissue of the stingray *Urolophus jamaicensis* were conducted (Dwivedi and Trombetta, 2006). After a minimum 30 d acclimation period, the animals were exposed to one of five experimental doses of (TBTO, 50, 500, 1000, 2000 or 4000 ng l^{-1}). Following 3 h of treatment, animals were sacrificed and gill tissue was analysed. These studies indicated that *U. jamaicensis* is hypersensitive to TBT exposure, where the elasmobranch gill showed a distorted, swollen epithelium with exfoliation following acute exposure to as little as 50 ng l^{-1}.

The mechanisms of action for the toxicity of TBT in the freshwater fish embryos of medaka, *Oryzias latipes*, were investigated in medaka embryos exposed to a single concentration of TBT at developmental stages that corresponded to the formation of structures and/or organs which might be potential targets (Bentivegna and Piatkowski, 1998). Times of exposure included day 0, oviposition, day 3, completion of somite formation, and day 5, liver formation. Endpoints for evaluating toxicity were 96 h acute embryo lethality, rate of embryo development, hatching success, gross abnormalities, as well as hatchling eye diameter and number of somites. The clear chorion of medaka embryos allowed staging and in ova observations. The results of this study indicated that TBT caused acute toxicity which was concentration and age-dependent. The 96 h LC50 for embryos exposed on day 0 was 55 μg l^{-1}, which was lower than that for days 3 and 5, 124 and 117 μg l^{-1}, respectively. Thus, day 0 embryos were the most sensitive to the acute toxicity of TBT. Subchronic endpoints showed that toxicity was concentration related and that embryos exposed on day 0 were more sensitive than those exposed on days 3 and 5. Developmental rate was slowed by TBT in a concentration-related manner; however, embryos treated with 12 and 25 μg l^{-1} were able to recover and hatch at the same time as controls. Types of gross abnormalities were similar regardless of day of exposure and consisted of tails bent at the tip, curled, and/or shortened. Finally, the results of this investigation also indicated that TBT's toxicity was not due to effects on an age-dependent target but one present throughout embryo development. Exposure on particular days did indicate that inhibition of liver cytochrome *P450* values was not an important mechanism of action in embryos, and thus the acute toxicity of TBT was unrelated to liver enzymes (Bentivegna and Piatkowski, 1998). The cytochrome *P450* enzymes (specifically, CYP1, 2 and 3) play a central role in the oxidative metabolism or biotransformation of a wide range of exogenous and endogenous compounds (Nelson et al., 1996). Because of their roles in the detoxification and activation of foreign compounds, alteration of the expressions of hepatic cytochrome *P450* enzymes affects the potential risks and benefits of xenobiotics in general and organotin compounds in particular, and is important from a toxicological point of view (Williams et al., 1998). It has been demonstrated that TBT may interact with *in vitro* and *in vivo* hepatic cytrochrome *P450* in marine and freshwater fish, leading to inactivation of enzyme activity levels (Fent and Bucheli, 1994; Fent and Stegemann, 1993; Fent et al., 1998). Furthermore, recent investigations of the effect of TBT at lower concentrations than those reported to date from the subchronic test of fishes have suggested an involvement of cytochrome *P450* enzymes in TBT metabolism or the androgenic effects of TBT in fish (Mortensen and Arukwe, 2007).

Normally, in aquatic marines where TBT is present, other biocides may also be present. The toxicity of antifouling biocides used in boat paints, including TBT (and Irgarol 1051, Kathon 5287, chlorothalonil, diuron, dichlofluanid, 2-thiocyanomethylthiobenzothiazole) to evaluate the toxic effects of these compounds, either as single biocide or as a mixture has been investigated on *Vibrio fischeri*, *Daphnia magna* and *Selenastrum capricornotum* (Fernandez-Alba et al., 2002). In most cases, the sensitivity of the organisms towards the toxicants followed the order: *S. capricornotum* > *D. magna* > *V. fischeri*. TBT was the most toxic biocide for *S. capricornotum* and for *D. magna*, and the second most toxic following Kathon 5287 for *V. fischeri*. For mixtures of compound, toxicities were additive in only 33% of the cases and 21% of mixtures were less toxic than expected based on the sum of concentrations of toxicants (antagonistic effect). Synergistic enhancements of toxicity were observed for a majority (46%) of the mixtures. This infers that the use of a protective sediment concentration for TBT must be addressed in a site specific basis when additional toxicants are considered.

6. Human exposure

With an increasing amount of public concern about the possible harmful effects on human health resulting from exposure to TBT, the consumption of either contaminated drinking water and beverages, and in particular marine food has been reported as an important route of human exposure (Azenha and Vasconcelos, 2002; Chien et al., 2002; Forsyth and Jay, 1997). Marine fishery products may contain high TBT concentrations (Table 4), and different diets are expected to result in different organotin loads in human tissues and blood (ATSDR, 2005; EFSA, 2004; EU-SCOOP, 2006; Lo et al., 2003). However, in spite of the evidence that such sources expose humans to organotin compounds, limited data on butyltin deposition in humans are available. Thus, human risk assessment has mainly been based on immunological

studies in experimental animals and estimated human intake of marine food sources.

Based on immune function studies, a Tolerable Daily Intake (TDI) value for TBT of 0.25 μg (kg bw)$^{-1}$ day^{-1} was established (Penninks, 1993). Because of uncertainties in human-rat toxicity extrapolation, human-rat kinetics extrapolation, and inter-individual differences for both toxicity and kinetics, a safety factor of 100 was used for the final calculation of the TDI. This TDI was based solely on reduced thymus weight resulting from feeding TBTO to adult rats. Furthermore, this TDI value has been adopted by the World Health Organisation (WHO-IPCS, 1999a).

Seafood samples collected from markets in Asian, European and North American cities presented TBT concentrations averaging 185 ng (g dw)$^{-1}$. Daily intakes of TBTO determined in Japan by the duplicated-portion method were 4.7±7.0 μg d^{-1} in 1991 (n=39) and 2.2±2.2 μg d^{-1} in 1992 (n=40). Using the market based method, the daily intake was estimated at 6–9 μg d^{-1} in 1991 and 6–7 μg d^{-1} in 1992 (Tsuda et al., 1995). Based on average per capita seafood consumption rates for each country, the amounts of TBT ingested did not exceed proposed thresholds for chronic effects, suggesting negligible risks to the average consumer (Cardwell et al., 1999; Keithly et al., 1999). Furthermore, the average intake of organotin compounds from foodstuffs was estimated in a Finnish market basket (Rantakokko et al., 2006). The study was conducted by collecting 13 market baskets, containing 115 different food items in the city of Kuopio. Organotin compounds were detected only in four baskets, with the fish basket containing the largest number of different organotin compounds. In fish and sea foods, the predominant compounds were TBT, MBT, TPhT, DBT and DPhT measured at levels up to 2.53, 1.52, 1.11, 0.25 and 0.14 ng g^{-1} fresh weights, respectively. Based on EU-SCOOP data, the median intake in Norway was 7 ng (kg bw)$^{-1}$ day^{-1}, and the corresponding value based on mean data was 33 ng (kg bw)$^{-1}$ day^{-1}. High consumers were exposed to 15 (median) and 70 (mean) ng (kg bw)$^{-1}$ day^{-1} (EU-SCOOP, 2003). Although the aforementioned values are below the TDI adopted by the WHO (WHO-IPCS, 1999b), a potential risk may exist for high consumers (EU-SCOOP, 2006) and persons weighing less, e.g. children (Belfroid et al., 2000). In the UK, a survey conducted using commercial species from many locations throughout the country showed that organotin levels were generally low, and it was suggested that they did not present a concern for health (FSA, 2005). The public health risks associated with TBT from shellfish for the general population and fishermen of Taiwan was also evaluated (Chien et al., 2002). TBT concentrations in various oysters ranging from 320 to 1510 ng g^{-1} dry wt. varied with sampling locations. The highest TBT concentration (where TBT presented the major composition of total butyltin compounds, 86–91%) in oysters of 1510 ng g^{-1} dry wt. was obtained from the Hsiangshan coastal area. The values of oyster consumption for fishermen were 94.1 and 250 g d^{-1} for typically and maximally exposed individuals, respectively. In particular, the highest intake (250 g d^{-1}) from fishermen was almost two times greater than that of the general population (139 g d^{-1}). These results indicated that people who are exposed to contaminated oysters presented potential health risks (estimated as THQ — target hazard quotient, daily intake/reference dose) (Chien et al., 2002). In particular, the THQ values of Hsiangshan's fishermen of 3.87 for TBT for maximally exposed individuals were higher than in other oyster culture areas (e.g. Taiwan area presented a THQ of 0.76). In France, within the framework of the study by Calipso (2006) concern was risen regarding the use of available data for purposes of risk evaluation due to their qualitative and quantitative disparity (EU-SCOOP, 2003, OT-SAFE, 2004).

The information on human exposure to butyltin compounds is also limited. In a study of eight volunteers from Germany (4 male, 4 female; age 18–54), the serum exhibited levels of organotins that were below the limits of detection, although TBT and TPhT were detectable at concentration ranges 0.02–0.05 μg l^{-1} and 0.17–0.67 μg l^{-1}, respectively (Lo et al., 2003). In contrast, a study that involved blood analysis of 38 volunteers from Michigan (US) showed a concentration of butyltin ranging from below the detection limit and up to 155 μg l^{-1} (Kannan et al., 1999b). Some blood samples had butyltin concentrations comparable to those exhibiting immunotoxic effects detected in *in vitro* experiments carried out with human blood cells (De Santiago and Aguilar-Santelises, 1999; Whalen et al., 1999). The mentioned study of 38 volunteers from Michigan indicated a fast clearance of TBT from the blood and that blood would thus not be the ideal biological compartment for estimating butyltin burden in humans, however their study showed that people are in fact exposed, and prompted the need for the characterisation of the routes of human exposure (Kannan et al., 1999a). Further information on butyltin deposition in humans was based on a few studies on hepatic deposition in four Japanese (Takahashi et al., 1999), nine Polish people (Kannan and Falandysz, 1997) and eighteen Danish men (Nielsen and Strand, 2002), the Japanese participants having a considerably higher dietary intake of marine food. In the two first studies concentrations refer to the sum of DBT and MBT as TBT levels and were within the range 59–96 ng g^{-1} and 2.4–11 ng g^{-1}, respectively. In the last study with Danish men concentration referred to TBT, DBT, MBT, and TPhT and were <0.3 ng g^{-1}, 0.8–28.3 ng g^{-1}, 0.3–4.7 ng g^{-1}, and <3 ng g^{-1} respectively. The above studies did not include correlated information on diet or other potential exposures to butyltin compounds. In general DBT appeared to be the main butyltin species deposited in human liver (Appel, 2004).

The danger posed by organotin compounds to humans depends not only on the solubilization but also on the possibility that they may degrade during human digestion. The intestinal permeation of butyltins using the Caco-2 *in vitro* intestinal cell-line model was investigated (Azenha et al., 2004). It was found that permeability pattern correlates well with the general *in vivo* toxicity pattern (trialkyltin > dialkyltin ≫ monoalkyltin), but was different from the accumulation pattern (DBT > TBT > MBT). It was suggested that the high accumulation of DBT in the Caco-2 cells may result from its strong chemical affinity for dithiol groups found in many enzymes (Snoeij et al., 1987). More recently, exposing hamster fibroblasts to mono-, di-, tri- and tetramethyltin it was observed that cellular uptake of organotin compounds is relatively low (<0.5%), where dimethyltin and tetramethyltin are most membrane permeable compounds.

Furthermore it has been suggested that the toxicological potential of organotin species depend on membrane permeability (Doop et al., 2007). Degradation of TBT to DBT and MBT and of DBT to MBT by the Caco-2 cells was not detected (Azenha et al., 2004). Similarly to the human enterocytes, the Caco-2 cell has been shown to express the main enzymes involved in drug metabolism, however, it fails to express the predominant enzyme of the cytochrome *P450* family, the CYP3A (Delie and Rubas, 1997), which may have impeded the degradation of TBT and DBT. These results could not be corroborated since there was no previous evidenced of TBT and DBT degradation at the intestinal tract.

Using *in vitro* gastrointestinal digestions as a sample preparation, in an attempt to mimic the initial steps of the gastrointestinal absorption of butyltin species in humans, it was observed that the most important degradation reaction was that of DBT to produce MBT (Rodriguez-Gonzalez et al., 2005). Additionally, investigations of the soluble and insoluble fractions of a commercial mussel tissue at the end of the complete *in vitro* digestion showed that 61% of the original total butyltin content present in the mussel tissue was solubilized with very little degradation of TBT (Rodriguez-Gonzalez et al., 2005). Later on, it was demonstrated that after ingestion, TBT compounds undergo dealkylation by cytochrome *P450* enzyme systems in mammals (Ohhira et al., 2006), producing metabolites that are generally less toxic than the parent compounds (Appel, 2004). Furthermore, it has been reported that butyltin compounds do not degrade during cooking (Massanisso et al., 2003), which makes the above results more significant.

Several animal experiments have suggested that the spectrum of potential adverse chronic systemic effects of organotins in humans is quite broad and includes primary immunosuppressive, endocrinopathic, neurotoxic metabolic, and enzymatic activity, as well as potential ocular, dermal, cardiovascular, upper respiratory, pulmonary, gastrointestinal, blood dyscrasias, reproductive/teratogenic/developmental, liver, kidney, bioaccumulative, and possibly carcinogenic activity (EU-SCOOP, 2006, Nakanishi, 2007; WHO-IPCS, 1999b). In fact, several studies on the butyltin/intestinal epithelium interaction have been conducted, using mostly rodents, and some suggestions derived from observations have been reported. For example, the low intestinal absorption of MBT as compared to those of DBT and TBT was suggested as a possible explanation for the non-hepatotoxicity of MBT, which contrasts with the hepatotoxicity observed for DBT and TBT in mice (Ueno et al., 1994). Additionally, the different susceptibility to ingested organotin toxicants observed for different animal species was suggested to be due, at least in part, to interspecies differences in gastrointestinal absorption (Boyer, 1989). Thus, ratios between accumulated TBT, DBT, and MBT differ across species, which is of considerable importance as toxicity has been demonstrated to depend on the number of butyl groups (TBT>DBT>MBT) (Whalen et al., 1999). In a multi-generation study it was observed that following oral administration of TBT, speciation in rat livers reflected metabolism in that MBT>DBT>TBT, and male rat livers contained less TBT than female rat livers, indicating a greater metabolic capacity in male rats (Omura et al., 2004).

Although many reports have described potential toxicity of organotins, the critical target molecules for the toxicity and mechanisms of toxicity of organotin compounds in humans remain unclear (Appel, 2004; Cooke, 2006; Nakanishi, 2007). In order to elucidate the target molecules, conducted *in vitro* experiments have demonstrated that butyltins exhibit structure-related inhibition of the catalytic activity of human aromatase protein from human placenta (Heidrich et al., 2001) or transfected cells (Cooke, 2006) — endocrine disrupting mechanisms. DBT acted as a partial but less potent inhibitor of human aromatase activity whereas tetrabutyltin and MBT had no effect (Heidrich et al., 2001). Nevertheless, at concentrations effective for the inhibition of these enzymes, TBT is generally toxic to mammalian cells because it causes apoptosis or necrosis (Nakanishi, 2007; Saitoh et al., 2001). It seems that organotin compounds are potential stimulators of human placental oestrogen biosynthesis and human chorionic gonadotropin production *in vitro* and that the placenta represents a potential target organ in pregnant women for organotin compounds (Nakanishi, 2007). With respect to mechanisms of action, several biochemical processes have been identified as targets for TBT and some of these are involved in fundamental processes such as mitochondrial respiration, ion channels, steroidogenesis, receptor activation, and gene transcription (Cooke, 2006; Schulte-Oehlmann et al., 2006). Studies conducted with pubertal rats exposed to 15 mg TBT and 6 mg TPhT resulted in a clear effect on the examined androgen-dependent endpoints of male reproduction, which may have been mediated by inhibition of cytochrome *P450* aromatase activity (Grote et al., 2004). Using human hepatic cytochrome *P450* systems it was observed that TBT was similarly metabolised by male and female human hepatic microsomes *in vitro* (Ohhira et al., 2006).

To finalize, it is emphasized that contaminated sediments remain one of the most challenging issues within the international scientific community. Investigations on experimental toxicity, dietary intake, potential human health effects and development of new sustainable technologies to remove TBT compounds coupled with new sampling approaches are clearly necessary.

A considerable number of previous studies have reported on the investigation of marine species responses to TBT in water, nevertheless more investigation is still required to understand the responses to TBT in sediments. It is still not clear whether organotins present more affinity to proteins or to lipids and what are the factors which may affect either affinity. Future toxicity studies need to consider that TBT is species-specific and that long periods of time may be required for tissue to achieve steady-state conditions and thus obtain more accurate responses. The use of biomarkers (imposex) instead of TBT concentrations in water, sediment and biological tissues should be contemplated due to the limitations that currently available analytical techniques present. The presence of a number of toxicants in real environmental matrixes may have a synergistic enhancement on TBT toxicity, which has as yet poorly been investigated. Climate change is one of the greatest environmental, social and economic threats facing the planet. In assessing climate-change

impacts in the coastal environments, changes in water temperature, solar radiation, dissolved CO_2, pH and salinity can affect TBT toxicity and thus their impact to the environment and human health need further investigation and should be included in future research plans. At present, the combined impacts of pollution and climate change on biodiversity an ecological status are unknown.

Nowadays, there is limited available data on organotin deposition in humans, and risk assessment based on immunological studies in experimental animals and estimated human intake of TBT contaminated food sources may raise concerns due to qualitative and quantitative data disparity. More research is still needed to elucidate what is the ideal biological compartment for estimating organotin burden in humans, what are the critical target molecules, and what are the mechanisms of toxicity of organotin compounds in humans.

Most immediate needs for sites with contaminated sediments include the development of tools for site assessment, contaminant monitoring, and fate and transport modelling as well as identifying methods to stabilize sediments to minimize risks before an adequate remediation strategy is implemented, particularly in those areas where the total TBT concentration give a total THQ in excess of 1. Advancements have been made to begin the process of mitigating impacted sediment sites and to understand the effect of in situ bioremediation strategies in sediments contaminated with ionisable hydrophobic organic contaminants (Antizar-Ladislao and Galil, 2006), however, the remediation of these sites is difficult (Abbott et al., 2000). The current state of the practice for remediation of contaminated sediments is primarily limited to only three strategies: dredging/excavation, capping, and monitored natural attenuation (MNA) (Saeki et al., 2007). Nevertheless, most available strategies can be problematic, due to the fact that the contaminants remain in the environment, and the issue of food chain bioaccumulation of pollutants is not eliminated. Hence, there is a need to establish alternatives to the existing, widely accepted sediment remediation approaches, currently under investigation.

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