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Organotin applications and environmental toxicity

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ABSTRACT

Organotin compounds have attracted global attention due to their extensive use for agricultural, industrial, medicinal, and domestic applications. These applications have made them enter the environment. This has caused environmental concerns due to the proven toxicological relevance of the compounds. Their toxic effects result in extensive damage to non-target organisms at ultratrace concentration levels (ppt) and accumulation in sediments and biota. This leads to the legislative restriction place on the uses of some of these compounds. Despite the legislative restriction, their environmental pollutions continue. Hence, this review which is aimed at providing an overview of the application of organotin compounds and their environmental toxicities.

Introduction

The environmental concerns regarding organotin compounds are of great importance due to their remarkable industrial, medicinal, agricultural, and domestic applications [1, 2]. Organotin compounds (OTCs) are among the most widely used organometallic compounds, these are compounds in which there is at least a bond between the tin cation and a carbon atom in the compound. The reactivity and application of OTCs are based on the stability of C-Sn bonds, the rate at which the anion can be displaced and the probability of making the coordination higher than four. Hence, this leads to its applications in a variety of chemical transformations including transmetallation reactions, addition to unsaturated compounds, catalysts and polyvinyl chloride (PVC) stabilizers etc. [3].

First logical studies of the series of OTCs was started by Edward Franklin in 1853, he synthesized diethyltin-diodide and tetraethyltin in 1859. Other studies followed and today more than 800 organotins (OTs) are known. Majority of these compounds originated from human activities except methyltins, which can also be produced by biomethylation. Although OTs have been known since 1850's, the first industrial use did not develop until 80 years later when it was used as polyvinyl stabilizers. In 1932, STANDARD OIL was issued a patent for the use of tetraalkyltin compounds as stabilizers of transformer oils. Yngve and his colleagues working in the Union Carbide Company in the 1930's were given the credit for the original development of OT stabilizers for vinyl plastics. There was a great change in the 1940's when the production of PVC in plastic industries began to increase. The PVC polymer becomes unstable under the effect of heat and light, as these change the colour and make it brittles. It was discovered that by adding certain OT derivatives, this thermal degradation process can be averted. This promoted considerable studies in the area which led to the synthesis of several OTCs. These compounds can also be used as fungicides, miticides, molluscicides, hermatocides, ovicides, rodent repellants, wood preservatives and antifouling paints [4].

The annual industrial world production of OTCs was less than 50 tons as at the time the systematic OT program started in Utrecht in 1950. In 1960, it was 2000 tons, while in 1965, 5000 tons and in 1969, it rose to about 14,000 tons, while in 1975, a production of 25,000 tons was attained. In 1992, up to about 50,000 tons was produced. High use of OTCs is observed in Southeast Asia and developing countries. Thailand has a large and ready market for application of OT principally in the agricultural sector [4]. The various technological and industrial applications as well as the distribution of OTCs have increased concern about the bioaccumulation and biomagnifications of these compounds and their toxic effects on the environment, since the environment consists of different ecosystems supporting a wide range of biota upon which human life depends. The uses of OTCs as toxic additives have created a well-established environmental threat since 1970s [5-8]. Run-off from OTCs used for agriculture account for the largest source of OT accumulation in the environment. These wide uses have resulted in the reckless release of these toxic compounds in the environment. The adverse environmental effects of the OTs have surpassed their usefulness in day to day applications, prompting bans on compounds such as tributyltin (TBT) chloride. Many countries worldwide have banned the application of TBT, beginning with France in 1982 and followed by the UK in 1986. In the USA, TBT was banned in 1988 and between 1987 and 1990; it was banned in Europe, Canada, Australia, New Zealand and Japan [9]. Despite the legislative restriction placed on the uses of some of these compounds, their environmental pollutions continue.

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They still pose a risk to the environment especially non-target organisms (both aquatic and terrestrial).

Regardless the different categories of OT, legislative restrictions are only on TBT pollution, whereas other OTs also show strong biocidic effects. Modern studies have shown that OTCs are released into the environment from various sources. For example, leaching and normal weathering of PVC products and plastics contribute dibutyltin (DBT) and its decomposition products to the environment. Some researches have shown that there are detectable levels of OTCs in house dusts collected in several European countries; indicating the presence of trisubstituted OTCs in household products such as fungicidesand pesticides etc.

However, only developed countries have taken steps in enforcing the legislative restrictions. There is no specific legislation controlling the use of TBT in food in Asian countries other than Japan and the Hong Kong Special Administrative Region of China [10]. There is still a lack of enforcement on their control in Africa. Therefore, there is need to know the environmental impact of these compounds in Africa in order to draw the attention of the government and different individuals on their toxicities and environmental implications. Presently in some African countries, there are empowerment schemes in which people are being trained on the production of insecticides, rodent repellants, and disinfectants among other chemical products. Some of the starting materials of these products are OTs, the populace have to be informed on the toxic effects of these compounds. Hence, this review which is aimed at providing an overview on the applications of OTCs and their environmental toxicities.

Classes and properties of organotin compounds

Organotin compounds are classified into Aliphatic and Aromatic organotins. These can be grouped depending on the number of carbon-tin bonds. They are designated as mono-, di-, tri, and tetraorganotin compounds with the general structure: $R_nSnX_{4-n,}$ where R = alkyl or aryl group, Sn = the central tin atom in the oxidation state +4 and X = a singly charged anion or anionic organic group (such as halides, hydroxide etc.).

The Sn-C bonds are stable in the presence of water, atmospheric oxygen, and heat. They are reported to be stable at temperatures up to 200 ^{0}C, so thermal decomposition has no significance under environmental conditions. This bond (Sn-C) can be cleaved by ultraviolet radiation, hydrolysis, Solvoylysis, acidic and basic attack and halogenations etc. The number of Sn-C bonds and the length of the alkyl chains have a significant effect on the chemical and physical properties of OTs. In general, the solubility of OTCs in water decreases with increasing number and length of the organic substitutes and depends on the particular X. The results of the experimentally determined aqueous solubility range between 20 gl^{-1} for the readily soluble Me_2SnCl_2 to less than 1 mgl^{-1} for sparingly soluble phenyl, cyclohexyl, and octyltin compounds.

Table 1. Physical properties of selected organotin compounds [4].

	m.p (^{o}C)	b.p (^{o}C)	Density (gcm^{-3})	Solubility ($mgdm^{-3}$)
Bu_4Sn	-97	145/1.3 kpa	1.06	-
Bu_3SnCl	-16	172/3.3 kpa	1.21	50[a] 5-17[b]
Bu_2SnCl_2	39-41	135/1.3 kpa	_	4-50[a] 92
$BuSnCl_3$	-	93/1.3	1.69	-
Me_3SnCl	37-39	154	_	-
$MeSnCl_2$	106-108	188-190	_	20 000[a]
$MeSnCl_3$	48-51	171	_	-

[a]Solubility in seawater; [b]Solubility in distilled water.

Synthesis

There are different routes of synthesizing OTCs. These are Grignard route, Wurtz route, alkylaluminium route and by direct synthesis. The first three routes involve two reaction steps in synthesizing OT halides. The first reactionstep is to make direct tin-carbon bond in the compounds. It involves the reaction of tin tetrachloride ($SnCl_4$) with fitting reagents to form different tetraaklytins compounds, R_4Sn. The second reaction step involves the reaction between the R_4Sn and $SnCl_4$ to produce less alkylated OT chlorides of the type R_3SnCl, R_2SnCl_2 or $RSnCl_3$ [4]. Other derivatives of tin can be directly synthesized from these chlorides for industrial uses. Figure 1 shows the various synthetic routes for organotin compounds.

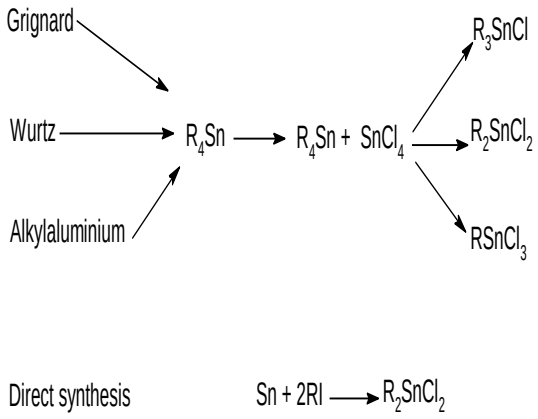

Figure 1. Synthetic routes for organotin compounds.

In the late 1940s, the commercial manufacturing of OTCs started in the USA at the Metal and Thermal Corporation's plant in Rathway, New Jersey by using the Grignard reagent (nRMgCl). Grignard route gives high yields, but the use of high volume of solvent is required. This is also the problem encountered while synthesizing via Wurtz route. This route of synthesis was ignored for industrial production because of large solvent volumes and sodium metal together with side reactions of uncompetitive economics. Alkylaluminium route for OTCs synthesis started in Germany at Schering AG, Industrial Chemicals Division, Bergkamen, in 1962. This process can be operated continuously and no solventis needed, which is an important advantage compared to the reactions in route 1 and 2. Organotin halides can also be directly synthesized by a reaction between tin metal or tin alloy and alkyl halides. The reactivity of alkyl halides with tin declines in the order RI > RBr > RCl. Direct synthesis route using alkyl iodides and bromides was developed in Japan in the early 1950s, methyltin stabilizers are produced by direct synthesis in the USA [4].

Applications of organotin compounds

Tin has a larger number of its organometallic derivatives in commercial use than any other element. Organotin compounds have product and process utility in three major areas: (1) Heat stabilizers, (2) Catalytic agents and (3) Biological active agents [11].

Heat stabilizers

The main industrial use of organotin compounds is as light and thermal stabilizers in the PVC industries, where less toxic mono- and dialkyltin compounds are used [12-15]. Originally, OTCs were developed as heat stabilizers for chlorinated hydrocarbons, which would be used in those applications for which there were strong possibilities of thermal degradation. However, as the chemistry of OTs became better comprehended, their applications expanded to catalytic chlorinated transformer oils.

Organotin compounds have been used as stabilizers for chlorinated transformer oils since 1932s; the transformer insulation consisted of paper and mineral oil as at this time. Large temperature gradients across the oil generated by power fluctuations in the transformer, caused decomposition of the mineral oil to ooze. This oxidative decomposition was prevented by the addition of tetraalkyl or tetraaryl tin. In 1957, General Electric developed replacements for mineral oils, which were trichlorobenzene, pentachlorodiphenyl, and pentachlorodiphenyl oxide. The chlorinated aromatic oils had more accurately defined heat transfer characteristics than did mineral oil. However, when arcing occurred in transformer operation, these compounds decomposed and liberated HCl, which corroded the interior of the transformer. Tetraalkyl and tretraaryl tin complexes were added to react with the liberated HCl to form OT chlorides (and alkanes or benzene). The motivation for using tetraorganotin complexes was the desirable volume to the efficiency factor for corrosion prevention; one mole of OT removed four (4) moles of HCl [3, 16-18].

PVC stabilizers

The largest proportion of OT stabilizer production is for the stabilization of PVC. PVC resin is a white powder produced by free radical, ionic, and emulsion polymerization. In order to mold the resin into finished products, the resin is softened by heating. For unplasticized PVC, this softening temperature approaches the thermal decomposition of the temperature of the resin. PVC polymers are particularly susceptible to thermal degradation during processing and use. This degradation occurs through progressive loss of hydrogen chlorides leading to a system of conjugated double bonds with resulting colour formation and loss of physical properties. Therefore, thermal stabilizers are essential additive for both rigid and flexible PVC products [12, 13, 19].

The process of degradation is accelerated in the presence of HCl and oxygen. To prevent this process certain OTs mainly mono- and diakylated derivatives, are added to the PVC at a level of 5-20 gkg^{-1}. The organic groups are mainly methyl, n-butyl, n-Octyl such as dibutyltin maleate, and dimethyltinS-S^{1}-bis (isooctylmercaptoacetate), etc. Organotin stabilizers act by inhibiting the dehydrochlorination reactions by exchanging their anionic group (*R*) with the Cl atoms in the PVC, reacting with and thereby scavenging the produced HCl, producing the compound *RH* which may inhibit other side reactions, preventing atmospheric oxidation of the PVC by acting as an antioxidant. Organotins stabilize for long periods of time. The scrap generated during processing can be recycled. The OT stabilizers probably come closest to being the ideal complexes for preventing the thermal degradation of PVC [20-26].

PVC stabilized by OTs can be used as bottles, insulators, pipes for drinking water, wastewater and drainage water, food packaging materials etc. [10]. Leaching of OTs from PVC pipes with a length of 45 m led to a concentration of 5 $mg(Sn)m^{-3}$ in the water after first use, and to a subsequent constant release of 1 $mg(Sn)m^{-3}$. The rate of leaching depends on different conditions, like the length of the alkyl chain in the stabilizer or the properties of the leaching medium (e.g. pH), but also on the type of PVC material [27]. Forsyth and Jay [28]revealed in laboratory experiments that (MBT) and DBT were leached by tap water from PVC pipes designed for potable water delivery.

Researches have shown that leaching of OT ingredients from PVC and related materials led to the contamination of foodstuff, beverages, drinking water, municipal water, sewage sludge; this can pose several health hazards [29, 30]. Different samples of ordinary plastic products purchased from a supermarket were analyzed by Takahashi, Mukai, Tanabe, Sakayama, Miyazaki and Masuno [31]and was discovered that 50% of the plastic product samples, including baking parchments made of siliconized paper, gloves made of polyurethane, sponges for dish washing and cellophane film for foodstuffs contained butyltins (BTs). A transfer of these pollutants to foodstuffs was proved by analyzing the cookies, which were baked on the investigated baking parchment. MBT, DBT and TBT were detected in these cookies. It implies that high temperatures are not effective in eliminating BT compounds from foods. It is important to emphasize that significant amounts of the BTs are left on the baking parchment of PVC, even its consequent disposal will lead to the accumulation of OTs (mono- and dialkylated derivatives) in the environment and possible long term effects on man and biota due to the little knowledge of OTCs mobilized by degradation of PVC materials in dumping sites [15, 30]. Variable amount of OTs have been found in foodstuff and beverages, including beans, vegetables, fruits, eggs, milk and meat [29, 30] and wine [32, 33]. The origin of dietary OTs is considered to be direct and indirect contact between different types of plastics and foodstuff [34]. In the European Union and United States, the use of OTs in plastic food packaging is regulated because of the inherent possibility of these compounds to migrate to the food [35].

Catalytic agent

Organotins are finding use as esterification, transesterification, and polyesterification catalysts etc. They are used to catalyze the room-temperature curing of silicone rubbers used in making dental impressions and encapsulating electronic parts [3, 36]. It is notable that in most of these uses, one of the reactants contains an OH group. The catalytic activities of the OTCs have been attributed to low-energy 5*d* orbital of the tin atom, which can form penta and hexacoordinate bonds. In this type of bond, the tin coordinates with either an oxygen or nitrogen. This coordination bond causes polarization of the carbon atom bonded to an oxygen or nitrogen atom, and makes the carbon atom more susceptible to attack by electrophilic reagent, such as alcohol, as in the urethane and esterification reactions.

Organotin compounds have distinct advantages as catalysts for esterification reactions because they have high catalytic efficiency, low tendency to eliminate water from secondary alcohols to form olefins, ability to produce coloured esters, absence of acidic or basic residues in the esters, ability to impart heat stabilization to condensation type polymers, ability to improve physical and electrical properties of the product. However, OTCs are less active catalysts than strong acids and bases, but have the advantage that they do not catalyze side reactions such as dehydration; thus when they are used, product purity is improved. They are limited by reaction temperature, which in the case of direct esterification

is usually greater than 180-200 ^{0}C and for transesterification is greater than 150 ^{0}C. An exception is transesterification of methyl methacrylate, which can be carried out at 100 ^{0}C using dibutyltin oxide as catalyst [3, 36-38].

Biological active agents

One of the fastest growing fields of application for OT is based upon their biological properties. The biological effects of OTCs on organisms depend on both the nature and the number of the organic groups bound to the tin cation in the OT compounds [39]. The biological properties of tri-substituted OT species were discovered in the late 1950s at the Institute of Organic Chemistry INO, Utrecht, Netherlands. The first biocidal application was the use of toxic ingredients bis(tributyltin) oxide (TBTO) in timber preservatives [4].

Most OTCs of antimicrobial interest are trialkyltin or triaryltin compounds. They are extremely active as antibacterial [40-42]. This is of interest in the control of staphylococcus aureus. As fungicides, OTs have a wide range of applications [43]. They are used to preserve paint, paper, textiles, wood, plastics, and anything else attacked by mildew or fungus. Industrial waters have been treated with OTs in paper mills, cooling towers and secondary oil recovery [18, 44] . Table 2 shows the different industrial uses of OTs.

Table 2. Industrial Uses of Organotin Compounds

Indusrial Application	Function	Organotin Compounds
PVC Stabilizers	Stabilization against decomposition by heat and light.	R_2SnX_2 and $RSnX_3$
Antifouling Paints	Biocide	R= Me, Bu, Oct R_3SnX
Poultry Farming	Dewormer	Bu_2SnX_2
Wood Preservation	Insecticide, Fungicide	R= Bu, Ph, Cy
Impregnation of textile	Insecticide, Antifeedant	Ph_3SnX ,Bu_3SnX
Glass Treatment	Precursor for tin (iv) oxide films on glass	Me_2SnX_2, $RSnX_2$
Material Protection (stone, leather, paper)	Fungicide, Algaecide, Bactericide	R= Me, Bu, Bu_3SnX
Agrochemical	Fungicide, Insectide, Miticide Antifeedant	R= Bu, Ph, R_3SnX

Key: Bu= Butyl- Cy= Cyclo-, Me= Methyl-, Oct= Octyl-, Ph= Phenyl-,

Wood preservation

Van der Kerk of Holland first reported that OTCs are effective wood preservatives in 1954. Wood can be attacked by bacteria, fungi and insects leading to the breakdown of the cellulose and other complex substances [45]. Wood preservation was carried out with TBTO dissolved in organic solvents such as kerosene because of its low solubility in water. The use of water as solvent became possible by the addition of quaternary ammonium salts by the development of water soluble biocides such as trialkyltin methanesulphonates and tributyl mesylimide. The application methods include dipping, spraying, brushing, and double vacuum impregnation in specially designed impregnation chambers. The latter is the most effective treatment and is often used in timber industries. In spite of care, wood treatment facilities can release TBT into the freshwater environment due to seepage, accidental spills, and effluents [4][21, 46].

Antifoulant

This is the second major biocidal applications of OTCs. They are used for the protection of ship hulls from aquatic organisms.Ship hulls were formerly being protected by coating with Cu_2O-based antifouling paints, but this coating became ineffective within one year, hence, the usage of the OT-based antifoulants. Antifouling paints consist of a film-forming material with a biocidal ingredient and a pigment. It works by releasing small amounts of the biocide from the painted hull into the water, forming a thin envelope of highly concentrated TBT around the boat. The toxic concentration repels the settling stages of fouling organism such as Teredo and Limnoria which are responsible for the decay of wood in marine environment as well as barnacles and molluscs which are very important in the fouling of ship bottoms [4, 45, 46]. The growth of aquatic organisms on vessel hulls creates roughness which causes an increase in the fuel consumption. For example, it was estimated that the use of antifouling paints save the US Navy an estimated 150 million US dollars of fuel annually and more importantly, reduces CO_2 emission and consumption of fossil fuel feed stock [47]. Tributyltin is quickly absorbed by organic materials such as bacteria and algae or adsorbed onto suspended particles in the water [48-51]. Afterwards, it is readily incorporated into the tissues of filter-feeding zooplankton, grazing invertebrates, and mammals where it accumulates [52-55].

Researchers have revealed that TBT species at concentrations of 1ngl^{-1} can induce imposex in sea snails, as a result, reproduction fails, and the population of snails in dog whelks declined drastically [56-59].

In November 1999, the International Maritime Organization (IMO) adopted an Assembly resolution that called on the Marine Environmental Protection Committee (MEPC) to develop an instrument, legally binding throughout the world, to address the harmful effects of antifouling systems used on ships. The resolution called for a global prohibition on the application of OTCs which act as biocides in antifouling systems on ships by 1 January 2003, and a complete prohibition by 1 January 2008. However, these restrictions cannot immediately solve the problem of pollution by OTCs due to their strong tendency to stick on suspended materials and sediments [10, 60, 61] and accumulate in filter-feeding molluscs [62]. Thus, the tendency of OTs to cause problems long after their ban remains a matter of concerns and requires monitoring for years to come [63, 64].

Agriculture

Organotins are used as pesticides in agriculture because of their biocidal effects [65-67]. Some linear trialkyltin compounds are extremely powerful biocides but their toxicities to plants is too high for practical uses in agriculture (e.g. butyltin derivatives). Tributyltin was first used as a pesticide in 1925 [21, 44, 68]. Derivatives of trimethyltin (TMT) show a high insecticidal activity, but their uses have been prohibited in agriculture because of their mammalian toxicity. The agricultural applications of OTCs in some regions are with restrictions due to their toxicities, but the restrictions are without consistency. For example, in Georgia (USA), Pecan orchards were sprayed 8-10 times per annum with OTCs while the application of these compounds to crops is restricted to just once in a year in Germany [4]. The pollution of the environment by OTs used as pesticides in agriculture has received less attention despite that their usage accounts for a significant portion of the pollutants in the environment, due to their direct input into soil, water, and air by spraying, leaching, and run-off.

Triphenyltins (TPTs) show a sufficiently side margin between fungitoxicity and phytotoxicity to enable them to be used in agriculture. Triphenyltin acetate and hydroxide control the fungus causing the late blight of potatoes, control Sigatoka

in bananas, and eleven (11) other fungal diseases of importance to crops. Triphenyltin compounds are effective molluscicides for the control of snails, which serve as vectors for schistosome infections in man. Dialkytin compounds have also been used to control parasitic diseases in poultry, sheep and swine [65, 67, 69]. Triphenyltin compounds have very good adhesive properties and are retained firmly by leaves on which they have been sprayed even after heavy rainfall. Nevertheless, the World Health Organization (WHO) pronounced TPT compounds as "safe agricultural chemicals" because the concentrations of the OTs in treated plants decrease rapidly due to the influence of light, losses in the wind and rain and degradation in the atmosphere. They argued that residues of OT substances in food, fruits, and vegetables can be partly or completely removed by washing, peeling or cooking before consumption. Researches have shown that cooking is not an effective way to eliminate OTCs from food [15, 69].

Another source of pollution by OTs is the spread of contaminated sewage sludge. Studies on OTCs in sewage treatment plants revealed that species monitored in wastewater samples can be efficiently removed from the water column majorly by adsorption and following sedimentation into the sludge. This contaminated sludge is disposed of in landfills or dumped into the sea, but in some countries it is also used in agriculture as a soil amendment to a large extent, giving a transfer path into the terrestrial and finally the aquatic environment[4].

Pharmaceuticals

Organotin compounds have been developed as pharmaceuticals such as anthelmintic, disinfectants and antitumour drugs [70-73]. Dialkyltin compounds are applied as anthelmintic. For example, dibutyltin dilaureate is used for tapeworm in chickens or turkeys and coccidiosis and hexamitiasis in turkeys, while DBT oxide is used for intestinal worms in freshwater fish such as trout.

Tributyltin compounds are active against gram-positive bacteria, their combination with a second chemical which combats gram-negative bacteria produce a highly effective disinfectant which may be used on open areas posing a risk of infection, such as hospital floors and sports as pavilions [74-76]. Bulten and co-workers widely investigated on the antitumour activity of OTCs with four coordination. Although OTs have been developed as pharmaceuticals, their uses have been limited or hindered majorly because of their toxicities [74].

Toxicity

The toxicity of OTCs varies widely, depending first on the number of organic groups attached to tin and second on the nature of the organic groups just like its biological effects. Inorganic tin compounds generally have very low toxicity. The high toxicity of OTs is observed in triorganotin compounds while diorganotin and monoorganotin compounds show successively lower toxicity. The toxicity of tetraorganotin compounds is low. However, under environmental conditions (degradation), they will decompose to toxic triorganotins. There are considerable variations in the toxicity of trialkyltin compounds. The toxicity decreases as the size and stability of the ligand increases [77, 78]. Organotins toxicities have great impacts on both animals and humans [21, 74, 79]. They have been internationally recognized as persistent toxic substances [10].

Studies since 1970s have shown that TBT is very toxic to a large number of organisms [10, 44, 80, 81]. Tributyltin shows the highest toxicity by disturbing the function of the mitochondria. It acts by blocking the absorption of oxygen in the mitochondria [62, 82-90]. But DBT is less, whereas MBT has no obvious toxic effect on mammals. The toxicity of OT is associated with cognitive and impairment in learning and memory processes [91, 92].

The hazard associated with the use of OTCs was unmasked by an episode of intoxication in 1954 in France involving over 200 cases, 100 of which were fatal. The cause was the ingestion of an oral preparation, Stalion containing diethyl diiodide at 15 $mgcapsule^{-1}$ and vitamin F (linoleic acid, 100 $mgcapsule^{-1}$). The Stalion was sold in capsules throughout France for the treatment of Furuncles and other staphylococcal skin infections, osteomyelitis, anthrax and acne. The main impurities were monoethyltin iodide and highly toxic triethyltin iodide. The most constant complaints of the patients were severe and persistent headaches. Other common symptoms were vomiting, retention, urine, vertigo, abdominal pain, photophobia, loss of weight, psychic disturbances, and several cases of hypothermia (35 ^{0}C). At autopsy, cerebral oedema of the white matter was found.

Tributyltin shows a high toxic effect to aquatic life at low nanomolar aqueous concentrations of 1-2 μgl^{-1}. It causes chronic and acute poisoning of the most sensitive aquatic organisms such as algae, zooplankton, molluscs and the larval stage of some fishes [86-88]. Lethal concentrations are in the range of 0.04-16 μgl^{-1} for short-term exposures, depending on the aquatic species [62, 80, 81, 84].

Triphenyltin is also dangerous to aquatic life. It was revealed that guppies (*Poecilia reticulate)* exposed to various concentrations of TPT in water died when the concentration of TPT got to 2.2 μgg^{-1}[69]. Fishes are more sensitive to TPT pollution in early life stages than in adults. Tributyltin and TPT pollution of aquatic environment may cause diverse symptoms on the affected organisms like thickening of the shell and failure of spat in Oysters, impotence of neogastropods and gastropods, reduction of the dogwhelk population, retardation of growth in mussels, and immunological dysfunction in fishes [65, 67, 69].

Fish larvae are very sensitive to TBT and often exhibit effects in the 0.05 μgl^{-1} range. The 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 concentrations [10, 93, 94]. The most severe effect of TBT apart from neurotoxicity is the endocrine-disrupting effects which lead to imposex [58, 63, 95, 96], imposex is the superimposition of male characteristics in female gastropod species [21]. Tributyltin can cause imposex in both male and female animals [95]. As a result of imposex, females can become sterile and the affected population may become locally extinct. Imposex is induced at a very low concentration of tin (as low as 1-2 ngl^{-1}). Tributyltin has been reported to cause imposex phenomenon in some of the gastropods in America, Canada, and Britain. It has also been reported to affect the visual and olfactory functions of tiger perch [39]. Triesbskorn, Kohler, Flemming, Braunbeck, Negele and Rahmann [97] stated that TBT can induce vacuolization in the optic tectum and optic nerve of rainbow trout. Furthermore, Zuo, Chen, Wu, Zhang, Su, Chen and Wang [98] revealed that chronic and repeat exposure to low doses of TBT could result in obesity and hepatic steatosis in animals. Tributyltin and TPT can inhibit enzyme activity in ovarian cells at concentrations as low as 2

$ngml^{-1}$ [99] and promote the development of prostate cancer cells at 100nM [10, 80, 81, 83, 84, 93, 94].

Trimethyltin, which is used as a PVC stabilizer, insecticide and disinfector, has strong neurotoxic effects. Its toxicity was associated with many neurological symptoms in the limbic system structures. Trimethyltin can pass the blood brain barrier and accumulate in the central nervous system. It can also induce lesions in the hippocampus and impaired spatial memory in mice and rats [74]. The toxic effects of TMT include ototoxicity, hyper-excitability, tremor, tonic-clonic convulsion, spontaneous seizures, tail mutilation, vocalization, epilepsy, hyper-reactivity, hypokalemia and death [63]. Long time exposure to low levels of OT can lead to nuclear anomalies in human red blood cells and DNA mutation [100-104].

Food contamination by OT can also cause poisoning. Poisoning can be categorized into three grades- mild, moderate, and severe according to the Diagnostic Criteria for Occupational Acute Trialkyltin Poisoning (GBZ26-2007) [79]. Organotins have been highlighted to be among the top seven endocrine-disrupting chemicals of concern in food in a recent report published by the Government of the Hong Kong Special Administrative Region [105]. A Chinese report of deadly poisonings after meals prepared from methyltin-contaminated food, analyses of the inner organs of one victim yielded high concentration levels of methyltins in liver (1.93 µgg-1 DMT, 1.42 µgg-1 TMT), Kidney (1.05 µgg-1 DMT, 0.47 µgg-1 TMT), stomach (0.104 µgg-1 DMT, 0.304 µgg-1 TMT), and heart (0.1 µg/g-1 DMT, 1.48 µg/g-1 TMT) [64](T. Nakashi, 2007). Recent studies have identified OTs in water, crop and food at concentrations that may be highly toxic to aquatic creatures and carcinogenic to humans [10, 58, 59].

Table 3 gives information on 829 cases of OT poisoning from 10 different regions in China from 1995-2013, this originated from 23 studies of the Chinese National Knowledge Infrastructure. There were number of cases (43.9%) caused by occupational exposure of people engaged in the processing and production of PVC, antifouling paint and heat stabilizers. Food contamination by OTs was also identified as another key factor that caused the poisoning. Trialkyltin and TMT-chloride were the major toxic compounds. The most common intoxication symptoms were dizziness, headache, somnipathy, nausea and vomiting. The level of intoxication is proportional to the severity of the symptoms [74].

Niu, Li and Li [74] analyzed 405 cases which were of OTs toxicities (Figure 2), these show the incidence of abnormal clinical examination results caused by occupational poisoning, food poisoning or both. There is a high incidence of abnormal results in three major clinical tests: potassium blood levels, electroencephalograph (EEG), electrocardiograph (ECG). As many as 68.9% patients with occupational poisoning suffered from hypokalemia, which may be caused by the damage of glomerular function. Only 40.5% of the patients had normal EEG results.Owing to the abnormal EEG results and the ubiquitous neurological symptoms with varying degrees of severity in the 405 cases, the researchers concluded that OTs could cause toxic encephalopathy. Furthermore, liver and renal damage were also the common side effects of OTs [74].

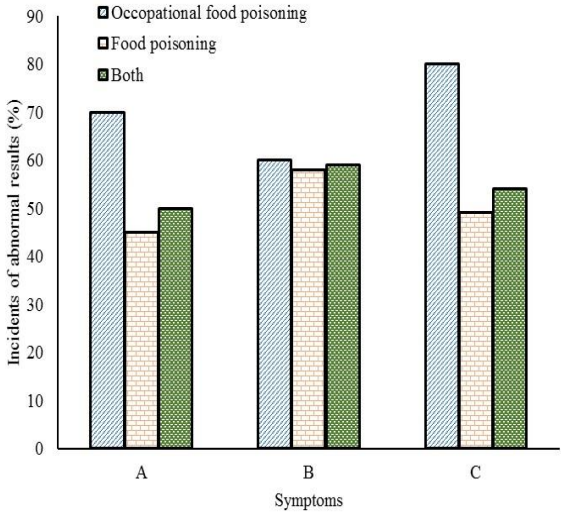

Figure 2. The abnormal results in three clinical examinations of 405 cases of organotin poisoning in China from 1995-2013. A- Hypokalemia, B- Abnormal EEG, C- Abnormal ECG [74].

Several animal experiments have suggested that the spectrum of potential adverse chronic effects of OTs in humans is quite broad and includes primary immunosuppressive, neurotoxic, metabolic and enzymatic activity as well as potential ocular, dermal cardiovascular, upper respiratory, pulmonary, gastrointestinal blood dyscrasis, to mention a few [6]. Being present in the water column at low and sub-ppb concentrations, they are strongly enriched in the trophic web and can reach significant ppb concentrations in fish and shellfish (up to 100 ng $Sngdw^{-1}$ in fish and up to 500-1000ng Sn/gdw in shellfish). Depending on the actual consumption of fish and shellfish in different countries, the individual populations may be at lower or higher risk from the exposure to OTCs through food. Though, in developed countries, the uptake of OTCs might not exceed the tolerable daily intake (TDI) level for OTCs for the average consumer, particular groups (e.g. children, high consumers of fish and fishery products) may still be at risk. The European Food Safety Authority has adopted a group TDI of $0.25\mu gkg^{-1}$ body weight per day for the sum of TBT, DBT, TPT and Dioctyltin (DOT), based on their similar toxicity and mechanism of action [106]. Although, there is a limited amount of information about OT contamination of food. However, studies revealed that the concentration of BTs in food in China appears to follow the following trend: freshwater fish > other animal foods (meat, eggs) > farm products (vegetables, potatoes, sugar) > liquid food (milk, wines and beverages). Also, BT contamination in foods is higher in well-developed industrial areas [107].

The principal toxicological difference among di-, tri- and tetra-substituted OTCs is that some tri-substituted compounds have a specific effect on the central nervous system producing cerebral oedema whereas disubstituted compounds do not produce this effect, but are potent irritants particularly in the bile duct. Toxicologically, the tetrasubstituted compounds resemble trisubstituted compounds, which are, generally, more toxic than the mono- and disubstituted derivatives.

Table 3.The information of 829 cases of organotin poisoning in China from 1995-2013 [74] and the references there in.

Areas	Number of Cases	Causes of Poisoning		Poison Level			Poison							
		Occupational Poisoning	Food Poisoning	Mild	Moderate	Severe	DBT	DBTDCl	TMT	TET	TBT	TMTCl	TeBT	MOTs
Zhejiang	206	203	3	107	62	37	7	3	153	16	10	3	5	9
Guangdong	183	79	104	141	37	5	0	0	0	0	0	183	0	0
Jiangxi	348	0	348	155	143	50	0	0	0	0	0	348	0	0
Shanghai	6	6	0	2	1	3	0	0	4	2	0	0	0	0
Liaoning	48	38	10	25	20	3	0	0	10	8	0	0	0	30
Jiangsu	9	9	0	3	0	6	0	0	0	0	0	9	0	0
Guangxi	7	7	0	4	1	2	0	0	0	0	0	7	0	0
Hunan	3	3	0	1	0	2	0	0	0	0	0	3	0	0
Hubei	16	16	-	3	0	13	0	0	0	0	0	5	0	11
Fujian	3	3	0	0	0	3	0	0	3	0	0	0	0	0
Summation	829	364	465	441	264	124	7	3	170	26	10	558	5	50

Diethyltin = DBT, Dibutyltin dichloride = DBTDCl, Trimethyltin = TMT, Triethyltin = TET, Tributyltin = TBT, Trimethyltin = TMTCl, Tetrabutyltin = TeBT, Mixed Organotins = MOTs.

Considering the adverse effects of OTCs, some of these compounds have been placed on the black and gray lists of several international agreements. Tributyltin has been included in the European list of priority pollutants [108].

Analytical methods

Since the toxicity of OTs depend on the nature of the alkyl groups, analysis of the environmental samples requires specific determination of the individual OTs. A significant number of various instrumental techniques have been reviewed in the literature. Methods that are sensitive enough for an accurate and simultaneous determination of OTCs at very low concentrations in different samples are imperative.

Sample preparation techniques for speciation analyses generally consist of several steps [109]. The steps depend on the physico-chemical properties of the analytes to be determined and of the matrix to be analyzed (e.g. water, sediments and biological materials). Nevertheless, the suitability of the sample preparation steps with the chosen technique must be reliable. The analytical steps required in the techniques (e.g. derivatization, extraction, separation, and detection) can afford the accuracy and precision of the final speciation results. Species selective analysis of OT is performed by coupled technique based on the combination of a chromatographic separation technique with a sensitive and element selective detection method. The most common technique is gas chromatography (GC) coupled with element-specific detection methods like atomic absorption spectrometry (GC/AAS), mass spectroscopy (GC/MS), inductively coupled plasma-mass spectrometry (GC/ICP-MS), microwave induced and inductively- coupled plasma atomic emission spectroscopy (GC/MIP-AES and GC/ICP-AES, respectively or flame photometric detection (GC/FPD), high-performance liquid chromatography (HPLC) and pulsed flame photometric detection (GC/PFPD) [110]. Majority of these methods used are multi-step, the main disadvantages include tedious and time-consuming extraction, and derivatization steps prior to the chromatographic analysis. The use of liquid chromatography with fluorescensce detection has also been reported for OT analysis [111]. However, single HPLC is incapable of detecting a large number of OTs, which lack chromophores in their structures. Although ICP-MS is a very sensitive technique, the OT structures cannot be identified and the interference of inorganic tin species cannot be eliminated.

Owing to this, modern trends have focused on eliminating potential error, reducing the number of procedural steps and the manual handling involved with samples. For example, more modern methods use on-line techniques that promote high pre-concentration factors, including solid-phase microextraction (SPME), solid-phase extraction (SPE) or stir-bar sorptive extraction (SBSE). For accurate internal quantification, isotope dilution (ID) is preferred due to its easy incorporation and its applicability to biotic, sediment and water matrices [110].

The extraction methods used for OTs have undergone a significant evolution from conventional liquid-liquid extraction (LLE), and solid-liquid extraction (SLE) procedures; where extraction can be time consuming, expensive and use high volumes of toxic solvents. Microwave assisted extraction (MAE) and accelerated sample extraction (ASE) (also known as pressurized liquid extraction) are more prevalent methods, providing benefits of autonomous rapid extraction times, high sample throughput and often reduced solvent consumption [112]. SPE is used widely because of its general availability, often yielding a higher pre-concentration factor relative to the other conventional techniques [113]. Octadecylsilyl commonly (C_{18}) is the most commonly used sorbent. Other sorbents such as Carbopack, $C_{2,}$ $C_{8,}$ C_{60}-fullerenes and cation-exchange phases are used to a lesser extent. On-line SPE coupled to LC is an attractive option, offering benefits in the reduction of analysis time, labour costs and a reduction in matrix effects [114]. Off-line SPE applications have also received attention. Methods include the in-situ extraction of OTs from water samples using dispersed molecularly imprinted polymers (MIPs). SPME and liquid-phase microextraction (LPME) have received much interest [115], because of their sensitivity, the reduction or elimination of harmful solvents and incorporation of simultaneous in-situ on-line extraction and derivatization. SPME can be used either with direct immersion (DI-SPME) or headspace sampling (HS-SPME), typically using polydimethylsiloxane (PDMS) as the pre-concentration phase (although alternative phases are emerging) [116]. Temperature, pH and stirring or agitation of the OTs on the SPME fibre; which with investment into auto-sampling equipment, can be undertaken automously (with on-line extraction, derivatization and desorption of analytes into the GC injector. For LC, a special desorption chamber is required to allow mobile phase access to the SPME fibre

[117]. SPME can suffer from sample matrix interferences (reduced using HS-SPME), increased sample carry over as well as significant costs associated with PDMS fibres [80]. LPME is an adaptation of liquid-liquid extraction (LLE) and is receiving attention because of the benefits in solvent reduction and the subsequent high pre-concentration factors from a decreased volumetric ratio of the solvent acceptor-donor phase [115]. LPME can achieve high sample throughputs with rapid extraction times, as well as increased selectivity using either a single solvent (α, α, α- trifluorotoluene) [118] or a mixture of solvents (e.g. methanol/tetrachloromethane [119]. Analysis of the resultant extracted OTs is by conventional GC injection. The most modern LPME methods used with OTs include disperse liquid-liquid micro-extraction (DLLME) [119], headspace-single drop micro-extraction (HS-SDME) [120] and direct immersion-single drop micro-extraction (DI-SDME) [118]; with limit of detections using tandem mass spectroscopy (MS-MS) and ICP-MS ranging between 0.4 and 3.0 ngl^{-1}[118, 120]. SBSE is similar to SPME with either solvent less direct immersion or headspace sampling applications. SBSE provides an increased pre-concentration capacity of 50-250 times SPME [120]. However, uptake and elution conditions must be optimized for the target analytes (e.g. temperature, stirring speed and sample pH). Recovery of extracted OTs is by liquid desorption [121] or on-line thermal desorption [122]. Using PDMS stir bars and 2D gas chromatography-tandem mass spectroscopy (GC-GC-MS-MS) or (LC-MS-MS) limit of detections of 0.01-0.8 ngl^{-1} for BTs in sea water have been reported [98, 123]. Among the detection techniques, MS-MS offers a number of advantages: more selective separation, element specificity, low detection limits, and high sensitivity [110].

Validation of the methods of analysis is commonly undertaken using commercially available Certified Reference Materials (CRM). These include: PAC-2 from the National Research Council Canada for BTs in marine sediments; BCR-646 from the European Commission Joint Research Centre for OTs (monobutytin (MBT), DBT and tributyltin (TBT), monophenyltin (MPT), diphenyltin (DPT) and triphenyltin (TPT) in fresh water sediments, ERM-CE 477 for BTs (MBT, DBT, TBT) in mussels from the Institute for Reference Materials and Measurements (IRMM) and NIES No. 11 from The National Institute for Environmental Studies (NIES) for TBT and TPT in fish tissue (non-certified) [110].

Derivatization strategies for OTs include alkylation using Grignard reagents or alkylborates (commonly sodium tetrahydroborate ($NaBEt_4$)) or conversion using borohydride species (e.g. sodium borohydride ($NaBH_4$)). Sodium teraethylborate ($NaBEt_4$) has become very popular as a derivatization reagent during the past years due to its application within aqueous matrices, its functionality in on-line and off-line simultaneous derivatization and extraction and its extended range to phenyltin compounds [120]. Sodium tetra(n-propyl)borate ($NaBPr_4$) has also been introduced as derivatization reagent. A comparison between $NaBEt_4$ and $NaBPr_4$ gave similar derivatization efficiency and limits of detection for both reagents [82, 124]. Grignard reagents (e.g. ethyl-, pentyl- or hexyl-magnesium bromides) are used for post extraction within a non-polar phase and can be used to manipulate GC retention times for OT derivatives. Although high derivatization yields are possible with most sample matrices. Grignard reagent is less favoured due to the requirement of expert handling techniques together with dry conditions to avoid reactions with water, acids ketones and alcohols [110]. Derivatization with $NaBEt_4$ is simpler; undertaken in the aqueous phase converting OTs into their ethyl derivatives. The pH must be regulated (pH 4-6) to allow for nucleophilic substitution of ethyl groups to the OT cation. $NaBEt_4$ is made-up at concentrations 1-5% within deionized water or methanol, having a short shelf life (~ 3-4 days at 4^0C). Reagent life-times can be extended by freezing, although most methods use a fresh solution for each batch of extractions [125].

Polar ionic organotin species need to be extracted from sample matrix and converted into fully alkylated more volatile forms before being separated with GC analytical system [126]. Extraction from water samples or sediment and soil samples after acid leaching followed by alkylation with Grignard reagent is the most common approach [125, 127]. Though, the Grignard reagent is sensitive to water, as a result, the OT species firstly need to be extracted into an apolar aprotic solvent by using complexation reagents like sodium diethyldithiocarbamate and tropolone. This method is usually multi-step, tedious and time consuming. It makes the sample preparation faster and easier because it enables an in situ derivatization and following extraction of the ethylated OTCs into organic phase (hexane, isooctane) which is then analyzed.

Sodium borohydride, ($NaBH_4$) can be used with aqueous matrices for simultaneous derivatization and extraction. However, due to the volatility of these OT derivatives losses can occur. $NaBH_4$ can suffer from interferences with complex matrices (e.g. biota and sediments); mainly from interactions with metals and formation Sn-H bonds on OTCs [110]. A detailed description of OT sample preparation and analyses is given in Brunori, Ipolyi, Massanisso and Morabito [128], Dietz, Sanz, Sanz, Muñoz-Olivas and Cámara [129], Nemanic, Milacic and Scancar [130], Cole, Mills, Parker, Bolam, Birchenough, Kröger and Fones [110].

Environmental levels of organotin

As a result of the extensive industrial application, a considerable amount of toxic OTCs have entered diverse ecosystems. Thus, notable concentrations of these pollutants and their metabolites have been discovered in the waters, suspended matter, sediments, and biota. The amount of the OTC detectable in the atmosphere is negligible, so that interactions from this source are unlikely to be remarkable [4].

Organotin in aquatic environment

In natural water, triorganotin compounds are present mainly as neutral TOT-OH (triorganotin hydroxide) species or as TOT^+ (triorganotin) cations depending on the pH value. The spread of tributyl species also depends on the pH and salinity. At pH 8, the major species are tributyltin hydroxide (TBT-OH) and tributyl carbonate while at pH < 5, TMT compounds basically occur as the trimethyltin cation Me_3Sn^+ and as Me_3SnOH at pH > 5. The primary species of DMT at pH < 4 is the cation $MeSn^{2+}$ while under environmental conditions (pH 6-8) the species mainly found is $Me_2Sn(OH)_2$ [4].

Researches concerning OT pollution in aquatic environment have been mainly restricted to areas with high shipping, harbours and shipyards. This is due to the direct emission of TBT from antifouling paints into the water, which gives rise to contamination of water and sediment of marinas, lake, and coastal areas. But high concentration of this contaminant can also be discovered far away from the coastal areas. Analysis of samples of the sea-surface microlayer and near-surface bulk water at 5 stations up to 200 km offshore in the North sea revealed that in a zone extended from 100 – 200 km offshore the TBT contents in the surface microlayer

exceed 20 ng(Sn)l^{-1}, which is 10 times higher than the concentration required to induce imposex in dogwhelks. It was reported that high occurrences of fish, egg and larval fish abnormalities were common in this area [131, 132].

Inputs from municipal wastewater and sewage sludge as well as from landfill leachates have to be considered [110]. Table 4 shows the concentrations of OTs in sewage sludge, landfill leachate and landfill gas.

Leaching and weathering of PVC materials containing OTs may release them on a large scale. However, BTs can be removed from water column by adsorption to suspended matter and sedimentation in the sludge. Studies found an average decrease of MBT concentrations in passing through the sewage treatment plant by 40%, with a range of 19-75% [4].

Researchers have reported that TBT concentrations in water have generally declined [9, 139, 140], and maximum concentrations in marine water rarely exceed 100 ngl^{-1}[141]. Exceptions to this general decline in organotin compounds, TBT in particular in bottom sediments have been reported at hot spots associated with ship channels, ports, harbours and marinas in Galveston Bay, Israel [142] and Japan [143].

Organotins in organisms

Researches have revealed that high concentration of OTCs are present in some aquatic organisms such as fishes, gastropods and filter-feeding organisms. A widespread deleterious effect induced by OT pollution is imposex. Imposex result to reproductive failure and thus, population decline [86-90]. Pollution of tributyltin may also cause the death of larvae flowing into the bay, and hence, results in failure to re- populate [144].

Though, there is a great concern for the toxic effect of OTs in diverse ecosystems, more data about the accumulation and toxic effect of OTs along the food chain is needed. The most obvious routes of OT exposure to biota and consequently to the food chain is through the diet and the accumulation from the surroundings [145-147]. Thus, the main routes of the higher trophic levels like birds and mammals are through their diets while invertebrates and fishes are from the direct uptake of organic contaminants from their surroundings. For example, water and sediment by skin or ventilator organs like gills. In a carnivore gastropod, it was found that about half of the accumulated amount of OT comes from their surroundings [147]. Lisicio, Carro and Magi [148] conducted an *in vivo* experiment on TBT using *Mytilus galloprovincialis*- a mussel species, the result showed bioaccumulation of TBT especially in the gills.

Studies from Japan and Europe reported that concentrations of OTCs in fishes have decreased significantly following the restriction on TBT as an antifouling agent [149, 150]. The average concentration of the three BT species normally monitored in marine food range from 100 – 1500 ngg^{-1} with highest concentrations present in cultured fishes and molluscs in Asian and Oceanian countries . Concentrations of TBT in zebra mussels in freshwater docks, up to 1440 ngg^{-1} wet weight has been reported. The presence of OTC 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*), mute swan (*Cygnus olor)*, flounder (*Platichthys flesus*), cod (*Gadus morrhua*), herring (*Clupea harengus*), sculpin (*Myoxocephalus scorpius*), eider duck (*Somateria mollissima*), common scoter (*Melanitta nigr*a), 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 characterized, and all the analyzed samples contained OTCs [146]. The highest hepatic concentrations of BTs 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. The lowest concentrations were found in seaweed and a plant-feeding bird [82, 146].

Higher levels of OTCs have been found in coastal waters up to 500 ng(Sn)g^{-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} (Table 4-6). It has been reported that organisms of higher tropic levels present higher OT levels than organisms of lower trophic levels, and higher than those expected to result through accumulation of water only. This confirmed that uptake via food may be an important accumulation route [82].

Human exposure

Due to the extensive use of OT in various areas of human activities, humans have been widely exposed to these compounds. These pollutants can enter human tissues by occupational exposure, indirect exposure to household items containing OTCs or by the consumption of contaminated food. Some household commodities made up of silicones, plastic polymers and polyurethane, examples are cellophane wrap, sponges, baking parchments, diaper cover, sanitary napkins and certain types of gloves contain several OT species. Though, the contamination level from these sources might be low, but it cannot be ignored [4, 14, 29, 30, 32-34, 79, 151, 152]. Humans can also be exposed indirectly to OTs by contact with clothes moistened with the vapour or liquid of OTs for textile impregnation [4, 33-35, 151] (Figure 3). Seafood such as fish, mussels and crabs gathered from coastal areas and lakes contain various amounts of BT compounds and humans at the highest level of the food chain are endangered by these foods. The ingestion of contaminated water, food etc. has been reported as an important route of human exposure [28-30, 33-35, 82, 106, 110, 147, 151, 153-155];[4, 88, 152]. Butyltins were first found in human blood in late 1990's and their residues in human livers were detected in samples collected from the Japanese and Polish people [2].

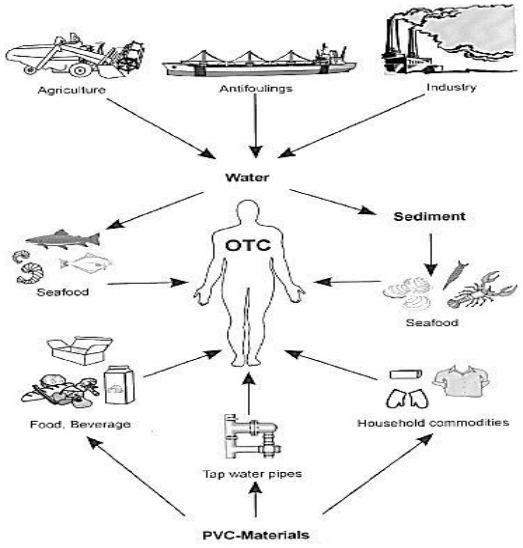

Figure 3. Human exposure to organotin

Table 4. Concentrations of OTs in sewage sludge, landfill leachate and landfill gas.

Sample type	Study	MMT	DMT	TMT	MBT	DBT	TBT	TPT	Unit	Ref
Sewage sludge	Data from review of micro-pollutants in sludge (3 studies)	-	-	-	ND-6000	ND-7500	ND-6000	<20-9000	ng^{-1}	[133]
Sewage sludge	GC-PFPD method for organotins in sewage sludge	-	-	-	265	376	100	-	ng^{-1}	[134]
Landfill leachate	Transformation compounds in landfill leachate. Municipal non-hazardous waste landfill, Ljubljana, Slovenia (excluding hazardous landfill)	99	188	289	149	16	23	-	ngl^{-1}	[135]
Landfill leachate	Municipal non-hazardous waste landfill, Barje, Ljubljana, Slovenia (excluding hazardous landfill)	144-258	54-198	167-469	161-195	57-141	9.7-51	-	ngl^{-1}	[136]
Landfill leachate	Municipal landfill, South of France (2005-2006)	ND-169	38-1002	165-8958	ND-458	ND-215	195-3314	-	ngl^{-1}	[137]
Landfill leachate	Municipal landfill (excluding hazardous landfill), Bavaria, Germany	ND-27	ND-1227	37-2894	ND-843	ND-411	ND-37	-	ngl^{-1}, as reported median(s)	[138]
Sample type	Study	TeMT	TMET	DMDET	TEMT	TBMT	TeET	TPT	Unit	Ref
Landfill gas (volatile OT species)	Municipal landfill (excluding hazardous landfill), Bavaria, Germany	6468->240,000	-	-	-	-	-	-	ngm^{-1}	[138]
Landfill gas (volatile OT species)	Municipal landfill, South of France (2005-2006)	2106->34,000	196-1467	948-6322	282-1392	ND	ND-24	-	ngm^{-1}	[137]

DMDET= Dimethyldiethyltin, DMT= Dimethyltin, GC= Gas chromatography, ND= Not below detection limit/not detected, PFD= Pulsed flame photometric detector, TMBT= Tributylmethyltin, TeET= Tetraethyltin, TEMT= Methyltriethyltin, TeMT= Tetramethyltin, TMT= Trimethyltin, TMET= Trimethylethyltin.

Average concentrations of BTs in livers of Polish people (2.4-11ngg^{-1} wet weight) were less than those in Japanese (59-96 ngg^{-1} wet weight). There have been reports to the adverse effects of TPT on humans via accidental exposure to TPT-based pesticides by farmers. These patients exhibited similar symptoms of OTs poisoning. TPT may also lead to possible impairment of the central nervous system and liver damage. For example in rats, TPT exposure can affect brain and gonadal aromatase activity in sex-dependent fashion. Triphenyltinwas detected in blood of Finnish people, the concentrations of TPT in blood of humans were greater in people who consumed greater amounts of seafood [156]. Despite the toxic effects cause by OTs and the contamination of humans, only limited data on the deposition of these pollutants in humans are available.

Researches showed that foodstuffs and beverages are being contaminated by OT ingredients from PVC and related materials.[29, 30, 33-35, 151]. The results of the analysis of Canadian drinking water distributed through PVC pipes carried out by Sadiki and Williams showed the presence of OTCs. The level of contamination ranged up to 291 ng(Sn)l^{-1} MMT, 49.1 ng(Sn)l^{-1} DMT, 28.5 ng(Sn)l^{-1} MBT, and 52.3 ng(Sn)l^{-1} DBT. Furthermore, 1.7−20 μgl^{-1} MBT, 0.3-160 μgl^{-1} DBT and 0.8-1.6 μgl^{-1} TBT were detected in various brands of wine collected across Canada [4, 32].

The average intake of OTCs from foodstuffs was estimated in Finnish market basket. From the study, which was conducted by collecting 13 market baskets, containing 115 several food items in the city of Kuopo, OTs were detected in 4 baskets, with these containing the highest level of different OTs [151]. The predominant OTs in fish and sea foods were MBT, DBT, DPT (diphenyltin), TBT, TPT measured at levels up to 1.52, 0.25, 0.14, 2.53, 1.11 ngg^{-1} fresh weights respectively. The median intake in Norway was 7 ng(kgbw)$^{-1}$ day^{-1}, based on EU-SCOOP (European Union-Scientific Cooperation) data. The corresponding value based on mean data was 33 ng(kgbw)$^{-1}$ day^{-1}. High consumers were exposed to 15 (median) and 70 (mean) ng(kgbw)$^{-1}$ day^{-1}[157]. Though, the listed values above are below the tolerable daily intake adopted by the WHO WHO-IPCS. World Health Organisation [158] but a potential risk may exist for high consumers (EU-SCOOP, 2006) and persons weighing less, e.g. children [159].Chien, Hung, Choang, Yeh, Meng, Sieh and Han [153] reported the investigation of the health risk associated with OTs particularly TBT from shellfish for fishermen and the general populace of Taiwan. The concentration of TBT in different Oyster ranging from 320 to 1510 ngg^{-1} dry weight varied with sampling locations. The TBT concentration of 1510 ngg^{-1} was detected in Oysters from the Hsiangshan coastal area where TBT was the major component of the total BT compounds, 86- 91%. The amount of Oysters consumed by fishermen was 94.1 and 250 gday^{-1} for typical and maximally exposed individuals respectively. The highest intake, 250 gday^{-1} from fishermen was about two times higher than that of the general populace, 139 gday^{-1}. These indicated that the people who are exposed to contaminated Oyster presented potential health hazard [10, 82, 106].

Although many reports have described potential toxicity of OTs, the acute target molecules for the toxicity and mechanisms of toxicity of OTCs in humans remain unclear. In order to elucidate the target molecules, conducted *in vitro* experiments have demonstrated that BTs exhibit structure-related inhibition of catalytic activity of human aromatase protein from human placenta or transfected cell — endocrine disrupting mechanisms [6, 82, 160]. Dibutyltin acted as a

partial but less potent inhibitor of human aromatase activity whereas tetrabutyltin (TeBT) and MBT had no effect [82]. However, at concentrations effective for the inhibition of these enzymes, TBT is generally toxic to mammalian cells because it causes apoptosis or necrosis. It seems that OTCs 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 OTCs [6, 82]. 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 [160, 161]. Researches conducted with pubertal rats exposed to 15 mg TBT and 6 mg TPT 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. Using human hepatic cytochrome *P450* systems it was observed that TBT was similarly metabolized by male and female human hepatic microsomes *in vitro* [82, 162].

The hazard posed by OTCs to humans depends not only on the solubilization but also on the possibility that they may degrade during human digestion. The study carried out on the intestinal permeation of BTs by Azenha, Evangenlista, Martel and Vasconcelos [163] revealed that the permeability pattern correlates well with the general *in vivo* toxicity pattern trialkyltin > dialkyltin >>monoalkyltin [82].

Conclusion

The increase percentage of organotin compounds in environment has raised much concern, their various applications and toxicities have been reviewed. As a result of lack of enforcement of laws on the control of organotin compounds in the environment, especially in Africa, there is need to carry out a detailed environmental assessment of organotin compounds in the environment. Thus, it remains necessary to investigate the environmental impacts as well as human health risks posed by these contaminants.

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