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TIN HAZARDS TO FISH, WILDLIFE, AND INVERTEBRATES: A SYNOPTIC REVIEW

by

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SUMMARY

Tin (Sn) has influenced our life style for the past 5,000 years. Today we are exposed to tin on a daily basis; including tinplated baby food cans; alloys such as pewter, bronze, brass, and solder; and toothpaste containing stannous flouride. These inorganic tin compounds are not highly toxic due to their low solubility, poor absorption, low accumulation, and rapid excretion. Synthetic organotin compounds, however, first manufactured commercially in the 1960's, may present a variety of problems to animals, including impaired behavior and reduced growth, survival, and reproduction. Some triorganotins--for example, in antifouling marine paints, in molluscicides, and in agricultural pesticides--can be harmful to sensitive species of nontarget biota at recommended application protocols.

Background concentrations of organotin compounds are frequently elevated--occasionally to dangerous levels--in aquatic organisms collected near marinas and other locales where organotin-based antifouling paints are extensively used. But more information is needed on background concentrations of organotins, especially those from terrestrial ecosystems.

Tributyltin compounds are especially toxic to aquatic organisms. Adverse effects were noted at concentrations of 0.001 to 0.06 ug/l on molluscs and at 0.1 to 1.0 ug/l on algae, fish, and crustaceans. In general, bioconcentration of organotins from seawater was high, especially by algae, but degradation was sufficiently rapid to preclude food chain biomagnification. In contrast, current environmental concentrations of some organotins are not likely to be directly toxic to birds and mammals. Birds seem to be relatively resistant to organotins, although data are scarce. Preliminary studies of 75 days duration suggest that diets containing 50 mg tin as trimethyltin chloride/kg were fatal to ducklings; 5 mg/kg killed 40%, and 0.5 mg/kg was not lethal. Trimethyltin compounds were lethal to other species of birds tested at doses of 1 to 3 mg/kg body weight. Other tests with ducklings and eleven other mono-, di-, tri-, and tetraalkyltin compounds at dietary levels equivalent to about 50 mg Sn/kg showed no adverse effects on survival. Small laboratory mammals were adversely affected by trimethyltin compounds at doses as low as 0.15 mg/l in drinking water (learning deficits), 0.63 mg/kg body weight (diet aversion), and 1.25 mg/kg body weight (death); neurotoxicological effects of trimethyltins were usually not reversible. Triethyltins were also toxic to small mammals, but effects--which were similar to those of trimethyltins--were usually reversible after cessation of exposure.

All evidence to date indicates that organotin compounds are not carcinogenic.

Methodologies and data necessary for the promulgation of effective criteria and standards to protect natural resources seem to be deficient in eight key areas: (1) routine analytical chemical methodologies for extraction, separation, and identification of inorganic and organic tin compounds and their chemical speciation products in biological and other samples; (2) mechanisms of toxicity for organotin compounds; (3) rates of uptake, retention, and translocation of organotins in biota; (4) persistence and mobility rates of organotins in nonbiological materials; (5) rates of tin methylation and biotransformation in biological and abiotic samples; (6) organotin interactions with other toxic chemicals; (7) quantitative structure activity relation for use in evaluating organotin toxicity; and (8) long-term environmental monitoring studies in terrestrial and aquatic ecosystems for establishment of baseline concentrations.

DISCLAIMER

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TABLES

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INTRODUCTION

Interest in the toxicity of tin compounds dates to the early 1800's when investigators demonstrated that inorganic tin compounds produced muscular weakness, loss of pain sensation, and immobility in dogs (Reiter and Ruppert 1984; Idemudia and McMillan 1986b). In man, organotins can be assimilated by inhalation, absorption through the skin, and from food and drinking water (Zuckerman et al. 1978). The first documented case of organotin poisoning of humans was in 1880 when workers complained of headaches, general weakness, nausea, and diarrhea after exposure to triethyltin acetate vapors (Reiter and Ruppert 1984). Renewed interest in the toxicity of organotin compounds resulted from a medical tragedy in France in 1954. "Stalinon," a proprietary compound of diethyltin diiodide plus linoic acid used to treat furuncles and other skin infections, caused 217 poisonings and 111 deaths (Piver 1973; Duncan 1980; Idemudia and McMillan 1986b). The identified toxic components in Stalinon were triethyltin contaminants; victims received a total dose of 3 grams over a 6- to 8-week period. Symptoms included constant severe headache, rapid weight loss, vomiting, urine retention, vertigo, hypothermia, abdominal pain, and visual and psychic disturbances. Some of the more severely affected patients had convulsions. Death usually occurred in coma or from respiratory or cardiac failure. In survivors, headaches and diminished visual acuity remained for at least 4 years.

Recent world production of organotin compounds is about 30,000 tons, although relatively few organotin compounds, perhaps only 25, are presently produced and used to any great extent (Laughlin and Linden 1985). Diorganotins are used in the manufacture of antioxidants, whereas triorganotins are used as general biocides against microbial and invertebrate pests and in marine antifouling paints (Laughlin and Linden 1985). The first antifouling paints incorporating an organotin compound as a biocide were developed in 1961. Because of their effectiveness and availability in a variety of colors, tributyltin antifouling paints are now the most commonly used type, replacing copper-, mercury-, and lead-based paints (Stebbing 1985). Worldwide synthesis of tributyltin compounds is about 900 metric tons annually for all applications (Laughlin et al. 1986a). Tributyltins are highly toxic to aquatic plants and animals, readily accumulate in fish and molluscs from contaminated localities, and are present in some harbors where their release from antifouling paints--found usually on small boats and recreational craft--is the putative source (Walsh et al. 1985; EPA 1986; Laughlin et al. 1986a). Tributyltin is a contributory factor and probably a major cause for the reproductive failure of the European flat oyster (*Ostrea edulis*) in recent years in some locations (Thain and Waldock 1986). in fact, tributyltins are capable of causing adverse biological effects at levels far below that of any previously reported marine pollutant (Lawler and Aldrich 1987).

The widespread agricultural applications of trialkyltin biocidal agents have greatly increased the relative exposure risks to workers handling these materials (Rosenberg et al. 1985). Internationally, tin was recognized as a potential environmental contaminant at the Paris and Helsinki conventions in 1974; in later conventions, organotin compounds were moved to the "black list" (Vrijhof 1985). Due to the increasing use of organotin compounds as a class, the Canadian government, in 1979, placed organotins on Canada's Category III Contaminant List. Category III indicates that additional data are needed on the occurrence, persistence, and toxicity of organotins for preparation of informed environmental and human health risk assessments (Chau et al. 1984).

Many reviews and bibliographies are available on the environmental impacts of inorganic and organic tin compounds.[1] These authorities agree that inorganic tin compounds are comparatively harmless and that many organotin compounds are potentially very hazardous to natural resources--especially tributyltin compounds to aquatic biota. One rare exception to this generalization involved 113 cases of acute gastrointestinal illness in Washington and Oregon in 1969 associated with ingestion of canned tomato juice contaminated by inorganic tin; detinning in many cans resulted in tin levels as high as 477 mg inorganic tin per liter of juice. It seems that excessive use of nitrate fertilizer on one tomato crop was the ultimate cause of the detinning (Barker and Runte 1972).

This report summarizes selected data on ecological and toxicological aspects of organic and inorganic tin compounds, with emphasis on fishery and wildlife resources. It is part of a continuing series of reports on chemical contaminants prepared in response to informational requests from environmental specialists of the U.S. Fish and Wildlife Service.

[1] Barnes and Stoner (1959); Piver (1973); Kimbrough (1976); CEC (1978); Zuckerman et al. (1978); Duncan (1980); Watanabe (1980); WHO (1980); Blunden and Chapman (1982); Blunden et al. (1984, 1985); Krigman and Silverman (1984); Reiter and Ruppert (1984); Reuhl and Cranmer (1984); Wilkinson (1984); Hall and Pinkney (1985); Laughlin and Linden (1985); McMillan and Wenger (1985); Thompson et al (1985); Blunden and Chapman (1986); Cardwell and Sheldon (1986); Chang (1986); Maton (1986); Sylph (1986a, b); EPA (1987); Snoeij et al. (1987).

CHEMICAL AND BIOCHEMICAL PROPERTIES

GENERAL

The chemical, physical, and biochemical properties of inorganic tin compounds differ dramatically from those of representative organotin compounds. There is general agreement that inorganic tins are not highly toxic due to their poor absorption and rapid turnover rate in tissues and to their being essential for growth in at least one species (rat). Of the 260 known organotin compounds, all but a few are manufactured, and 36 are listed as toxic (Watanabe 1980). Most authorities agree on several points regarding organotin compounds: information concerning the mechanism of toxic action is incomplete; there is no evidence of carcinogenicity; trialkyltin compounds are the most toxic; and there are large differences in resistance between and within species.

INORGANIC TIN

Elemental tin has an atomic number of 50, an atomic mass of 118.69, and exists in three allotropic forms: white tin at room temperature, nonmetallic grey tin at <13.3 C, and brittle tin at >161 C. White tin is a stable silver-white, lustrous, soft metal with a density of 7.27, a melting point of 231.9 C, and a boiling point of 2,507 C. Tin has 10 stable isotopes (Sn-112, -114, -115, -116, -117, -118, -119, -120, -122, and -124), the most for any element. Inorganic tin compounds exist in the +2 (stannous) and +4 (stannic) oxidation states. Stannous compounds are generally more polar than stannic compounds, are unstable in dilute aqueous solutions, are easily oxidized, and normally contain some Sn+4. Stannic oxide occurs naturally as the mineral cassiterite, has a melting point of 1,127 C, and has wide application in industry. Additional information on inorganic tin chemistry is listed in Zuckerman et al. (1978), WHO (1980), and Davies and Smith (1982).

Signs of inorganic tin poisoning in mammals include local effects such as vomiting, diarrhea, and eye and nose irritation; however, these vary considerably among species (WHO 1980). The major systemic effects include ataxia, twitching of limbs, weakness of limbs, paralysis, growth retardation, decreased hemoglobin levels, and--at extremely high doses--testicular degeneration, pancreatic atrophy, formation of spongy brain white matter, and kidney necrosis. In humans, symptoms of inorganic tin intoxication include nausea, vomiting, diarrhea, stomach ache, fatigue, and headache. The lowest concentration producing outbreaks was about 250 mg Sn per liter in canned orange and apple juice. Ingestion of 50 mg of tin through eating canned peaches that contained Sn concentrations of about 450 mg/kg caused acute symptoms in 2 of 7 human volunteers (WHO 1980). Inhalation of SnO_2 dust is a hazard in the deep-mining of tin; deposits in lungs are easily detectable as "stannosis" (Krigman and Silverman 1984).

Inorganic tin and its salts are not highly toxic due to their poor absorption, relative insolubility of their oxides, and rapid tissue turnover (WHO 1980; Hassett et al. 1984; Krigman and Silverman 1984; Blunden and Chapman 1986). The absorption of ingested inorganic tin is usually less than 5%, although up to 20% has been reported. Stannous compounds are more readily absorbed from the gastrointestinal tract than stannic compounds, but absorbed tin leaves the vascular system rapidly. Bone is the main site of tin deposition, followed by lung, liver, and kidney. Penetration of the blood-brain and placental barriers by inorganic tin seems to be very slight. Except for lung, inorganic tin does not accumulate in organs with increasing age. Absorbed inorganic tin is excreted mainly in the urine, although excretion through the bile may account for up to 15% of the total. Tin and its inorganic compounds do not produce significant dermatitis or allergic reactions to skin epithelium, and results of all long-term studies of carcinogenicity, teratogenicity, and mutagenicity have been negative to date (WHO 1980).

The half-time (Tb 1/2) of inorganic tins in animals was reviewed by WHO (1980). Studies with Sn+2 in mouse, rat, monkey, and dog show that in all species elimination is a four-compartment process regardless of the route of administration (i.e., intraperitoneal or intravenous). The Tb 1/2 for the longest-lived Sn component

was >3 months. In studies with rats, for example, radiotin-113 in skeleton following intramuscular administration had a Tb1/2 of 3 to 4 months, but for oral administration of Sn+2 and Sn+4 it was only 28 to 40 days in bone and 10 to 20 days in liver and kidney.

Inorganic tin can be biomethylated by microorganisms in the aquatic environment and subsequently mobilized in the ecosystem (Tugrul et al. 1983; Yemenicioglu et al. 1987). The process is slow and usually does not proceed beyond the monomethyltin stage (Zuckerman et al. 1978), although dimethyltin formation by *Pseudomonas* bacteria has been reported (Smith 1978b).

Tin is an essential nutrient for growth in the rat, and a tin-deficient diet leads to reduced growth (WHO 1980; Krigman and Silverman 1984). The mechanism of action is unclear, but involves increasing metabolic activity of liver lysosomes and liver hydrolytic enzymes during regeneration (Dwivedi et al. 1985a,b).

ORGANOTINS

Organotins are compounds with at least one tin-carbon bond. In most organotin compounds, tin is in the tetravalent oxidation state. Four series of organotin compounds are known: R_4Sn, R_3SnX, R_2SnX_2, and $RSnX_3$ wherein R is usually a butyl, octyl, or phenyl group, and X is commonly chloride, fluoride, oxide, hydroxide, carboxylate, or thiolate (CEC 1978). The possible molecular composition and structure of the R groups are virtually unlimited (Laughlin et al. 1985). At least 260 organotin compounds presently are known, of which 36 are listed as toxic chemicals (Watanabe 1980). Except for some methyltin compounds, all organotins are manufactured (Laughlin et al. 1985). Most commercially used organotins are characterized by low mobility in the environment because of low aqueous solubility, low vapor pressure, and high affinity for soils and organic sediments (Blunden and Chapman 1986). Solubility data for organotin compounds are incomplete. In general, their solubility in water is limited to about 5 to 50 mg/l, but they are very soluble in many common organic solvents (WHO 1980). The presence of chloride in seawater reduces the solubility of tributyltin and triphenyltin compounds, probably by association with the hydrated cation to form the covalent organotin chloride (Blunden et al. 1985). Organotin compounds are analyzed in aqueous media by spectrophotometric, fluorometric, and electrochemical techniques. However, if picomole per liter concentrations are required, additional techniques must be used. More work needs to be done on analytical detection methods of organotins in sediments and biota (Thompson et al. 1985).

Methylation of inorganic and methyltin compounds has been reported with the formation of mono-, di-, tri-, and tetramethyltin compounds. In addition, tributylmethyltin and dibutylmethyltin species have been found in harbor sediments, which suggests that some butyltin compounds may be methylated in aquatic systems (Guard et al. 1981; Thompson et al. 1985; Donard et al. 1987).

Abiotic and biological degradation of organotins generally occurs through sequential dealkylation or dearylation (Zuckerman et al. 1978; WHO 1980; Smith 1981b; Chau et al. 1984; Blunden et al. 1985). Organotin compounds undergo successive cleavage of tin-carbon bonds to ultimately produce inorganic tin as follows: $R_4Sn \xrightarrow{k4} R_3SnX \xrightarrow{k3} R_2SnX_2 \xrightarrow{k2} RSnX_3 \xrightarrow{k1} SnX_4$. The reaction rate, k, usually proceeds as k4 > k3 > k2 = k1. The breaking of a Sn-C bond can occur by a number of different processes, including ultraviolet irradiation (UV), biological cleavage, chemical cleavage, gamma irradiation, and thermal cleavage (WHO 1980; Blunden and Chapman 1982, 1986; Blunden et al. 1985; Thompson et al. 1985). In general, UV and biological cleavage are the most important processes. The main abiotic factors that seem to limit organotin persistence in the environment are elevated temperatures, increased intensity of sunlight, and aerobic conditions (Table 1). A probable environmental degradation scheme for tributyltin and triphenyltin compounds is shown in Figure 1.

The tendency of an organotin compound to be concentrated by an organism depends on its partition behavior between lipid and aqueous phases. In general, compounds highly soluble in octanol and only slightly soluble in water have high Kow values. Kow values of organotins increase with number and molecular weight of organic groups attached to the tin atom, with significant bioaccumulation potential for organotins with R groups of butyl and larger (Thompson et al. 1985). Kow values for tributyltins in seawater vary from 5,500 to 7,000, but can be significantly modified by salinity and speciation products (Laughlin et al. 1986b). Thus, organotins would be expected to accumulate in lipid-rich surface microlayers of natural waters (Cardwell and Sheldon 1986) and

in biota (as discussed later). However, the ability of microorganisms, algae, and higher organisms to reduce various organotins into less toxic metabolites that can be rapidly excreted seems to preclude food chain biomagnification and to lessen the potential hazards to natural resources from consumption of organisms with elevated organotin residues (Table 1; Cardwell and Sheldon 1986).

Most authorities now agree on five points: (1) information concerning the mechanism of the toxic action of organotin compounds is inadequate; (2) results of all studies with various organotins for possible carcinogenicity are negative; (3) triorganotin compounds are the most toxic group of organotins; (4) large inter- and intraspecies differences exist in resistance to organotin compounds; and (5) organotins can alter enzyme activity levels in many organs and tissues including brain, liver, and kidney (Piver 1973; Duncan 1980; WHO 1980; Davies and Smith 1982; Maguire et al. 1982; Arakawa and Wada 1984; Dwivedi et al. 1985b; Blunden and Chapman 1986).

The monoorganotin compounds, $RSnX_3$ have a generally low toxicity and do not seem to have any important biological action in mammals (Duncan 1980; Davies and Smith 1982; Krigman and Silverman 1984; Blunden and Chapman 1986).

Dialkylorganotins, R_2SnX_2, are associated with hepatotoxicity (ethyl, propyl, butyl, and pentyltins), immunotoxic effects to T-cells (butyl and octyltins), and skin and eye irritation (methyl, ethyl, propyl, butyl, and octyltins; Watanabe 1980; Krigman and Silverman 1984). The diorganotins combine with coenzymes or enzymes possessing dithiol groups and exert their toxic action by inhibiting alpha-keto acid oxidation and blocking mitochondrial respiration (Duncan 1980; WHO 1980; Davies and Smith 1982). Resistance to diorganotin toxicity varies widely among species. For example, dibutyltins and dioctyltins--unlike other organotins tested--were toxic to rat thymocytes, but did not induce similar effects on lymphoid atrophy in mice, guinea pigs, or Japanese quail (Seinen et al. 1977b). Selected dibutyltins are effective as antihelminthics and are used to kill parasitic worms in chickens and turkeys without harm to host birds (Davies and Smith 1982).

Table 1. Biological and abiotic degradation times of selected organotins.

Degradation route, organism or compartment, and tin compound	Time for 50% degradation and other variables (reference)
Biological	
Microorganisms	
Tributyltin	1 to 2 weeks in aerated medium in dark, 6 to 13 weeks in aerated medium in light, <1 year in anaerobic medium (Cardwell and Sheldon 1986)
Triphenyltin	60 to 140 days under aerobic, light conditions (Smith 1981b)
Algae, *Ankistrodesmus falcatus*	
Tributyltin	25 days (Maguire et al. 1984)
Bivalve molluscs, 3 species	
Tributyltin	10 to 14 days (Cardwell and Sheldon 1986; Laughlin et al. 1986a)
Sheepshead minnow, *Cyprinodon variegatus*	
Tributyltin	14 to 28 days (Cardwell and Sheldon 1986)
Abiotic	
Distilled water	
Tributyltin	>89 days at initial concentration of 0.7 mg Sn/L, 18 days at 2.0 to 4.0 mg Sn/L (Walsh et al. 1986a)
Freshwater	

Tributylin	3 to 89 days (Duncan 1980; Smith 1981b; Ward et al. 1981; Maguire and Tkacz 1985; Walsh et al. 1985)
Triphenyltin	8 months at 1.0 to 2.5 mg/L, 100 days at 0.5 mg/L (Duncan 1980)
Diphenyltin	2 to 3 days (Soderquist and Crosby 1980)
Seawater	
Tributyltin	6 to 19 days; most rapid at low initial concentrations under high illumination (Seligman et al. 1986)
Triphenyltin	About 140 days (Duncan 1980)
Sediments	
Trimethyltin	About 80 days at 16 C to form the more volatile $(CH_3)_4Sn$ (Guard et al. 1981)
Tributyltin	At least 10 months at 20 ºC (Maguire and Tkacz 1985)

In any member of the organotin series R_nSnX_{4-n}, progressive substitution of organic groups at tin produces a maximum biological activity for the triorganotin derivatives, R_3SnX (Davies and Smith 1982). Among triorganotin compounds, trimethyltins are highly toxic to insects, birds, and mammals; triethyltins to mammals; tripropyltins to gram-negative bacteria; tributyltins to fish, molluscs, fungi, and gram-positive bacteria; triphenyltins to fish, fungi, and molluscs; and tricyclohexyltins to mites (Duncan 1980; Davies and Smith 1982; Maguire et al. 1982; Blunden and Chapman 1986). In mammals, the lower triorganotin homologues (trimethyltins, triethyltins) are essentially neurotoxic, the intermediate trialkyltins and triphenyltins are primarily immunotoxic, and the higher homologues are only slightly toxic or not toxic (Krigman and Silverman 1984; Snoeij et al. 1985). The toxicity of triorganotin compounds is probably due to their ability to bind to proteins and to inhibit mitochondrial oxidative phosphorylation (Smith 1978b; Duncan 1980; WHO 1980; Davies and Smith 1982; Blunden and Chapman 1986). Triorganotins also interfere with phagocytosis and exocytosis and other pathways where sulfhydryl groups play a pivotal role (Elferink et al. 1986), and inhibit uptake of gamma-aminobutyric acid and Na^+-K^+-ATPase in brain (Costa 1985). Impairment of phagocytosis and related activities of polymorphonuclear leukocytes may enhance susceptibility for infection (Elferink et al. 1986).

Trimethyltins are the most toxic trialkyltins to mammals, regardless of the nature of the substituent (X group) according to Smith (1978b). They induce pathological lesions in brain and overt neurological and behavioral changes in rodents (Chang 1986). Trimethyltins are neurotoxins that damage the limbic system, cerebral cortex, and brain stem and can traverse the placenta and accumulate in the fetus (Reuhl aid Cranmer 1984). Trimethyltins (but not inorganic, monomethyl, or dimethyltins) inhibit brain protein synthesis by 47% and can cause a decrease of 4.2 °C in body temperature of mice within 1 hour postadministration of 3.0 mg/kg body weight (Costa and Sulaiman 1986). Raising the ambient temperature to 35 °C prevented hypothermia in treated mice and resulted in only a 20% inhibition in protein synthesis. More research is needed on the role of protein synthesis in organotin-induced neurotoxicity.

Triethyltins modify phosphorylation processes in subcellular fractions of rat brain proteins (Piver 1973; Neumann and Taketa 1987). Signs of triethyltin poisoning in rodents include weakness of hindlimbs, dyspnea, and peripheral vasodilation (Watanabe 1980). Internally, acute triethyltin intoxication is characterized by a transient edema of the central and peripheral nervous systems manifested by extensive intramyelinic vacuolation due to splitting of myelin lamellae; changes are reversible (Watanabe 1980; Reuhl and Cranmer 1984). Neuronal death is reported following triethyltin intoxication during the neonatal period, possibly as a result of elevated intracranial pressure (Reuhl and Cranmer 1984). In rabbit brain, triethyltins alter activity of pyruvate dehydrogenase (Neumann and Taketa 1987).

Studies on tributyltin uptake and depuration from food or water by rats, crabs, oysters, and fish showed that in all species it was accumulated and metabolized, at least partly, within 48 hours to dibutyltins, monobutyltins, and more polar metabolites; however, oysters (*Crassostrea virginica)* metabolized significantly less tributlytin than did other species tested (Lee 1985). The accumulation of tributyltin compounds in different tissues

correlated well with lipid content nd supports a partitioning mode of uptake (Laughlin et al. 1986a). The mixed function oxygenase system from hepatic tissues was able to metabolize tributyltins by forming hydroxylated metabolites (Lee 1985). Tributyltins are also potent cytotoxicants in rabbit erythrocyte and skin cultures (Gray et al. 1985).

The potential of tricyclohexyltins to modify the inducibility of cytochrome P-450 by various substances, such as 3-methylcholanthrene, is of considerable toxicological importance (Rosenberg et al. 1985). Significant metabolic interactions can result from a combination of environmental chemicals and drugs that produce alterations in heme and mixed function oxygenase activity (Rosenberg et al. 1985), suggesting that more research is needed on interaction effects of organotins with other environmental substances or contaminants.

The biological effects of the tetraorganotin compounds, R_4Sn, seem to be caused entirely by the R_3SnX derivative that is produced by their rapid in vivo dealkylation (Duncan 1980; Davies and Smith 1982; Blunden and Chapman 1986). Increasing toxicity of tetra- and triorganotins in mammals has been shown to be associated with decreasing length of their ligands, as reflected by solubility in biological fluids (Arakawa et al. 1981). It is not known if damage is produced by the metal or by its alkyl derivative, but the presence of trialkyl groups seems to enhance the toxicity of tin--probably by increasing its partition into lipids, thus aiding the absorption of the metal and speeding its distribution to the site of action (Arakawa et al. 1981).

SOURCES AND USES

Metallic tin is derived mainly from the mineral cassiterite (SnO_2) and to a lesser extent from the sulphide ore stannite Cu_2S-FeS-SnS_2, although it can be derived from rarer minerals such as malayaite, $CaSnSiO_5$. (Blunden et al. 1985). Tin is one of the earliest metals known and has influenced our life style through the ages. Tin alloy artifacts dating from about 5,000 years ago have been unearthed at Ur, the site of ancient Babylonia (Zuckerman et al. 1978). Today we are exposed to tin on a daily basis through the use of tinplated food cans; of alloys such as pewter, bronze, brass, and solder; and from toothpaste containing stannous flouride (Zuckerman et al. 1978). Inorganic tin compounds are also used in a variety of industrial processes such as the strengthening of glass, as a base for colors, as catalysts in various chemical reactions, as stabilizers in perfumes and soaps, and as dental anticariogenic agents (WHO 1980). Organotin use is increasing rapidly in antifouling marine paints, in molluscicides, and in agriculture, which often causes serious adverse effects on nontarget biota.

In 1975, the total world tin production was 236,000 tons, of which 72% was produced by China (10%), Indonesia (8%), Malaysia (35%), Thailand (7%), and 6% each by the UK and USSR (WHO 1980). The world production of recycled tin was about 20,000 tons, of which France produced about half (WHO 1980). The production and consumption of tin chemicals, especially organotins, has increased markedly in the past several decades (Table 2).

The United States is the major consumer of tin and organotin compounds, followed by Japan, the UK, Germany, and France (WHO 1980). In 1976, for example, the United States consumed 11,000 tons of organotins, or about 39% of the world organotin production (Chau et al. 1984). The projected total demand for primary tin up to the year 2000 is estimated at 7.5 million tons. Total reserves currently are about 6.5 million tons; however, it is likely that new discoveries and increases in known reserves will result in sufficient new tin to meet the demand for this period (WHO 1980).

The uses of inorganic and organotin compounds are numerous and increasing (Table 3). Industrial consumption of organotins, for example, rose from about 5,000 tons in 1965 to about 35,000 tons in 1980. At present, the uses of nontoxic organotin compounds (R_2SnX_2 and $RSnX_3$ types) account for about 67% of the total world production, although use of R_3SnX types as selective biocides has increased disproportionately in recent years (Davies and Smith 1982). Tin now has more of its organometallic derivatives in commercial use than any other element (Blunden et al. 1985).

Table 2. Annual tin production and consumption.

Chemical group and other variables	Amount, in metric tons	Reference[a]
Organotins		
Production Worldwide		
Total		
1950	<5,000	1
1955	~5,000	2
1976	24,000 to 28,000	3, 4, 5, 6
1986	30,000	2
Triorganotins	8,000	2
Tributyltins	900	7
Di- and monoorganotins	27,000	2
USA		
1965	2,300	8
1976	10,400	8
1986	25,000	8
Consumption		
Worldwide		
Total		
1965	5,000	9
1967	8,000	10
1975	25,000	10
1980	30,000 to 35,000	9
Biocidal applications		
1975	10,000	10
Total tin, Production, worldwide,		
1975, Total	236,000	4
1975, Primary tin	217,000	4
1976, Total	180,000 to 200,000	2, 3, 5
1976, Total	155,000	1
Tinplate	52,700	1
Solder	48,100	1
Chemicals	20,000	1
Other uses	34,200	1
1976, Total	225,000	4
Ores	157,500	4
Scrap metal	67,500	4

[a]References: 1, Blunden et al. 1985; 2, Blunden and Chapman 1986; 3, Zuckerman et al. 1978; 4, WHO 1980; 5, Chau et al. 1984; 6, Guard et al. 1981; 7, Laughlin et al. 1986a; 8, Walsh et al. 1985; 9, Davies and Smith 1982; 10, CEC 1978.

Table 3. Major uses of inorganic and organic tin compounds.

Compounds, uses, and references (in parentheses)
INORGANIC TIN COMPOUNDS: Tin plate, solder, brass, bronze, and other alloys; heat stabilizers for polyvinyl chloride manufacture; tin and tin alloy electroplating baths; catalysts for silicone and polyurethane foam production; in glass manufacture; flame retardants for woolen fabrics; in toothpastes and dentifrices; for control of parasitic worms in sheep; radiopharmaceuticals; in ceramic glazes and pigments; in fluorescent phosphors, in weighting and dying of silk; stone polishing; corrosion inhibitors; color and perfume stabilizers in soaps (WHO 1980; Blunden et al. 1985).
MONOORGANOTINS: Polyvinyl chloride stabilizers, catalysts, SnO_2 precursors (CEC 1978; WHO 1980; Chau et al. 1984; Blunden et al. 1985, Blunden and Chapman 1986).
DIORGANOTINS: Catalysts for silicones, polyurethane foams; polyvinyl chloride stabilizers; precursor for forming SnO_2 films on glass; antihelminthics for poultry; lubricating oil additives (Piver 1973; CEC 1978; WHO 1980; Chau et al. 1984; Blunden et al. 1985; Blunden and Chapman 1986).
TRIORGANOTINS: Agrochemical fungicides, herbicides, miticides, insecticides, nematocides, acaricides, antifeedants; biocide in marine paints; slimicide in paper pulp mills and cooling towers; rodent repellant; molluscicides; wood preservative fungicides; disinfectants; stone preservation; textile and leather protection (Piver 1973; Hunter 1976; Kumpulainen and Koivistoinen 1977; CEC 1978; WHO 1980; Davies and Smith 1982; Chau et al. 1984; Subramanian 1984; Wilkinson 1984; Blunden et al. 1985; Maguire and Tkacz 1985; Thompson et al. 1985; Blunden and Chapman 1986),
TETRAORGANOTINS: Used in manufacture of R_nSnX_{4-n} compounds from $SnCl_4$; catalysts for olefin polymers; stabilizers for transformer oils; corrosion inhibitor in lubricating oils (CEC 1978; WHO 1980; Davies and Smith 1982)

Biocidal applications of organotins to control marine fouling communities, agricultural pests, and as selective molluscicides merit brief additional comment. The use of antifoulants on ships is necessitated by the damage some organisms can cause to wooden structures and by the reduced fuel efficiency and speed due to drag when vessels become heavily fouled (Laughlin et al. 1984). Until recently, the most widely used antifouling paint contained a copper base that is biocidally active when copper leaches as an ion from the paint (Hall et al. 1987). However, short effective lifetimes and high costs have limited the usefulness of copper-based paints. Organocompounds of arsenic, mercury, or lead have also been used in antifouling paints, but these paints have been removed from the commercial market due to the toxicological risks during preparation and application and to their hazards to the environment (Blunden et al. 1985; Hall et al. 1987). Organotin coatings are currently promoted because of their excellent antifouling action, long lifetime (up to 4 years), and lack of corrosion (Messiha and Ikladious 1986). Oganotin coatings, especially tributyltins, present potential environmental problems to nontarget aquatic biota due to their extreme toxicity.

Use of organotin antifouling paints on recreational and commercial water craft has increased markedly in recent years. In Maryland, for example, 50% to 75% of the recreational boats used in Chesapeake Bay are covered with organotin paints (Hall et al. 198). The organotin biocide released by hydrolysis from the surface of the paint film into seawater provides the antifoulant action. In consequence, the depleted outer layer of paint film, containing hydrophilic carboxylate groups, is easily eroded by moving seawater exposing a fresh surface layer of organotin acrylate polymer. In continuing tests by the U.S. Navy, ablative organotin fouling coatings have demonstrated more than 48 months of protection (Blunden et al. 1985). As discussed later, the use of organotin compounds in antifouling paints has been severely curtailed. Several organotins have been used extensively as agricultural pesticides, especially tricyclohexyltin and triphenyltin compounds (Hunter 1976;

Kumpulainen and Koivistoinen 1977; Blunden et al. 1985). In general, these compounds showed low phytotoxicity, low toxicity to nontarget organisms, no evidence of development of resistant insect strains, and degradation to form harmless tin residues. It is probable that agricultural uses of organotins will increase. The toxicity of triorganotin compounds to aquatic invertebrates, especially slow release formulations of tributyltins, is usually high, and this property has been used advantageously to eradicate certain species of freshwater snails that are intermediate vectors of schistosomiasis, i.e., *Biomphalaria* spp., *Bulinus* spp. (Chliamovitch and Kuhn 1977; CEC 1978; Duncan 1980; Seinen et al. 1981). Unfortunately, nontarget biota, including some sensitive species of fishes, are killed at recommended application levels (EPA 1987).

Organotins enter air, soil, and water primarily as a result of routine agricultural, industrial, municipal, and biocidal operations (Table 4). Deposition rates of organotins from air into soils and water are unknown at present, but may be significant around urban and industrialized areas. Total tin concentrations--primarily inorganic tin--in the atmosphere of the northern hemisphere are significantly higher than those in the southern hemisphere and are dominated by anthropogenic sources (Table 5). The most important of these sources seems to be the incineration of municipal wastes, which accounts for most of the tin flux to the atmosphere (Byrd and Andreae 1986a). Riverine fluxes of tin to the oceans vary between 36 and 71 million kg annually, almost all of it in particulate fractions (Byrd and Andreae 1986b).

Table 4. Possible modes of entry of organotins into air, soil, and water (Blunden et al. 1985).

Environmental compartment and organotin group	Sources
Air	
R_3SnX	Agricultural spraying, volatilization from biocidal treatments, antifouling paint sprays
R_3SnX, R_2SnX_2, $RSnX_3$	Incineration of organotin-treated or -stabilized waste materials
R_2SnX_2, $RSnX_3$	Glass coating operations to produce SnO_2 films
Soil	
R_3SnX	Agricultural applications, wood preservation
R_3SnX, R_2SnX_2, $RSnX_3$	Burial of waste materials containing organotins
WaterR_3SnX	Antifouling coatings, molluscicides, overspray from agricultural operations, land runoff from agricultural use, industrial processes (i.e., slimicides in paper manufacture)
R_2SnX_2, $RSnX_3$	Leaching from organotin stabilized polyvinyl chloride

Table 5. Total tin flux to the atmosphere and hydrosphere (modified from Byrd and Andreae 1986a, b).

Environmental compartment and other variables	Annual flux, in millions of kilograms
Atmosphere	
Northern hemisphere	
Anthropogenic	16.6
Natural	1.2
Total	17.8

Southern hemisphere	
Anthropogenic	1.6
Natural	0.7
Total	2.3
Hydrosphere	
Riverine flux to oceans	
Dissolved fraction	0.09
Particulate fraction	35.6–71.2

BACKGROUND CONCENTRATIONS

GENERAL

In aquatic environments, organotin concentrations were elevated in sediments, biota, and surface water microlayers collected near marinas, aquaculture rearing pens, and other facilities where organotin-based antifouling paints were used. In some cases, organotin concentrations in the water column were sufficiently high to pose a substantial risk to sensitive species. Data are now extremely limited on background concentrations of organotins in all environmental samples, especially in terrestrial ecosystems, and this may be attributed, in part, to limitations in routine chemical analytical capabilities.

NONBIOLOGICAL

Tin concentrations in water, air, soils, sediments, and other nonbiological materials are documented but information is scarce except for aquatic systems (Table 6). In aquatic systems, several trends were evident. First, tin and organotin compounds tend to concentrate in surface microlayers by factors up to 10,000X relative to subsurface water; in the case of organotins, this may be due to partitioning into the film of petroleum hydrocarbons commonly present on water surfaces (Maguire et al. 1982; Cleary and Stebbing 1987; Hall et al. 1987). Second, organotin concentrations, especially tributyltins, were highest in the vicinity of marinas and harbors, and this is consistent with its use as an antifouling agent in some paints for boats, ships, and docks (Chau et al. 1984; Maguire et al. 1986; Randall et al. 1986; Valkirs et al. 1986). Peak tributyltin concentrations occurred in late spring and early summer in association with postwinter launching of freshly painted boats (Hall et al. 1987). Third, organotin levels throughout the water column of marinas in numerous freshwater and marine locations were sufficiently elevated to cause chronic toxic effects in sensitive organisms including algae, copepods, oysters, mussel larvae, and fish (Maguire et al. 1982, 1986; Waldock and Thain 1983; Chau et al. 1984; Maguire and Tkacz 1985; Beaumont and Newman 1986; Cardwell and Sheldon 1986; Thain and Waldock 1986; Cleary and Stebbing 1987; Hall et al. 1987; Stromgren and Bongard 1987). Fourth, methyltin species were infrequently detected. Their occurrence was positively correlated with the presence of relatively high concentrations of inorganic tin and was due primarily to biotic and abiotic methylation of both organotin and inorganic tin compounds (Chau et al. 1984; Maguire et al. 1986). Finally, butyltin species were detected in harbor sediments at concentrations that were toxicologically hazardous to benthic fauna (Waldock and Thain 1983; Chau et al. 1984; Maguire et al. 1986). Tributyltin species can be accumulated from the sediments by oligochaetes (*Tubifex tubifex, Limnodrilus hoffmeisteri*), thus making it potentially available to bottom-feeding fish; oligochaetes can also degrade tributyltins by a sequential debutylation, with Tb1/2 estimates of 5 months in water and 4 months in water-sediment mixtures (Maguire and Tkacz 1985).

Table 6. Tin concentrations in nonbiological materials.

Sample (units), tin species, and other variables	Concentration[a]	Reference[b]
Saline waters (µg/L)		
Total tin		
Chesapeake Bay	Max. 0.46	1

San Diego Bay	Max. 0.07	1
Southwest UK, 1984	Max. 3.2	2
France, Arcachon Bay		
1982	5.05	3
1983	2.20	3
1985	1.00	3
Northeastern Mediterranean	Max. 0.32	4
Total organotin		
England		
Subsurface		
Southwest	Max. 0.29	1
Southeast	Max. 0.06	1
Surface microlayer		
Southwest	Max. 1.1	1
Southeast	Max. 0.06	1
France, Arcachon Bay		
1982	0.20	3
1983	<0.15	3
1985	<0.15	3
Inorganic tin		
San Diego Bay, California	Max. 0.009	5
Northeastern Mediterranean	Max. 0.24	6
Methyltin		
Western Florida	<0.009	7
Gulf of Mexico	<0.015	7
Dimethyltin		
Western Florida	<0.005	7
Gulf of Mexico	<0.007	7
Baltimore Harbor, Maryland	Max. 0.1	7
Trimethyltin		
Western Florida	<0.0005	7
Gulf of Mexico	<0.001	7
Baltimore Harbor, Maryland	Max. 0.02	7
Tetramethyltin		
Baltimore Harbor, Maryland	Max. 0.3	7
Butyltin		
Tejo estuary, Portugal	0.0011	7
Baltimore Harbor	Max. 0.3	7
San Diego Bay	Max. 0.05	5
Dibutyltin		
San Diego Bay	Max. 0.46	5
San Diego Bay	Max. 0.13	8
Chesapeake Bay, 1985–86		

Surface microlayer	Max. 1.16	8
Water column		
Marinas	(0.02–0.15)	8
Other locations	<0.04	8
Tributyltin		
Coastal waters, UK	Max. 0.43	7
Marinas, UK	Max. 2.3	7
San Diego Bay, California	Max. 0.93	5
Main channel	Max. 0.06	7
Boat basin	Max. 0.55	7
Surface microlayer	(0.06–0.25)	8
Water column	(0.01–0.18)	8
Chesapeake Bay, 1985–86		
Surface microlayer	Max. 1.2	8
Water column		
Marinas	(0.05–1.0)	8
Other locations	0.02	8
Southwest UK, 1984	Max. 0.88	2
Maryland		
Baltimore Harbor		
Surface microlayer	Max. 4.57	8
Annapolis, water column	0.07	8
Tetrabutyltin		
Chesapeake Bay	ND	8
Freshwater (µg/L)		
Total tin		
Drinking water	Usually <1.0, Max. 30.0	9
Great Lakes		
Subsurface	Max. 1.2	1
Surface microlayer	Max. 24.9	1
Inorganic tin		
Canadian marinas, 1982–84		
Lake St. Clair	6.7	10
Whitby	37.2	10
Port Hope	9.9	10
Methyltin		
Canada		
Marina	1.2	11
Harbors, lakes, rivers	(0.06–1.0)	7
USA rivers	<0.002	7
German rivers	<0.08	7
Florida lakes, ponds, rivers	<0.012	7
Dimethyltin		

Canadian marina	Max. 0.4	11
USA rivers	0.004	7
German rivers	Max. 0.26	7
Florida lakes, ponds, rivers	<0.008	7
Trimethyltin		
Canadian marina	Max. 0.05	11
Lake Superior	0.05	7
USA rivers	0.002	7
German rivers	0.002	7
Florida lakes, ponds, rivers	<0.008	7
Butyltin		
Canada		
Marinas		
Whitby	0.62	10
Port Hope	0.42	10
Lake St. Clair	8.5	11
Hamilton Harbor, Canada	0.02	7
Subsurface waters		
33 locations	detectable	12
188 locations	ND	12
Dibutyltin		
Canada		
Marinas		
Whitby	1.46	10
Port Hope	0.08	10
Lake St. Clair		
Subsurface	7.3	11
Surface microlayer	107.0	11
Harbor areas, lakes, rivers	(0.01–0.3)	7
Surface microlayer	(0.7–2,600)	7
Subsurface waters		
27 locations	detectable	12
194 locations	ND	12
Surface waters	(0.01–7.3)	8
Tributyltin		
Canada		
Marinas		
Lake St. Clair		
Subsurface	0.18	10
Surface microlayer	50.9	11
Whitby	4.2	10
Port Hope	5.7	10
Harbor areas, lakes, rivers	(0.01–1.0)	7

Surface microlayer	(0.2–60.0)	7
Subsurface waters		
1 location	2.34	12
7 locations	(0.4–1.8)	12
13 locations	(0.07–0.4)	12
22 locations	detectable	12
178 stations	ND	12
Surface waters	(0.01–2.9)	8
Air (µg/m^3)		
USA cities	Usually <0.01 (0.003–0.3); Max. 0.8 (Boston)	9
Japan		
Near furnaces	(10–640)	9
700 m distant	(3.8–4.4)	9
Soils (mg/kg)		
In mineral soils containing tin	>1,000	9
In unmineralized soils	(2.0–<200)	9
Sediments (mg/kg)		
Inorganic tin		
Toronto Harbor	Max. 0.62	13
Sault St. Marie	15.5	10
Lake Superior	0.7	10
Wabigoon River	(0.3–1.2)	10
Turkey	(0.5–1.1)	14
Northeast Mediterranean	Max. 2.3	6
Great Bay, New Hampshire	(0.40–0.63)	15
Methyltin		
Lake Superior	ND	10
Wabigoon River	0.1	10
Turkey	0.3	14
Northeast Mediterranean	Max. 0.01	6
Great Bay, New Hampshire	Max. 0.08	15
San Diego Bay	Max. 0.003	7
Chesapeake Bay	Max. 0.0008	7
Dimethyltin		
Turkey	Max. 0.01	14
Great Bay, New Hampshire	Max. 0.05	15
San Diego Bay	Max. 0.003	7
Trimethyltin		
Turkey	Max. 0.02	14
Great Bay, New Hampshire	ND	15
San Diego Bay	Max. 0.0002	7

Butyltin		
Toronto Harbor	Max. 0.08	13
Sault St. Marie	0.15	10
Wabigoon River	(0.04–0.11)	10
Great Bay, New Hampshire	(0.003–0.03)	15
Canada		
Marinas	0.02	7
Other locations	(0.014–0.58)	7
San Diego Bay	Max. 0.007	7
Mission Bay, California	Max. 0.011	7
Dibutyltin		
Toronto Harbor	Max. 0.26	13
Great Bay, New Hampshire	(0.001–0.015)	15
Canada		
Marinas	0.074	7
Harbors, lakes, rivers	(0.05–0.35)	7
Tributyltin		
Toronto Harbor	Max. 1.28	13
Great Bay, New Hampshire	(0.012–0.044)	15
Lake St. Clair, marina	0.125	7
Canadian harbors, lakes, and rivers	(0.11–0.54)	7
Minerals (mg/kg)		
Total tin		
Shale	4.1	16
Igneous rock	2.5	16
Oceanic clay	2.4	16
Oceanic carbonate	0.4	16
Sandstone	0.12	16

[a]Concentrations are expressed as mean, (minimum-maximum), maximum (Max.), and nondetectable (ND).

[b]References: 1, Cleary and Stebbing 1987; 2, Cleary and Stebbing 1985; 3, Alzieu et al. 1986; 4, Salihoglu et al. 1987; 5, Valkirs et al. 1986; 6, Yemenicioglu et al. 1987; 7, Hall and Pinkney 1985; 8, Hall et al. 1987; 9, WHO 1980; 10, Chau et al. 1984; 11, Maguire et al. 1982; 12, Maguire et al. 1986; 13, Maguire and Tkacz 1985; 14, Tugrul et al. 1983; 15, Randall et al. 1986; 16, Thompson et al. 1985.

BIOLOGICAL

Information on background concentrations of total tin in tissues of field populations of animals and plants was abundant, but few data were available on organotin species (Table 7).

Tin concentrations in marine algae and macrophytes varied between 0.5 and 101 mg total Sn/kg dry weight and clearly demonstrated that most species of aquatic flora bioconcentrate tin from seawater (Table 7). Marine plants are also important in the cycling of tin. Living algae are effective in immobilizing tin from seawater and regulating the formation and degradation of toxic methyltin compounds (Donard et al. 1987). Dead and decaying algae accumulate inorganic and organotin compounds, release them, and ultimately remove tin from the estuary to the atmosphere by formation of tetramethyltins (Donard et al. 1987).

Organotin content in fish tissues is quite variable, ranging from a low of 3% to 6% of the total tin body burden (Tugrul et al. 1983) to 18% for goatfish (*Upeneus moluccensis)* to 5% for *Mullus barbatus*, another species of goatfish (Salihoglu et al. 1987). By contrast, the limpet (*Patella caerulea*) contains 35% to 75% of its total tin body burden as organotin (Tugrul et al. 1983).

In January 1982, France banned organotin compounds for use in antifouling paints. By 1985, tin and organotin concentrations in seawater and Pacific oysters (*Crassostrea gigas*) were 5 to 10X lower than those found in 1982 (Alzieu et al. 1986). In Arcachon Bay, France, a decrease in the incidence and extent of anomalies in oyster calcification mechanisms was noted that seemed to be correlated with decreases in tin contamination (Alzieu et al. 1986). Crassostreid oysters can accumulate radiotin (Sn-113) to a higher degree than other species of bivalve molluscs, a characteristic that may be useful as a bioindicator in the event of contamination due to this isotope (Patel and Ganguly 1973).

Antifouling paints containing tributyltin compounds are used widely on netting panels of sea cages at fish and shellfish aquaculture units to minimize the obstruction of water exchange through the cages (Davies et al. 1987). Under these conditions, tributyltin paints were detrimental to the growth and survival of juvenile scallops and to calcium metabolism and growth of adult oysters (Paul and Davies 1986) and resulted in elevated concentrations of tributyltin in salmon tissues (Short and Thrower 1986; Davies and McKie 1987). Scallops (*Pecten maximus)* reared in sea pens for 31 weeks on nets coated with tributyltin oxide contained 2.5 mg total Sn/kg fresh weight soft parts (1.9 mg tributyltin/kg), but lost up to 40% during a 10-week depuration period. Scallop adductor muscle contained 0.53 mg tributyltin/kg, suggesting that this tissue--the one consumed by humans--is a probable tin storage site (Davies et al. 1986). Pacific oysters (*Crassostrea gigas*) reared for 31 weeks on tributyltin-exposed nets contained a maximum of 1.4 mg tributyltin/kg FW at week 16 (controls 0.12 mg/kg), but lost 90% during a 10-week depuration period (Davies et al. 1986). Atlantic salmon (*Salmo salar)* held for 3 months during summer in cages with tributyltin-treated net panels contained 0.75 to 1.5 mg tributyltin/kg fresh weight muscle vs. 0.28 mg/kg at start (Davies and McKie 1987). Based on laboratory studies, it is probable that Atlantic salmon were exposed to approximately 1.0 ug tributyltin/l during this interval (Davies and McKie 1987). Chinook salmon (*Oncorhynchus tshawytscha)*, reared in sea pens treated with tributyltin paints, contained <0.013 mg tributyltin/kg muscle fresh weight when introduced into the pens. Concentrations were 0.3 mg/kg after 3 months, 0.8 mg/kg at 13 months, and 0.9 mg/kg at 19 months. Cooking did not destroy or remove organotins from salmon muscle tissues (Short and Thrower 1986).

Table 7. Tin concentrations in field collections of living flora and fauna. Unless indicated otherwise, all values are in mg total Sn/kg fresh weight (FW) or dry weight (DW) tissue.

Taxonomic group, organism, and other variables	Concentration, in ppm[a]	Reference[b]
Algae and higher plants		
Algae, marine		
Whole, 10 species	(11–49) DW	1
Whole, 2 species	(96–101) DW	1
Swiss chard, whole,		
Beta vulgaris cicla		
Grown in soil at pH		
5.5	(12–51) DW	2
6.0	8 DW	2
6.5	<0.5 DW	2
Mangrove, *Bruguiera*		

caryophylloides, leaf		
Controls	1.3 DW	2
On Sn drainage	9.4 DW	2
Green alga, *Enteromorpha* spp.		
Inorganic tin	0.4 FW; 4.4 DW	3
Monomethyltins	0.5 FW	3
Dimethyltins	0.5 FW	3
Trimethyltins	<0.001 FW	3
Tetramethyltins	ND	3
Monbutyltins	0.006 FW; 0.4 DW	3
Tributyltins	0.05 FW; 0.6 DW	3
Seaweeds, whole, 5 species		
May	(0.5–1.8) DW	1
June	(0.5–2.2) DW	1
June	(0.1–0.5) FW	1
Wheat, *Triticum vulgare*		
Japan	0.5 FW	2
USA	(5.6–7.9) FW	2
Elm, *Ulmus americana*		
Wood, Vermont		
40 years old	1.7 FW; 1.8 DW	2
80 years old	1.4 FW; 1.5 DW	2
Vegetation		
Near tin smelter	(338–2,165) DW	2
Corn, *Zea mays*	0.1 FW	2
Invertebrates		
Pacific oyster, *Crassostrea gigas*		
Soft parts		
Arcachon Bay, France, July		
1982		
Total tin	Max. 7.0 DW	4
Organotin	Max. 1.6 DW	4
1983		
Total tin	Max. 4.0 DW	4
Organotin	Max. 0.8 DW	4
1985		
Total tin	Max. 0.9 DW	4
Organotin	Max. 0.4 DW	4
Soft parts		
Controls	0.1 FW	5
Reared in sea cages painted with tributyltin for 16 weeks		

Total tin	1.4 FW	5
Tributyltin	0.9 FW	5
American oyster, *Crassostrea virginica*		
Shell	<0.1 DW	2
Soft parts	1.4 FW	2
Crustaceans, marine		
Edible tissues		
5 species	(0.6–0.7) FW	6
8 species	(0.7–0.9) FW	6
3 species	(0.9–2.0) FW	6
American lobster, *Homarus americanus*		
Muscle	0.6 FW	2
Molluscs, marine		
Edible tissues		
3 species	(0.3–0.5) FW	6
7 species	(0.5–0.7) FW	6
4 species	(0.7–0.9) FW	6
4 species	(0.9–2.0) FW	6
Mussel, *Mytilus edulis*		
Soft parts	(1.3–7.1) DW	7
Hepatopancreas		
San Diego harbor	(1.9–3.5) DW	8
Offshore	(<0.7–2.0) DW	8
Common dogwhelk, *Nucellus lapillus*		
Soft parts, uncontaminated		
Total tin	Max. 0.3 FW	9
Total tin	(0.1–0.2) DW	10
Tributyltin	(0.1–0.2) DW	10
Dibutyltin	(0.01–0.05) DW	10
European oyster, *Ostrea edulis*		
Uncontaminated area		
All tissues	<0.1 FW	11
River Crouch, UK		
Flesh	(0.27–0.33) FW	11
Eggs	0.33 FW	11
Larvae	0.30 FW	11
Limpet, *Patella caerulea*		
N.E. Mediterranean, 1980		
Shell		
Total tin	0.013 DW	12
Methyltin	0.0004 DW	12

Dimethyltin	0.0002 DW	12
Trimethyltin	0.0009 DW	12
Soft parts		
Total tin	0.075 DW	12
Methyltin	0.001 DW	12
Dimethyltin	0.009 DW	12
Trimethyltin	0.026 DW	12
Scallop, *Pecten maximus*		
Reared in sea pens with tributyltin-coated netting for 3 weeks		
Total tin		
Gonad	0.6 FW	5
Adductor muscle	0.6 FW	5
Gills	0.6 FW	5
Digestive gland	1.0 FW	5
Tributyltin		
Gonad	0.4 FW	5
Digestive gland	0.5 FW	5
Adductor muscle	0.5 FW	5
Gills	0.6 FW	5
Fish		
Pacific herring, *Clupea harengus pallasi*		
Whole, Vancouver, Canada 1984		
Inorganic tin	0.04 FW	13
Butyltin	0.06 FW	13
Dibutyltin	0.05 FW	13
Tributyltin	0.24 FW	13
Lake whitefish, *Coregonus clupeaformis*, muscle	(0.8–3.6) FW	2
Northern pike, *Esox lucius,* muscle		
Manitoba, Canada	(0.7–5.4) FW	2
Lake Erie	0.5 FW	
Fish, marine		
Liver		
27 species	(<0.1–0.4) FW	6
45 species	(0.4–0.8) FW	6
10 species	(0.8–2.0) FW	6
Muscle		
8 species	(0.2–0.4) FW	6
110 species	(0.4–0.6) FW	6
34 species	(0.6–0.8) FW	6
7 species	(0.8–2.0) FW	6
Whole		

2 species	(0.3–0.6) FW	6
12 species	(0.8–2.0) FW	6
3 species	(2.0–9.0) FW	6
Atlantic cod,		
Gadus morhua, muscle	(0.5–3.7) FW	2
Atlantic halibut,		
Hippoglossus hippoglossus, muscle	1.2 FW	2
Rainbow smelt,		
Osmerus mordax, muscle	1.2 FW	2
Yellow perch, *Perca flavescens,* muscle	0.6 FW	2
Winter flounder,		
Pseudopleuronectes americanus, muscle	3.2 FW	2
Atlantic salmon, *Salmo salar*		
Muscle	0.07 FW	14
Gonad	0.15 FW	14
Gill	0.03 FW	14
Kidney	0.06 FW	14
Liver	0.04 FW	14
Lake trout, *Salvelinus namaycush*		
Whole, Canada, 1982–84		
Methyltin	(0.2–0.9) FW	15
Dimethyltin	(ND–0.2) FW	15
Trimethyltin	ND	15
Inorganic tin	(0.2–0.3) FW	15
Inorganic tin	Max. 0.9 FW	13
Spiny dogfish, *Squalus acanthias*		
Muscle	2.0 DW	2
Birds		
Ruffed grouse,		
Bonasa umbellus, liver	0.5 FW	2
Chicken, *Gallus gallus*		
Muscle	1.7 FW	2
Egg	0.9 FW	2
Mammals		
Cow, *Bos bovis*		
Muscle	Max. 2.8 FW	2
MilkMax. 0.9 FW	2	
Beaver, *Castor canadensis,* heart	7.3 FW	2
Woodchuck, *Marmota monax*, liver	1.8 FW	2
White-tailed deer,		
Odocoileus virginianus		
Liver	0.8 FW	2
Kidney	Max. 2.2 FW	2

Heart	ND	2
Muskrat, *Ondatra zibethicus,* liver	0.3 FW	2
Sheep, *Ovis aries*		
Liver	0.3 FW	2
Muscle	1.4 FW	2
Harbor seal, *Phoca vitulina*		
All tissues	<0.1 FW	2
Fox, *Vulpes* sp., liver	3.5 FW	2

[a]Concentrations are expressed as mean, (minimum-maximum), maximum (Max.), and nondetectable (ND).

[b]References: 1, Eisler 1981; 2, Jenkins 1980; 3, Donard et al. 1987; 4, Alzieu et al. 1986; 5, Davies et al. 1986; 6, Hall et al. 1978; 7, Karbe et al. 1977; 8, Young et al. 1979; 9, Davies et al. 1987; 10, Bryan et al. 1986; 11, Thain and Waldock 1986; 12, Tugrul et al. 1983; 13, Maguire et al. 1986; 14, Davies and McKie 1987; 15, Chau et al. 1984.

LETHAL AND SUBLETHAL EFFECTS

GENERAL

Inorganic tin compounds are of low toxicologic risk due largely to their low solubility, poor absorption, low accumulations in tissues, and rapid excretion. By contrast, some organotin compounds--especially trialkyltins--produce a variety of harmful effects resulting in impaired behavior and lowered growth, survival, and reproduction. Among aquatic organisms, tributyltin compounds were especially potent. Adverse effects were noted in molluscs at water concentrations of 0.001 to 0.06 ug/l and in algae, fish, and other species of invertebrates at 0.1 to 1.0 ug/l. Bioconcentration of organotins was high, but degradation was sufficiently rapid to preclude food chain biomagnification. Birds seem to be relatively resistant to organotins, although data are extremely scarce. Preliminary data suggest that diets containing 50 mg of tin as trimethyltin chloride/kg are fatal to all mallard ducklings in 75 days; however, no deaths occurred in 75 days at 50 mg/kg of eleven other mono-, di-, tri-, and tetraalkyltin compounds. Trimethyltin was lethal to other species of birds tested at doses of 1 to 3 mg/kg body weight. Trimethyltins and triethyltins were the most toxic organotin compounds tested on small laboratory mammals. Neurotoxicological effects of trimethyltins were usually not reversible, while those caused by triethyltins were reversible after exposure. Adverse effects of trimethyltins were produced at concentrations as low as 0.15 mg/l in drinking water (learning deficits), 0.625 mg/kg BW (diet aversion), and 1.25 mg/kg BW (death).

AQUATIC ORGANISMS

Results of acute toxicity tests with several organotin compounds and *Daphnia magna* indicated several distinct trends: toxicity increased with length of alkyl group from methyl to butyl; the anion substituents are relatively unimportant; and bioavailability is correlated with increasing solubility in lipids, which is a direct function of Kow, the n-octanol/water partition coefficient (Vighi and Calamari 1985). Structure-activity relations seem to have high predictive capacity in hazard assessment, and those for organotins seem particularly promising (Vighi and Calamari 1985). For example, studies on the biocidal properties of structurally distinct diorganotins (R_2SnX_2) and triorganotins (R_3SnX) to zoeae of a marine crab show, within a homologous series, that diorganotins are less toxic than the corresponding triorganotins (Table 8). It was concluded that the toxicity of organotins to crab zoeae seems to be a function of the hydrophobic characteristics conferred by the number and structure of the organic ligands (Laughlin et al. 1985).

Table 8. Toxicity of selected diorganotin and triorganotin compounds to zoeae of the marine mud crab (*Rithropanopeus harrisii*) exposed from hatching to age 14 days (modified from Laughlin et al. 1985).

Compound tested and formula	Lowest concentrations tested, in mg/L, producing Some deaths, but <50%		At least 50% mortality	
	Total product	Tin only	Total product	Tin only
Diorganotins				
Deimthyltin dichloride, $(CH_3)_2SnCl_2$	10.0	5.4	20.0	10.8
Diethyltin dichloride, $(C_2H_5)_2SnCl_2$	2.5	1.2	5.0	2.4
Dipropyltin dichloride, $(C_3H_7)_2SnCl_2$	2.5	1.1	5.0	2.2
Dibutyltin dichloride, $(C_4H_9)_2SnCl_2$	0.25	0.097	2.0	0.78
Dephenyltin dichloride, $(C_5H_{11})_2SnCl_2$	0.5	0.18	0.75	0.27
Dicyclohexyltin dichloride, $(C_6H_{13})_2SnCl_2$	0.125	0.041	0.25	0.082
Triorganotins				
Trimethyltin hydroxide, $(CH_3)_3SnOH$	0.075	0.05	0.1	0.067
Triethyltin hydroxide, $(C_2H_5)_3SnOH$	0.075	0.04	0.1	0.053
Tripropyltin oxide, $(C_3H_7)_3Sn)_2O$	0.025	0.015	0.05	0.03
Tributyltin oxide, $((C_4H_9)_3Sn)_2O$	0.01	0.005	0.02	0.011
Triphenyltin hydroxide, $(C_5H_{11})_3SnOH$	0.01	0.003	0.02	0.007
Tricyclohexyltin bromide, $(C_6H_{13})_3SnBr$	0.006	0.0016	0.009	0.0023

Signs of tributyltin poisoning in rainbow trout and other freshwater teleosts include sluggishness; loss of appetite; altered body pigmentation; air gulping; loss of positive rheotaxis; increased rate of opercular movements; damaged gills, cornea, and epithelial cells of bile duct; and increases in blood hemoglobin, erythrocyte number, and hematocrit (Chliamovitch and Kuhn 1977; Thompson et al. 1985). These changes were consistent with the known inhibitory effects on mitochondrial and oxidative phosphorylation of triorganotin compounds. Suppression of regeneration in echinoderms, and presumably other aquatic groups, may be due

primarily to neurotoxicological action of orginotins, or secondarily by direct action on tissue at the breakage point (Walsh et al. 1986b).

Studies on lethal and sublethal effects of tin compounds to representative species of aquatic organisms demonstrate that organotin compounds are more toxic than inorganic tin compounds; triorganotin compounds are more toxic than mono-, di-, or tetraorgano forms; and tributyltin compounds are the most toxic triorganotin compounds tested (Table 9). Adverse effects of tributyltins were noted at water concentrations of 0.001 to 0.06 ug/l in marine gastropod and bivalve molluscs and at 0.1 to 1 ug/l in algae, echinoderms, fish, crustaceans and coelenterates (Table 9). In order of toxicity, tributyltins were followed by tripropyltins (harmful effects recorded at 0.001 to 10 ug/l to gastropods, fish, and algae), triphenyltins (0.6 to 1 ug/l to diatoms and annelids), triethyltins (3.8 to 10 ug/l to fish and algae), trimethyltins (20 ug/l to algae and crustaceans), and tripentyltins (50 to 100 ug/l to gastropods). Because many organotin compounds are slow-acting poisons, short-term toxicity tests seriously underestimate the toxicity of these compounds (Laughlin and Linden 1985).

Biological factors known to modify lethal and sublethal effects of organotins include age of the organism, inherent interspecies resistance, and tissue specificity. Abiotic modifiers include exposure route, and physicochemical regimen. Early developmental stages were more sensitive to organotins than later developmental stages in marine annelids (Walsh et al. 1986a), mysid shrimp (Hall and Pinkney 1985), and rainbow trout (Thompson et al. 1985). Mortality of zoeae of fiddler crabs (*Uca pugilator*) to trimethyltins was greatest at elevated temperatures and low salinities (Thompson et al. 1985). Mussels exposed through a diet of algae showed slow accumulation of organotins when compared to exposure from the medium; the reverse was observed for crabs (Evans and Laughlin 1984; Hall and Pinkney 1985; Laughlin et al. 1986a). A marine diatom (*Thalassiosira pseudonana*) showed no adaptation or resistance to triphenyltins or tributyltins (Walsh et al. 1985), but another diatom (*Amphora coffeaeformis*) was extremely resistant (Thomas and Robinson 1986, 1987). Finally, mortality was substantially higher when organisms were exposed simultaneously to organotins through water and sediments; in the case of grass shrimp (*Palaemonetes pugio*), the addition of contaminated sediments increased mortality by up to 1,000X (Clark et al. 1987).

Table 9. Lethal and sublethal effects of inorganic and organic tin compounds in ambient medium to selected species of aquatic organisms.

Compound and organism	Concentration (µg/L)	Effect	Reference[a]
Inorganic tins			
Dab (fish), *Limanda limanda*	35	No deaths in 96 h	1
Marine diatoms, 2 species	316 to 325	50% growth inhibition in 72 h	2
Monmethyltins			
Marine diatom, *Skeletonema costatum*	78	50% growth inhibition in 72 h	2
Dimethyltins			
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
Trimethyltins			
Alga, *Scenedesmus quadricauda*	20	LC-87 (30 days)	3
Alga, *Chlorella vulgaris*	20	LC-100 (30 days)	3
Alga, *Asteromonas gracilis*	20	LC-100 (12 days)	3
Cladoceran, *Daphnia magna*	20	LC-61 (30 days)	3
Marine diatoms, 2 species	214	50% growth inhibition in 72 h	2
Tetramethyltins			
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
Diethyltins			

Snail, *Biomphalaria glabrata*	50 to 100	LC-50 (24 h)	4
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
Triethyltins			
Marine diatom, *Thalassiosira pseudonana*	3.8	LC-50 (72 h)	2
Sevyuga sturgeon, *Accipenser stellatus*, larvae	10	LC-100 (48 h)	3
Common carp, *Cyprinus carpio*	10	BCF's after 45 days ranged between 5x in muscle and 88x in blood	3
Marine diatom, *Skeletonema costatum*	40.2	LC-50 (72 h)	2
Tetraethyltins			
Marine diatoms, 2 species	127 to 142	50% growth inhibition in 72 h	2
Tripropyltins			
Snail, *Lymnaea stagnalis*	0.001 to 1.0	Fecundity reduced after exposure for 3 months	3
Sheep sturgeon, *Accipenser nudiventris*	0.001	Larvae die when exposed from fertilization	3
A. nudiventris	0.01	Prolarvae die when exposed continuously from fertilization	3
Loach (fish), *Misgurnis fossilis*, larvae	<1	Normal development	3
M. fossilis	10	No development	3
Algae, Lake Ontario	4	50% reduction in primary productivity in 4 h	3
Alga, *Ankistrodesmus falcatus*	14	50% growth reduction in 8 days	3
Snail, *B. glabrata*	40 to 280	LC-50 (24 h)	4
Monobutyltins			
Golden orfe (fish), *Leuciscus idus melanotus*	>45,000	LC-50 (48 h)	5
Dibutyltins			
Duck mussel, *Anodonta anatina*	15	After 7 months, tin localized exclusively in epithelial cells of kidney, accompanied by significant decrease in cellular glycogen content	6, 29
Marine diatom, *S. costatum*	35 to 56	50% growth inhibition in 72 h	2
Golden orfe	1,000	LC-50 (48 h)	5
Tributyltins			
Dogwhelk, *Nucella lapillus*	0.001 to 0.02	Development of male characteristics in 13%	

		of female snails after 31 days, 27% in 91 days and 41% in 120 days. Whole body BCF values about 19,000x in 31 days, 36,000x in 91 days,78,000x in 120 days	7
Snail, *B. glabrata*	0.001	Reduction in egg deposition on continuous exposure from hatching	8
B. glabrata	0.1	Exposure for 34 days followed by 50-day recovery period produced 60% mortality, 80% reduction in egg deposition, and reduced growth	3
B. glabrata	0.4	LC-99 (30 days)	9
B. glabrata	1.0	50% reduction in egg laying after exposure for 2 to 3 weeks	3
B. glabrata	3	BCF of 48x in muscle after 120 h	3
B. glabrata	7	LC-100 (20 days)	9
B. glabrata	15	LC-100 (5 days)	9
B. glabrata	75	LC-100 (24 h)	4
Pacific oyster, *Crassostrea gigas*	0.01 to 0.02	Spat show reduced growth and hypoxia compensation after 2 weeks	10
C. gigas	0.15	Reduced growth and shell thickening after 8 weeks	11
C. gigas	0.2	BCF of ~ 6,000x in adult soft tissues in 21 days, 11,400x in whole spat in 56 days	3
C. gigas, larvae	1.0	LC-100 (12 days)	8
C. gigas, larvae	1.6	LC-100 (48 h)	12
C. gigas	1.6	No growth. BCF after 8 weeks varied from 2,300x to 3,100x	11
Copepod, *Eurytemora affinis*	0.0125	No adverse effects in 13 days	34
E. affinis	0.1	LC-74 (13 days)	34
E. affinis	0.5	Reduction in brood size in 48 h	34
E. affinis	0.6	LC-50 (72 h)	34
E. affinis	2.2	LC-50 (48 h)	34
Bay mussel, *Mytilus edulis*	0.05	Some larval deaths in 96 h	13
M. edulis, larvae	0.1	LC-50 (15 days)	14
M. edulis, larvae	0.24	Growth reduction after 45 days	12, 14
M. edulis	0.31	No shell growth in 66 days	14
M. edulis	0.4	Reduction in shell growth rate in 7days	15
M. edulis, adults	0.97	LC-50 (66 days)	14, 16
M. edulis, larvae	0.5	LC-100 (96 h)	13
European oyster, *Ostrea edulis*	0.06	Reduced growth rate in 10 days	14
O. edulis	0.24	No larval release after	

		exposure for 74 days; BCF of 875x	17
O. edulis	2.6	Reduced growth in 74 days; BCF of 397x	17
O. edulis, larvae	3.4	LC-50 (48 h)	17
Marine algae, 3 species	0.1	Reduced growth rate in 48 h	18
Brittle star, *Ophioderma brevispina*	0.1	Arm regeneration inhibited	19
Sheepshead minnow, *Cyprinodon variegatus*	0.18 to 1.0	Maximum BCF's after 167 days were 1,600x in muscle, 3,900x in viscera, 52,000x in liver; no adverse effects on growth or reproduction	20
C. variegatus	0.96	LC-50 (21 days)	8
C. variegatus	1.6	Maximum BCF's after 58 days were 1,810x in muscle, 2,120x in head, 4,580x in viscera, and 2,600x in whole fish. Loss after 28 days depuration ranged from 64% to 80%	20
C. variegatus	3.2	LC-100 (21 days)	20
C. variegatus	5 to 8	LC-50 (96 h)	3
C. variegatus	18	LC-50 (7 days)	8
Oysters, several species	0.2	LC-70 (113 days)	8
Rainbow trout, *Salmo gairdneri*	0.2 to 1.0	Exposure of yolk-sac fry for 110 days produced liver disfunction, reduced growth, and altered blood chemistry; no deaths	8, 21
S. gairdneri	5	Kidney degeneration in 12 days, some deaths	21
S. gairdneri	11. to 20	LC-50 (96 h)	5, 22
S. gairdneri	11.7	Bile duct pathology after 5 days; destruction of corneal epithelium after 7 days	3
S. gairdneri	21	LC-50 (48 h)	9
S. gairdneri	28	LC-50 (24 h)	23
Baltic amphipod, *Gammarus oceanicus,* larvae	0.3	Reduced survival after 5 weeks	24
G. oceanicus	3	LC-100 (16 days)	3
Alga, *Skeletonema costatum*	0.33 to 0.36	50% growth inhibition in 72 h	2
Copepod, *Acartia tonsa*	0.4	50% immobilization in 144 h	25
A. tonsa	0.55	LC-50 (6 days)	8
A. tonsa	1.0	LC-50 (96 h)	25
Fiddler crab, *Uca pugilator*	0.5	Limbs regenerated during	

		19 days showed a variety of deformities and retardation of regenerative growth	26, 35
U. pugilator	0.5 to 50	Non-dose dependent reduction in burrowing activity in 15 to 60 min; hyperactivity in 1 to 3 weeks	36
Mysid shrimp, *Metamysidopsis elongata,* juveniles	0.5 to 1.0	LC-50 (96 h)	3
American oyster, *Crassostrea virginica*	0.73 to 1.9	Reduced larval growth in 66 days	16
C. virginica, larvae	0.9	50% immobilization in 48 h	12
Hydroid, *Campanularia flexuosa*	1.0	100% growth inhibition in 11 days	3
Cladoceran, *D. magna*	1.0	Reduced survival and impaired reproduction in 15 days	14
D. magna	1.7	LC-50 (48 h)	12
D. magna	3	LC-50 (24 h)	23
American lobster, *Homarus americanus*	1.0	No effect on larval metamorphosis in 6 days	8
H. americanus, larvae	5	LC-100 (6 days)	25
H. americanus, larvae	20	LC-100 (24 h)	3
Shrimp, *Crangon crangon*, larvae	1.5	LC-50 (96 h)	12
C. crangon, adults	41	LC-50 (96 h)	12
Copepod, *Nitroca spinipes*	2	LC-50 (96 h)	25
Round Crucian carp, *Carassius carassius grandoculis*	2	BCF after 7 days of about 500x in vertebra, 630x in muscle, 3,160x in kidney, and 5,020x in liver	27
Sole, *Solea solea*, larvae	2	LC-50 (96 h)	3
Lugworm, *Arenicola cristata*	2	LC-0 (168 h)	28
A. cristata, larvae	4	LC-100 (96 h)	23
Algae, various species	3 to 16	50% reduction in primary productivity in 4 h to 8 days	3
Barnacle, *Balanus amphitrite*	4	LC-50 (24 h) nauplii	3
Freshwater clam, *Anodonta anatina*	5	LC-100 (6 weeks)	29
Mud snail, *Nassarius obsoletus*	5 to 6	Induced male characteristics in females in 64 days	3
N. obsoletus	8	LC-50 (61 days)	3
Tubifex worm, *Tubifex tubifex*	6	LC-50 (48 h)	9
Amphipod, *Orchestia traskiana*	6	LC-47 (9 days)	3
O. traskiana	10	LC-80 (9 days)	3
O. traskiana	15	LC-93 (9 days)	3
Mud crab, *Rithropanopeus harrisii*	6	BCFs after 4 days were 650x in muscle,	

		4,400x in hepatopancreas, and 1,300x in gill	37
R. harrisii	15	Weight loss after 15 days	3, 37
Bluegill, *Lepomis macrochirus*	7.6	LC-50 (96 h)	12
L. macrochirus	33	LC-50 (48 h)	8
Mysid shrimp, *Mysidopsis bahia*	8	LC-50 (96 h)	30
Mummichog (fish), *Fundulus heteroclitus*	9	Avoidance	3
F. heteroclitus	24	LC-50 (96 h)	12
Crab, *Carcinus maenus*	10	LC-50 (96 h)	3
Amphioxus, *Branchiostoma caribaeum*	10	LC-100 (96 h)	30
Snail, *Neritina* sp.	10	LC-100 (6 days)	3
Snails, *Biomphalaria* spp.	10 to 30	LC-50 (24 h)	8
Channel catfish, *Ictalurus punctatus*	12	LC-50 (96 h)	8
Marine diatom, *S. costatum*	14.7	LC-50 (72 h)	2
Snail, *Lymnaea* sp.	15	LC-100 (~5 days)	3
Atlantic menhaden, *Brevoortia tyrannus*	15	Avoidance by juveniles	3
Speckled sanddab, *Citharichthys stigmaeus*	20	LC-50 (96 h)	3
Grass shrimp, *Palaemonetes pugio*	20	LC-50 (96 h)	30
Green alga, *Ankistrodesmus falcatus*	20	BCF of ~ 30,000x at day 7	23
A. falcatus	40	BCF of 8,600x at day 7	23
Guppy, *Poecilia reticulata*	21 to 30	LC-50 (96 h)	8
P. reticulata	26 to 34	LC-50 (48 h)	5
Mozambique tilapia, *Tilapia mossambica*	28	LC-50 (24 h)	8
Duckweed, *Lemna media*	30	Reduced growth in 10 days	31
Snail, *Australorbis glabratus*	30	LC-100 (5 days)	31
European frog, *Rana temporaria*, tadpole	30	LC-50 (5 days)	32
R. temporaria, tadpole	75	LC-100 (24 h)	9
Harlequin fish, *Rasbora heteromorpha*	42	LC-50 (48 h)	8
Jewelfish, *Hemichromus bimaculatus*	45	LC-70 (48 h)	8
Fathead minnow, *Pimephales promelas*	45	LC-50 (96 h)	8
Golden orfe	50	LC-50 (48 h)	5
Cladoceran, *Daphnia longispina*	60	LC-100 (72 h)	31
Bleak (fish), *Alburnus alburnus*	70 to 400	LC-50 (96 h)	5
Goldfish, *Carassius auratus*	75	LC-100 (24 h)	31
Duckweed, *Lemna media*	500	LC-100 (10 days)	31
Tetrabutyltins			
Golden orfe	10,000	LC-50 (48 h)	5

Tripentyltins			
Snail, *B. glabrata*	50 to 100	LC-50 (24 h)	4
Triphenyltins			
Marine diatoms, 2 species	0.6 to 1.1	50% growth inhibition in 72 h	2
Lugworm, *A. cristata*	0.75–1.0	Abnormal larval development	28
A. cristata, larvae	1.5 to 2.5	LC-0 (168 h)	28
A. cristata, larvae	4 to 10	LC-100 (96 h)	23
Algae, various species	2 to 20	50% growth inhibition in 4 h to 8 days	3
Marine diatom, *S. costatum*	4.3 to 13.8	LC-50 (72 h)	2
Copepod, *Nitroca spinipes*	8	LC-50 (96 h)	3
Snail, *B. glabrata*	10 to 1,000	LC-50 (24 h)	4
Rainbow trout	15	LC-50 (96 h)	30
Snail, *Biomphalaria sudanica*	17	LC-50 (24 h)	3
Cladoceran, *D. magna*	20	LC-100 (30 days)	3
Cladoceran, *D. longispina*	50	LC-100 (48 h)	33
Snail, *Australorbis glabratus*	50	LC-100 (7 days)	33
A. glabratus	200	LC-100 (72 h)	33

[a]References: 1, Taylor et al. 1985; 2, Walsh et al. 1985; 3, Hall and Pinkney 1985; 4, Duncan 1980; 5, Blunden and Chapman 1986; 6, Herwig and Holwerda 1986; 7, Bryan et al. 1986; 8, Thompson et al. 1985; 9, Chliamovitch and Kuhn 1977; 10, Lawler and Aldrich 1987; 11, Waldock and Thain 1983; 12, Champ 1986; 13, Dixon and Prosser 1986; 14, Cardwell and Sheldon 1986; 15, Stromgren and Bongard 1987; 16, Valkirs et al. 1987; 17, Thain and Waldock 1986; 18, Beaumont and Newman 1986; 19, Walsh et al. 1986b; 20, Ward et al. 1981; 21, Seinen et al. 1981; 22, Douglas et al. 1986; 23, Maguire et al. 1984; 24, Laughlin et al. 1984; 25, U'ren 1983; 26 Weis et al. 1987; 27, Tsuda et al. 1986; 28, Walsh et al. 1986a; 29, Holwerda and Herwig 1986; 30, Clark et al. 1987; 31, Floch et al. 1964; 32, Laughlin and Linden 1982; 33, Floch and Deschiens 1962; 34, Hall et al. 1988; 35, Weis and Kim 1988; 36, Weis and Perlmutter 1987; 37, Evans and Laughlin 1984.

Aside from direct toxic effects that antifouling paint residues may have on marine life, there is no evidence of any risk from cytogenetic damage. Tributyltins, for example, were not genotoxic to larvae of the mussel (*Mytilus edulis*) based on results of sister chromatid exchange and analysis of chromosomal aberrations (Dixon and Prosser 1986). Teratogenic effects, however, were detected in larvae of the lugworm (*Arenicola cristata*) at sublethal concentrations of tributyltins (Walsh et al. 1986a), and algae (*Nitzschia liebethrutti*) exposed to 15 mg inorganic Sn/l for 14 days had frustule abnormalities (Saboski 1977).

Bioconcentration of inorganic and organic tin compounds from the medium is considerable. Bioconcentration factors (BCF's) for inorganic tin and marine algae were about 1,900X; moreover, tin-resistant bacteria contained a remarkable 3.7 to 7.7 grams Sn/kg dry weight (Maguire et al. 1984). BCF's for organotin compounds varied from about 400X to 30,000X among various species of molluscs, algae, and crustaceans and were highest when ambient tin concentrations were <1.0 ug/l, when exposure times were comparatively lengthy, and when organism lipid content was elevated (Thompson et al. 1985;Champ 1986; Laughlin et al. 1986a; Thain and Waldock 1986). Sheepshead minnows (*Cyprinodon variegatus*) were unable to reach equilibrium with a medium containing 1.61 ug tributyltin/l after 58 days of exposure and maximum BCF values recorded were 2,600X in whole fish, 1,810X in muscle, 4,580X in viscera, and 2,120X in the remainder of the carcass; however, whole body loss was 52% after depuration for 7 days and 74% after 28 days (Ward et al. 1981). Sheepshead minnows were able to metabolize tributyltins into lower alkyl moieties, which were less toxic. Thus, even though significant bioconcentration occurred, the chronic toxicity of tributyltins to sheepshead minnow was not significantly greater than its acute toxicity (Ward et al. 1981).

Benthic fauna are probably capable of transferring organotins from sediments to bottom-feeding teleosts. For example, sediments spiked with 0.98 mg Sn/kg dry weight, as tributyltin, resulted in concentrations of 4.41 mg/kg whole body dry weight in oligochaete annelid worms after 22 weeks, up from 0.38 at the start (Maguire and Tkacz 1985).

Imposex--the superimposition of male characteristics onto a functionally normal female reproductive anatomy--is a phenomenon documented in populations of marine gastropod molluscs in the vicinity of yacht basins and marinas and is a sensitive indictor of tributyltin contamination. A female with imposex displays one or more male characteristics such as a penis, a vas deferens, or convolution of the normally straight gonadal oviduct. It is measured by frequency of occurrence in the adult females and by the intensity of expression of all male characteristics in bearer females. Imposex is prevalent in mud snails (*Nassarius obsoletus*) near estuarine marinas and has been induced experimentally in that species by exposure for 60 days to three tributyltin compounds at concentrations of 4.5 to 5.5 ug/l (Smith 1981a,b). Imposex has been documented extensively in declining populations of the common dogwhelk (*Nucella lapillus*), especially in southwestern England (Bryan et al. 1986, 1987; Gibbs and Bryan 1986; Davies et al. 1987; Gibbs et al. 1987). These authorities agree on six points: (1) dogwhelk populations near centers of boating and shipping activity show the highest degrees of imposex, coinciding with the introduction and increasing use of antifouling paints containing tributyltin compounds; (2) imposex is not correlated with tissue burdens of arsenic, cadmium, copper, lead, silver, or zinc, but is correlated with increasing concentrations of tributyltin and dibutyltin fractions; (3) transplantation of dogwhelks from a locality with little boating activity to a site near a heavily used marina causes a marked increase in the degree of imposex and in tissue accumulations of tributyltins; (4) imposex can be induced in female dogwhelks by exposure to 0.02 ug Sn/l leached from a tributyltin antifouling paint; after exposure for 120 days, 41% of the females had male characters and whole body residues of 1.65 mg Sn/kg dry weight soft parts (vs. 0.1 in controls), of which almost all was tributyltin (1.64 vs. 0.08 mg/kg in controls). Concentrations as low as 0.0015 ug tributyltin/l can initiate imposex in immature females; (5) declining dogwhelk populations studied were characterized by a moderate to high degree of imposex, relatively fewer functional females, few juveniles, and a general scarcity of laid egg capsules. Many females in late imposex contained aborted capsules as a result of oviduct blockage, resulting in sterility and premature death; and (6) there was no evidence that loss of tin leads to any remission of imposex; in fact, all evidence indicates that gross morphological changes that occur in late imposex are irreversible. It is clear that additional research is needed on the imposex phenomenon in molluscs and on its implications to vertebrates and other taxonomic groups.

BIRDS

Information is scarce on the effects of tin and organotin compounds on birds. However, limited data suggest that triorganotin compounds, especially trimethyltins--and to a lesser extent triethyltins--are the most toxic (Table 10).

Dr. W. James Fleming of the Patuxent Wildlife Research Center has recently concluded a 75-day feeding study with mallard ducklings (*Anas platyrhynchos*) and 12 organotin compounds. Preliminary results indicated that trimethyltin was the most toxic compound tested. A dietary level of 50 mg of Sn as trimethyltin chloride/kg food was fatal to all ducklings; 5 mg/kg killed 40%, but all survived at 0.5 mg/kg diet. Death was preceded by mild to severe tremors, progressing to ataxia and lethargy. Large neurons of the pons, medulla oblongata, gray matter of the spinal cord, and cells of the cerebral cortex exhibited degeneration and necrosis. All ducklings survived exposure to 50 mg/kg ration of tetraethyltin, tetrabutyltin, tetraphenyltin, triethyltin chloride, tripropyltin chloride, tributyltin chloride, tributyltin oxide, triphenyltin chloride, tricyclohexyltin chloride, dimethyltin chloride, and dibutyltin chloride (Fleming, personal communication). Sublethal effects were recorded at 50 mg triethyltin chloride/kg (low body weight, vacuolization of spinal cord and brain white matter), at 50 mg tributyltin chloride/kg (enlarged liver), and at 50 mg tetrabutyltin/kg (elevated kidney weight). Residue and other analyses are now in progress.

Table 10. Lethal and sublethal effects of selected organotin compounds to birds.

Compound and organism	Effect (reference)
Dialkyltins	
Japanese quail, *Coturnix japonica*	No measurable effect at dietary levels of 150 mg/kg for 2 weeks (Seinen et al. 1977b)
Trialkyltins	
Mallard, *Anas platyrhynchos*	Ducklings fed diets containing 50 mg trimethyltin chloride/kg died within 60 days (personal communication, Dr. W. James Fleming, Patuxent Wildlife Research Center)
Pigeon, *Columba* sp.	Trimethyltin injections (3 intra-muscular injections, 2 weeks apart) at 1.0 mg/kg body weight interfered with ability to perform motor tasks; no evidence of cumulative effects (Idemudia and McMillan 1986b)
Domestic chicken, *Gallus* sp.	Single oral dose of 3 mg trimethyltin/kg body weight produced tremors, convulsions, and death within 24 h (Stoner et al. 1955)
Pigeon	Triethyltin injections (4 intramuscular injections, 2 weeks apart) at 1.75 mg/kg body weight resulted in total suppression of pecking behavior for 3 h; recovery underway by 27 h post-injection (Idemudia and McMillan 1986a)
Domestic chicken	Single oral dose of 3 mg triethyltin sulfate/kg body weight resulted in immediate collapse, salivation, convulsions, and death in a few min; at 2 mg/kg, bird was unconscious for 1 to 1.5 h postadministration, with recovery beginning in 1 day (Stoner et al. 1955)
Domestic chicken	Feeding of 160 mg triethyltin hydroxide/kg diet for 15 weeks was not fatal, but caused muscular weakness and some diet avoidance (Stoner et al.1955)
Japanese quail	Acute oral LD-50 of tricyclohexyltin hydroxide varies between 255 and 390 mg/kg body weight; dietary levels of 20 mg/kg had no measurable effect on growth, survival, or reproduction (Zuckerman et al. 1978)
Domestic chicken	Acute oral LD-50 of 654 mg of tricyclohexyltin hydroxide (Smith 978a)
Tetraalkyltins	
Domestic chicken	Daily doses >0.0001 mg tetraethyltin/ kg body weight produced Adverse effects on blood chemistry and CNS (Duncan 1980)

MAMMALS

Inorganic tin compounds and some heterocyclic organic tin compounds are of low toxicologic risk to mammals (Table 11), due largely to their low solubility, poor absorption, low tissue accumulations, and rapid tissue excretion (Hiles 1974; Kimbrough 1976). Inorganic tin compounds accumulate mostly in liver and kidney, rarely in brain, in proportion to dose and regardless of the exposure route (Hassett et al. 1984). Noncyclic organotin compounds, by contrast, have produced adverse effects on the skin, eyes, gastrointestinal tract, liver, bile duct, kidney, hematopoietic system, central nervous system, reproduction, growth, and chromosomes of small laboratory animals (Table 11). Effects of diorganotin compounds can be distinguished from those of tri- and tetraorganotin compounds. The chief toxicological difference is that some trialkyltins have a specific effect on the central nervous system resulting in cerebral edema, whereas diorganotins do not produce this effect but are potent irritants that induce inflammatory reactions. The tetraorganotins resemble triorganotins, which are usually more toxic than either mono- and diorganotins (WHO 1980; Table 11).

Diorganotin compounds cause cerebral edema and inhibit mitochondrial respiration by preventing the oxidation of keto acids, presumably through inhibition of alpha-keto oxidase activity (Piver 1973; WHO 1980). Large interspecies variability exists in the capacity of diorganotins to induce lymphoid atrophy. For example, dioctyltins and dibutyltins were selectively cytotoxic to rat thymocytes after dietary exposures of 50 to 150 mg/kg diet for 2 weeks; in contrast, no lymphoid atrophy occurred in mice, guinea pig, or Japanese quail given similar dosages and exposures (Seinen et al. 1977a,b). Route of exposure can also modify effects of diorganotins. Oral exposure to dibutyltin compounds, for example, produces inflammatory changes in bile duct of rat and necrotic changes in liver of mice and rats; dermal exposure causes bile duct injury in rats and rabbits; and intravenous administration produces pulmonary edema in rats (WHO 1980). Intratesticular administration of high doses of some dibutyltins produced marked degeneration in rat testes within 7 days, including atrophy of seminiferous tubules and complete arrest of spermatogenesis; however, similar results have been reported for cadmium, zinc, and copper salts (Saxena et al. 1985).

Table 11. Effects of tin compounds on selected species of animals.

Tin compound, organism	Dose	Effect (reference)[a]
Inorganic tins		
Rat, *Rattus* sp.	6.7 mg/kg body weight (BW)	Single intraperitoneal (ip) injection caused deficits in auditory startle habituation tests (1)
Dog, *Canis familiaris*	54 mg/kg BW	LD-100, single oral dose (2)
Rat	20 to 30 mg/kg BW, or 1.0 g/kg diet	No observed effect level after 13 weeks (3)
Rat	188 mg/kg BW	LD-50, single oral dose of tin fluoride (4)
Rat	700 mg/kg BW	LD-50, single oral dose of tin chloride (4)
Rat	2,275 mg/kg BW	LD-50, single oral dose of Sn^{+2} (3)
Rat	10 g/kg diet	Normal growth after 4 weeks (3)
Rat	>10 g/kg BW	LD-50, single oral dose of SnO (4)
Mouse, *Mus* sp.	Radiotin-113	50% clearance after 29 days following ip injection (5)
Methyltins		
Rat	120 mg/L drinking water	Impaired learning of pups when dam consumed Sn-laced water throughout 21-day gestation (6)
Rat	575 to 1,370 mg/kg BW	LD-50, single oral dose (7, 8)

Rat	600 mg/L	LC-50, aerosol dose for 1 h (7)
Ethyltins		
Rat	200 mg/kg BW	LD-50, single oral dose (7)
Butyltins		
Mouse	1,400 to >6,000 mg/kg BW	LD-50, single oral dose (3)
Rat	2,220 to 2,300 mg/kg BW	LD-50, single oral dose (7)
Octyltins		
Rat	2,400 to 3,800 mg/kg BW	LD-50, single oral dose (7)
Mouse	4,600 mg/kg BW	LD-50, single oral dose (3)
Dimethyltins		
Rat	74 to 237 mg/kg BW	LD-50, single oral dose (7)
Rat	1,070 mg/L	LC-50, aerosol dose for 1 h (7)
Diethyltins		
Rat	40 to 100 mg/kg BW	LD-50, single oral dose (9)
Dibutyltins		
Rat	0.1 and 1.0 mg/kg BW	Kidney damage after 12-month dietary exposure (3)
Mouse	1 to 10 mg/L drinking water	Reduction in tumor growth rates (10)
Rat	2 mg/kg BW daily or 40 mg/kg diet	No observable effect level after 90 days (9)
Rat, mouse	10 mg/kg BW	Dermal application daily for 10 days causes severe effect on skin and bile duct (3)
Mouse	35 to 112 mg/kg BW	LD-50, single oral exposure (9)
Rat	80 mg/kg diet	Slight reduction in growth rate and food intake; mild anemia after 90 days (9)
Rat	100 to 520 mg/kg BW	LD-50, single oral dose (8)
Dioctyltins		
Rat	50 or 150 mg/kg diet	After 6 weeks altered immune function as evidenced by inhibition of T-lymphocyte activity (11)
Guinea pig, *Cavia* sp.; mouse	50 or 150 mg/kg diet	No evidence of altered immune function (11)
Rat	945 to 7,000 mg/kg BW	LD-50, single oral exposure (7, 8, 9)
Mouse	1,140 to 4,000 mg/kg BW	LD-50, single oral exposure (9)
Trimethyltins		
Rat	0.15 to 1.0 mg/L in drinking water	Dams consuming contaminated water throughout 21-day gestation pro-

		duced pups with decreased learning ability at age 11 days (6)
Rat	0.625 mg/kg BW	3 ip doses resulted in flavor aversion (12)
Cynomolgus monkey, *Macaca fascicularis*	0.75 mg/kg BW	Single intravenous (iv) injection produced reduced appetite 7 days postexposure (13)
Cynomolgus monkey	1.1 mg/kg BW	Single iv injection resulted in tremors, hyperactivity, ataxia, stupor, unconsciousness (13)
Cynomolgus monkey	1.25 mg/kg BW	Single iv injection is fatal within 4 days (13)
Cynomolgus monkey	1.5 mg/kg BW	Single iv injection is fatal within 2 days (13)
Cynomolgus monkey	3.0 mg/kg BW	Single iv injection is fatal within 24 h (13)
Hamster, *Cricetus* sp.	About 3.0 mg/kg BW	LD-100, single oral dose (14, 15)
Rat	3.0 mg/kg BW	Loss in body weight and disrupted diurnal pattern of drinking and in rearing young after single oral dose, 2-week observation period (16)
Mouse	3.0 mg/kg BW	Single ip dose produced hypoactivity and impaired motor activity (12)
Marmoset, *Callithrix jacchus*	About 3.0 mg/kg BW	LD-50, single oral dose (14, 15)
Gerbil, *Gerbillus* sp.	About 3.0 mg/kg BW	LD-50, single oral dose (14, 15)
Man, *Homo sapiens*	About 3.0 mg/kg BW	LD-50, single oral dose (14, 15)
Rat	<4 mg/kg BW	No effect following stomach gavage route of administration (1)
Rat	5 mg/kg BW	Single oral dose produces hyperactivity (12)
Rat	6 mg/kg BW	No significant effect on behavior (17)
Rat	7 mg/kg BW	Significantly altered behavior (17)
Rat	>8 mg/kg BW	Lethal within 4 days after stomach gavage (1)
Rat	9.1 to 30 mg/kg BW	LD-50, single oral dose (9, 18)
Rat	15 mg/kg diet	Neuronal degradation in 2 weeks (19)
Rat	16 mg/kg BW	LD-50, single ip dose (2)
Rat	30 mg/kg BW	LD-100, single oral dose (7)
Triethyltins		
Rat	0.25 mg/kg BW	Impaired response to pain after 14 subcutaneous (sc) injections (12)
Rat	0.38 mg/kg BW	Flavor aversion after 2 ip doses (12)
Rat	1.0 mg/kg BW	Reduced amplitude startle response after 3 oral doses (12)
Rat	1.5 mg/kg BW	Hypoactivity, single sc injection (12)
Mouse	2.0 mg/kg BW	Hypoactivity, 27 days after single ip injection (12)
Rat	4.0 to 9.0 mg/kg BW	LD-50, single oral dose (8)

Guinea pig	5 to 10 mg/kg BW	LD-50, single oral dose (9)
Rat	5 mg/L in drinking water for 15 days followed by 10 mg/L for 15 days	Brain edema (20)
Rat	10 mg/kg BW	LD-50, single ip dose (2)
Rat	10 mg/kg BW	LD-100, single oral dose (7)
Rabbit, *Lepus* sp.	10 mg/kg BW	LD-50, single ip dose (2)
Rabbit	10 mg/kg BW	LD-50, single oral dose (8)
Rabbit, rat, guinea pig	10 mg/kg BW	LD-100, single oral dose (21)
Rat	15 mg/kg diet	Cerebral edema in 2 weeks (19)
Rat	20 mg/kg diet	After 7 days, decreased food intake; after 3 to 4 weeks, hind limb weakness and some deaths; on return to normal diet, signs of poisoning gone in 7 days with normal weight in 4 weeks (21)
Rabbit	40 mg/kg diet	Muscular weakness after chronic exposure (21)
Tripropyltins		
Rat	44 to 120 mg/kg BW	LD-50, single oral dose (4, 8)
Tributyltins		
Rabbit	0.04 mg/kg BW	After 16 weeks, central nervous system dysfunction (20)
Guinea pig	0.2 mg/L air	Ocular and nasal irritation, asphyxic convulsions, death within 1 h (20)
Mouse	0.2 mg/kg BW	Reduces mammary tumor growth rate; adversely affects thymus gland growth (22)
Rat	0.36 to 0.95 mg/kg BW	Single dermal application causes skin irritation (3)
Rat	10 mg/kg BW	LD-50, single ip dose (2)
Rabbit	12 mg/kg BW	Daily doses for 6 months were not fatal; signs of intoxication disappeared within a few weeks after withdrawal (20)
Guinea pig	20 mg/kg BW	LD-50, single oral dose (9)
Rat	32 mg/kg diet	Impaired growth after 30 days (20)
Mouse	46 to 230 mg/kg BW	LD-50, single oral dose. LD-50 values were lowest for tributyltin acetate (46 mg/kg BW) followed by benzoate

		(108), chloride (117), laurate (180), and oleate (230) (9)
Rat	50 to 380 mg/kg BW	LD-50, single oral dose (7, 8, 9)
Rabbit	60 mg/kg BW	LD-50, single oral dose (9)
Rat	150 mg/kg diet	61% reduction in thymus weight after 2 weeks (19)
Rat	320 mg/kg diet	Some deaths in 30 days (20)
Triphenyltins		
Rat	0.6 mg/kg BW daily	After 6 weeks, diminished exploratory behavior in maze and significantly more errors in maze learning (23)
Guinea pig	3.7 mg/kg BW	LD-50, single ip dose (2)
Guinea pig	10 to 24 mg/kg BW	LD-50, single oral dose (2, 9)
Guinea pig	25 to 50 mg/kg diet	At 25 mg/kg, 83% dead in 77 days; at 50 mg/kg, all dead by day 29 (7)
Rat	25 to 300 mg/kg diet	No measurable effect at 25 mg/kg in 170 days; some lesions at 50 mg/kg in 105 days; impaired growth at 200 mg/kg in 70 days; weight loss and some deaths at 300 mg/kg in 117 days (7)
Rat	34 mg/kg BW	LD-50, single ip dose (23)
Mouse	81 to 245 mg/kg BW	LD-50, single oral dose (3)
Rat	118 to 268 mg/kg BW	LD-50, single oral dose (7, 8)
Trihexyltins		
Rat	1,000 mg/kg BW	LD-50, single oral dose (8)
Tricyclohexyltins		
Dogs, rats	6 to 12 mg/kg diet	Some weight loss in 2 years, but no other toxic effects (20)
Rat	13 mg/kg BW	LD-50, single ip dose (2)
Sheep, *Ovis* sp.	15 to 150 mg/kg BW	No observed effect at injected dose of 15 mg/kg BW; adverse effects at 25 to 50 mg/kg; death at 150 mg/kg (8)
Rat	25 mg/kg BW	Gastroenteritis after 19 days (3)
Rat	235 to 650 mg/kg BW	LD-50, single oral dose (20)
Rabbit	500 to 1,000 mg/kg BW	LD-50, single oral dose (7)
White-footed mice, *Peromyscus leucopus*	710 mg/kg BW	LD-50, single oral dose (3)
Guinea pig	780 mg/kg BW	LD-50, single oral dose (7)
Dogs, monkeys, cats (*Felis domesticus*)	>800 mg/kg BW	LD-50, single oral dose (8)
Mouse	1,070 mg/kg BW	LD-50, single oral dose (3)
Trioctyltins		
Rat	29,200 mg/kg BW	LD-50, single oral dose (7)

Tetramethyltins		
Rat	195 to 331 mg/kg BW	LD-50, single oral dose (7)
Tetraethyltins		
Rabbit	7 mg/kg BW	LD-50, single oral dose (8)
Rat	9 to 16 mg/kg BW	LD-50, single oral dose (8)
Mouse	40 mg/kg BW	LD-50, single oral dose (3)
Guinea pig	40 mg/kg BW	LD-50, single oral dose (3)
Tetrabutyltins		
Rat	6,000 mg/kg BW	LD-50, single oral dose (7)

[a]References: 1, Hassett et al. 1984; 2, Kimbrough 1976; 3, WHO 1980; 4, Blunden et al. 1985; 5, Brown et a. 1977; 6, Noland et al. 1982; 7, Smith et al. 1978a; 8, Zuckerman et al. 1978; 9, Piver 1973; 10, Cardarelli et al. 1984a; 11, Seinen et al. 1977a; 12, Reiter and Rupert 1984; 13, Reuhl et al. 1985; 14, Aldridge et al. 1981; 15, Brown et al. 1984; 16, Bushnell and Evans 1985; 17, McMillan and Wenger 1985; 18, Watanabe 1980; 19, Snoeij et al. 1985; 20, Duncan 1980; 21, Stoner et al. 1955; 22, Cardarelli et al. 1984b; 23, Lehotzky et al. 1982.

Trimethyltin, triethyltin, and tributyltin compounds are highly toxic to animals and man. Trimethyltin and triethyltin compounds are more toxic to mammals than are the higher triorganotin homologues, probably because of poorer absorption of higher trialkyltin compounds from the gastrointestinal tract (Kimbrough 1976; WHO 1980). Trimethyltin and triethyltin compounds are potent inhibitors of oxidative phosphorylation in the mitochondria for which these compounds have a high binding affinity (WHO 1980). Different triorganotin compounds cause different neuronal patterns of toxicity in adult animals (Reiter and Rupert 1984). Trimethyltins, for example, produce largely irreversible behavioral impairments, such as hyperactivity and impaired learning and performance, and these are consistent with reported neuronal cell death in limbic system structures. Triethyltins, with their direct effect on muscle--consistent with reports of myelin vacuolation and cerebral edema--produce largely reversible effects (Reiter and Ruppert 1984). Differences in chronic toxicity between triethyltins and trimethyltins have resulted in different strategies in assessment of hazard. Evaluations of triethyltin have focused on repeated testing throughout dosing, followed by a recovery period. But evaluations of trimethyltin-induced behavioral impairments have generally focused on testing weeks to months after exposure (Reiter and Rupert 1984).

Symptoms of trimethyltin intoxication in man include irritability, headache, depression, aggressiveness, disorientation, appetite loss, memory deficits, and decreased libido; changes were largely reversible following cessation of exposure (Reiter and Ruppert 1984; Reuhl et al. 1985). At high doses, trimethyltins cause death in primates and humans, preceded by seizures, anorexia, and emotional lability (Brown et al. 1984). Trimethyltin produced adverse effects in laboratory animals over an unusually narrow dose range, with differences of 10X or less between doses producing no observable effects and those producing 100% mortality in all species tested (McMillan and Wenger 1985). Trimethyltin effects in small laboratory animals are usually not reversible. Signs of trimethyltin poisoning include tremors, hyperexcitability, aggressive behavior, weight loss, neuronal destruction in hippocampus and other portions of the brain, seizures, learning and memory impairment, self-mutilation, altered sensitivity to stimuli, and disrupted patterns of drinking and eating (Aldridge et al. 1981; Brown et al. 1984; Hassett et al. 1984; Reiter and Ruppert 1984; Bushnell and Evans 1985; McMillan and Wenger 1985; Reuhl et al. 1985). Trimethyltin-induced behavioral disruptions usually peak 3 to 5 days after exposure, but effects persist for extended periods and seem to be irreversible (Reiter and Ruppert 1984; McMillan and Wenger 1985). Rats sometimes survive the trimethyltin behavior syndrome and appear outwardly normal, although later neuropathological examination shows extensive bilateral damage, including hippocampus shrinkage and cell loss (Aldridge et al. 1981).

Triethyltins were the most potent organotins tested on mammals, although other organotins produced similar signs of poisoning (Table 11). Mammals poisoned by triethyltin compounds showed muscle weakness within hours of dosing; after a short period of recovery, tremors developed, leading to convulsions and death 2 to 5 days after dosing. Although toxicity produced by triethyltins becomes more pronounced with continued exposure, reversal of behavioral deficits occurs within weeks after dosing is terminated (Reiter and Ruppert 1984). Initial reaction to triethyltin exposure in rats was fluid accumulation in white matter of the central nervous

system, which persisted for as long as the compound was administered; after administration the effects reversed (Piver 1973). There is general agreement that triethyltin-induced behavioral changes are accompanied by cerebral edema, neurodegenerative disorders, interference with oxidative phosphorylation, and disrupted metabolism of glucose and enzyme activity (Kimbrough 1976; Hassett et al. 1984; Reiter and Ruppert 1984; McMillan and Wenger 1985; Reuhl et al. 1985; Linee and Hennon 1986).

Triphenyltins are skin and eye irritants to rats and rabbits (WHO 1980). They do not accumulate in rats, dogs, and guinea pigs although some triphenyltin acetate was partly absorbed by cattle and sheep--with most excreted in 6 to 8 weeks (Duncan 1980). Thymus atrophy was associated with a lymphocyte depletion in the thymic cortex and is the predominant effect of the intermediate trialkyltins. Intermediate trialkyltin homologues caused a dose-related reduction of thymus weight in male rats after 2 weeks on diets containing 150 mg organotin/kg; decreases were 19% for triphenyltin, 47% for tripropyltin, and 61% for tributyltin (Snoeij et al. 1985). Tributyltins and other organotins induce chromosomal aberrations in mammals, although this was not observed in tests with aquatic invertebrates (Dixon and Prosser 1986).

Tetraorganotin compounds produce muscular weakness, paralysis, respiratory failure, tremors, and hyperexcitability as acute effects in mice and dogs; latent effects are similar to those seen in triorganotin poisoning (WHO 1980). Tetramethyltin, for example, produces the same toxic syndrome as trimethyltin in rats because it is rapidly dealkylated in vitro to the latter compound (Aldridge et al. 1981). Signs of triorganotin poisoning in rabbits were evident shortly after administration of tetraorganotin compounds, suggesting that triorganotins were soon distributed to the site of action in amounts sufficient to produce signs of poisoning (Arakawa et al. 1981). The dealkylation and distribution of tetraorganotins are related to alkyl chain length and to their accumulations in tissues, including brain. In 3-hour studies with rabbits, at intravenous dosage rates of 2 to 3 mg/kg BW, tetraethyltin was quickly distributed to liver, but tetrapropyltin and tetrabutyltin were slowly distributed (Arakawa et al. 1981). Tetraethyltin was more readily converted into the corresponding trialkyltin than was tetrapropyltin. About 20% of the tetraethyltin, 4% of the tetrapropyltin, and 1% of the tetrabutyltin were converted to their corresponding trialkyltins. Thus, the extent of formation of triorganotins decreased as the size and stability of the ligand increased. There was poor distribution of tetraorganotins to brain, but the amounts of triorganotin metabolites found in brain increased over time. Particularly, the transfer of triethyltin to the brain was significant and compatible with the appearance of signs of toxicity. It was concluded that the extent of the dealkylation and the toxicity of organotin compounds depends on the length of their alkyl group, which was associated with their rate of absorption and ultimate distribution (Arakawa et al. 1981).

Organotin compounds are not mutagenic, teratogenic, or carcinogenic, as judged by largely negative but incomplete evidence (Duncan 1980; WHO 1980; Cardarelli et al. 1984b). It has been suggested that some organotins retard the onset and growth of cancer in laboratory animals and that the anticarcinogenic action is mediated through the thymus gland (Cardarelli et al. 1984b). The absence of tin in tissues may also be associated with tumor development (Cardarelli et al. 1984)). In one study, mice with cancer-prone mammary glands and transplanted mammary tumors had significantly reduced tumor growth rates after oral dosing with tributyltin fluoride (Cardarelli et al. 1984b). In another study, tumor growth rates were significantly reduced in mice continuously exposed to various diorganotin compounds in drinking water at I and 10 mg/l (Cardarelli et al. 1984a). It is hypothesized that the unknown thymic organotins are antagonistic to cancers in mice and possibly man (Cardarelli et al. 1984a, b). Additional research on potential anticarcinogenic properties of organotins is clearly indicated.

TERRESTRIAL INVERTEBRATES

Resistance to organotin acaricides has been reported in several populations of spider mites. After cyhexatin and fenbutatin oxide were used for 10 to 17 years on pears and apples to control mites, populations of McDaniel spider mite (*Tetranychus mcdanieli*), two-spotted spider mite (*T. urticae*), and European red mite *Panonychus ulmi*) slowly began to develop strains that were resistant to these chemicals (Croft et al. 1987).

CURRENT RECOMMENDATIONS

Proposed organotin criteria for the protection of aquatic life, domestic animals, and human health, vary substantially (Table 12). The most stringent criteria now proposed are for triorganotins and aquatic life; these vary from 0.002 to 0.008 ug/l (Table 12). But even these comparatively low concentrations will not protect certain species of gastropod molluscs or larvae of the sheep sturgeon (*Accipenser nudiventris*) from tributyltin

impacts, as discussed earlier. No criteria are currently proposed for protection of mammals against trimethyltins and triethyltins, the most toxic organotins tested in this group. Trimethyltins, for example, produce nonreversible neurotoxicological effects to certain species of small laboratory animals at concentrations as low as 0.15 mg/l drinking water or 0.625 mg/kg BW and are fatal at 1.25 mg/kg BW.

Hazard evaluation posed by organotin compounds to natural resources is predicated partly on their chemical composition, partly on their concentration and persistence in abiotic materials and diet items, and partly on their availability from these materials to organisms. In each of these areas, key data are missing for promulgation of effective regulations. It seems that additional research is needed in eight areas to acquire these data: (1) the development of sensitive and rapid analytical schemes for the extraction and separation of inorganic tin and organic tin compounds and their chemical speciation products from water, sediments, and biological materials (WHO 1980; Reuhl and Cranmer 1984; Hall and Pinkney 1985; Laughlin and Linden 1985; Thompson et al. 1985; Blunden and Chapman 1986); (2) elucidation of mechanisms and modes of toxicity for organotin compounds, especially those involving sublethal chronic exposures and cellular and subcellular impacts (WHO 1980; Reuhl and Cranmer 1984; Hall and Pinkney 1985; Thompson et al. 1985; Vrijhof 1985); (3) acquisition of data on organotin toxicokinetics, including data on routes of exposure, uptake, retention, and translocation. Studies should emphasize whole organisms, to determine if food chain biomagnification is a potential problem; reproductive organs, in which organotin burdens may affect proliferation; and edible tissue , especially muscle and liver, which are selectively consumed by humans and various animal species (WHO 1980; Reuhl and Cranmer 1984; Wilkinson 1984; Hall and Pinkney 1985; Thompson et al. 1985); (4)determination of the persistence and mobility of organotin compounds-- especially in aquatic abiotic materials, such as sediments, sediment interstitial waters, suspended particulates, and the water column--and on the partitioning of these compounds between the surface microlayer and subsurface waters (Wilkinson 1984; Thompson et al. 1985); (5) determination of the extent of tin methylation and the biotransformation and pharmacodynamics of organotins (WHO 1980); (6) measurement of biological interaction effects of organotins with other toxic chemicals under stressful environmental conditions of temperature, oxygen, and other variables (Thompson et al. 1985); (7) development of quantitative structure activity relations for use in evaluating toxicity of organotin compounds (Hall and Pinkney 1985; Laughlin and Linden 1985; Laughlin et al. 1985; Laughlin 1987); and (8) initiation of long-term environmental monitoring studies in terrestrial and aquatic ecosystems to establish appropriate baseline concentrations and to separate these from contaminant effects (Kumpulainen and Koivistoinen 1977; WHO 1980; Hall and Pinkney 1985; Thompson et al. 1985).

Table 12. Proposed organotin criteria for protection of natural resources and human health.

Resource, organotin compound	Criterion or effective tin concentration	Reference[a]
Aquatic life		
Freshwater		
Triorganotins		
North Carolina	<0.008 µg/L	1
Triethyltins		
Max. permissible concentration	<100 µg/L	2
Tributyltins		
Acute value	<0.97 µg/L	3
Chronic value	<0.30 µg/L	3
Safe level	0.12 to <0.27 µg/L	2
Saltwater		
Triorganotins		
North Carolina	<0.002 µg/L	1, 4

Safe level, USA	<0.05 µg/L	5
Tributyltins		
4-day average	<0.017 µg/L (not to be exceeded more than once in 3 years)	6
Chronic value	<0.064 µg/L	3
Acute value	<0.22 µg/L	3
1-h average	<0.43 µg/L (not to be exceeded more than once in 3 years)	6
Safe level, UK	<0.02 µg/L	4
Water		
Dibutyltins		
Dibutyltin dichloride, USSR	<2,000 µg/L	7
Dibutyltin disulfide, USSR	<20,000 µg/L	7
Tributyltins		
USA, Canada	<0.2 µg/L	8
In schistosomiasis control	<0.1 µg/L	9
Tetraethyltin, USSR	<200 µg/L	7
Marine antifouling paints		
Organotins	<4 grams/L	4
Sediments		
Freshwater		
Tributyltins		
4-day average	<30 µg/kg	3
1-h average	<48 µg/kg	3
Saltwater		
Tributyltins		
4-day average	<7 µg/kg	3
1-h average	<1 µg/kg	3
No effect level on annelids, mysids, clams	<610 µg/kg	3
Domestic and laboratory animals		
Diet		
Dibutyltins		
Rat, age 3 months	<40 mg/kg diet	10
Rat, age 6 months	<20 mg/kg diet	10
Triphenyltins		
Guinea pig,		

daily intake	<0.1 mg/kg body weight (BW)	10
Tricyclohexyltins		
Rat, daily	<3 mg/kg BW	10
Dog, daily	<0.75 mg/kg BW	10
Intrarumenal dose		
Tricyclohexyltins		
Sheep, single dose	<15 mg/kg BW	10
Drinking water		
Tributyltins		
Rat	<0.007 µg/L	11
Human health		
Air		
Organotins	<100 µg/m^3	7, 12
Organotins, daily	<200 µg/kg BW	7
Triethyltins, occupational exposure	<100 µg/m^3	13
Tricyclohexyltins	<1,200 µg/m^3	7
Diet		
Total tin		
Daily intake	0.2 to 8.8 mg	7
Daily intake		
From fresh foods	1 to 4 mg	10
From water	<0.03 mg	10
Daily intake, adult	0.003 to <0.13 mg/kg BW	7
Daily intake, adult	0.2 to 17 mg/kg BW	10
Composition of diet		
Inorganic tin	~1 mg/kg	10
Organic tin	<2 mg/kg	10
Tricyclohexyltins		
Peaches	<4 mg/kg	8
Apples, pears	<2 mg/kg	7
Meat	<0.2 mg/kg	7
Milk	<0.05 mg/L	7
Total daily intake	<0.0075 mg/kg BW	7, 14

[a]References: 1, Anon. 1985; 2, Duncan 1980; 3, Cardwell and Sheldon 1986; 4, Side 1987; 5, USN 1984; 6, Hall et al. 1987; 7, Zuckerman et al. 1978; 8, Thompson et al. 1985; 9, Chliamovitch and Kuhn 1977; 10, WHO 1980; 11, Simmonds 1986; 12, Blunden and Chapman 1986; 13, Watanabe 1980; 14, CEC 1978.

Antifouling paints containing organotin compounds have been associated with a number of adverse effects to marine biota, including contamination of salmon farmed in sea cages with treated net panels (Side 1987) and reduced growth of oysters (Cleary and Stebbing 1985). The United States Navy, however, proposes to implement fleetwide use of organotin antifouling paints that contain tributyltin as a biocide. This procedure will

result in a 15% fuel consumption reduction, increase the interval between cleaning ship hulls from 2 years (with cuprous oxide-based antifouling paints) to about 7 years, and increase ship speed up to 40% as a direct result of reduced drag (USN 1984). Since naval vessels rarely remain moored for extended periods in coastal areas, hazard effects to the environment are minimal--despite the size of the vessel--when compared to boating practices at local marinas (USN 1984). Accordingly, civilian use of marine paints containing organotin compounds has been severely restricted in recent years. France banned tributyltin compounds in antifouling paints in January 1982 for use on vessels under 25 m (82 feet) length (Waldock and Thain 1983; Side 1987). The State of Virginia enacted legislation that prohibits the use of tributyltin paints on nonaluminum vessels under 25 m (Anon. 1987). Similar legislation is pending in at least 12 coastal and Great Lakes States (Anon. 1988). In April 1987, England banned the retail sale of antifouling paints containing organotin compounds at concentrations greater than 4 grams of total tin per liter (Side 1987).

Because of their hazards, use of the more toxic triorganotin biocides should be curtailed to prevent their entry into the environment (Piver 1973). Continued monitoring of tributyltin levels is highly recommended at present, especially in areas of extensive boating activity (Simmonds 1986).

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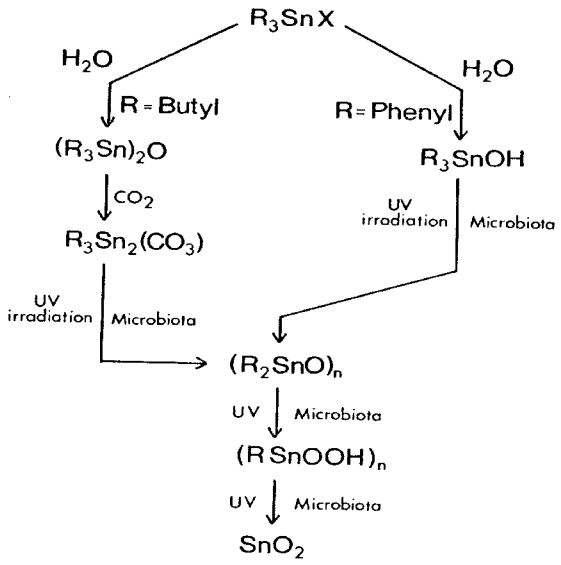

Figure 1. Environmental degradation scheme for tributyltin and triphenyltin compounds. Modified from Smith (1978b).