In the regulation of life processes, metal ions play an unique role by regulating the osmotic phenomena within cells and tissues and also function as constituents of oxygen carriers. They also act as biocatalysts such as co-enzymes and enzymes. Metals like iron, copper and vanadium are present in the oxygen-carrying systems in the blood of vertebrates, many invertebrates and tunicates, respectively. The role of magnesium in chlorophyll, Zinc in the enzyme carbonic anhydrase and cobalt in cobalamin (vitamin B_{12}) are well established. On the other hand many metal ions are more or less toxic toward living organisms.

Fungi require iron, copper, zinc and a few other metals for proper growth and development. But when zinc or especially copper ions are supplied in more than optimal amounts, they behave as fungicides. Certain other metals like silver, mercury, cadmium, nickel and lead which are fungicidal and have no known physiological functions. The

organometallic compounds form another category of fungicides. They also, in general, enhanced fungicidal activities than the corresponding metal ions. Thus stannous or stannic tin compounds hardly have any biological activity whereas, organotin compounds (particularly triorganotin derivatives) exhibit high biocidal activity, probably due to their lipid solubility, which facilitates better transport to the reaction sites than the corresponding inorganic tin compounds.

Though more than 70 elements of the periodic table are metals, there are a number of constraints in the biological activities of the organometallic compounds. Except mercury, the metals of the first three groups of the periodic table have very little aqueous stabilities which in turn restricts their biological activities. The organo transition metal compounds so far do not show any extensive biocidal activities. Only metals of fourth and fifth main group elements show considerable biocidal activities[1].

Organomercurials are one of the most effective biocidal agents and have been found to be in the forefront of fungicidal compounds due to their high effectiveness in minute amount against a broad spectrum of both pathogenic and non pathogenic fungi. Until, recently there was an annual world use of around 12,000 tons of mercury

in the form of organomercurials for a multitude of biocidal applications. Due to their high mammalian and phytotoxicities the use of organomercurials is now under hard scrutiny and may disappear within a few years, except for some restricted agricultural uses. A number of present applications of organomercurials may be partly taken over by highly effective but relatively non toxic organotin preparations in near future[2].

Apart from mercury, organometallic compounds of group four and five of the periodic table, such as those of germanium, lead, arsenic, antimony, bismuth show considerable biological activities. Organoarsenic compound, for example, have had a long and colourful history from Ehrlich's Salvarsan [4,4'-diarsenobis (2-amino phenol) dihydrochloride trihyd] to the methylarsonic acid salts still used today as crabgrass herbicides and to control other grassy weeds. Series of tetra-, tri-, di- and monosubstituted germanium and lead compounds have been prepared and tested for biological activities. Of these tri substituted compounds show by far the best activities against a number of pathogenic and non pathogenic fungi and bacteria as apparent from the table 1-4.

Table -1[3]

Minimum inhibitory concentration of trisubstituted organogermanium and lead acetates*

Compound	Botrytis allii	Penicillium italicum	Aspergillus niger	Rhizopus nigricans
Germanium compounds:				
Trimethylgermanium acetate	>500	>500	>500	>500
Triethylgermanium acetate	50	200	50	200
Tripropylgermanium acetate	50	500	50	100
Tributylgermanium acetate	>500	>500	>500	>500
Tripentylgermanium acetate	>500	>500	>500	>500
Triphenylgermanium acetate	>500	>500	>500	>500
Lead compounds:				
Trimethyllead acetate	100	200	200	>500
Triethyllead acetate	20	20	20	30

Contd..

Table - 1 (Contd..)

Compound	Botrytis allii	Penicillium italicum	Aspergillus niger	Rhizopus oligosporus
Tripropyllead acetate	2	5	10	5
Tributyllead acetate	0.1	0.6	0.5	0.5
Tripentyllead acetate	0.1	0.2	0.5	0.5
Trihexyllead acetate	0.5	2	2	100
Triheptyllead acetate	50	100	100	>500
Trioctyllead acetate	>500	>500	>500	>500
Triphenyllead acetate	2	2	2	5

*Concentrations in $\mu g/ml$

Table - 2[4]

Antifungal activity of oxo- and disubstituted arsenical compounds*

Compound	Botrytis allii	Penicillium italicum	Aspergillus niger	Rhizopus nigricans
Phenyllead triacetate	100	200	200	200
Dimethyllead diacetate	>500	>500	>500	>500
Diethyllead diacetate	>500	>500	>500	>500
Dipropyllead diacetate	500	500	500	500
Dibutyllead diacetate	10	10	20	10
Dipentyllead diacetate	10	20	20	20
Dibenzyllead diacetate	20	50	50	100
Diheptyllead diacetate	500	500	>500	>500
Diphenyllead diacetate	50	50	50	50

*Concentration in μ g/ml

Table - 3[6,6,7]

Antibacterial activity of tri- and disubstituted organogermanium compounds*

Compound	Bacillus subtilis	Mycobacterium phlei	Streptococcus lactis	Escherichia coli	Pseudomonas fluorescens
Trimethylgermanium acetate	>500	>500	>500	>500	>500
Triethylgermanium acetate	>500	500	50	>500	>500
Tripropylgermanium acetate	>500	20	5	>500	>500
Tributylgermanium acetate	>500	2	1	>500	>500
Tripentylgermanium acetate	>500	5	2	>500	>500
Triphenylgermanium acetate	>500	>500	20	>500	>500
Triphenylgermanium acetate	>500	>500	>500	>500	>500
Diethylgermanium dichloride	>500	>500	>500	>500	>500
Dibutylgermanium dichloride	>500	>500	>500	>500	>500
Diphenylgermanium dichloride	>500	>500	>500	>500	>500

*Concentration in $\mu g/ml$

Table -4 (6,7,8)

Antibacterial activity of tri- and disubstituted organolead compounds*

Compound	Bacillus subtilis	Mycobacterium phlei	Streptococcus lactis	Escherichia coli	Pseudomonas fluorescens
Trimethyllead acetate	100	100	200	200	100
Triethyllead acetate	50	50	50	50	20
Tripropyllead acetate	2	2	2	5	10
Tributyllead acetate	0.5	0.2	1	20	20
Tripentyllead acetate	0.5	0.1	5	50	50
Trihexyllead acetate	5	0.2	10	> 500	> 500
Triheptyllead acetate	20	5	-	> 500	> 500
Trioctyllead acetate	50	20	200	> 500	> 500
Triphenyllead acetate	1	0.05	1	20	50
Dimethyllead diacetate	0.2	0.2	1	50	50
Diethyllead diacetate	0.2	1	5	5	5

Contd..

Table - 4 (Contd..)

Compound	Bacillus subtilis	Mycobacterium phlei	Streptococcus lactis	Escherichia coli	Pseudomonas fluorescens
Dipropyllead diacetate	0.2	0.2	0.5	1	2
Dibutyllead diacetate	0.1	0.1	0.2	1	10
Dipentyllead diacetate	0.2	0.2	0.5	2	500
Dihexyllead diacetate	0.5	0.5	1	5	>500
Diheptyllead diacetate	2	2	10	100	>500
Dioctyllead diacetate	20	20	50	>500	>500
Diphenyllead diacetate	1	2	1	10	100

*Concentration in $\mu g/ml$

Arsenic, antimony and bismuth of the fifth main group elements of the periodic table, form a large number of organometallic derivatives of the following types.

Trivalent RM^{III} $RM^{III}X$ $RM^{III}X_2$

Pentavalent RM^{V} $RM^{V}X_2$ $RM^{V}X_3$ $RM^{V}X_4$

/ where R = group attached to the metal atom by means of a carbon atom; X- denotes a group not linked to the metal atom via carbon /. The biocidal activities of some representative compounds of the above types are given in the table 5. Comparable data are not available for the tri- and disubstituted trivalent arsenic compounds, may be due to their extremely unpleasant physiological properties.

Within self-evident limitations such as the stability of the metal-carbon bond, it would seems at present that every metal can give rise to at least one type of organometallic compound which exhibits an outspoken physiological activity. So far, in addition to mercury, only the fourth and fifth main group metals have been explored in this respect. Earlier efforts were mainly directed to explore medical applications but recent emphasis is on the applications of diverse biocidal activities in a much broader area. It is

Table - 5[9]

Antifungal and antibacterial activity of organoantimony and -bismuth compounds*

Compound	Fungi			Bacteria		
	Penicillium funiculosum	Aspergillus flavus	Candida albicans	Staphylococcus aureus	Aerobacter aerogenes	Pseudomonas aeruginosa
Antimony compounds:						
R_3Sb^{1}						
Triphenylantimony	>500	>500	250	16	31	125
Tributylantimony	125	250	63	8	31	63
Diphenylantimony	>500	>500	>500	>500	>500	>500
R_2SbX						
Diphenylantimony chloride	125	250	31	2	4	4
$RSbX_2$						
Phenyl antimony dichloride	250	250	63	2	8	4
R_3SbX_2						
Triphenyl antimony dichloride	>500	>500	>500	63	>500	>500
Bismuth compounds:						
R_3Bi^{1}						
Tributylbismuth	250	250	63	0.5	4	2
Triphenylbismuth	>500	>500	>500	>500	>500	>500

Contd..

Table -5 (Contd..)

Compound	Fungi			Bacteria		
	Penicillium funiculosum	Aspergillus flavus	Candida albicans	Staphylococcus aureus	Escherichia coli	Pseudomonas aeruginosa
Et_3Bi Diphenylbismuth chloride	>500	>500	63	0.5	4	8
$EtBiCl_2$ Butylbismuth dichloride	500	>500	125	0.5	8	2
Phenylbismuth dichloride	>500	>500	63	0.125	2	2
Et_3Bi Triphenylbismuth dichloride	>500	>500	125	8	31	31

* Concentration in $\mu g/ml$

difficult to make a meaningful comparison between the biocidal activities of fourth and fifth group organometallics due to lack of sufficient relevant data, yet a few facts are worth mentioning. In the case of fourth group compounds the antimicrobial activity of R_3MX and R_2MX_2 with the possible exception of R_2SnX_2, are all stable and act as such, the antimicrobial compounds of the fifth group of the types R_3M, R_2MX and RMX_2 presumably all act as compounds of the type MX_2, into which compounds of types R_3M and R_2MX are in many cases transformed. It is believed that the activity of R_2MX (group four) and RMX_2 (group five) is due to inhibition of the same enzyme system. It may be pointed out that in former case, the metal is in its highest valence state, whereas in the latter group it is in the lowest. The availability of the two reactive bonds at the metal atom is the decisive factor for activity. The mode of action of the fourth group compounds of the type R_2MX is different again and not identical to that of any type of compounds of the fifth group metals. Highest fungicidal activity has been found for tin and lead compounds of the type R_3MX.

Organotin compounds, after their discovery around 1850, long remained of purely scientific interest. The first

practical application of organotin compounds were mentioned in a patent around 1925 as rotproofing agents[10], though they have never been used as such. But in 1936, a patent was filed claiming the use of organotin compounds as a stabilizer for vinyl resins[11]. In this function, organotin compounds proved to be outstanding.

The systematic studies of biological activities of organotins were initiated in 1950 by the pioneering work of the TNO group[12] (Institute for Organic Chemistry, Utrecht, Netherland). Van der Kerk, Luijten and others have laid a very strong foundation to the various biocidal and commercial uses of organotin compounds. They systematically studied the organotin compounds of the following types R_4Sn R_3SnX R_2SnX_2 $RSnX_3$ (R = hydrocarbon radical; X = anionic group) and have found that some representatives of the type R_3SnX possessed high fungitoxicity (table-6). The first tests were carried out with tetraethyltin, triethyltin chloride, diethyltin dichloride and ethyltin trichloride. Of these only triethyltin chloride inhibited the growth of test fungi at concentration below 10 mg/l. Detailed studies were latter carried out with other derivatives.

Table -3[12a]

Minimum inhibitory concentrations of organotin compounds to Aspergillus niger *

Type of compound	R = Ethyl	R = Butyl	R = Phenyl
R_2H	>500	>500	>500
R_3HX	2	1	0.5
R_2HX_2	>500	>500	10
RHX_3	>500	>500	>500

*Concentration in µg/ml

They also observed the variation of acid radicals had only a minor influence on the activity of triethyltin salts. Subsequent examinations of a series of tri-n-alkyltin acetates, on the other hand, showed a profound influence of the length of the alkyl chains (Table-7). The most active compound in the series of tri - n- alkyltin acetates were tri-n-propyl and tri-n-butyltin acetates. They inhibited

Table - 7[3]

Antifungal activity of some triorganotin acetates.

$R_3Sn.OCOCH_3$ R =	Minimal concentration in ug/l causing complete inhibition of growth of the fungi			
	Botrytis allii	Penicillium italicum	Aspergillus niger	Rhizopus nigricans
CH_3	200	500	200	500
C_2H_5	1	10	2	2
n-C_3H_7	0.5	0.5	0.5	0.5
i-C_3H_7	0.1	0.5	1	1
n-C_4H_9	0.5	0.5	1	1
i-C_4H_9	1	1	10	1
n-C_5H_{11}	5	2	5	5
cyclo -C_5H_9	0.5	0.5	5	0.5
n-C_6H_{13}	>500	>500	>500	>500
cyclo -C_6H_{11}	50	25	50	25
C_6H_5	10	1	0.5	5

the growth of the test fungi at concentrations of 1 mg/l or even less[13].

Experiments by ITRI group with unsymmetrical trialkyltin acetates i.e. compounds in which tin has different alkyl groups, reveal that the activity depend not on the nature of the individual group but on the total number of carbon atoms in the three groups. Van der Kerk and Luijten[14] showed diethylbutyl, diethylhexyl-, diethyloctyl-, dimethyloctyl- and dimethyldodecyltin acetate as well as ethyldipentyltin acetate all exhibited the same order of activity like tributyltin acetate; dimethylbutyltin acetate exhibited the same activity as triethyltin acetate but less active than tributyltin acetate. From these results they concluded that the maximum activity among the trialkyltin acetates is associated with a total number of 9 to 12 carbon atoms regardless of the nature of individual groups. But a similar rule does not apply to mixed aliphatic - aromatic compounds[15].

Introduction of functional groups into triorganotin compounds in most cases diminishes the antimicrobial activity[16]. $(CH_3)_2(ClCH_2)SnCl$ has the same antifungal activity as trimethyltin chloride; $(n\text{-}C_3H_7)_2(ClCH_2CH_2CH_2)SnOCOCH_3$ and $(n\text{-}C_3H_7)_2(CH_3COOCH_2CH_2)SnBr$ are far less active than

tripropyltin acetate; $(NaOOCH_2CH_2)_3SnOH$ is inactive even at 100 g/ml. Thus the introduction of hydrophilic groups appears to abolish activity.

With the sole exception of diphenyltin dichloride[17], which inhibit the growth of Botrytis allii, Penicillium italicum, Aspergillus niger and Rhizopus nigricans at concentrations of 10 - 30 mg/l, no active compounds were ever found among the types R_3Sn, R_2SnX_2 and $RSnX_3$, inspite of careful screening although there are some unsubstantiated claims[18,19,20,21]. R_4Sn type of compounds can show some activity only when R_3SnX compound was present as an impurity or when it is cleaved off one of the R group by the reaction. For example, in the case of tributyl (cyanomethyl) tin, the cyanomethyl group undergoes cleavage easily under hydrolytic circumstances[16].

Butyltin triacetate at 0.01% concentration has been claimed as effective as similar fungicides containing 0.1% 2,4,5-T in an East German patent[20], by Klotzer et al. He also claimed in another patent that monobutyltin trifluoride or monophenyltin triformate have no phytotoxic properties and have a low toxicity in warm blooded animals[21]. [LD_{50} for rats - 400 and 300 mg/kg respectively]. The

nonobutyltin compounds in a spore germination test against Phytophthora infestans, Alternaria tenuis and Botrytis cinerea showed effectiveness in concentrations of 0.01, 0.01 and 0.0001% respectively. Inspite of the above claims, it is generally accepted that nonorganotin compounds do not show any significant biological properties and are therefore not used as commercial fungicides. However, a series of stannatranes, $RSn(OCH_2CH_2)_3N$ have been prepared which were tested for fungicidal activity at the Institute for Organic Chemistry, T.N.O., Utrecht[18]. They have found remarkable and unusual antifungal activity of certain nonorganotin compound [7]. Results are given in table -3-.

Table -3

Fungicidal activity of Stannatranes*

Compound	B.allii 2 days	B.allii 3 days	A.niger 2 days	A.niger 3 days	Cl.cucumerinum 2 days	Cl.cucumerinum 3 days
$Bu_3Sn(OCH_2CH_2)_3N$	>500	>500	>500	>500	>500	>500
$Br(CH_2)_4Sn(OCH_2CH_2)_3N$	>500	>500	>500	>500	>500	>500
$OctSn(OCH_2CH_2)_3N$	>500	>500	>500	>500	>500	>500
$PhSn(OCH_2CH_2)_3N$	20	50	10	10	2	2

*Concentration in mg/l.

Besides the T.N.O. group, a number of workers have studied the biocidal properties of triorganotin compounds. Baumann[22] and Hartel[23] have carried out independent research on simple alkyl and aryltin compounds with a practical aim, which led to the development of the first agricultural organotin fungicide, 'Brestan' based on triphenyltin acetate. Other workers have extended the above results. In most cases, the influence of varying the acid radical in triorganotin salts were studied[24],[25],[26].

Smara Dijpesteijn et al studied the antibacterial activities with organotin compounds and have found that, in general, organotin compounds are much more active towards gram-positive bacteria like Bacillus subtilis, Mycobacterium phlei and Streptococcus lactis than towards gram-negative ones like Escherichia coli and Pseudomonas fluorescens[8,27]. The most active compounds, inhibiting growth of gram-positive species at 0.1 - 5.0 mg/l, belong to the type R_3SnX. Figure - 1 shows the typical relationship between chain length of di- and tri substituted organotin compounds and their minimum inhibitory concentration for gram-positive Mycobacterium phlei. Triphenyltin acetate is as active as the most active trialkyltin acetates.

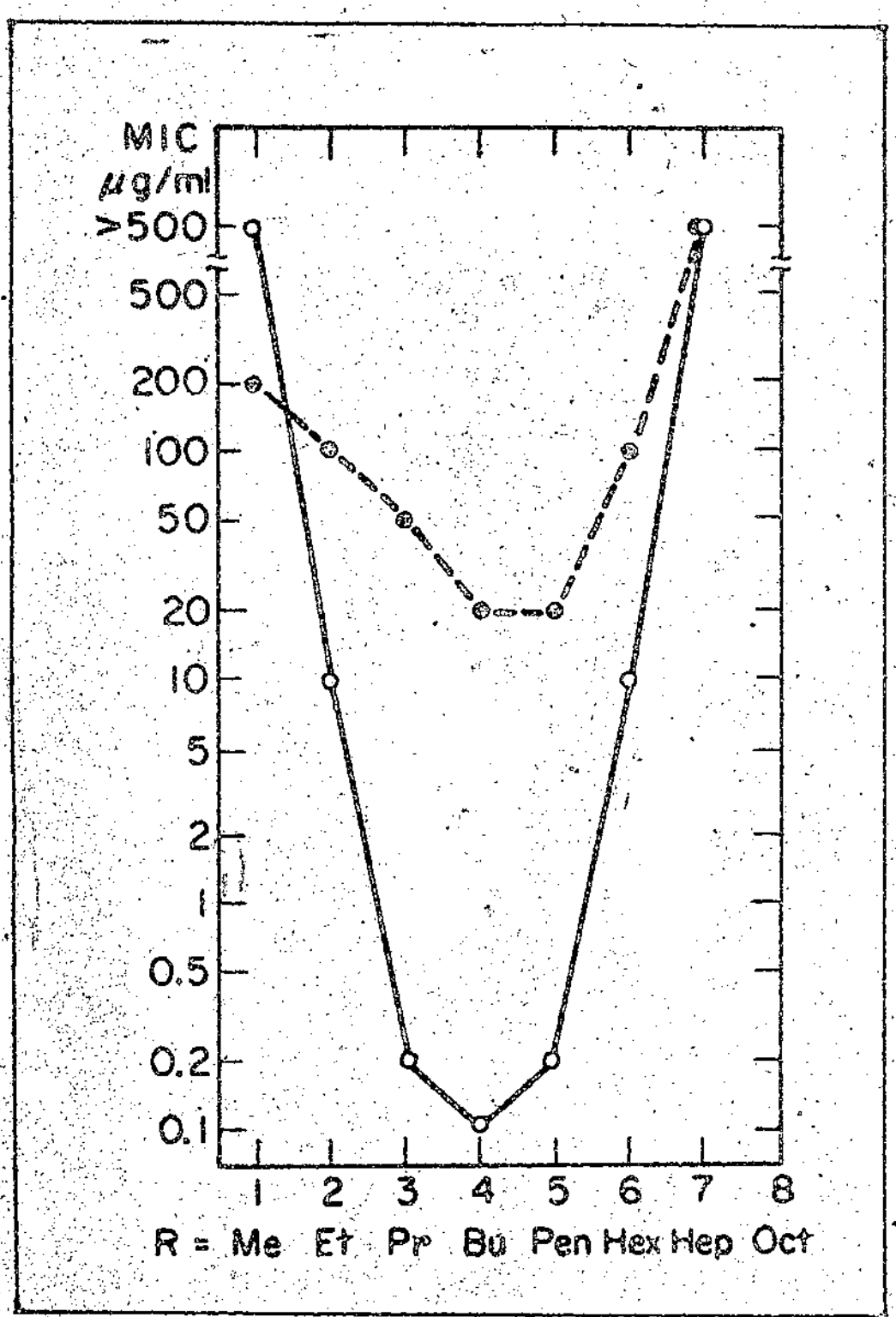


Figure-1 Influence of chain length of di- and trisubstituted tin compounds on minimum concentration inhibitory to Mycobacterium phlei. legend; O——O, trialkyltin compounds; ●——●, dialkyltin compounds.

For the gram-negative bacteria, triethyl and tripropyltin acetates are the most active and require 20-50 mg/l for the growth inhibition. Dipropyl, dibutyl and dipentyltin dichloride have no antifungal properties but inhibit the growth of gram-positive bacteria at a concentration of 20-50 mg/l.

The trialkyltin compounds also been tested against pathogenic bacteria, notably Staphylococcus aureus (gram-positive) and some Pseudomonas species (gram-negative). The results obtained[28,29], confirm the trends indicated as above.

In addition to the antifungal and antibacterial activities of organotin compounds, particularly of triorganotin derivatives, a large number of other activities have been reported of these compounds, which in some cases has led to successful commercial utilisation. Following are some areas where organotins are being used.

(I) Slime control in paper mills

Paper making involves the use of large quantities of water which due to its nutrient contents etc. promotes vigorous growth of bacteria leading to the formation of slime which impairs the quality of paper. Bis-tributyltin oxide (T.B.T.O) at a concentration of few hundredths of a mg/l, though can not completely inhibit the growth of

slime but can effectively control the number of bacteria in such a way that causes no harm to paper. Moreover S.B.P.O. renders the paper to be fungistatic and bacteriostatic[30].

(II) Sanitising of textiles

What is meant here is a treatment of fabrics, particularly undergarments and shorts which renders them as bacteriostat. This will prevent the bacterial decomposition of wheat, which is the cause of odour. Sadler mentions the use of S.B.P.O. at a concentration of 0.025 - 0.050%, which does not irritate the skin[31]. This of course is a minor application.

Textile preservation

Rueck and Luijten found that S.B.P.O. in 0.1% concentration makes wool resistant to attack by the clothes - moth (Tinsola biselliella) and the carpet - beetle (Anthrenus verna) similar to DDT[32].

(III) Water treatment

This application is closely related to the slime control in the paper mills. The treatment of cooling water to keep it clean from algae, fungi and bacteria result in one of the major use of S.B.P.O. in U.S.A. Some times quarternary ammonium compounds are combined with S.B.P.O. to solubilise the organotin compounds and also for

broadning the antimicrobial spectrum[31].

(IV) Paint preservation

Emulsion paints may be spoiled in the can by bacteria, and molds may grow on painted surface. In most cases mold growth originates from a source under the paint film, generally a wall. Mold growth on top of a film may occur in a humid atmosphere. T.B.T.O. alone is not suitable for paint preservation in can because of its ineffectiveness against gram-negative bacteria. A suggestion has been made to combine organomercurial with T.B.T.O. for paint preservation in can[33]. Johnson mentioned the use of tributyltin acetate for oil based paints for the use in humid tropical areas[34].

(V) Anthelmintic activity

Man and his domestic animals may become infected with several kinds of parasitic worms. Anthelmintics are substances that kill those worms or remove them from the organism. Guthrie et al in 1941 carried out first *in vivo* test with organotin compounds as tetraethyltin, tetra-isobutyltin, tetraphenyltin and triphenyltin chlorides to chickens artificially infected with the cestode Hymenolepis cesticillus, but found no active compound of sufficient low toxicity[35,36]. Kerr in 1952 observed that a single dose of 70 mg/kg body weight of dibutyltin

dilaurate effectively removed R.contortillus from chicken[37]. Following this investigation, dibutyltin dilaurate is used in U.S.A. under the trade name 'Butynorate'[38]. Another preparation 'Normal' also contains dibutyltin dilaurate-along with piperazine and phenothiazine[39]. However, no anthelmintic containing organotin compounds so far has been found suitable for the treatment of animals.

(VI) Molluscicidal activity

Several kinds of mollusc are the intermediate host in the life cycle of certain parasitic worms which,in man, give rise to a diseased condition known as bilharziasis, a severe problem for hundreds of millions of people particularly in the underdeveloped countries[40]. The most promising way to break the life cycles of the parasites is the chemical control of the vector snails. Triphenyltin chloride and acetate are highly active against Biomphalaria glabrata and Bulinus contortus[41]. The time required to kill the snails depends on the concentration. 1 mg/l kill the snails in 24 hours whereas 0.25 mg/l in 48 hours. The high toxicity of organotin compounds to other forms of aquatic life presented some disadvantages. A safe method for the introduction of organotin toxicants has been developed by Goodrich[42]. Recently P.J.Smith et al have

studied some more molluscicides from the point of structure-activity relationship[43].

(VII) Protection of surfaces (ship, piers etc) from attack by sea organisms.

A number of organisms both plants and animals can grow on the hull and other parts of ships and various other objects immersed in sea water. This kind of growth is called fouling and can seriously impair the function of the attached objects which can lead to increased consumption of fuel and other difficulties. World shipping industry loses millions of dollars every year due to fouling. T.B.T.O. or tributyltin fluoride have come to the forefront as an effective weapon against the fouling nuisance.

In 1963, triethyllead oleate and triethyltin stearate were claimed as ingredients of antifouling paints[44]. T.B.T.O. gives better control for antifouling than these compounds[45]. Tributyltin fluoride is used in Japan as antifouling agent. Development of organotin based antifouling paints has been reviewed by Evans[46]. Several techniques are at present being used for organotin antifouling agents.

(VIII) Antitumour activity

Recently a series of diorganotin dihalide complexes, $R_2SnX_2.L_2$ where R = methyl, ethyl, n-propyl, n-butyl or phenyl; X = F, Cl, Br, I or NCS and L = O or N donor organic ligands have been found to possess reproducible therapeutic activity *in vivo* towards P-388 lymphocytic leukaemia in mice, particularly the diethyltin dihalide and dipseudohalide complexes. A.J.Crowe and P.J.Smith[47] discussed the activities of organotin compounds as an antitumour agents. This is a new and novel use of organotin compounds with high potentialities as they display, unlike many platinum complexes, the absence of a high nephrotoxicity, although their activities are comparatively weaker.

(IX) Insecticidal activity

Around 1925, organotin compound was claimed as moth proofing agent[10]. Later, a Dutch patent claimed that trialkyltin chlorides can control insects other than moths[48]. Blum et al[49] showed that triethyltin compounds are highly active against house fly. They carried out detailed investigations with 40 organotin compounds to find a high activity for the trisubstituted compounds $[LD_{50} = 0.1 - 1\ \mu g/fly]$, a moderate activity for compounds of the types R_2Sn and $RSnX_3$ $[LD_{50} = 10 \mu g/fly]$

and a low activity for those of the type R_3SnX. The similar result was obtained by Cras et al.[50] Kochkin et al[51] extended the number of insects species to include flies, bed bugs, cockroaches, mosquitos and fleas, and observed LD_{50}'s correspond with those observed by Blum et al in the case of flies. Kubo[52] found some triphenyltin organophosphates as contact insecticides against the adult Azukibean weevil (Callosobruchus chinensis). Various other insects can also be controlled by organotin compounds. One of the interesting aspect of organotin compound in controlling the insects is that, in addition to a toxic effect these compounds can exert an antifeedant effect[53]. Another effect exerted by organotin compounds at low concentrations and likewise only demonstrated for triphenyltin compounds is their ability to interfere with insect reproduction. Kenaga[54] observed this effect in house flies. Similar effect has been observed on German cockroach (Blatella germanica) andthe confused flour beetle (Tribolium confusum).

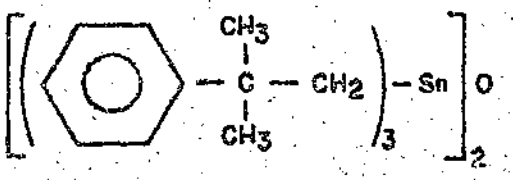
(8) Wood preservation

The most common cause of decay of wood is fungal attack. Since organotin compounds show strong fungitoxicity. Hof and Luijten[55] showed that triethyl and tributyltin

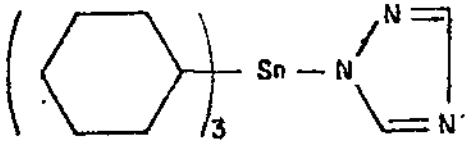
compounds are highly active against wood destroying fungi. The use of triethyltin compounds must be discouraged because of their disagreeable handling properties and high mammalian toxicity. On the other hand tributyltin compounds offer vast possibilities. In recent years, there are more than 60 wood preservatives based on T.B.T.O. in the U.K. market(56).

(XI) Miticidal activities

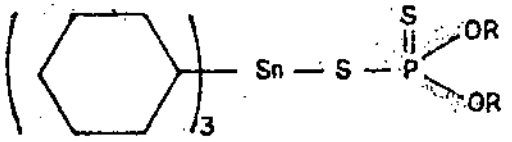
In the year 1968, tricyclohexyltin hydroxide, the result of a join research effort by M & T Chemicals and Dow Chemical Co. was introduced under the name 'Plictran' for controlling the phytophagous (plant-feeding) mites on apples and pears(57). It is now also used on citrus, stone fruit, hop, tea, vegetable etc. Plictran is very selective and gives good control of harmful arachnids with little toxicity towards other insects such as honey bees. It shows also the antifeedant activity against some insects larvae(58). There are now three other organotin miticides of following types.



VENDEX (SHELL)



PEROPAL (BAYER, CHEMAGRO)

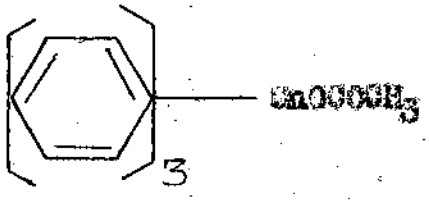


R – 28627 (STAUFFER)

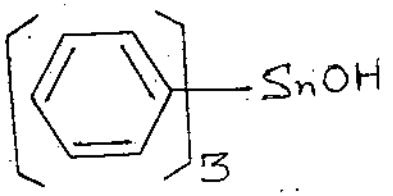
Regarding the phytotoxicity, the pesticides are well tolerated by crops which normally require an acaricide to protect them except the hop plant. Apples, grape, tomato, bean, cabbage and cotton plants, all showed good tolerance to Peropal[59].

(XII) Agricultural uses

Control of fungal diseases in agriculture by organotin compounds is probably the second largest application of organotins. The first organotin compound triphenyltin acetate (also called fentin acetate or Brestan) was introduced commercially as a fungicide in Europe in 1960, by Farbwerke Hoechst and shortly later Philips Duphar introduced fentin hydroxide (called Du - Ter) with active ingredient of triphenyltin hydroxide. Both Brestan and Du-ter have same spectrum of disease control[60].



Fentin acetate (Brestan)



Fentin hydroxide (Du - Ter)

Triphenyltin acetate or hydroxide were recommended for the control of Phytophthora (late blight) on potatoes and Cercospora on sugar beets at the rate of few gram per acre. At present in U.S.A., Du-ter is registered for controlling fungi on potatoes, sugarbeets, peanuts, pecans etc(60). These compounds are highly effective protectant fungicides against almost the same range of fungi as the copper fungicides but at about one-tenth the dosage(61). Organotin compounds can also be used for the control of leaf spot or celery, blast and algal control on rice. Recently organotin fungicides are being used to control coffee leaf rust and also for antifeedant for the giant looper. Coffee leaf rust is wide spread throughout the coffee growing areas of Kenya where organotins are being increasingly used(62).

Problem of toxic residue from sprays of organotin compounds has been extensively investigated. Organotin compounds have a relatively short half-life (3-4 days) on plant leaves in the field[63,64,65]. The amount of organotin residue in potato tubers has been found less than 0.1 mg of tin per kg, after the foliage were repeatedly sprayed with Brestan[66]. When the cows are fed with sugarbeet leaves which were extensively sprayed with Brestan, very little amount of triphenyltin acetate ingested is found in the milk (about 4 μg/l)[67].

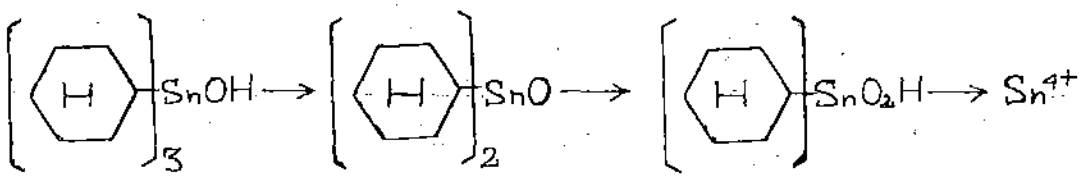
Chemicals are important tools in modern crop protection and the search of suitable compounds has been primarily directed towards finding those which can rapidly eliminate most of the pest population on the crop. Since late 1940, organochlorines and subsequently organophosphorus compounds were being used. Recently, however, these pesticides, particularly organochlorines have come under severe criticism on the following grounds[68]. These compounds have a broad spectrum of activity, which means that beneficial and non-target pests may also be adversely affected. It has been found in several cases that spraying a crop with such compounds has resulted in a subsequent out break of the target pest far worse than before, because the pest's natural enemies have also been killed. An added

problem with such pesticide is that many of these are persistant in environment and can remain toxic for a long time before being degraded to less harmful products. Moreover, excessive uses of insecticides has resulted in many pest populations building up resistance to such compounds. Considering these difficulties, organotins can possibly offer some answer to these problems as they are very effective at very low doses and degrade to non toxic inorganic tin within a short period. Moreover, organotin has remarkable antifeedant activities and can also behave as chemosterilant[54] and no field resistance of pests have so far been reported. This is why, some tri-organotin compounds have been cleared by WHO as safe agricultural pesticides.

Environmental impact of organotin pesticides

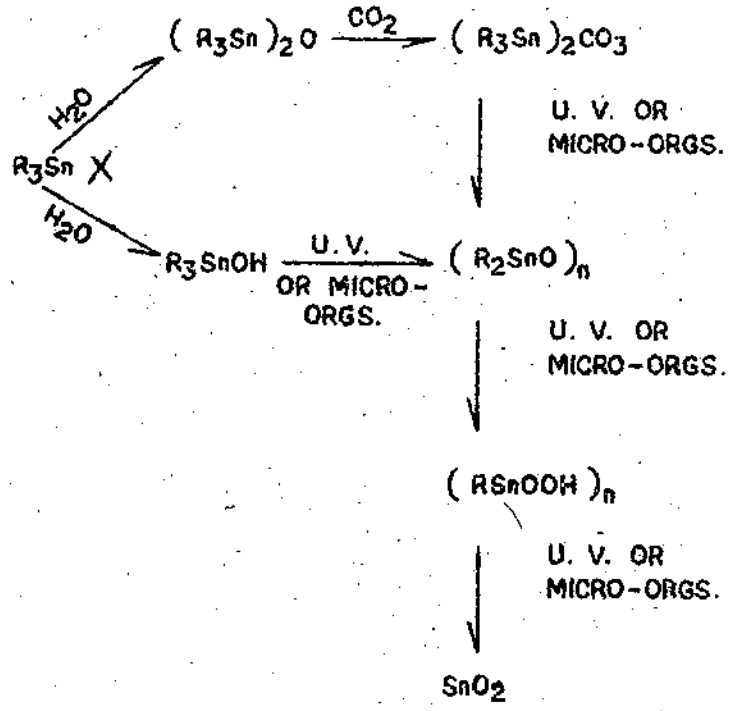
Organotin pesticides, that are in current use donot considerably accumulate in the soil with successive applications. They are metabolised readily in animals and soils to inorganic tin compounds which are not taken up by the plants[65]. When radio-labelled Plictran was fed to rats, 99.9% of radioactivity was excreted, indicating no significant absorption in the gastrointestinal tracts[61]. The

metabolism of the compound in animals is by stepwise cleavage of cyclohexyl groups from the tin atom as shown below:



It was also found that when Plictran was sprayed in three different locations during a period of three years, build-up of tin residues in the upper six-inches of the soil was negligible.

In view of the very large number of industrial applications of the organotins, a knowledge of their environmental breakdown pattern is obviously important to ensure their continued safe use. A generalised degradation scheme for the tributyl - and triphenyltin derivatives, based on that proposed by Cholden[GB], which is probably applicable to other organotins, is as follows:



Fish and his co-workers[70,71] have shown that tributyltins are metabolised *in vitro* and *in vivo* in mammals to di- and monobutyltins via carbon-hydroxylated intermediates. Fungal degradation of T.B.T.O. to di- and monobutyltins by *Coniophora cerebella* and *Polystictus*

Versicolor has also been reported recently[72].

Unlike mercury compounds, there is no evidence of methylation of organotins, on account of their lack of accumulation and ready breakdown to non toxic inorganic tin compounds, making these are quite acceptable from environmental considerations[61].

Mode of action of organotins

The biological activity of organotins has been extensively studied and it has been found that tetraorganotins are not biologically active unless they are degraded to triorganotin derivatives under *in vivo* and *in vitro* conditions. The biological activity pattern of the triorganotins, R_3SnX, is now well known, with the compounds showing a marked species dependence, according to the nature of R group, but relatively independent of the anionic radical[73], X. This may be summarised as follows[43].

Species	R in most active R_3SnX compounds
Insects	Me
Mammals	Et
Gm. negative bacteria	n^{n}Pr
Gm. positive bacteria, fish, fungi, molluscs	n^{n}Bu
Fish, fungi, molluscs	Ph
Mites	cyclo-C_6H_{11} / Neophyl

and is illustrated in Figure -2 which show the dependence of the biological activity of the tri-n-alkyltin acetates on the nature of the n-alkyl group for various species.

The lower alkyltin compounds are able to inhibit mitochondrial oxidative phosphorylation[74] and it has been suggested by Hall and Duckerman[75] that their biological activity pattern may be dependent upon the effectiveness of their interaction at an active site or sites which involves co-ordination to certain amino acids. The exact chemical nature of the binding sites on the protein has been the subject of considerable attention recently and it has been suggested that the most probable binding sites for triorganotins on proteins appear to be viz the -SH and imidazole -NH groups[43].

The published reports generally confirm the initial observation of relative unimportance of the nature of anionic portion of the triorganotin molecule to the over all biological activity, although there are occasional unsubstantiated reports of dependence. Fuller has reported that once the R$_3$Sn group gets to the site of biochemical reaction i.e. at cell mitochondria, it may not matter what the X- group is but the latter can be significantly involved in transporting the biocide to the reactive site[76]. He has designed the X group in such a way that the solubility

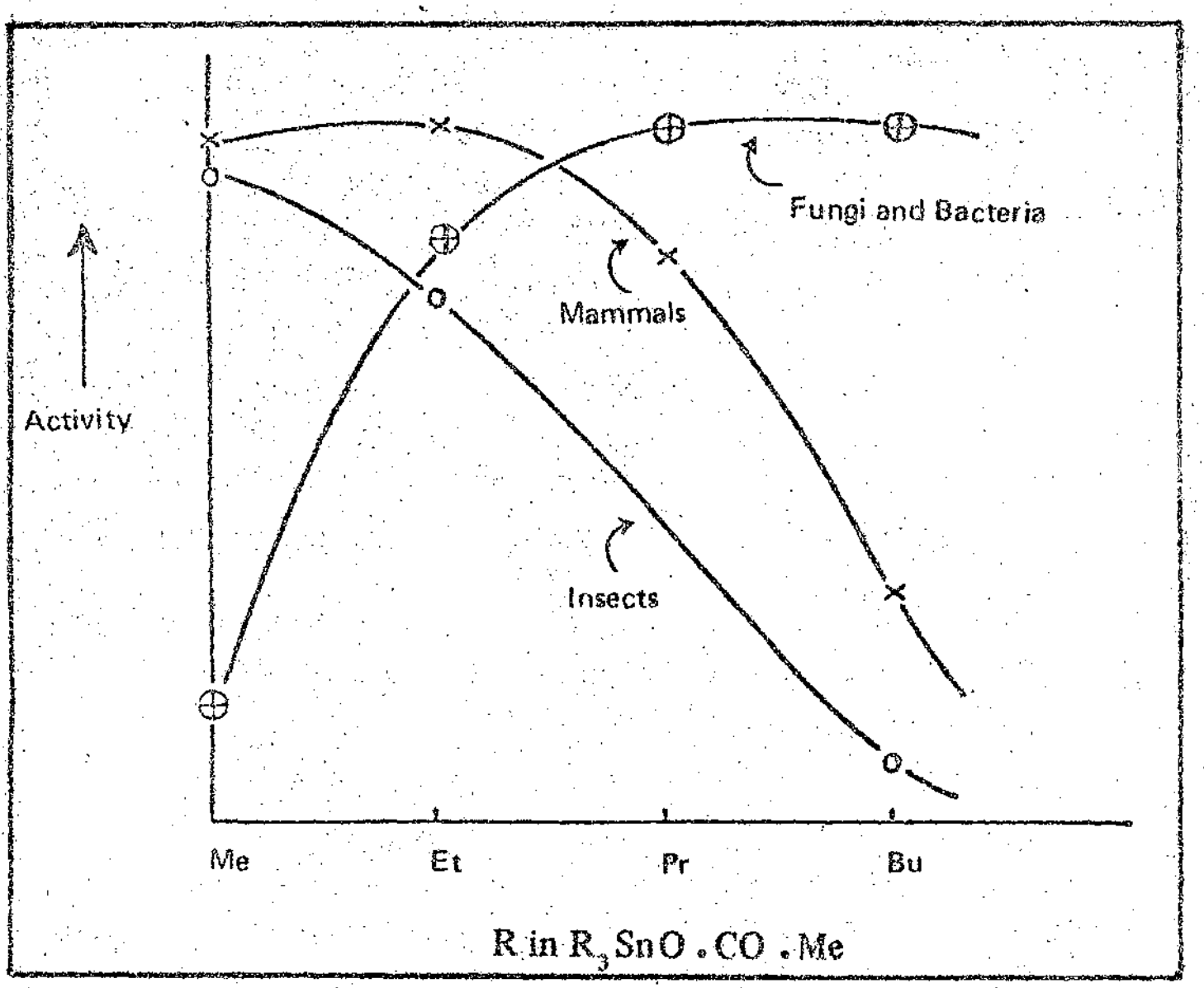
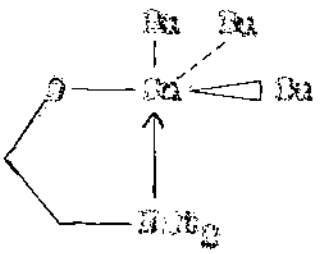


Figure 2 Dependence of the biological activity on tri- n- alkyltin acetate on the nature of the alkyl group for different species[43]

of the resulting R_3SnX compound was substantially increased. He prepared a few sucrose derivatives which show better fungicidal activities against paint destroying fungi, although their tin content is much smaller than the commercial organotin paint preservatives.

Schicke et al[77] reported that, in laboratory and green house test against Phytophthora infestans on tomato, Septoria apii on celery and Cercospora beticola on sugar beet, the tin complexes (I) $Ph_3(Cl)Sn \longleftarrow OSMe_2$(II) and $(Ph_3SnClBr)^-$ $(Ph_3PC_{10}H_{21})^+$(III) were superior to triphenyltin acetate, triphenyltin chloride and triphenyltin hydroxide at corresponding doses. Field test on potatoes, celery and sugar-beets also proved that the complexes gave field protection.

But several workers have found considerably lower fungitoxicities of organotin chelated compounds. It has been reported that $Bu_3SnOCH_2CH_2NEt_2$, which contains an intramolecularly co-ordinating diethylaminoethanol ligand shows the lowest activity as a molluscicide[78]. This is probably due to a reduced tendency for this compound to attack the active sites on the snail protein, rather than to any profound variation in the ease of penetration of the compound to reach the site of toxic action. Tzschach and co-workers[79] have found that a similar intramolecularly



chelated tributyltin dialkylaminoalkoxide is approximately eight times less toxic orally to mice than T.B.T.O. So, it would appear that the toxicity of the trialkyltin compounds, R_3SnX, may be somewhat dependent on the nature of X group, if the X group is a ligand which can form a intramolecularly chelated complex.