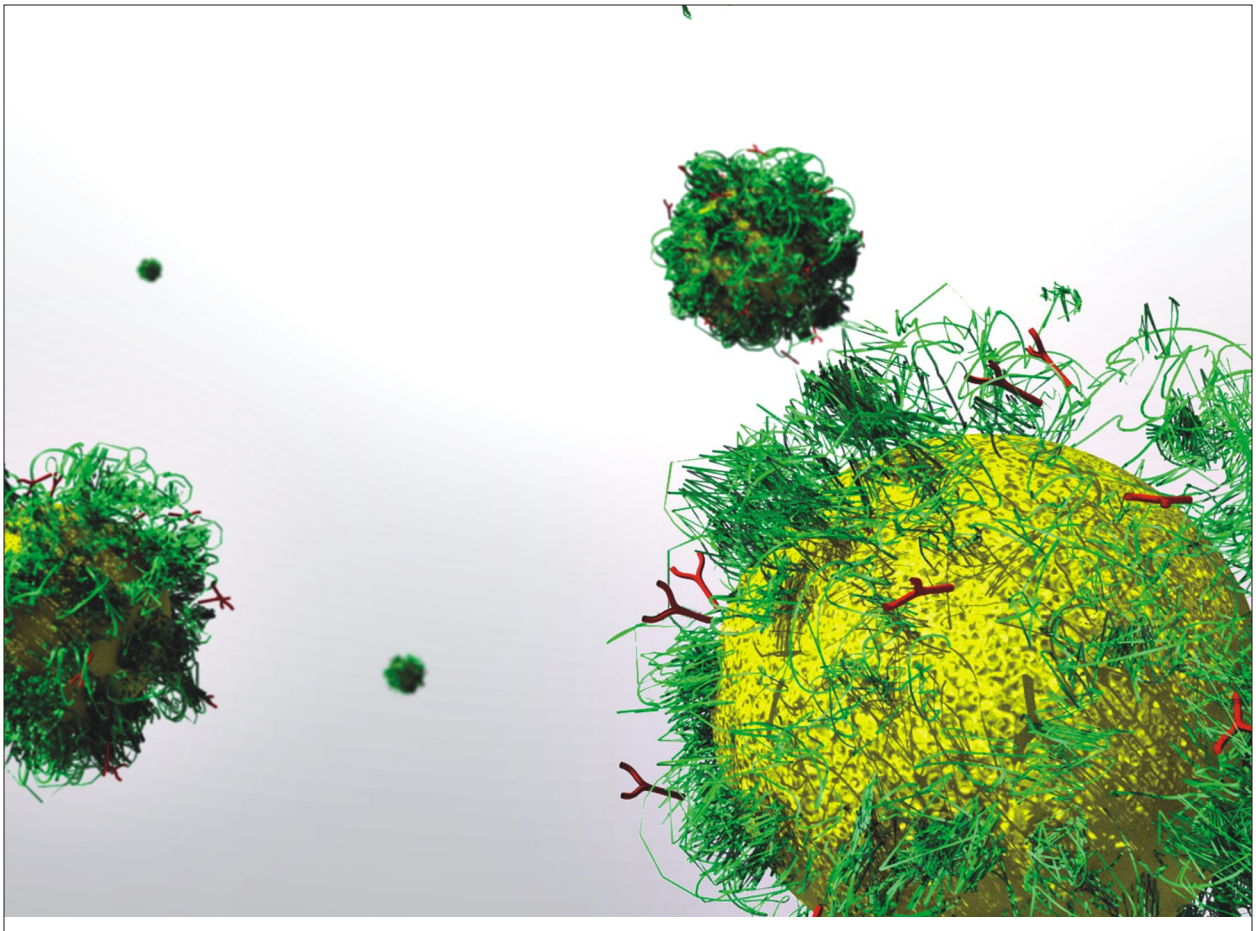

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Synthesis and Evaluation of Diorganotin(IV) and Triorganotin(IV) Derivatives of Aspirin, Paracetamol and Metronidazole as Antimicrobial Agents

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ABSTRACT

A large number of organotin complexes are used as pharmaceuticals, pesticides, stabilizers and fire retardants. In an attempt to explore its pharmaceutical profile, new diorganotin (IV) R_2SnA_2 (R = n-Bu, n-Oct) and triorganotin (IV) R_3SnA_2 (R= n-Bu) derivatives where A is the anion of 2-acetoxybenzoic acid (Aspirin), N-(4-hydroxyphenyl) acetamide (Paracetamol) and 2-(2-methyl-5-nitroimidazol-1-yl) ethanol (Metronidazole) have been synthesized. The complexes 1-9 were characterized by elemental analysis as well as FTIR, nuclear magnetic resonance (^1H, ^{13}C and ^{119}Sn) spectroscopy. On the basis of these spectroscopic studies it is proposed that diorganotin complexes of Paracetamol and Metronidazole having 1:2 stoichiometry, show tetrahedral geometry while the complexes of Aspirin show octahedral arrangement around tin metal ion with bi-dentate nature of carboxylate group. Triorganotin complexes of Aspirin, Paracetamol and Metronidazole having 1:2 stoichiometry show trigonal bipyramidal geometry with monodentate nature of the carboxylate group around the organotin moiety in the complexes of Aspirin. The ligand molecules bound to the Sn atom through carboxyl oxygen atoms in Aspirin and hydroxyl oxygen in Paracetamol and Metronidazole. The anti-fungal activity of complexes 1, 4 and 9 has been determined against *Candida albicans*. It is observed that the activity increases on complexation and highest antifungal activity has been found for the triorganotin complex of metronidazole.

Key words: Organotin, aspirin, paracetamol, metronidazole, *Candida albicans*

INTRODUCTION

The importance of metal ions in biological system is well known as they show indispensable chemistry in various physico- chemical processes (Theophanides, 1984). Advances in understanding metal trafficking and the role of metals in curing diseases have suggested targeting metals, themselves as a useful therapeutic strategy. The success of *cis*-platin and its congeners suggests that metals can also be developed as therapeutic agents. *cis*-platin was the first in this field with its use as an anti-tumor drug (Sun *et al*., 2007) but it is having major disadvantage as having lower water solubility and imposing several side defects. These challenges have changed the face of current research towards non-platinum chemotherapeutics. Organometallic complexes of group 14 elements, especially tin (IV) and silicon (IV) derivatives, have been the subject of considerable interest (Casas *et al*., 2000; Dakternieks *et al*., 1997) owing to their unique physical, chemical and

structural properties favorable to the environment (Ukita *et al.*, 1999). Recently we have published few papers on the chemistry of silicon compounds and silatranes (Puri *et al.*, 2011, 2009, 2008a). Now we are attempting to explore the chemistry of tin (IV) complexes. A large variety of organotin complexes can be prepared using multiple mechanisms of action that can prevent the development of drug resistance which is the major side effect in case of *cis*- platin. Organotin complexes are an active area of research owing to rich variety of their wide applications as stabilizers for PVC plastics, industrial biocides, wood preservatives and marine anti- fouling paints (Craig, 1998). In recent years, investigations have been carried out to test their antitumor activity and it has been observed that indeed several di- and tri-organotin (IV) species were found to be active against various types of cancer (Baul *et al.*, 2009; Fei and Mun, 2007). These kinds of complexes attract particular interest in structural studies because of many possible bonding modes between the ligand and tin atom. Many di- and tri-organotin complexes were synthesized and characterized (Stefano *et al.*, 2002). Since fast and effective relief of pain and inflammation in humans with minimum side effects continues to be a major challenge for medicinal chemistry researchers, many diorganotin (IV) derivatives have been found to have the potential to be placed in the class of non-steroidal anti-inflammatory drugs (NSAIDs) (Nath *et al.*, 2006, 2004a, b, 2003, 1999). Organotin (IV) complexes are also used as templates which combines two functional groups of the substrate (Puri *et al.*, 2008a, b).

As a part of our interest in to the bioinorganic chemistry of the Tin, many di- and tri-organotin derivatives with various drugs mostly non-steroidal anti-inflammatory drugs (NSAIDs) have been synthesized. These NSAIDs are frequently used medicinal drugs. Aspirin is a derivative of salicylic acid. It has analgesic, anti-inflammatory and antipyretic actions and inhibits *prostaglandrin synthetase* while Paracetamol is a derivative of 4-aminophenol which also has analgesic and antipyretic action. Paracetamol is useful in treatment of pain such as headache, toothache, rheumatism and neuralgia (Lawal and Obaleye, 2007). Synthesis and Characterization of complexes of Aspirin and Paracetamol has been studied with Co^{+2}, Ni^{+2} and Fe^{+3} metal ions. Metronidazole is a derivative of nitroimidazole. It is most frequently used drug in treatment of amebiasis and trichomoniasis. Metronidazole is an antiprotozoa drug could be labeled with the 99m Tc (Ibrahim, 2009). It is useful in the treatment of infection caused by susceptible organism particularly anaerobic bacteria and protozoa. In the lieu of this, we are reporting the synthesis, spectroscopic characterization and biological activities of series of di- and triorganotin (IV) complexes of aspirin (L^1H), paracetamol (L^2H) and metronidazole (L^3H) (Fig. 1).

MATERIALS AND METHODS

Chemistry: The interaction of R_2SnO {R = Bu, Oct} and $(R_3Sn)_2O$ {R = Butyl} with Aspirin, Paracetamol and Metronidazole in 1:2 (Metal:Ligand) molar ratio, leads to the formation of complexes 1-9 with an azeotropic removal of water (scheme 1). All the organotin (IV) complexes were obtained in a good yield of (67-71%) and were stable towards air and moisture. All the complexes 1-9 were identified by elemental analysis (Table 1).

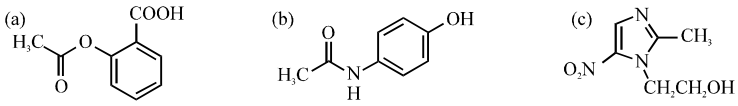

Fig. 1(a-c): Chemical structure of (a) Aspirin (L^1H), (b) Paracetamol (L^2H) and (c) Metronidazole (L^3H)

Table 1: Elemental analysis and some physical properties of organotin (IV) complexes

Compound	State	Melting point (°C)	Yield (%)	Molecular formula	Molecular weight	Contents (calc/found) (%) C	H	N
$Bu_2Sn(L^1)_2$	White solid	202	70	$C_{26}H_{32}O_8Sn$	591.186	52.82/52.81	5.45/5.43	
$Oc_2Sn(L^1)_2$	White solid	208	71	$C_{34}H_{48}O_8Sn$	703.378	58.05/58.06	6.87/6.86	
$Bu_3Sn(L^1)_2$	White solid	220	67	$C_{30}H_{41}O_8Sn$	648.289	55.58/55.56	6.37/6.39	
$Bu_2Sn(L^2)_2$	White solid	205	68	$C_{24}H_{34}N_2O_4Sn$	533.196	54.06/54.09	6.42/6.44	5.25/5.240
$Oc_2Sn(L^2)_2$	White solid	207	70	$C_{32}H_{50}N_2O_4Sn$	645.388	59.55/59.56	7.80/7.82	4.34/4.330
$Bu_3Sn(L^2)_2$	White solid	223	68	$C_{28}H_{43}N_2O_4Sn$	590.299	56.97/56.95	7.33/7.32	4.74/4.760
$Bu_2Sn(L^3)_2$	White solid	210	69	$C_{20}H_{34}N_6O_6Sn$	573.178	41.91/41.92	5.97/5.98	14.66/14.63
$Oc_2Sn(L^3)_2$	Light yellow solid	222	70	$C_{28}H_{50}N_6O_6Sn$	685.370	49.06/49.05	7.35/7.36	12.26/12.27
$Bu_3Sn(L^3)_2$	White solid	225	69	$C_{24}H_{43}N_6O_6Sn$	630.281	45.73/45.74	6.87/6.88	13.33/13.32

Table 2: Growth media and conditions of indicator microorganisms

Name of organism	Gram nature	Growth medium	Nature	Incubation temperature	Incubation	Incubation time (days)
Candida albicans MTCC 183		YEPD	Aerobic	30°C	48 h	15
Bacteriodes fragilis MTCC 1045		RCB	Anaerobic	37°C/6.8	5 days	30
Escherichia coli MTCC 1650		Man	Aerobic	37°C/7.2	24 h	30
Pseudomonas aeruginosa ATCC 10662		NB	Aerobic	30°C/7.4	24 h	30
Salmonella enterica (isolate)		BHI/NB	Aerobic	37°C/7.4	24 h	15
Vibrio cholerae ATCC 14104		NB	Aerobic	37°C/7.4	24 h	15
Listeria monocytogenes (MTCC 657)		BHI/NB	Aerobic	37°C/7.4	24 h	30

Biological activity: The biological activity for the complexes 1-9 was studied on *Candida albicans,* a representative model organism used to screen the antifungal activity and six indicator strains. Indicator strains including *Candida albicans* were procured from different sources as few from Microbial Type Culture Collection, Chandigarh, Punjab, India. *Bacteroides fragilis* MTCC 1045, *Candida albicans* MTCC 183, *Listeria monocytogenes* MTCC 657 and All other cultures including *Pseudomonas aeruginosa* ATCC 10662, *Vibrio cholera* ATCC 14104 were purchased from American Type Culture Collection. *Salmonella enterica* is a lab isolate. To study the effect of complexes, these were dissolved in dimethyl sulfoxide chloroform/methanol/ethanol and dichloromethane and kept at 4°C till further use. The organism was cultured in sabouraud dextrose broth medium, at 30°C and then subcultured after every 36 h so as to maintain it in log phase. For all the experiments, actively proliferating log phase cells were taken and the antifungal activities of various complexes were studied by growing the cells at the final concentrations of 0.80 and 0.40 mg mL^{-1} in total of 2 mL culture media. 1×10^5 cells of *Candida albicans* (as counted by haemocytometer) were used per ml of the media as inoculum. Growth of cells was measured by Optical Density (OD) measurements at 600 nm. Experiments were conducted with yeast form of *Candida albicans* grown at 30°C in presence of above complexes at the final concentrations of 0.80 and 0.40 mg mL^{-1}. Cell turbidity was measured after 24 h at 600 nm. Growth conditions of other organisms are mentioned in Table 2.

Percentage inhibition of tri- and diorganotin (IV) complexes are presented in Table 3. Highest Inhibitory activity (up to 80%) has been found with triorganotin complexes of Metronidazole

Table 3: Anti-fungal activity for organotin(IV) complexes of aspirin, paracetamol and metronidazole

	Average % inhibition after 24 h	
	Candida albicans	
Solvent/complex	Conc. (0.80 mg mL^{-1})	Conc. (0.40 mg mL^{-1})
$CHCl_3/Bu_2Sn(L^1)_2$	43.9	50.0
$CHCl_3/Bu_2Sn(L^2)_2$	7.5	-
$DMSO/Bu_3Sn(L^3)_2$	77.0	78.8

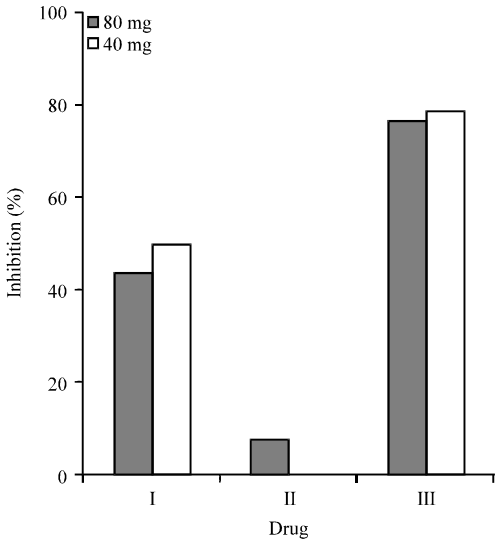

Fig. 2: Inhibition of cellular growth of the organism vs. drugs

(complex III, Fig. 2) which shows very promising results as an antifungal drug. Since, we obtained similar inhibition pattern at two different concentrations of these drugs, studies will be done to find their IC_{50} value.

Experimental protocols: All the di- and tri-organotin (IV) oxides were purchased from Merck, U. S. A. and were used as such. All the reactions were carried out under anhydrous conditions. The solvents used were dried before use by the methods reported in the literature (Armarego and Chai, 2003).

Preparation and characterization of the complexes: Dialkyl/trialkyltin (IV) oxide {1 mmol} and the ligands (L^1H, L^2H, L^3H) 2 mmol were dissolved in a mixture of dry benzene (30 mL) and absolute ethanol (L^1H and L^2H)/methanol (L^3H) (10 mL). The reaction mixture was then heated at reflux and the water removed by azeotropic distillation. The dialkyl, respectively trialkyltin (IV) oxide dissolved within 10-15 min to give a clear solution. Refluxing was further continued for 3-4 h and the contents were filtered and then cooled. Excess of solvent was removed by distillation to leave behind a solid complex. These were recrystallized from the same solvent and dried *in vacuo* at 40-50°C for 2-3 h. Purity of the complexes was checked by TLC using silica gel-G as adsorbent. Melting points were determined in a capillary tube on an electrothermal melting point apparatus. IR spectra for the complexes 1-9 were recorded on a Perkin Elmer FTIR spectrophotometer at

4000-200 cm^{-1}. The ^{1}H-NMR and ^{13}C-NMR were recorded on a Bruker Avance II 400 NMR Spectrometer. All chemical shift values were reported with respect to TMS as internal solvent. CHN analysis of the samples was performed on the Perkin Elmer model 2400 C H N analyzer.

RESULTS AND DISCUSSION

Reaction scheme:

Scheme 1: Reaction pathway for $R_2Sn(L^n)_2$ and $R_3Sn(L^n)_2$

$R_2SnO+2\ L^nH \rightarrow R_2Sn(L^n)_2+H_2O$

(1) R = Bu; n = 1; (2) R = Oc; n = 1

(4) R = Bu; n = 2; (5) R = Oc; n = 2

(7) R = Bu; n = 3; (8) R = Oc; n = 3

$(R_3Sn)_2O+2L^nH \rightarrow R_3Sn(L^n)_2+H_2O$

(3) R = Bu; n = 1

(6) R = Bu; n = 2

(9) R = Bu; n = 3

All the compounds were obtained as crystalline solids. Compounds 1 and 4 are soluble in chloroform while compound 9 is soluble in dimethyl sulfoxide while rest of the compounds are soluble in chloroform with one drop of dimethyl sulfoxide.

Spectroscopic data

Infrared spectra: Characteristic IR frequencies (in cm^{-1}) for organotin (IV) derivatives are presented in Table 4. The (O-H) bands which appeared in the range 2500-2800 cm^{-1} for the acid, were absent in the spectra of complexes 1-3 showed the deprotonation and coordination of the carboxylate anion. In complexes 1-3 $\Delta\nu$ between ν_{asy}(COO) and ν_{sym}(COO) is important because these frequencies can be used to determine the type of bonding between metal and carboxyl group. The values of $\Delta\nu$ can be divided in to three groups: (a) in compounds where $\Delta\nu$ (COO)>350, hence the compounds contain the high probability of monodentate carboxylate group, (b) when $\Delta\nu$ (COO)<200, hence the carboxylate groups of the compounds can be considered as bidentate, (c) in compounds where $\Delta\nu$ (COO)<350 and >200 are considered as intermediate between monodentate and bidentate which is called anisobidentate. In complexes 1-3, peaks at 1602-1670 and 1335-1526 cm^{-1} have been assigned to ν_{asy}(COO) and ν_{sym}(COO) group. In complexes 1 and 2, $\Delta\nu$ value corresponds to the bidentate behavior of carboxylate group comparable to that of sodium salt

Table 4: Characteristic IR frequencies (cm^{-1}) of di- and triorganotin(IV) derivatives of aspirin, paracetamol and metronidazole

ν (C = O)	ν (COO) asy	ν (COO) sym	ν (Sn-O)	ν (Sn-C)	ν (C-O)	ν (N-H)	ν (NO_2)
1702	1602	1511	489	529	-	-	-
1769	1618	1526	435	560	-	-	-
1725	1670	1335	479	539			
1654	-	-	513	566, 598	1255	3324	-
1657	-	-	515	570, 596	1257	3326	-
1660			503	576	1267	3400	
-	-	-	502	563, 597	-	-	1370
-	-	-	503	558, 604	-	-	1368
-	-	-	502	558	-	-	1369

Table 5: ^{1}H-NMR chemical shifts (δ, ppm) of di- and triorganotin (IV) complexes

Phenyl protons	Imidazole-H	-CH_3	-NH	Sn-H-α/H-β/H-γ/H-δ up to H-ω	-NCH_2	-CH_2O
6.72 (m, 8H)		3.01 (s, 3H)		1.66-.75		
6.53 (m, 8H)		2.53 (s, 3H)		1.51-0.71		
7.11-7.53 (m, 8H)		2.08 (s, 3H)		1.77-0.86		
7.34-7.30 (m, C_6H_4,8H)	-	3.02 (s, 6H)	9.52 (b,s,2NH)	1.66-0.75		
7.34-7.29 (m, C_6H_4, 8H)	-	3.21 (s, 6H)	9.53 (b,s,2NH)	1.60-0.78		
7.44-7.40 (m, C_6H_4, 8H)		2.02 (s, 6H)	8.02 (b,s,2NH)	1.78-0.75		
-	7.81 (s, 2H)	2.42 (s, 6H)		1.3-0.96	4.41	4.95
-	8.02 (s, 2H)	2.42 (s, 6H)		1.4-0.96	4.44	4.92
-	7.80 (s, 2H)	2.41 (s, 6H)		1.32-0.94	3.80	4.49

α β γ δ α β γ δ θ λ μ ω

Sn-CH_2-CH_2-CH_2-CH_3; Sn-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_3

while in complex 3, Δν value shows the monodentate nature of carboxylic group around the organotin moiety and is comparable to that of ester (Chandra *et al.*, 1980). In IR spectra of the complexes 4-9, the absence of bands in 3200-3400 cm^{-1} region due to the hydroxyl group suggested deprotonation of this group and its subsequent coordination through the oxygen atom. The appearance of ν(Sn-O) band in the region 435-515 cm^{-1} further confirms the complexation in 1-9. A strong absorption peak at 1370 cm^{-1}, assigned to nitro group of free metronidazole does not suffer significant downfield shift in the spectra of complexes 7, 8 and 9 show its non-coordinating behavior in complex formation.

Multinuclear (^{1}H, ^{13}C and ^{119} Sn) NMR spectra

^{1}H-NMR spectra: ^{1}H-NMR spectral data of organotin (IV) complexes are presented in Table 5. The signals at 2.2, δ 3.4 and δ 11.21 ppm attributed to -OH group of hydroxyl group of metronidazole, paracetamol and carboxylic proton of aspirin, respectively, is absent in the spectra of complexes 1-9. The absence of these signals in the spectra of complexes 1-9 confirms the deprotonation of the respective groups and their subsequent coordination around organotin moiety. The -NH signal at δ 9.54 ppm in paracetamol remains unchanged which indicates that this group is not involved in the formation of complexes 4-6. The resonances due to the aromatic proton of the ring suffered a downfield shift on complex formation in 1-9. The observed downfield shift may be ascribed to the deshielding of these protons due to the drainage of electron density from ring to tin metal atom (Sagdinc and Bayari, 2004; Chen *et al.*, 2009). All the protons in the complexes 1-9 have been identified and total number of protons calculated from the integration curves is in agreement with the proposed molecular formulae.

^{13}C-NMR spectra: ^{13}C-NMR spectral data along with the assignment of characteristic peaks of all the synthesized organotin (IV) complexes are presented in Table 6. The formation of the complexes 1-3 was evident from the δ (COO) value in the ^{13}C-NMR spectra. The complexes 1-3 exhibited a δ(COO) signal in the range of 173.4-176.7 ppm which undergo downfield shift as compared to that of their parent acids (173.02 ppm), indicating the participation of the carboxylate anions in the coordination to the tin (IV) atom. This phenomenon resulted from the decrease of the electron density in the carboxylate anions upon coordinated to the tin atom moiety during complexation. The signal of the carbonyl group for aspirin and paracetamol were observed in the range of

Table 6: ^{13}C-NMR spectral data of di- and triorganotin (IV) complexes

C = O	-COO	Ph-C	Sn- (C-α to C-ω)	C-N	-NCH_2	-CH_2O
177.7	173.4	125.3, 118.1, 118.1, 110.7	32.4, 27.5, 26.7, 25.4	-	-	-
177.5	175.4	118.2, 117.2, 110.2, 109.4	32.0, 38.9, 29.3, 28.5, 27.1, 25.6, 22.7, 14.1	-	-	-
174.9	176.7	126.3-111.5	33.3-26.4			
168.1		115.2-131.7	40.7-39.4	135.6		
168.4	-	117.4-132.8	41.7-40.4	134.6		
164.4		117.4-134.2	42.7-40.4			
-	-	-	34.6-25.3	151.9	48.5	59.7
-	-	-	37.6-27.4	159.1	48.3	60.3
-	-	-	41.5-29.7	156.6	46.2	64.5

α β γ δ α β γ δ θ λ μ ω

Sn-CH_2-CH_2-CH_2-CH_3; Sn-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_3

Table 7: ^{119}Sn-NMR spectral data of di- and triorganotin (IV) complexes (4-9)

Compound No.	δ (ppm)
4	56
5	42
6	-132
7	-67
8	-98
9	-142

164.4-177.7 ppm. No significant changes were detected in the ^{13}C-NMR signals for complexes 1-6 upon coordination. The positions of phenyl carbon signals in the range of 115-125 ppm undergo significant downfield shift in the complexes 1-6, compared to those observed in the free aspirin and paracetamol. The presence of Sn-C peaks of butyl and octyl groups in the range of 14.1-42.7 ppm in 1-9 confirms the incorporation of organotin moiety (Sandhu and Kaur, 1990). All magnetically non-equivalent carbons of alkyl or phenyl groups attached to the tin have been identified and their chemical shifts are in close agreement with the reported values.

^{119}Sn-NMR: The possibility of detecting the presence of coordinative different organotin (IV) moieties was explored by acquisition of ^{119}Sn-NMR spectra. The ^{119}Sn- chemical shifts usually cover a range, quoted relative to tetramethyltin, with increasing coordination number of tin producing a large upfield shift for **δ** (^{119}Sn). In complexes 4-9, only a single peak indicates the formation of single species. In 4, 5, 7 and 8, **δ** value lie in range -98-56 ppm, corresponds to the tetrahedral environment (Holecek *et al.*, 1986; Kapoor *et al.*, 2003) around the tin atom while in 6 and 9, **δ** value lie in range -132 to -142 ppm, corresponds to the trigonal bipyramidal geometry (Table 7).

Biological activity: The biological activity for the complexes 1-9 was studied on *Candida albicans,* a representative model organism used to screen the antifungal activity and six indicator strains results of all the 9 drugs complexes (Table 8) are as Complex 1 and two are give good inhibition against all the six strains and two different concentration 100 and 500 ppm have been used. Complex 3 have not shown any inhibition against *Listeria monocytogenes* MTCC 657 and *Bacteroides fragilis* MTCC 1045 even at 500 ppm of drug. Complexs 4 and 7 have not shown any inhibition against *Listeria monocytogenes* MTCC 657 and *Bacteroides fragilis* MTCC 1045 at

Table 8: Zone of inhibition for organotin complexes against various strains

Pseudomaonas aeurigenosa ATCC 10662 (ppm)		*Salmonella enterica* (isolate) (ppm)		*Escherichia coli* MTCC 1650 (ppm)		*Listeria monocytogenes* MTCC 657 (ppm)		*Vibrio cholerae* ATCC 14104 (ppm)		*Bacteriodes fragilis* MTCC 1045 (ppm)	
100	500	100	500	100	500	100	500	100	500	100	500
15.5	16.0	19.0	24.0	15.5	16.0	15	16	19.0	20	15	16
12.0	17.0	20.0	22.0	12.0	17.0	14	16	17.5	19	14	16
14.0	16.0	17.5	20.0	14.0	16.0	-	-	13.0	14	-	-
9.00	12.5	13.0	14.5	9.0	12.5	-	17	19.0	22	-	17
15.0	16.5	18.0	23.0	15.0	16.5	13	15	16.0	18	13	15
15.5	16.0	19.0	24.0	15.5	16.0	13	14	12.0	14	22	12
9.00	12.5	13.0	14.5	9.0	12.5	-	17	19.0	22	-	17
13.0	14.0	14.0	16.0	12.0	13.5	14	16	14.0	16	14	15
15.5	16.0	19.0	24.0	15.5	16.0	15	16	19.0	20	15	16

100 pm but it has shown good results with 500 ppm. Good inhibition zones were observed by Complexes 5, 6 8, 9. Maximum zone of 24 mm was observed be complex 6 and 9 against *Salmonella enterica*. the antifungal activities of various complexes were studied by growing the cells at the final concentrations of 0.80 and 0.40 mg mL^{-1} in total of 2 mL culture media. The 1×10^5 cells of *Candida albicans* (as counted by haemocytometer) were used per mL of the media as inoculum. Growth of cells was measured by OD measurements at 600 nm.

Percentage inhibition of tri- and diorganotin (IV) complexes are presented in Table 7. Highest Inhibitory activity (up to 80%) has been found with triorganotin complexes of Metronidazole (complex III, Fig. 1) which shows very promising results as an antifungal drug. Since, we obtained similar inhibition pattern at two different concentrations of these drugs, studies will be done to find their IC_{50} value.

CONCLUSIONS

Organotin (IV) complexes of Aspirin, Paracetamol and Metronidazole have been synthesized in 1:2 (Metal: Ligand) molar ratio through azeotropic removal of water. The spectral studies of complexes 1-9 suggest a tetrahedral geometry in diorganotin complexes of Paracetamol and Metronidazole while octahedral environment around tin metal ion in the complexes of Aspirin. In triorganotin complexes of Aspirin, Paracetamol and Metronidazole, trigonal bipyramidal geometry is observed. The anti-fungal activity of all the studied complexes revealed that the activity increases on complexation and it has been observed that the highest antifungal activity has been found for the triorganotin complex of metronidazole. The results obtained from zone of inhibition method are in same lines with those observed from turbidity method. Zone of inhibition (Table 8) increases with increasing concentration of drugs except in one strain *Listeria monocytogenes* MTCC 657.

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