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Organotin(IV) and organolead(IV) complexes as biocides and fertility regulators: synthetic, spectroscopic and biological studies

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Biocidal, antifertility and spectroscopic aspects of organotin(IV) and organolead(IV) complexes with amino acids(L) and 2,2-bipyridine(L′) are described with the support of elemental analysis, IR, ^{1}H, ^{13}C, ^{119}Sn and ^{207}Pb NMR spectroscopy. The spectral data suggest that the ligand L acts in a monodentate and ligand L′ in a bidentate manner, coordinating through the nitrogen atoms. The complexes have been characterized on the basis of molecular weight determinations and conductivity measurements. The isolated products are coloured solids, soluble in dimethylsulfoxide (DMSO), dimethylformamide (DMF) and methanol. All the complexes are monomeric in nature, as indicated by their molecular weight determinations. Conductivity measurements in dry DMF show them to be non-electrolytes. The complexes have been screened against a number of fungi and bacteria to assess their growth inhibiting potential. The results are positive. In addition to these studies, the complexes show good antimicrobial properties as compared with their starting materials. The testicular sperm density, sperm morphology, sperm motility, density of cauda epididymis, spermatozoa and fertility in mating trials and the biochemical parameters of the reproductive organs of rats were examined and are discussed in detail. Copyright © 2006 John Wiley & Sons, Ltd.

KEYWORDS: organotin; organolead; biochemical perspectives; antifertility activity; antimicrobial properties

INTRODUCTION

Many organometallic compounds exhibit interesting antitumour activity against several human cancer cell lines, and organotin(IV) compounds are a widely studied class of metal-based antitumour drugs. Their intensive investigations has led to the discovery of compounds that in many cases have disappointingly low *in vivo* toxicity.[1,2] Organotin(IV) compounds have a range of pharmacological applications. The use of organotin(IV) halides as anti-inflammatory agents against different types of oedema in mice has been reported.[3] Organotin(IV) complexes are also used in agriculture. They are efficient fungicides and bactericides.[4,5] Organotin(IV) chelates with nitrogen sulfur and oxygen donor ligands have received much attention during the last few years.[6] The considerable developments over recent decades in the use of organotin compounds as reagents or intermediates in organic synthesis prompted the preparation of many new organotin compounds.[7] The chemistry of organotin(IV) complexes (R_mSnX_n) has been extensively studied due to their biopotency.[8–10] Lead complexes are used in the treatment, management or diagnosis of the disease. Lead complexes with N_4-macrocyclic moiety have been designed to possess a broader spectrum of antimicrobial activities, low toxicity and lack of cross resistance.[11,12]

The present study aims to briefly cover the interactions based on our recent work in the promising interdisciplinary field. This communication deals with the synthesis, characterization and antimicrobial properties of the organotin(IV) and organolead(IV) derivatives of amino acids. Emphasis has been put on the antifertility property of the complexes.

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EXPERIMENTAL

Glass apparatus with standard quick-fit joints was used throughout the work. Adequate precautions were taken to exclude moisture from the system. The chemicals and solvents used were dried and purified by standard methods.

Synthesis of the complexes [$LSnPh_3bipy$]

To a solution of tyrosine (0.44 g; 0.002 mol) in dry methanol (15 ml) was added a solution of 2,2′-bipyridine (0.38 g; 0.002 mol) in the same solvent. The resulting mixture was refluxed for 20 h after adding a solution of triphenyltinchloride (0.93 g; 0.002 mol) in methanol (20 ml). The mixture was allowed to stand overnight in the refrigerator. The solid product obtained was isolated by filtration, washed with ether and dried *in vacuo*. Similarly, other complexes were prepared by the reactions of 2,2′-bipyridine and tyrosine or phenylalanine with triphenyltin chloride, dimethyltin chloride, triphenyllead chloride or dimethyllead chloride in 1 : 1 : 1 molar ratio, as shown in the following equations:

$$L + R_3MCl \xrightarrow{+bipy} [LMR_3(bipy)] + HCl \quad (1)$$

$$L + R_2MCl_2 \xrightarrow{+bipy} [LMR_2Cl(bipy)] + HCl \quad (2)$$

where, L = tyrosine (L^1) or phenylalanine (L^2), M = Sn or Pb and R = phenyl or methyl group.

Analytical methods and physical measurements

The molecular weights were determined using the Rast Camphor method. Conductivity measurements in dry dimethylformamide were performed with a conductivity bridge type 305 (Systronics). Infrared spectra were recorded on a Nicolet Magna FT IR 550 spectrophotometer in KBr pellets. The far infrared spectra of the complexes were recorded on the same spectrophotometer in Nujol Mulls using a CsI cell. ^1H and ^{13}C NMR spectra were recorded on a Jeol FX 90Q spectrometer. ^{13}C NMR and ^{119}Sn NMR spectra were recorded on the said instrument using TMS as the internal standard at 22.49 MHz and at 33.35 MHz using DMSO-d_6 as the solvent. The chemical shifts were determined relative to the external reference tetramethyltin and are supposed to be accurate to ±1 ppm. The electronic spectra were recorded on a Perkin Elmer UV–visible spectrophotometer in the range 200–600 nm, using dry methanol as the solvent. The ^{207}Pb spectra were recorded in dry methanol using $PbMe_4$ as the internal standard.

Biopotency

Percentage disease control

In this method, the compounds were tested in the field to control the disease caused by the organism. Two concentrations, 100 and 200 ppm, were applied to the different plots and observations were recorded.

$$\text{Percentage disease incidence (PDI)} = \frac{\text{Number of infected plants}}{\text{Total number of plants observed}} \times 100$$

$$\text{Percentage disease control} = \frac{\text{PDI in treated plants} - \text{PDI in untreated plants}}{\text{PDI in untreated plants}} \times 100$$

The fungus *Alternaria alternata* in brinjal (aubergine/eggplant) plants was used for this purpose.

The efficacy of the starting materials and their metal complexes *in vitro* and in field conditions was studied. The field experiments were laid out in a randomized block design with three replicates. Brinjal plants were raised in each plot. Compounds were also sprayed with a standard fungicide, Bavistin, to check the spray.

Forty-five days after sowing, the plants were inoculated artificially by spraying with conidial suspension. The conidial suspension was prepared by crushing infected leaves in water. Inoculation was performed in the evening. The first spray of the fungicide was given when the lesions were first seen and was repeated after 12 days. Disease intensity was observed 12 days after the second spray. The data were analysed statistically and disease control was determined.

Antibacterial activity

The antibacterial activity was evaluated by the paper disc method. In this technique, sterilized hot nutrient [composition: peptone (5 g), beef extract (5 g), NaCl (5 g), agar-agar (20 g) and distilled water 1000 ml] and 5 mm diameter Whatman no. 1 paper discs were used. The agar medium was poured into the Petri plates. After solidification, the plates were stored and frozen in the inverted position so that there was water condensation in the upper lid. Solutions of the test compounds in methanol at 500 and 1000 ppm concentrations were prepared into which either the discs were dipped and then placed on seeded plates or the required quantity of test sample was pipetted onto the disc. The Petri dishes containing the discs and the seeded agar were then subjected to low temperature for 2 h to allow diffusion of the chemical before being incubated at the suitable optimum temperature (28 ± 2 °C) for 24–30 h. After the filter expiry of the incubation period, the clear zone of inhibition associated with the treated disc was measured (mm). The organisms used in these investigations were *Pseudomonas cepacicola* and *Staphylococcus aureus.*

Antifertility activity

In the present investigations, healthy adult male albino rats (*Rattus norvegicus*) each having weight between 200 and 250 g of proven fertility were used. These were preferred over other laboratory mammals because of their medium size, relatively docile nature, ease of handling and maintenance, covertly observable sex and libido and relatively short gestation

period of 25–30 days. Animals were regularly checked for any disease and if found infected were isolated and treated. Animals were fed on a diet of rat feed pellets obtained from Hindustan Lever Ltd, Mumbai, and water was provided *ad libitum*.

The LD_{50} is a statistically derived single dose of a substance that can be expected to cause death in 50% of the animals. In a prohibited analysis method of LD_{50}, the selected dose levels should bracket the expected LD_{50} value with at least one dose level higher than the expected LD_{50} but not causing 100% mortality and one dose level below the expected LD_{50} but not causing 0% mortality. Toxicity of the complexes was determined by calculating the LD_{50} values. Symptoms of poisoning and mortality were observed and results of toxicity were analysed for determination of LD_{50} values of the complexes. On the basis of the LD_{50} values, a single dose of the compounds was determined for the experiment (Tables 1 and 2).

Antifertility and toxicity are inseparable issues, but metal complexes which show good antifertility with high toxicity cannot be used for the desired purpose.

Thirty adult male albino rats of an inbred colony were housed in an air-conditioned animal room at $24 \pm 2\,^{\circ}C$ with 24 h light with water and food given *ad libitum*. They were divided into five groups containing six animals each. The first group served as olive oil-treated control. The 12.5 mg/kg second group was treated with the compound [L^1SnPh_3.bipy].

Table 1. LD_{50} for the organotin complexes

Sample no.	Dose (mg/kg)	Animals taken	Death
1	250	50	50
2	200	50	45
3	150	50	35
4	100	50	30
5	50[a]	50	25
6	25	50	20
7	12.5	50	5

[a] 50 mg/kg LD_{50}.

Table 2. LD_{50} for the organolead complexes

Sample no.	Dose (mg/kg)	Animals taken	Death
1	250	50	50
2	200	50	50
3	150	50	45
4	100	50	35
5	50	50	35
6	25	50	30
7	12.5[a]	50	25
8	6.2	50	23

[a] 12.5 mg/kg LD_{50}.

The third, fourth and fifth groups were treated with [L^2SnPh_3.bipy], [L^1SnMe_2Cl bipy] and [L^2SnMe_2Cl bipy], respectively; 12.5 mg/kg body weight were suspended in olive oil and given orally over a period of 60 days. These animals were screened for fertility and autopsied for detailed biochemical studies.

RESULTS AND DISCUSSION

The 1 : 1 : 1 molar reactions of amino acids and 2,2′-bipyridine with organotin and organolead chlorides (Ph_3SnCl, Me_2SnCl_2, Ph_3PbCl and Me_2PbCl_2) in dry methanol proceed smoothly. The resulting products were filtered and washed several times with the same solvent. All the products are coloured solids and are completely soluble in most organic solvents. All these complexes were purified by recrystallization. Their purity was further checked by thin-layer chromatography using silica gel-G. It was observed that the spot moves as such for a particular type of compounds. The molecular weight determinations show these compounds to be monomers. The molar conductivity in dry dimethylformamide was found to be in the range 8–19 $ohm^{-1}\,cm^2\,mol^{-1}$, indicating non-electrolytic behaviour (Table 3).

Spectral Aspects

The electronic spectra of the complexes were recorded in carbon tetrachloride. The prominent peaks were observed at 217–225 and 255–263 nm in the UV region and assigned to the $\pi-\pi^*$ electronic transitions due to MLCT.

The IR spectra of the starting materials and their metal complexes supported the formation of the complexes with the proposed coordination mode. The amino acids exhibited the ν(OH) band of the carboxylate group[13] at ca. 3200 cm^{-1}. However, the IR spectra of the complexes did not show this band, indicating the deprotonation of the carboxylic group. This was further supported by the appearance of a new medium intensity band in the region 520–555 cm^{-1} attributed to M–O stretching vibrations, indicating the coordination of the metal through the oxygen atom. No splitting was observed in the band at ca. 1650 cm^{-1} due to (COO)asym and (COO)sym vibrations. In the free bipyridine molecule, strong interactions between C═C and C═N gave rise to two groups of doublets (1555–1582 and 1440–1480 cm^{-1}). These bands underwent remarkable changes due to coordination and new bands were found to appear in the spectra of the complexes at 1600–1610 and 1560–1565 cm^{-1},confirming the bidentate (NN) coordination of bipyridine.[14]

A medium to sharp intensity band observed in the far IR region of the metal complexes at 345–360 cm^{-1} was assigned to the ν(M–Cl) mode. It has been suggested that the *cis* form of such complexes gives rise to two ν(M–N) bands, whereas in the *trans* form only one IR active band is observed. The presence of only one ν(M–N) band in the metal complexes suggests that the complexes exist in the *trans* form.[15] Similarly,

Table 3. Physical properties and analytical data of the organotin(IV) and organolead(IV) complexes

Compound	Reactant g (mol)			Colour and state	Yield (%)	Melting point (°C)	Analysis found (Calcd) (%)					Molecular weight found (calcd)
	Amino acid	R_3MCl/ R_2MCl_2	2,2′-Bipyridine				C	H	N	M	Cl	
[L^1SnPh_3.bipy]	0.44 (0.002)	0.93 (0.002)	0.38 (0.002)	Light yellow solid	72	128	64.55 (64.65)	4.89 (4.99)	5.31 (6.11)	16.79 (17.27)	—	664 (687.39)
[L^2SnPh_3.bipy]	0.43 (0.002)	1.00 (0.002)	0.41 (0.002)	Light yellow solid	75	139	66.08 (66.29)	4.86 (4.96)	5.48 (6.27)	17.25 (17.70)	—	651 (670.39)
[L^1SnMe_2Cl.bipy]	0.46 (0.002)	0.55 (0.002)	0.39 (0.002)	Cream solid	73	187	48.16 (48.36)	4.73 (4.83)	7.33 (8.06)	18.66 (19.09)	6.39 (6.80)	506 (521.62)
[L^2SnMe_2Cl.bipy]	0.45 (0.002)	0.59 (0.002)	0.42 (0.002)	Cream solid	70	131	48.76 (49.98)	4.68 (4.79)	7.58 (8.33)	23.06 (23.52)	6.59 (7.02)	481 (504.62)
[L^1PbPh_3.bipy]	0.43 (0.002)	0.17 (0.002)	0.37 (0.002)	Off-white solid	72	202	57.19 (57.28)	4.22 (4.42)	4.69 (5.42)	26.27 (26.68)	—	760 (775.89)
[L^2PbPh_3.bipy]	0.46 (0.003)	1.32 (0.002)	0.43 (0.002)	Off-white solid	74	210	57.42 (58.56)	4.19 (4.38)	4.82 (5.54)	26.79 (27.28)	—	733 (758.89)
[L^1PbMe_2Cl.bipy]	0.48 (0.003)	0.81 (0.002)	0.41 (0.002)	Yellow solid	70	219	41.20 (41.31)	4.03 (4.13)	6.17 (6.88)	33.44 (33.90)	5.36 (5.81)	584 (610.63)
[L^2PbMe_2Cl.bipy]	0.44 (0.002)	0.82 (0.002)	0.47 (0.002)	Yellow solid	76	216	42.38 (42.49)	4.06 (4.07)	6.39 (7.08)	34.44 (34.87)	5.56 (5.97)	569 (593.63)

Table 4. IR spectral data (cm^{-1}) of the organometallic complexes

Compound	ν(M–O)	ν(M–N)	M–CH_3/M–Ph
[L^1SnPh_3.bipy]	535	380	270
[L^2SnPh_3.bipy]	540	387	272
[L^1SnMe_2Cl.bipy]	520	390	1170
[L^2SnMe_2Cl.bipy]	545	392	1177
[L^1PbPh_3.bipy]	550	383	290
[L^2PbPh_3.bipy]	530	381	299
[L^1PbMe_2Cl.bipy]	555	390	1220
[L^2PbMe_2Cl.bipy]	525	395	1243

the presence of only one Sn–C stretching frequency at 560 cm^{-1} also suggests that the complexes exist in the *trans* form. One strong to medium intensity band appearing in the spectra of the complexes in the region 1170–1242 cm^{-1} can be assigned to M–CH_3 stretching vibrations. A new band observed at 270–299 cm^{-1} may be assigned to ν (M-Ph) (Table 4).[16]

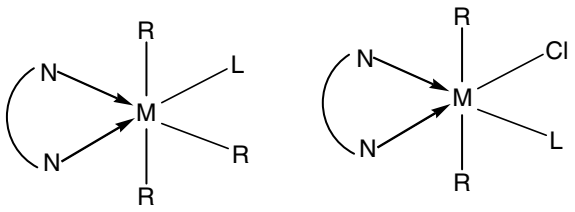
The ^1H NMR spectra were recorded in DMSO-d_6. The chemical shift values relative to the TMS peak are shown in Table 5. A doublet was observed in the high field at δ 3.04–3.10 ppm due to –CH_2 protons of tyrosine or phenylalanine. A complex pattern in the region δ 3.68–3.80 ppm was assigned to NH_2–CH. The phenyl proton signals appeared in the region δ 7.40–8.79 ppm. Proton signals due to –COOH proton were absent in the ^1H NMR spectra of the complexes and this confirmed the coordination through the carbonyl group which is already supported by the M–O peak in the far-IR spectra. The additional singlets in the region δ 1.00–1.30 ppm are due to the CH_3–M group and those at δ 7.20–7.55 ppm are due to the Ph–M group. The C–Sn–C angles were calculated using the equation θ (C–Sn–C) = 0.0161 $[^2J(\text{Sn–H})]^2$–1.32 $[^2J(\text{Sn–H})]$ + 133.4.[17] ^{13}C NMR spectra of the complexes exhibit the carboxylic carbon signal at δ 177.33–177.96 ppm (showing upfield shift from the free amino acid) attributed to the monodentate nature of the carboxylic group. The ^{13}C NMR spectral data of the complexes are listed in Table 6. On the basis of the spectral evidence, it may be inferred that the carboxylic acid of the amino acid (tyrosine or phenylalanine) behaves as monodentate in these complexes and the complexes are octahedral in shape with a coordination number 6 around the metal atom. The values of the θ (C–Sn–C) angle of these complexes were estimated using the formula:[18]

$$J^1(^{119}\text{Sn},^{13}\text{C}) = 11.4\,\theta(\text{C–Sn–C}) - 875$$

The values 128 and 131° are very near to 126 and 130.8°, which were calculated from the ^2J (Sn–H) coupling constant for organomethyltin(IV) complexes. ^{119}Sn NMR spectra of the organotin(IV) complexes display sharp signals

Table 5. ^{1}H NMR spectral data (δ, ppm) of the organotin(IV) and organolead(IV) complexes

Compound	Bipyridine moiety	Tyrosine/phenylalanine moiety	CH_2	M–CH_3/ M–Ph_3	NH_2–	^{119}Sn NMR/ ^{207}Pb NMR	^2J (Sn–H) (Hz)
[L^1SnPh_3.bipy]	7.40–8.60	6.65–6.90	3.04	7.20	3.80	−342	—
[L^2SnPh_3.bipy]	7.49–8.66	6.60–7.12	3.09	7.23	3.77	−345	—
[L^1SnMe_2Cl.bipy]	7.50–8.57	6.33–7.18	3.07	1.00	3.70	−330	76
[L^2SnMe_2Cl.bipy]	7.58–8.71	6.62–7.09	3.05	1.07	3.68	−334	80
[L^1PbPh_3.bipy]	7.43–8.79	6.44–7.08	3.10	7.35	3.71	−2209	—
[L^2PbPh_3.bipy]	7.60–8.60	6.56–7.20	3.07	7.55	3.73	−2215	—
[L^1PbMe_2Cl.bipy]	7.53–8.65	6.59–7.08	3.08	1.27	3.75	−2245	—
[L^2PbMe_2Cl.bipy]	7.55–8.62	6.49–7.07	3.05	1.30	3.79	−2249	—



N⌒N = donor site of 2,2′-bipyridine
M = Sn(IV) or Pb(IV)
R = Ph or Me

Figure 1. Proposed structures for the complexes.

at $\delta - 330$ to -345 ppm, clearly showing the hexacoordinated environment around the tin atom.[19] ^{207}Pb NMR spectra of the organolead(IV) complexes exhibit sharp signals at $\delta - 2209$ to 2249 ppm and supports the 6-coordinated state of the lead atom.[20] Thus on the basis of the above spectral factors, as well as on the analytical data and literature evidence,[15,21–23] hexacoordinated octahedral geometry has been established for these complexes (Fig. 1).

Bio-chemical aspects

Antimicrobial mode of action

The degradative enzymes produced by the microorganisms are important in host infection, food deterioration and breakdown of organic matter. The enzyme production is here intended to mean both the synthesis of the enzyme by the microorganisms and the activity of the enzyme in the medium after it is produced. Since the organometal(IV) complexes inhibit the growth of the microorganisms, it is assumed that the production of the enzymes is affected; hence, the organisms are unable to utilize the food and consequently growth ceases.

Owing to the greater lipid solubility, complexes facilitate their diffusion through the spore membrane to the site of the action within the spores, ultimately killing them by combining the –SH groups of certain cell enzymes. The variation in the effectiveness of different biocidal agents against different organisms, as suggested by Saxena and Singh[24] depends upon the impermeability of the cell. The effect of resonating rings on the toxicity may be appraised in the light of modern electronic theory. The resonant energy is the energy in excess of the sum of the energy of the separate bonds making up the molecule. The Arrhenius activation theory states that an excess of the molecular energy activates molecules and produces a more rapid rate of chemical reaction. Resonating structures, such as benzene rings (in the present case), may serve as a powerhouse to activate potentially reactive groupings.

The results of the antimicrobial screening were compared with a conventional fungicide, Bavistin, and a conventional bactericide, Streptomycin, taken as standards in either case (Tables 7 and 8). The results also reveal that the complexes show greater antimicrobial activity as compared with the starting materials. The complexes containing a halogen atom attached directly to the metal atom also showed moderate activity. The mode of action of these compounds may involve the formation of a hydrogen bond with the active centres of the cell constituents, resulting in interference with normal cell processes.

Antifertility activity

The testicular morphology, testicular sperm density, sperm motility, density of cauda epididymal spermatozoa and fertility in mating trials and biochemical parameters of the reproductive organs with the complexes were examined. The results show that the complexes were able to inhibit fertility due to the synergistic effects of tin. The results of the study are grouped under the following headings:

- *Body and organ weights*—body weights of the rats were not affected after the tin complexes were administrated. However, the weights of testes, epididymis, seminal vesicle and ventral prostate were significantly decreased (Table 9).
- *Fertility test*—the sluggish motile spermatozoa were unable to fertilize normal cyclic females. The test was 50–85% negative in rats treated with the compounds.

Table 6. ^{13}C NMR spectral data of the organotin(IV) and organolead(IV) complexes

Compound	Bipyridine moiety	Tyrosine/ phenylananine	–CH	$-CH_2$	C=O	C–Sn–C angle, $\theta°$	Estimated C–Sn–C angle, $\theta°$	$^1J(^{119}Sn,^{13}C)$ (Hz)	$^2J(^{119}Sn,^{13}C)$ (Hz)	$^3J(^{119}Sn,^{13}C)$ (Hz)
$[L^1SnPh_3.bipy]$	C_1 142.01; C_2 128.10; C_3 149.02	Cα, 154.21; Cβ, 115.66, Cγ, 129.30; Cδ, 132.81	63.22	38.88	177.78	141	142	751	40.8	125.0
$[L^2SnPh_3.bipy]$	C_1 142.20; C_2 128.3; C_3 148.62	Cα, 154.40; Cβ, 115.83, Cγ, 129.40; Cδ, 132.85	63.36	39.26	177.33	140	142	748	38.9	128.0
$[L^1SnMe_2Cl.bipy]$	C_1 143.06; C_2 128.40; C_3 149.06	Cα, 154.44; Cβ, 115.60, Cγ, 129.08; Cδ, 132.49	63.59	39.24	177.60	126	128	587	—	—
$[L^2SnMe_2Cl.bipy]$	C_1 143.02; C_2 128.41; C_3 149.20	Cα, 154.50; Cβ, 115.70, Cγ, 129.59; Cδ, 132.33	63.48	39.68	177.59	130.8	131	622	—	—
$[L^1PbPh_3.bipy]$	C_1 143.01; C_2 128.80; C_3 149.00	Cα, 125.42; Cβ, 128.43, Cγ, 127.30; Cδ, 140.60	63.56	38.45	177.78	—	—	—	—	—
$[L^2PbPh_3.bipy]$	C_1 142.57; C_2 128.80; C_3 149.00	Cα, 125.48; Cβ, 128.96, Cγ, 127.44; Cδ, 140.56	63.44	38.16	177.68	—	—	—	—	—
$[L^1PbMe_2Cl.bipy]$	C_1 142.52; C_2 129.06; C_3 148.52	Cα, 125.48; Cβ, 128.66, Cγ, 127.26; Cδ, 140.55	63.77	38.25	177.96	—	—	—	—	—
$[L^2PbMe_2Cl.bipy]$	C_1 142.50; C_2 129.50; C_3 148.42	Cα, 125.43; Cβ, 128.77, Cγ, 127.89; Cδ, 140.63	63.96	39.76	177.56	—	—	—	—	—

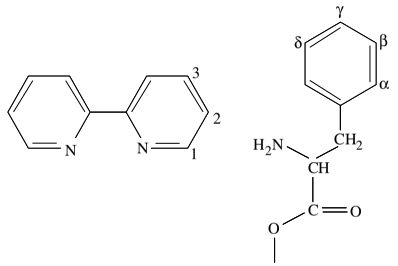


Table 7. Efficacy of organotin(IV) and organolead(IV) complexes with respect to leaf spot on brinjal plants caused by *Alternaria alternata* using the percentage disease incidence method

Treatment	Concentration (ppm)	Inhibition replicates (out of 60) R_1	R_2	R_3	Percentage disease incidence	Percentage disease control
Ph_3SnCl	100	44	47	54	80.35	19.45
	200	40	45	50	75.0	25.0
Me_2SnCl_2	100	37	44	43	68.88	31.12
	200	36	38	42	64.44	35.56
2,2′-Bipyridine	100	34	40	47	67.22	32.78
	200	30	38	43	61.66	38.34
$[L^1SnPh_3.bipy]$	100	22	18	19	32.77	67.23
	200	18	12	15	25.00	75.00
$[L^2SnPh_3.bipy]$	100	20	17	16	29.44	70.56
	200	18	15	15	26.67	73.33
$[L^1Me_2SnCl.bipy]$	100	13	14	13	22.22	77.78
	200	10	9	9	15.56	84.44
$[L^2Me_2SnCl.bipy]$	100	15	14	14	23.88	76.12
	200	12	10	12	18.88	81.12
Bavistin 6.2%	—	11	13	11	19.44	80.56
Control (water spray)	—	41	46	50	76.11	23.89

Table 8. Antibacterial screening data of the starting materials and their organotin(IV) and organolead(IV) complexes

Compound	Inhibition (mm) after 24 h (concentration in ppm) *Pseudomonas cepacicola* 500	1000	*Staphylococcus aureus* 500	1000
Ph_3SnCl	5	9	5	8
Me_2SnCl_2	6	10	5	10
2,2′ Bipyridine	4	6	4	7
Tyrosine	2	4	3	4
Phenylalanine	3	4	—	4
$[L^1SnPh_3.bipy]$	10	12	9	13
$[L^2SnPh_3.bipy]$	9	15	8	14
$[L^1SnMe_2Cl.bipy]$	16	16	14	14
$[L^2SnMe_2Cl.bipy]$	15	15	14	15
$[L^1PbPh_3.bipy]$	13	13	11	13
$[L^2PbPh_3.bipy]$	16	16	15	16
$[L^1PbMe_2Cl.bipy]$	18	19	19	18
$[L^2PbMe_2Cl.bipy]$	16	17	17	17
Streptomycin	3	5	15	17

- *Sperm motility*—the sperm motility declined significantly after treatment with the complexes (Table 10).
- *Sperm density*—the sperm density in testes and cauda epididymis declined significantly after treatment (Table 10).
- *Biochemical changes*—total protein and sialic acid contents of testes, epididymis, ventral prostate and seminal vesicle were depleted significantly after treatment with the complexes. The acid phosphatase levels of testes, epididymis and ventral prostate were also reduced significantly. A significant decrease in seminal vascular fructose contents was also noticed, whereas the testicular cholesterol control contents were increased significantly after treatment with the various compounds (Table 11).

DISCUSSION

The present study revealed that administration of the tin complexes caused a significant reduction in the weights of testes and other sex accessory glands. The prostate and seminal vesicle are well-documented androgen-dependent processes.[25] Sperm motility is considered as an important parameter in evaluating the fertility potential.[26] The tin(IV) complexes significantly reduce the fertility of male rats. Since a number of androgen-sensitive parameters (protein, sialic acid, fructose, acid phosphatase and total cholesterol) in target organs were found to be altered by these complexes, it is probable that the structure and function of epididymis and other sex accessory organs had changed. Our findings indicate that the complexes $[L^1Sn\ Me_2Cl.bipy]$ and $[L^2SnMe_2Cl.bipy]$ have a more pronounced effect of fertility on various biochemical parameters of reproductive organs as compared with other complexes discussed in this paper.

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Table 9. Effects of organotin(IV) complexes on the body and reproductive organ weights on male rats

Group	Treatment	Body weight (g)		Organ weight (mg)			
		Initial	Final	Testes	Epididymis	Seminal vesicle	Ventral prostate
A	Control	208.0 ± 15.3	230.0 ± 11.2[c]	1380.0 ± 30.3	490.0 ± 20.2	520.0 ± 20.4	490.0 ± 11.8
B	[L^1SnPh_3.bipy]	215.0 ± 10.3	238.0 ± 15.5[c]	1130.0 ± 10.8	380.0 ± 25.8[a]	445.0 ± 20.2[a]	425.0 ± 12.4[a]
C	[L^2SnPh_3.bipy]	210.5 ± 13.2	220.0 ± 12.6[c]	990.0 ± 30.5[a]	335.0 ± 18.6[b]	370.5 ± 13.2[b]	380.0 ± 17.3[a]
D	[L^1SnMe_2Cl.bipy]	218.0 ± 10.4	238.0 ± 10.5[c]	950.0 ± 25.6[a]	325.0 ± 14.8[b]	355.0 ± 17.9[b]	330.0 ± 11.8[b]
E	[L^2SnMe_2Cl.bipy]	225.0 ± 15.8	240.0 ± 14.5[c]	850.0 ± 19.2[b]	295.0 ± 13.9[b]	315.0 ± 13.2	300.0 ± 10.5[b]

Group B compared with group A.
Groups C, D and E compared with group A.
Mean ± SEM of five animals: [a] $p \leq 0.01$; [b] $p \leq 0.001$; [c] n.s.

Table 10. Effects of organotin(IV) complexes on the reproductive parameters on male rats

Group	Treatment	Sperm motility cauda epididymis (%)	Sperm density million/cm^3		Fertility test (%)	
			Testes	Cauda epididymis		
A	Control	85.0 ± 2.9	5.0 ± 0.60	55.5 ± 3.9	100%	Positive
B	[L^1SnPh_3.bipy]	65.0 ± 3.5[a]	4.1 ± 0.63[a]	45.0 ± 1.0[a]	50%	Negative
C	[L^2SnPh_3.bipy]	60.0 ± 3.0[a]	3.7 ± 0.25[a]	35.5 ± 2.0[a]	55%	Negative
D	[L^1SnMe_2Cl.bipy]	35.0 ± 3.0[b]	1.9 ± 0.15[b]	25.0 ± 2.0[b]	80%	Negative
E	[L^2SnMe_2Cl.bipy]	33.0 ± 3.5[b]	2.1 ± 0.15[b]	22.0 ± 2.5[b]	85%	Negative

Group B compared with group A.
Groups C, D and E compared with group A.
Mean ± SEM of five animals: [a] $p \leq 0.01$; [b] $p \leq 0.001$.

Table 11. Testicular biochemistry of organotin(IV) complexes

Group	Treatment	Glycogen (mg/gm)	Total protein (mg/gm)	Total cholesterol (mg/gm)	Sialic acid (mg/gm)	Phosphatase mg/ip/g/h	
						Acid	Alkaline
A	Control	3.90 ± 0.55	220.0 ± 10.9	5.90 ± 0.25	5.40 ± 0.20	3.15 ± 0.15	10.30 ± 0.80
B	[L^1SnPh_3.bipy]	4.5 ± 0.10[a]	1.85 ± 13.4[a]	6.65 ± 0.12[a]	4.58 ± 0.19[a]	4.15 ± 0.15[a]	13.40 ± 0.70[a]
C	[L^2SnPh_3.bipy]	5.95 ± 0.15[b]	142.5 ± 15.4[a]	8.20 ± 0.20[b]	3.85 ± 0.20[a]	5.50 ± 0.10[b]	15.4 ± 0.15[b]
D	[L^1SnMe_2Cl.bipy]	6.15 ± 0.10[b]	130.0 ± 10.5[b]	8.40 ± 0.20[b]	3.00 ± 0.10[b]	5.75 ± 0.11[b]	16.80 ± 0.14[b]
E	[L^2SnMe_2Cl.bipy]	6.75 ± 0.20[b]	110.0 ± 9.0[b]	9.40 ± 0.30[b]	2.75 ± 0.12[b]	6.10 ± 0.15[b]	17.85 ± 0.15[b]

Group B compared with group A.
Groups C, D and E compared with group A.
Mean ± SEM of five animals: [a] $p \leq 0.01$; [b] $p \leq 0.001$.

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