

# Antifungal, Antibacterial and Antifertility Activities of Biologically Active Macrocyclic Complexes of Tin(II)

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**Abstract:** Synthetic, structural and biological aspects of tetraazamacrocyclic complexes of Tin(II) have been described. The complexes were characterized by elemental analysis, molecular weight determination conductance measurements and electronic, infrared, <sup>1</sup>H, <sup>13</sup>C and Sn NMR spectral studies. Ligand and their unsymmetrical complexes have been tested for their antimicrobial effects on several pathogenic fungi and bacteria. The testicular sperm density, testicular sperm morphology, sperm motility, density of cauda epididymal spermatozoa and fertility in mating trails and bio-chemicals parameters of reproductive organs have been examined in male albinorats in vivo.

**Keywords:** Unsymmetrical, antimicrobial effects, pathogenic fungi and bacteria.

## INTRODUCTION

The complexes have been prepared by the template method using 3,10-dimethyl-4,9-diazadodecane-3,9-diene-2,11-dione. The field of macrocyclic chemistry of metals is developing very rapidly because of its importance in the area of coordination chemistry [1-5] Synthetic macrocyclic ligands are of significance because porphyrin play vital role in biological systems, such chelating molecules are important since they are capable of furnishing an environment of controlled geometry and ligand field strength [6]. These compounds have also been screened for toxicological effects [7-9]. The coordination and organometallic compounds having metal-nitrogen bonding occupy an important position amongst the recent developments related to bioinorganic systems. Metal ion recognition is of fundamental importance to broad areas of both chemistry and biochemistry. The importance of metal ion in biological systems as macrocyclic compounds is well established because of their catalytic behaviour in a number of redox reactions of biological significance. Thus much of the current interest in macrocyclic coordination chemistry arises from the hope that the unusual

geometrical relationship imposed into metal ions by the macrocyclic donor set may be transformed on to unusual bonding situation. A review on macrocycles has revealed the importance of macrocyclic complexes in biological processes such as photosynthesis and dioxygen transport[10] their potential applications as extractant and as radio-therapeutic and medical imaging agents. Macrocyclic polyamines have attracted increasing attention because of their unique property, namely to form very stable chelates with various heavy metal ions[11]. The transition and lanthanide metal ions have been used as templates in the synthesis of 10, 12, 13, 14 and 18-membered polyaza macrocyclic complexes[12]. The potential of macrocyclic ligand systems with their central cavity for use as metal ion selective reagent has been widely recognized now a days[13]. Apart from more obvious parameters such as donor atom, radii and type of hybridization, a range of other structural factors, including chelate ring size, extent of ligand rigidity and the presence or absence of ring substituents can all influences the geometry of the binding cavity often in subtle ways[14]. For a number of systems in which the metal ion fully occupies the macrocyclic cavity,

there is a tendency for maximum stability to occur at the ligand for which the cavity size best matches the radius of the ion [15]. In continuation of our earlier work on macrocycles of Sn(II) have been prepared and thoroughly characterized.

## MATERIALS AND METHOD

### Preparation of ligand

These ligand were prepared by the condensation of 2,3-butanedione with 1,2-diaminoethane in ethanol in presence of acidic medium. The reaction was carried out in 2:1 molar ratio and heated under reflux for 12 hours. The reaction mixture was cooled and the reddish brown crystalline product separated out. The product collected and washed with benzene (yield 70%).

### Preparation of complexes

The reaction mixture containing ligand, tin(II) chloride and different diamine in 1:1:1 molar ratio in methanol was heated under reflux for 10-12 hours. The solution was cooled, transferred to a evaporating dish and kept overnight at room temperature in a desiccator. The solid, dark coloured complex separated out. The complexes were repeatedly washed with dry cyclohexane so as to ensure its purity and dried in vacuo. The product was recrystallized from ethanol and finally from cyclohexane. The analytical data and physical properties have been given in Table 1.

## RESULT AND DISCUSSION

All the resulting solids are soluble in DMF and DMSO. The Rast Camphor method for determination of molecular weights showed them to be monomeric in nature. The molar conductivity values of all the complexes in DMF are in the range

12-18 ohm<sup>-1</sup>cm<sup>2</sup>mol<sup>-1</sup> suggesting their non ionic nature. The presence of chloride in the coordination sphere is supported by the fact that its presence is evident only after the chemical decomposition of complexes.

### Infrared Spectra

A comparative study of the starting material and their complexes show the absence of uncondensed functional groups (–NH<sub>2</sub> and >C=O) in all the complexes [16,17] due to the elimination of two water molecules. The band assigned to ν (>C=N) at 1620-1630 cm<sup>-1</sup> registers a substantial decrease in the metal complexes as a result of chelation [18]. The bands characteristic of the methyl moiety appeared in all the complexes at 3035 cm<sup>-1</sup> (ν<sub>asy</sub> CH<sub>3</sub>) and 2825cm<sup>-1</sup> (ν<sub>sym</sub> CH<sub>3</sub>). All the complexes and ligand show two distinct sharp bands occurring at *ca* 2810 and 1425 cm<sup>-1</sup> assigned to C-H stretching and bending vibrations [19].

### <sup>1</sup>H NMR Spectra

The structure proposed for the unsymmetrical complexes in the foregoing discussion further get support from the <sup>1</sup>HNMR spectral data. The <sup>1</sup>HNMR spectra of ligand does not show NH<sub>2</sub> band any more indicating that the proposed macrocyclic skeleton has been formed. A singlet observed at δ 3.20-3.60 ppm in the complexes as well as ligand assigned to methylene protons adjacent to nitrogen. The shift of signals towards lower field is an identification of the coordination of the ligand. The complexes show multiplets in the **region δ 7.16-8.64** ppm attributable to aromatic protons[20] Chemical shift values are given in Table 2.

**Table1 Analyses and Physical Properties of the ligand and Tin (II) Complexes**

Compound	Colour	M.p. (°C)	% Analyses			Mol.Wt.
			Sn	N	Cl	
C <sub>10</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	Reddish brown	156	-	7.13(7.27)	-	196.248 (226.21)
[Sn(C <sub>16</sub> H <sub>20</sub> N <sub>4</sub> )Cl <sub>2</sub> ]	Yellowish brown	220	25.92 (25.69)	3.06(3.23)	7.74 (7.88)	457.97 (467.94)
[Sn(C <sub>15</sub> H <sub>19</sub> N <sub>5</sub> )Cl <sub>2</sub> ]	Cream	110	25.86 (25.98)	3.05 (3.26)	7.72 (7.95)	458.96 (472.79)
[Sn(C <sub>14</sub> H <sub>25</sub> N <sub>5</sub> )Cl <sub>2</sub> ]	Sandy Brown	> 300	26.20 (26.62)	3.09 (3.46)	7.82 (8.15)	452.99 (468.66)
[Sn(C <sub>20</sub> H <sub>22</sub> N <sub>4</sub> )Cl <sub>2</sub> ]	Light Brown	140	23.36 (23.71)	2.75 (2.93)	6.98 (7.06)	508.03 (533.80)

**Table 2.  $^1\text{H}$  NMR Spectral Data ( $\delta$ , ppm) of ligand and its Complexes**

Complexes	$>\text{N}-\text{CH}_2$ (bs)	-R	$-\text{CH}_3$ (s)	$>\text{NH}$
$\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_2$	2.97(4H)	-	1.19(12H)	-
$[\text{Sn}(\text{C}_{16}\text{H}_{20}\text{N}_4)\text{Cl}_2]$	3.55(4H)	8.68( $\text{H}_{2,5}\text{d}$ ) 7.97( $\text{H}_{3,4}\text{d}$ )	1.95(12H)	-
$[\text{Sn}(\text{C}_{15}\text{H}_{19}\text{N}_5)\text{Cl}_2]$	3.16(4H)	8.46( $\text{H}_{2,4}\text{s}$ ) 7.88( $\text{H}_3\text{d}$ )	1.25(12H)	-
$[\text{Sn}(\text{C}_{14}\text{H}_{25}\text{N}_5)\text{Cl}_2]$	3.95(12H)	-	1.86(12H)	4.40
$[\text{Sn}(\text{C}_{20}\text{H}_{22}\text{N}_4)\text{Cl}_2]$	3.08(4H)	7.79( $\text{H}_{2,7}\text{b}$ ) 7.71( $\text{H}_{3,6}\text{b}$ ) 7.74( $\text{H}_{4,5}\text{d}$ )	1.77(12H)	-

**Electronic Spectra**

Electronic spectra of the ligands consist of a band around 375 nm due to  $n-\pi^*$  transitions of the  $>\text{C}=\text{N}$  chromophore which shifted to *ca* 10nm, which is consistent with the nitrogen coordination of macrocyclic ligand. This suggests the formations of azomethine grouping on complexation. The band around 270 nm and 305 nm in the complexes are assigned to  $\pi-\pi^*$  transitions within the benzenoid ring [21-22] in the complexes.

 **$^{13}\text{C}$  NMR Spectra**

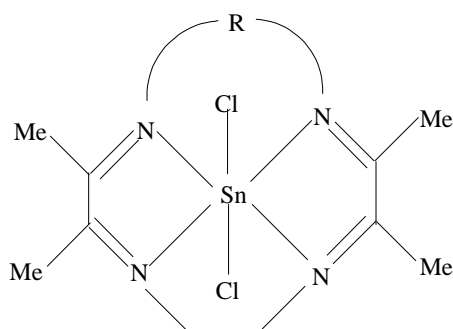
$^{13}\text{C}$  NMR spectra of the ligand and their complexes were recorded in  $\text{DMSO}-d_6$ [23]. The signals observed at  $\delta$ 124.38 - 136.60 ppm have been assigned to aromatic carbon attached to nitrogen atoms. Carbon atoms which have a distance from nitrogen atoms show upfield shift. A signal observed at 168.34 ppm may be assigned to carbonyl ( $>\text{C}=\text{O}$ )

carbons in the ligand which disappear in the complexes. Similarly a band appeared in the range  $\delta$  151.98 - 165.70 ppm due to two  $>\text{C}=\text{N}$  bands in the complexes, indicates cyclisation of the ligand. Signals observed for  $>\text{N}-\text{CH}_2$ ,  $\text{CH}_2$  and  $\text{CH}_3$  carbons have also been assigned in the ligands and their complexes without any appreciable shift (Table 3).

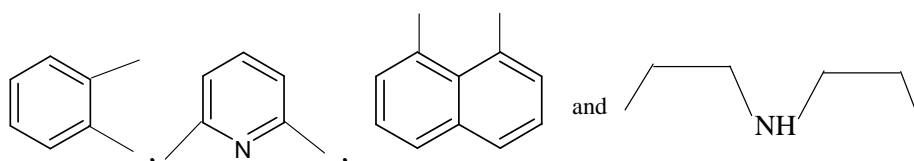
**X-Ray diffraction**

The possible geometry of the product  $[\text{Sn}(\text{C}_{14}\text{H}_{25}\text{N}_5)\text{Cl}_2]$  has been deduced on the basis of X-ray powder diffraction studies. The results show that the compound belong to the orthorhombic crystal systems, having unit cell dimensions  $a = 21.712 \text{ \AA}$ ,  $b = 35.317 \text{ \AA}$  and  $c = 6.700 \text{ \AA}$ . The  $d$ -spacing in  $\text{\AA}$ ,  $h$ ,  $k$ ,  $l$  values and  $2\theta$  angles are reported in Table 4.

Thus on the basis of above evidences, the following structures can be assigned to these metal complexes .



Where, R=



**Table 3.  $^{13}\text{C}$  NMR spectral data ( $\delta$ , ppm) of ligand and its Complexes**

Complexes	$>\text{C}=\text{O}$	$>\text{N}=\text{CH}_2$	$>\text{C}=\text{N}$	$-\text{CH}_3$	$-\text{R}$	$-\text{CH}_2$
$\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_2$	173.25	41.82	154.29	12.43	-	27.28
$[\text{Sn}(\text{C}_{16}\text{H}_{20}\text{N}_4)\text{Cl}_2]$	-	44.25	169.14	16.78	$\text{C}_{1,6}$ 128.71 $\text{C}_{2,5}$ 126.28 $\text{C}_{3,4}$ 124.36	32.31
$[\text{Sn}(\text{C}_{15}\text{H}_{19}\text{N}_5)\text{Cl}_2]$	-	46.51	159.47	12.17	$\text{C}_{1,5}$ 134.64 $\text{C}_{2,4}$ 126.48 $\text{C}_3$ 124.36	26.57
$[\text{Sn}(\text{C}_{14}\text{H}_{25}\text{N}_5)\text{Cl}_2]$	-	41.21	167.31	18.94	-	33.08
$[\text{Sn}(\text{C}_{20}\text{H}_{22}\text{N}_4)\text{Cl}_2]$	-	45.94	162.81	13.51	$\text{C}_{2,7}$ 127.96 $\text{C}_{3,6}$ 128.34 $\text{C}_{4,5}$ 127.62	36.91

**Table 4. X-Ray powder diffraction data of  $\text{Sn}(\text{C}_{14}\text{H}_{25}\text{N}_5)\text{Cl}_2$** 

Peak No.	$2\theta$ (deg.)	d-spacing (obs.) ( $\text{\AA}^\circ$ )	h	k	l
1.	16.61	6.700	0	1	0
2.	19.24	5.800	3	1	0
3.	22.97	4.870	7	0	1
4.	26.07	4.300	6	1	1
5.	28.44	3.140	2	5	0
6.	29.68	3.015	5	4	0
7.	30.77	2.919	1	5	2
8.	33.43	3.370	6	1	4
9.	35.38	3.190	0	2	2
10.	40.46	2.800	6	2	2
11.	42.75	2.115	9	4	0
12.	45.58	2.500	14	0	0
13.	51.21	2.240	12	0	6
14.	53.85	2.140	14	1	4
15.	58.94	1.770	1	3	5

## **BIOLOGICAL STUDIES**

### **Antibacterial Activity**

The activity against bacteria was evaluated by the inhibition zone technique [24]. Flat bottomed 90mm Pyrex Petridishes were used. 15ml. nutrient agar medium, having the composition peptone-5g, beef extract-5g, NaCl-5g, agar-agar-20g and distilled water-1000ml., was pipetted into the Petridish. After the agar solidified, 5ml of warm seeded agar was applied. The seeded agar was prepared by cooling the molten agar to  $40^\circ\text{C}$  and then adding the amount of bacterial suspension. The

compound were dissolved in methanol in 500 and 1000ppm concentrations.

Paper disc of Whatman No.1 filter paper with a diameter of 5mm. were soaked in these solutions of varied concentrations. The discs were dried and placed on the medium previously seeded with the organism in Petriplates at suitable distances. The Petriplates were stored in an incubator at  $28\pm 2^\circ\text{C}$  for 24 hours. The zone of inhibition, thus formed around each disc containing the test compounds, was measured accurately in mm. The organisms used in the present investigations included *Escherichia coli*(-) and *Staphylococcus aureus*(Table 5).

**Table 5. Bactericidal screening data of ligand and Complexes**

Compound	Diameter of inhibition zone after 24 hrs. at $28 \pm 2^\circ\text{C}$			
	Escherichia coli(-) (conc. in ppm)		Staphylococcus aureus (+) (conc. in ppm)	
	500	1000	500	1000
$\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_2$	2	4	4	6
$[\text{Sn}(\text{C}_{16}\text{H}_{20}\text{N}_4)\text{Cl}_2]$	5	8	7	8
$[\text{Sn}(\text{C}_{15}\text{H}_{19}\text{N}_5)\text{Cl}_2]$	9	11	11	13
$[\text{Sn}(\text{C}_{14}\text{H}_{25}\text{N}_5)\text{Cl}_2]$	3	6	5	7
$[\text{Sn}(\text{C}_{20}\text{H}_{22}\text{N}_4)\text{Cl}_2]$	12	13	13	15
Streptomycin	17	18	15	17

**Table 6. Fungicidal Screening Data of ligand and its Complexes**

Compound	Average Percentage in inhibition after 4 days					
	Fusarium oxysporum			Macrophomina phaseolina		
	50	100	200	50	100	200
$\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_2$	31	43	52	26	38	47
$[\text{Sn}(\text{C}_{16}\text{H}_{20}\text{N}_4)\text{Cl}_2]$	52	67	71	46	58	60
$[\text{Sn}(\text{C}_{15}\text{H}_{19}\text{N}_5)\text{Cl}_2]$	69	71	79	55	63	74
$[\text{Sn}(\text{C}_{14}\text{H}_{25}\text{N}_5)\text{Cl}_2]$	37	52	66	32	46	59
$[\text{Sn}(\text{C}_{20}\text{H}_{22}\text{N}_4)\text{Cl}_2]$	73	77	82	62	71	80
Bavistin	85	100	100	82	100	100

### Antifungal Activity

The antifungal activities were evaluated by Radial Growth Method using Czapek's agar medium [24], having the composition glucose-20g, starch-20g, agar-agar-20g and distilled water 1000ml., which was prepared in a flask and sterilized. The requisite amount of the compound, after being dissolved in methanol so as to get a certain concentration (50,100,200ppm.) The medium then poured into the petriplates and a small disc (0.7cm.) of the fungus culture was cut with a sterile cork borer and transferred aseptically to the centre of a petridish containing the medium with a certain amount of the compound. These Petriplates are wrapped in polythene bags containing a few drops of alcohol and were placed in an incubator at  $25 \pm 2^\circ\text{C}$ . The controls were also run and three replicates were used in each case. The colony diameter, after 96 hours, compared with control was taken as a measure of fungitoxicity. The amount of growth inhibition was calculated by the equation.  $100(d_c - d_t)/d_c$ , where  $d_c$  and  $d_t$  are the diameter of the fungus colony in the control and test plates, respectively. The organism used in these investigations included *Fusarium oxysporum* and *Macrophomina phaseolina*. (Table 6).

The results recorded in Tables 5 and 6 pointed out that the complexes have greater inhibiting power than other compounds, it can possibly be concluded that the chelation as well as the addition of a substrate enhance the activity of complexes.

However the fungicide & bactericides do react readily with M-N bonds. At lower concentration, inhibition is less severe, the activities of the organism will only be slowed down and it may be able to grow at a slow rate, while at higher concentration, more enzymes will become inhibited leading to a quicker death of the organism. As currently viewed, all fungicides or bactericides are metabolic inhibitors; that is, they block some vital metabolic process [25-26]. Organic fungicides are extremely efficient, most of them newer fungicides also have very low phytotoxicity and most of them readily degraded thus prevented their accumulation in soil. Fungicidal and bacterial action is expressed in one of two physically visible ways [25].

- 1) The inhibition of spore germination
- 2) The inhibition of fungus growth.

Most fungicides prevent spore germination or kill the spore immediately following germination. Some of these chemical inhibitors or toxicants also retard or halt fungus growth when applied after the infectious stage has developed. The newer systemic fungicides have eradicant properties and stop the progress of existing infections. Since the metal complexes inhibit the growth of microorganisms it is assumed that production of the ATP [27] and enzymes is being affected as microorganisms is unable to utilize food for itself or intake of nutrients decreases and consequently growth diminishes.

### 4.3 Antifertility Activity

The salts of transition [28]. A large number of these complexes [29] have been shown to cause atrophy of testis, prostate and epididymis in male mice have been undertaken Twenty adult male mice (body weight 40-50g )were divided into four groups of five animals each. The animals were kept in plastic cages 10inx8inx8in,25cm x20cmx20cm and three animals were housed in each case. The animals fed pellets and tap water was provided ad libitum. of four groups, one was used as a control group received 0.2 cm<sup>3</sup> olive oil day<sup>-1</sup> per animal ,orally. The ligand and its complexes were suspended in olive oil separately and given to animals at adose level of 20mg/kg body weight day<sup>-1</sup> orally by gauge tube for 20 days. Twenty four hours after the administration of the organic moiety and its complexes .A significant decrease ( $p<0.01$ ) in motility from  $79.33\pm2.02$  to  $29\pm3\%$  was observed in the animals treated with ligand and the sperm count also decreased ( $p<0.001$ )from  $28.66 (\pm0.66)\times10^6$  to  $14\pm1.562\times10^6\text{cm}^{-3}$ .A highly significant ( $p<0.001$ )decline in the motility of sperm was observed in the case of tin complexes .This may be due to an interference with enzyme reaction including the oxidative phosphorylation uncoupling. The data recorded in (Table 8) indicate that the ligand and its complexes affect the motility as well as the sperm count in male mice .It could be correlated with loss of total membrane protein and fall in circulating androgen . Further it is also observed that the ligand itself is able to inhibit fertility, but due to the added synergistic effects of tin complexes ,its activity is enhanced. Thus, it can

be postulated that further intensive studies in this direction will lead to quite interesting results.

Values means  $\pm$  SE of six determinations

a=p 0.05group B compared with group A

b=p 0.001 group C and D compared with group B

c=p = NS,group E and F compared

### Fertility Test

The mating exposure tests of all the animals were performed from day 55<sup>th</sup> to 60<sup>th</sup>.They were cohabited with proestrous females in the ratio 1:3.The vaginal plug and the presence of sperm in the sites on day 16<sup>th</sup> of pregnancy through leprotomy.

### Body and Organ Weight

No significant change was observed in the body weight after treatment with the compounds. A significant reduction in the weight of testes, epididymis, seminal vesicle and ventral prostate was observed after treatment with the ligand and compounds.(Table 7)

Values means  $\pm$  SE of six determinations:

a=p 0.05group B compared with group A

b=p 0.001 group C and D compared with group B

c=p=NS group E and F compared

### Sperm Dynamics

Sperm motility in cauda epididymis and sperm density in testes and caudaepididymis were significantly reduced after treatment with both the ligand and their compounds.(Table 8)

**Table 7.Changes in the body weight of reproduction organs after treatment with various compounds.**

Group	Treatment	Body weight (gm)		Testes Epididymis mg/100gm body wt.		Ventral Prostate	Seminal Vesicle
		Initial	Final				
A	Control	250 $\pm$ 16	265 $\pm$ 10 <sup>c</sup>	1355 $\pm$ 40	610 $\pm$ 15	325 $\pm$ 10	680 $\pm$ 20
B	C <sub>10</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	235 $\pm$ 9	243 $\pm$ 11	1125 $\pm$ 20 <sup>c</sup>	515 $\pm$ 20 <sup>a</sup>	290 $\pm$ 15 <sup>c</sup>	570 $\pm$ 10 <sup>a</sup>
C	[Sn(C <sub>16</sub> H <sub>20</sub> N <sub>4</sub> )Cl <sub>2</sub> ]	225 $\pm$ 9	232 $\pm$ 12 <sup>c</sup>	1040 $\pm$ 30 <sup>b</sup>	455 $\pm$ 10 <sup>b</sup>	210 $\pm$ 15 <sup>b</sup>	555 $\pm$ 12 <sup>b</sup>
D	[Sn(C <sub>15</sub> H <sub>19</sub> N <sub>5</sub> )Cl <sub>2</sub> ]	247 $\pm$ 11	253 $\pm$ 14	1020 $\pm$ 20 <sup>b</sup>	435 $\pm$ 15 <sup>b</sup>	195 $\pm$ 10 <sup>b</sup>	500 $\pm$ 9 <sup>b</sup>
E	[Sn(C <sub>14</sub> H <sub>25</sub> N <sub>5</sub> )Cl <sub>2</sub> ]	238 $\pm$ 10	24 $\pm$ 7 <sup>c</sup>	900 $\pm$ 35 <sup>b</sup>	410 $\pm$ 10 <sup>b</sup>	176 $\pm$ 5 <sup>b</sup>	550 $\pm$ 15 <sup>b</sup>
F	[Sn(C <sub>20</sub> H <sub>22</sub> N <sub>4</sub> )Cl <sub>2</sub> ]	215 $\pm$ 15	223 $\pm$ 13 <sup>c</sup>	889 $\pm$ 20 <sup>b</sup>	400 $\pm$ 20 <sup>b</sup>	150 $\pm$ 10 <sup>b</sup>	458 $\pm$ 8 <sup>b</sup>

**Table 8.Antifertility activity after treatment with ligand and their complexes**

Group	Treatment	Sperm motility (%) Cauda Epididymis	Sperm Density (Million/ml) Cauda Testes Epididymis		Fertility (%)
A	Control	76.4 $\pm$ 2.2	4.5 $\pm$ 0.26	57.2 $\pm$ 4	100
B	C <sub>10</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	63.6 $\pm$ 7.0 <sup>a</sup>	2.8 $\pm$ 0.4 <sup>b</sup>	48 $\pm$ 2.0 <sup>b</sup>	86
C	[Sn(C <sub>16</sub> H <sub>20</sub> N <sub>4</sub> )Cl <sub>2</sub> ]	48 $\pm$ 4.0 <sup>b</sup>	1.8 $\pm$ 0.03 <sup>b</sup>	33 $\pm$ 1.0 <sup>b</sup>	92
D	[Sn(C <sub>15</sub> H <sub>19</sub> N <sub>5</sub> )Cl <sub>2</sub> ]	42 $\pm$ 5.0 <sup>b</sup>	1.6 $\pm$ 0.02 <sup>b</sup>	27 $\pm$ 3.0 <sup>b</sup>	93
E	[Sn(C <sub>14</sub> H <sub>25</sub> N <sub>5</sub> )Cl <sub>2</sub> ]	35 $\pm$ 3.7 <sup>b</sup>	1.0 $\pm$ 0.2 <sup>b</sup>	22 $\pm$ 3.3 <sup>b</sup>	96(-ve)
F	[Sn(C <sub>20</sub> H <sub>22</sub> N <sub>4</sub> )Cl <sub>2</sub> ]	32 $\pm$ 3.0 <sup>b</sup>	0.9 $\pm$ 0.2 <sup>b</sup>	16 $\pm$ 1.0 <sup>b</sup>	96(-ve)

**Biochemical parameters leading to infertility****Total Protein**

Treatment with the ligands as well as their complexes resulted in a significant reduction in the total protein contents of testes, epididymis, seminal vesicle and ventral prostate (Table 9)

**Sialic Acid**

A significant reduction in sialic acid contents of testes, epididymis, seminal vesicle and ventral prostate was observed after the treatment in all experimental groups.(Table 9)

**Cholesterol**

Cholesterol contents of testes were decreased significantly in all experimental groups. (Table 10)

**Fructose**

A significant decrease in the seminal vesicular fructose was noticed in all experimental groups(Table 10).

**Glycogen**

Testicular glycogen was depleted significantly in all experimental groups(Table 10). Present study showed that oral administration of  $\text{SnCl}_2 \cdot \text{C}_4\text{H}_6\text{O}_2$  and their complexes resulted in the reduction of weight of testes, epididymis, seminal vesicle and ventral prostate. The weight, size and secretory activities of sex accessories are closely regulated by androgen levels. Reduction in sperm density and motility in cauda epididymis is of importance with regards to fertilization. Significant reduction in the sperm motility and sperm density was observed in treated animals. This may be due to inhibitory effect of these compounds on the enzyme oxidative phosphorylation [30]. In our study various androgen dependent parameters that is total protein sialic acid, fructose, cholesterol and glycogen revealed a significant decrease indicating that administration of these compounds resulted in the fall of circulating androgen [31,32]. It is inferred that compounds of Sn are found to be more effective than the starting materials in inhibiting the fertility.

**Table 9.Effects of various complexes on total protein and sialic acid contents of various reproductive organs of male rats**

Group	Treatment	Testes	Total protein (mg/gm) Epididymis	Ventral Prostate	Seminal Vesicle	Testes	Sialic Acid(mg/gm) Epididymis	Ventral Prostate	Seminal Vesicle
A	Control	178±5	270±11	168±8	192±100	4.5±0.4	6.1±0.1	5.4±0.2	4.5±0.2
B	$\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_2$	160±2 <sup>a</sup>	218±15 <sup>a</sup>	148±5 <sup>a</sup>	155±5 <sup>a</sup>	3.5±0.1 <sup>a</sup>	5.2±0.2 <sup>a</sup>	4.5±0.3 <sup>a</sup>	3.8±0.3 <sup>a</sup>
C	$[\text{Sn}(\text{C}_{16}\text{H}_{20}\text{N}_4)\text{Cl}_2]$	128±11 <sup>b</sup>	185±5 <sup>a</sup>	115±3 <sup>a</sup>	127±2 <sup>b</sup>	2.8±0.2 <sup>b</sup>	4.2±0.02	4.4±0.2 <sup>b</sup>	3.1±0.1 <sup>b</sup>
D	$[\text{Sn}(\text{C}_{15}\text{H}_{19}\text{N}_5)\text{Cl}_2]$	122±6 <sup>b</sup>	152±8 <sup>b</sup>	100±4 <sup>b</sup>	118±5 <sup>b</sup>	2.6±0.11 <sup>b</sup>	3.8±0.01	4.2±0.2 <sup>b</sup>	3.0±0.1 <sup>b</sup>
E	$[\text{Sn}(\text{C}_{14}\text{H}_{25}\text{N}_5)\text{Cl}_2]$	106±12 <sup>b</sup>	132±11 <sup>b</sup>	98±7 <sup>b</sup>	109±8 <sup>b</sup>	2.5±0.3 <sup>b</sup>	3.8±0.02	4.0±0.2 <sup>b</sup>	2.8±0.2 <sup>b</sup>
F	$[\text{Sn}(\text{C}_{20}\text{H}_{22}\text{N}_4)\text{Cl}_2]$	101±16 <sup>b</sup>	112±6 <sup>b</sup>	100±6 <sup>b</sup>	104±7 <sup>b</sup>	2.6±0.04 <sup>b</sup>	3.6±0.3	3.7±0.1 <sup>b</sup>	2.7±0.1 <sup>b</sup>

**Table 10.Changes in Tissue Cholesterol,Glycogen and Fructose Contents after treatment with various complexes in male rats**

Group	Treatment	Testicular Cholesterol (mg/gm)	Testicular Glycogen (mg/gm)	Seminal Vesicular Fructose (mg/gm)
A	Control	7.8±0.2	4.5±0.4	450±15
B	$\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_2$	6.7±0.04 <sup>b</sup>	4.0±0.4 <sup>a</sup>	400±11 <sup>b</sup>
C	$[\text{Sn}(\text{C}_{16}\text{H}_{20}\text{N}_4)\text{Cl}_2]$	6.1±0.04 <sup>b</sup>	3.8±0.06 <sup>b</sup>	320±20 <sup>b</sup>
D	$[\text{Sn}(\text{C}_{15}\text{H}_{19}\text{N}_5)\text{Cl}_2]$	5.9±0.04 <sup>b</sup>	3.7±0.03 <sup>b</sup>	260±15 <sup>b</sup>
E	$[\text{Sn}(\text{C}_{14}\text{H}_{25}\text{N}_5)\text{Cl}_2]$	5.5±0.05 <sup>b</sup>	3.6±0.05 <sup>b</sup>	250±15 <sup>b</sup>
F	$[\text{Sn}(\text{C}_{20}\text{H}_{22}\text{N}_4)\text{Cl}_2]$	5.0±0.08 <sup>b</sup>	3.0±0.05 <sup>b</sup>	210±15 <sup>b</sup>

Cf Table 7

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