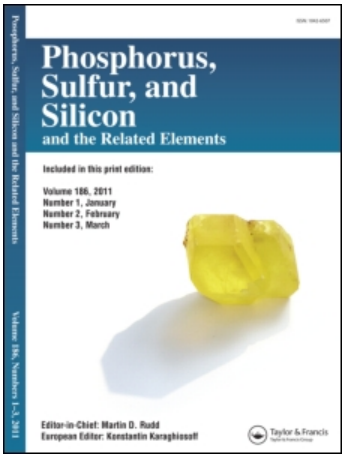

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Sulfur-Bonded Organogermanium (IV) Complexes of Biopotent Bases and Their Antiandrogen and Biocidal Properties

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Sulfur-Bonded Organogermanium (IV) Complexes of Biopotent Bases and Their Antiandrogen and Biocidal Properties

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In the search for the better fungicides, bactericides and antiandrogen agents, studies have been carried out to assess the growth-inhibiting potential of the newly synthesized organogermanium(IV) complexes against various pathogenic fungal and bacterial strains as well as on reproductive organs of the male albino rats. The results of these studies have been compared with the standard fungicide Bavistin *and bactericide* Streptomycin*. The studies demonstrate that the ligands and their trimethylgermanium(IV) complexes have comparable antimicrobial activity. The results also indicated that the weights of the body and vital organs were not affected after the treatment suggesting that the complexes have no side effect or toxicological effect and maintained normal physiology of the animals throughout the experiment. It has also been revealed that the organogermanium(IV) complexes showed more antifertility effect than the bases. These complexes were synthesized by the reactions of trimethylgermanium(IV) chloride with biologically potent N∩SH donor bases and characterized by elemental analyses, conductance measurements, molecular weight determinations and IR, ^{1}H NMR, ^{13}C NMR and electronic spectral studies.*

Keywords Antiandrogen aspect; benzothiazolines and biopotent bases; biocidal properties; triorganogermanium(IV) complexes

INTRODUCTION

With the ever-growing world population, contraception is an important health issue for the 21st century. Fertility is an issue of global and national public issues concerning the rapid growth of the country. The rapid increase of population has an adverse effect on the national economy and as the increase is only limited to the developing countries, the

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problem becomes an acute on the fruits of improvement in the different sectors, which are being eroded by the growing population. Moreover, the increasing number of births has a deleterious effect on the health of mother and child, and it hinders social and economic progress. The regulation of human fertility has global consequences in terms of resources depletion, population, and poverty. Now, it is one of the priorities of the national Family Programs, and therefore, there is an urgent need to improve the access and the quality of contraceptive service in the country. The primary requisite of an antifertility agent for human is that it should be non-toxic, non-teratogenic, and it should not interfere with the normal metabolic and behavioral process. Further, the method should be reversible. Therefore, exhaustive and prolonged studies on the safety and efficacy of contraceptive agents including their effect on progeny in laboratory animals should precede studies on human volunteers. Each contraceptive method has its unique advantages and disadvantages. The success of any contraceptive method depends not only on its effectiveness in preventing pregnancy, but on the rate of continuation of proper use, as well. Currently, there are many methods available for the women including oral contraceptive pills, implants, intrauterine devices, cervical caps, female condom, and tubule legation but for men, contraceptive choices are limited, in contrast to the great variety of female methods men who want to take responsibility for contraception today have only two option condoms and vasectomy (male sterilization). Out of the two male methods, although condoms protect against sexually transmitted disease, many couples find them too inconvenient, expensive, unreliable for long use physiological resistance and a 3–15% failure rate and vasectomy is not reliably reversible and thus are not acceptable for those who may want children in the future. Chemicals can interfere with hormonal control, the male reproductive tract and directly alter the male reproductive tract function. The chemical control of fertility in the male has received attention since quite some time and a large number of synthetic compounds have been tested for their antispermatogenic and antiadrogenic effects.[1] Many simple chemicals have been shown to be capable of affecting epididymal spermatozoa, so that they are useless when ejaculated. Chemically their action probably depends upon donating methyl group to important cell components. Spermatozoa obtained from the epididymis during the sterile phase were non-motile.

The organic germanium has been used clinically in many parts of the world to treat a wide spectrum of illnesses, and has been the subject of extensive research in many disciplines: pathology, biochemistry, pharmacology, immunology, oncology, and neurochemistry. Organic germanium has been used in a broad spectrum of regimes—on its own,

with diet and stress counseling, and as a drug in clinical trials of cancer therapy, in conjunction with chemotherapy, radiation therapy, and surgery. Drawing these sources of information together gives quite a solid overview of the fundamental aspects of organic germanium. Measurement of urinary Ge can detect occupational exposure to inorganic Ge and its compounds. It is prudent to recommend the monitoring of renal variables in workers exposed to germanium.[2] A histological comparison of the liver, spleen, bone marrow, circulating young erythrocytes, and differential count in mature male and female albino rats receiving germanium dioxide with their litter controls not receiving this compound was made.[3] The aim of the present investigations is to find the effect on the testes and accessory sex glands together with metabolic disturbance and disease when exposed to bases and their germanium(IV) complexes; for these findings, the experiments have been done on male albino rats.

EXPERIMENTAL

All the experimental work and handling of the compounds was carried out in the absence of moisture. Chemicals and solvents were dried and purified by the standard methods.

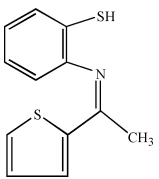
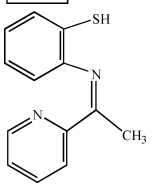
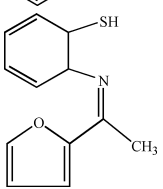
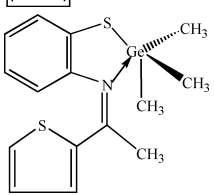
Preparation of the Bases

The bases, i.e. benzothiazolines, L_1H, L_2H, and L_3H used during these investigations were prepared[4] by the condensation of unimolar ratio of [1-(thien-2-yl)ethanone] (5.20 g, 41.20 mmol), [1-(pyridin-2-yl)ethanone] (6.20 g, 51.20 mmol) and [1-(furan-2-yl)ethanone] (5.50 g, 49.20 mmol), respectively with 2-mercaptoaniline (2.78 g, 22.20 mmol, 3.39 g, 27.00 mmol, 3.16 g, 25.20 mmol) in dry ethanol (50 mL)) on a magnetic stirrer for 3–4 h. The crystalline products so obtained were filtered, washed with ethanol, and dried in vacuo for 2 h. Analyses of these bases for carbon, hydrogen, nitrogen, and sulfur agreed with the theoretical values within the limits of experimental errors and the physical properties are given in Table I.

Synthesis of Trimethylgermanium(IV) Complexes

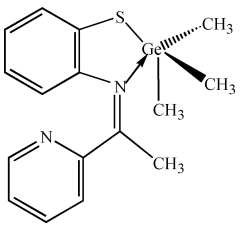
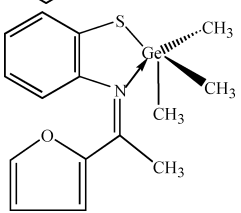
To a weighed amount of trimethyl germanium chloride (1.0 g, 6.52 mmol) was added the requisite amount of the sodium salt (prepared by reacting the base with freshly cut sodium metal in 20 mL dry methanol) (1.66 g, 22.2 mmol, 1.63 g, 26.91 mmol, 1.56 g, 25.2 mmol) of the base in a dry solvent mixture of benzene (20 mL) and methanol (30 mL).

TABLE I Physical Properties and Analytical Data of the Bases and Their Germanium(IV) Complexes

Compound	Empirical Formula	M.P. (°C)	Yield (%)	Analysis (%) C Found (Calcd.)	H Found (Calcd.)	N Found (Calcd.)	S Found (Calcd.)	Ge Found (Calcd.)	Mol. Wt. Found (Calcd.)
	$C_{12}H_{11}NS_2$	85	75	60.80 (61.76)	4.91 (4.75)	6.26 (6.00)	28.30 (27.48)	—	235 (233.35)
	$C_{13}H_{12}N_2S$	87	90	68.74 (68.39)	5.60 (5.29)	12.51 (12.26)	14.54 (14.04)	—	217 (228.31)
	$C_{12}H_{11}NSO$	84	90	65.53 (66.33)	5.64 (5.10)	7.05 (6.44)	15.30 (14.75)	—	225 (217.29)
	$C_{15}H_{19}NS_2Ge$	116	80	51.02 (51.46)	5.85 (5.47)	4.38 (4.00)	18.45 (18.32)	21.00 (20.73)	352 (350.04)

(Continued on next page)

TABLE I Physical Properties and Analytical Data of the Bases and Their Germanium(IV) Complexes *(Continued)*

Compound	Empirical Formula	M.P. (°C)	Yield (%)	Analysis (%) C Found (Calcd.)	H Found (Calcd.)	N Found (Calcd.)	S Found (Calcd.)	Ge Found (Calcd.)	Mol. Wt. Found (Calcd.)
	$C_{16}H_{20}N_2SGe$	102	80	55.48 (55.70)	6.01 (5.84)	7.98 (8.11)	8.97 (9.29)	21.25 (21.04)	336 (345.00)
	$C_{15}H_{19}NSOGe$	108	92	53.00 (53.94)	6.12 (5.73)	4.70 (4.19)	9.68 (9.60)	21.38 (21.73)	305 (333.97)

The reaction mixture was refluxed for 8–9 hours during which a white solid (NaCl) separated out; the contents were then cooled and filtered. Benzene (15 mL) was added to the filtrate and it was again refluxed. The process of refluxing and filtration was repeated two or three times until all the sodium chloride had precipitated. The solvent was then removed by distillation under reduced pressure and the resulting product repeatedly washed with dry *n*-hexane and petroleum ether. It was finally dried in vacuo under reduced pressure. The purity was further checked by TLC using silica gel-G. The details of the physical properties and analytical data of the newly synthesized complexes are recorded in Table I.

Analytical Methods and Physical Measurements

Carbon and hydrogen analyses were carried out at CDRI, Lucknow. Germanium was determined gravimetrically as GeO_2. Nitrogen and sulfur were determined by the Kjeldahl's and Messenger's method, respectively. Molar conductance measurements were made by using Systronic conductivity bridge, Model 305. Molecular weights were determined by the Rast Camphor method. The ^{1}H NMR spectra were recorder on a JEOL FX 90 Q spectrometer in DMSO-d_6 using TMS as the internal standard at 89.55 MHz. ^{13}C NMR spectra were recorded from saturated solutions using DMSO as a solvent at 22.49 MHz on the same instrument. The IR spectra were recorded on a Perkin-Elmer 577 grating spectrophotometer in KBr pellets. The electronic spectra were recorded on a Pye-Unicam SP-8-100 ultraviolet spectrophotometer in the range, 200–500 nm.

Biocidal Activity

The synthesized organogermanium compounds and bases were tested for the in vitro growth inhibitory activity against pathogenic fungi, viz., *Macrophomina phaseolina, Fusarium oxysporum* and *Aspergillus niger* and bacteria, viz., *Staphylococcus aureus*, *Klebsiella aerogenous, Escherichia coli* and *Pseudomonas cepacicola*. Proper temperature, necessary nutrients, and growth media free from other microorganisms were employed for the preparation of cultures of fungi and bacteria using aseptic techniques.[5] The Radial Growth Method and Paper-disc Plate Method were employed to evaluate the antifungal and antibacterial activities,[6] respectively.

Antifungal Activity

A culture of the test fungus was grown on PDA medium (glucose), starch, agar-agar and 1000 mL of H_2O) at $25 \pm 2^\circ$C and the compounds

after being dissolved in 50, 100, and 200 ppm concentrations in methanol were mixed in the medium. The linear growth of the fungus was obtained by measuring the diameter of the colony in petri plates after four days, and the percentage inhibition was calculated by the following relationship : % inhibition = $100(C\text{-}T) \times C^{-1}$, where C and T are the diameters of the fungus colony in check and test plate, respectively.

Antibacterial Activity

The nutrient agar medium (peptone, beef extract, agar-agar, and NaCl) and 5 mm diameter paper discs of Whatman No.1 were used to evaluate bactericidal activity. The compounds were dissolved in dry methanol in 500- and 1000-ppm concentrations. The filter paper discs were soaked in different solutions of the compounds, dried, and then placed in the petri plates previously seeded with the test organism. The plates were incubated for 24–30 hours at $30 \pm 1^{\circ}C$, and the inhibition around each disc was measured.

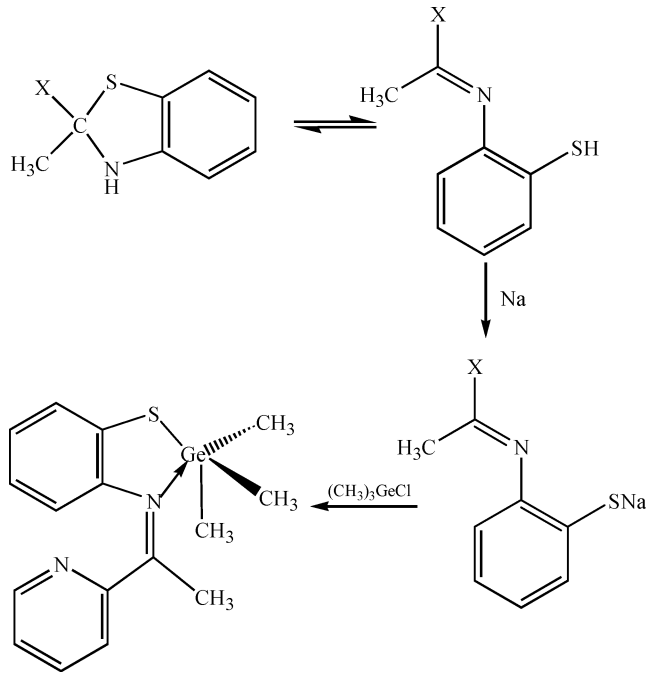
RESULTS AND DISCUSSION

The reactions of trimethyl germanium chloride with the sodium salt of the bases in the solvent mixture of benzene and methanol proceed smoothly with the precipitation of sodium chloride, which was removed by filtration. The complete reaction has been shown with X = pyridine.

All the newly synthesized complexes are colored solids, soluble in most of the common organic solvents and are non-electrolytes (molar conductivity below 13 $ohm^{-1}cm^2mol^{-1}$). These are monomeric in nature (Table I).

Infrared Spectra

The free bases show neither ν(SH) at 2600–2500 cm^{-1} nor ν(C=N) at 1625–1600 cm^{-1} but show NH stretching band at 3350–3150 cm^{-1}. This is an indicative of the benzothiazolines rather than the Schiff base structure.[7] In the spectra of the germanium complexes, bands due to νNH vibrations disappear indicating the chelation of nitrogen with the germanium atom, and a new band at about 1600 cm^{-1} is observed, which may be assigned to the >C=N vibrations. The appearance of this band suggests that the complexes are germanium—Schiff base derivatives, as the benzothiazoline ring opens to give the Schiff base structure in the presence of the germanium atom. Several new bands in the germanium complexes in the regions, 680-660 cm^{-1} and 410–415 cm^{-1} are



SCHEME 1 Synthetic route of the complexes.

due to the Ge←N[8] and Ge-S[9] stretching vibrations, respectively and this further lends support to the proposed coordination.

Ultra-Violet Spectra

The ultra-violet spectra of the bases, benzothiazolines consist of two broad and strong bands around 270 and 315 nm, characteristic of the cyclic form of the bases. The bands were attributed to the $\phi - \phi^*$ and $\pi - \pi^*$ (benzenoid) transitions, respectively.[10,11] These bands do not undergo any change during the complexation. However, an additional band in the organogermanium (IV) complexes is also observed around 400 nm due to the n-π^* electronic transitions of the azomethine group. The appearance of this new band in the complexes clearly indicated the formation of the azomethine grouping on complexation and subsequent isomerization of the bases into the azomethine form.[12]

^{13}C NMR Spectra

The ^{13}C NMR spectra of the bases and their corresponding germanium complexes recorded in dry DMSO are given in Table II. A considerable

TABLE II ^{13}C NMR Spectral Data (δ, ppm) of the Bases and Their Corresponding Trimethylgermanium(IV) Complexes

Compound	C—N/C=N	C—S	—CH_3	Aromatic
L_2H	151.24	139.68	13.15	123.19, 121.75, 120.40, 121.80, 125.81, 126.51, 125.73, 125.63, 125.70, 126.90
$Me_3Ge(L_2)$	170.22	154.13	14.41	124.26, 121.54, 121.13, 121.98, 126.61, 126.64, 126.24, 125.97, 125.63, 126.65
L_3H	148.71	134.46	11.26	123.44, 120.84, 115.56, 115.18, 113.88, 124.54, 126.38, 128.82, 130.18
$Me_3Ge(L_3)$	166.70	152.28	18.64	124.01, 120.70, 121.08, 116.31, 115.86,122.24, 123.67, 12.00, 125.25

change in the chemical shift of carbons attached to nitrogen and sulfur is an indication of the role of these elements in coordination and also an evidence for the pentacoordinated state for germanium, i.e., the signals of C—N group in the bases L_2H and L_3H appeared at δ 151.24 and 148.71 ppm, respectively and which shifted at δ 170.22 and 166.70 ppm in the germanium complexes in the form of C=N which clearly indicated that the benzothiazolines after converting into the Schiff base forms coordinated through the nitrogen atom of the azomethine group. Similarly the shifting of carbon signals of C—S group from δ 139.68 (L_2H) and 134.46 ppm (L_3H) to δ 154.13 (Me_3GeL_2) and 152.28 ppm (Me_3GeL_3), which also indicates the involvement of sulfur atom in bond formation. Based on these observations, it is clear that five bonds have been formed with the germanium atom including one by nitrogen, one by sulfur, and three by methyl groups and thus the complexes are pentacoordinated. Several penta-coordinated complexes have also been reported by other authors in the literature.[13,14]

^{1}H NMR Spectra

The different signals observed in the proton magnetic resonance spectra of the bases and their corresponding organogermanium(IV) complexes have been recorded in Table III. The broad signals due to the NH protons in the bases disappear in the case of the organogermanium(IV) complexes and thus confirms the coordination of the germanium with the nitrogen and sulfur atoms. The methyl proton signals in the bases undergo deshielding and appear at a downfield shifted position in the spectra of the complexes again indicating the coordination of the nitrogen to the germanium atom. The complex multiplet for the aromatic protons also shows a slight downfield shift in the spectra of the organogermanium (IV) complexes.

TABLE III ^{1}H NMR Spectral Data (δ, ppm) of the Bases and Their Corresponding Trimethylgermanium(IV) Complexes

Compound	—NH(S)	$H_3C-\overset{\vert}{C}-N(S)$ or $H_3C-\overset{\vert}{C}=N$	Aromatic (m)	Me_3Ge (s)
L_1H	3.42	3.10	7.36–6.44	—
$Me_3Ge(L_1)$	—	3.46	7.50–6.65	1.08
L_2H	5.40	3.36	7.30–6.75	—
$Me_3Ge(L_2)$	—	3.60	7.50–6.80	0.96
L_3H	5.44	3.40	7.20–6.42	—
$Me_3Ge(L_3)$	—	3.72	7.16–6.60	0.95

s : singlet; and m : multiplet.

Based on these studies, the structures for the bases and their organogermanium(IV), complexes have been shown in Figure 1.

Biological Aspects

Fungicidal and bactericidal activities of the bases and their corresponding organogermanium(IV) complexes against pathogenic fungi and bacteria are recorded in Tables IV and V.

The results are quite promising. The antimicrobial data reveal that the complexes are superior to the free bases. The enhanced activity of the germanium complexes may be ascribed to the increased lipophilic nature of these complexes arising due to the chelation.[15] The activity increased as the concentration was increased. Further, the results of bioactivity were compared with the conventional fungicide *Bavistin* and the conventional bactericide *Streptomycin*, taken as standards in either case.

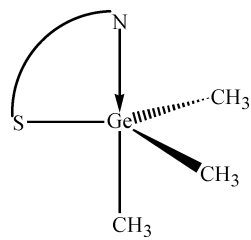


FIGURE 1 Structure of the complexes.

TABLE IV Fungicidal Screening Data of the Bases and Their Respective Trimethylgermanium(IV) Complexes. Average Percentage Inhibition after 96 Hours

	(Conc. in ppm)								
	Macrophomina phaseolina			*Fusarium oxysporum*			*Aspergillus niger*		
Compound	50	100	200	50	100	200	50	100	200
L_1H	23	31	52	31	35	41	38	46	58
$Me_3Ge(L_1)$	36	66	75	48	72	85	56	73	92
L_2H	28	37	52	24	35	58	30	41	54
$Me_3Ge(L_2)$	50	69	84	44	74	86	56	76	95
L_3H	15	24	40	17	27	52	23	31	50
$Me_3Ge(L_3)$	20	35	73	33	42	84	49	69	90
Bavistin	82	100	100	86	100	100	91	100	100

In case of fungicidal activity, it has been observed that all of the organogermanium (IV) complexes were able to inhibit and kill the pathogens at 50-ppm concentration, while at the 100-ppm concentration of only the standard proved invariably fatal. In case of the bactericidal activity, the germanium complexes exhibited remarkable potential in inhibiting the growth of pathogens. It is emphasized that in some cases the complexes were found to be even more active than the standard *Streptomycin* against gram-negative bacteria. Thus, it can be postulated that further intensive studies of these complexes in this direction as well as in agriculture could lead to the interesting results.

TABLE V Bactericidal Screening of the Bases and Their Respective Trimethylgermanium(IV) Complexes. Inhibition after 24 Hours (Conc. in ppm)

	Diameter of inhibition zone (mm)							
	Staphylococcus aureus (+)		*Klebsiella aerogenous (–)*		*Escherichia coli (–)*		*Pseudomonas cepacicola (–)*	
Compound	500	1000	500	1000	500	1000	500	1000
L_1H	6	9	4	5	4	8	5	8
$Me_3Ge(L_1)$	12	16	8	10	7	14	11	14
L_2H	6	8	3	5	5	7	4	6
$Me_3Ge(L_2)$	9	14	8	9	10	13	10	11
L_3H	4	6	2	3	3	4	2	3
$Me_3Ge(L_3)$	7	10	6	7	7	8	6	9
Streptomycin	15	17	3	5	17	18	2	3

Antiandrogen Activity

For checking the efficiency of these compounds as well as the bases, some experiments have been done on male albino rats (*Rattus norvegicus*). The rats selected for these studies were with the weights between 200–250 g. These rats were regularly checked for any disease and if found infected were isolated and treated. The rats were fed on a diet of rat feed pellets obtained from Hindustan Lever Limited, Mumbai and water was provided ad libitum. During, these experiments doses of the bases and their compounds were given orally after mixing in olive oil with the help of hypodermic syringe having pearl point needle for 60 days and withdrawal for 30 days. After the completion of the treatment, the fertility test was done. On day 61, the rats were autopsied and blood was extracted from the heart. The serum was separated and used for serum biochemistry. Reproductive tissues and vital organs were blotted free of blood, weighed and used for the tissue biochemistry observations. The following observations were recorded :

The Body and Organ Weights

The experiments indicated that the body weights of the rats were not much altered after the treatment of the complexes. However, a general decrease in the reproductive organ weights was observed in the weights of the testis ($p < 0.001$), epididymis ($p < 0.001$), was deferens ($p < 0.01$), seminal vesicle ($p < 0.001$) and ventral prostate ($p < 0.01$).

Sperm Dynamics and Fertility

A significant decrease in sperm density in testes and cauda epididymis were observed in the bases and their germanium complexes. Also, the sperm motility in Cauda epididymis was decreased significantly in the bases and their germanium treated rats ($p \leq 0.001$) as shown in Table VI.

Biochemical Changes

When the results of these investigations were compared with the control, the marked reductions in sialic and protein contents of testes, epididymis, ventral prostate and seminal vesicle were deserved in the bases and their organogermanium(IV) complexes treated rats. On the other hand, a sharp increase in testicular cholesterol and acid and alkaline phosphatase contents were observed in various treated

TABLE VI Altered Sperm Dynamics and Fertility after Treatment with the Bases and their Germanium Complexes

Group	Compound	Sperm motility *Cauda epididymis*	Sperm density (million/ml) Testes	Epididymis	Fertility test (%)
A	Control	70.0 ± 6.1	1.90 ± 0.20	51.0 ± 1.85	98 +ve
B	L_1H	45.0 ± 3.2	0.72 ± 0.10	25.0 ± 1.80	75 –ve
C	Me_3Ge (L_1)	48.0 ± 5.0	0.70 ± 0.20	22.0 ± 1.30	96 –ve
D	L_2H	57.0 ± 6.0	0.82 ± 0.11	28.0 ± 1.60	70 –ve
E	Me_3Ge (L_2)	44.0 ± 7.0	0.73 ± 0.10	26.0 ± 1.70-	81 –ve
F	L_3H	61.0 ± 4.0	1.10 ± 0.10	42.0 ± 1.70	65 –ve
G	Me_3Ge (L_3)	50.0 ± 6.0	0.80 ± 0.11	30.0 ± 1.80	75 –ve

Values are mean ± SEM six determinations. Group A compared with Groups B, D, and F; Group C compared with Group B; Group E compared with Group D; and Group G compared with Group F.

groups. Seminal vesicular fructose contents were decreased significantly (Table VII).

What we have done in the present investigations, the bases and their germanium complexes were given to the rats at the dose levels of 9–50 mg/kg/day for sixty days. At the completion of the experiments marked alterations in the weights of testes, epididymis, seminal vesicle, and ventral prostate were observed. Significant decline in the testes weight may be due to the decrease in the number of spermatogenic elements and spermatozoa.[16] Reduction in the weights of sex accessory organs directly support the reduced availability of androgens.[17] Suppression of gonadotropins might have caused decrease in sperm density in testes.[18] Low caudal epididymal sperm density may be due to the changes in the androgen metabolism,[19] and 95% negative fertility may be attributed to lack of forward progression and reduction in the density of spermatozoa and altered biochemical milieu of *Cauda epididymis*. Decline in the total protein concentration in testes and other accessory reproductive organs indicated suppressed androgen activity.[20] Furthermore, reduced contents of sialic acid in various reproductive organs reported herein suggest adverse effects on the metamorphosis and maturational stages of spermatid.[21,22] The rise in the testicular cholesterol contents due to various compounds treatment suggests suppressed androgen biosynthesis.[23] An increase in testicular acid and alkaline phosphatase activities indicates metabolic disturbance and impairment of the functional integrity of the testes.[24] Thus, the present investigations reveal that the bases and their organogermanium(IV) complexes altered the reproductive function of male rats and the complexes are more active

TABLE VII Effects of the Bases and Their Germanium Complexes on Tissue Biochemistry

		Total protein (mg/g)				Sialic acid (mg/g)				Cholesterol	Fructose	Phosphatases (mg/ip liberated/hr/mg tissue)	
Group	Compound	Testes	Epididymis	Seminal vesicle	Ventral prostate	Testes	Epididymis	Seminal vesicle	Ventral prostate	(mg/g) testes	(mg/g) Seminal vesicle	Acid	Alkaline
A	Control	250.0 ± 17.0	230.0 ± 20.0	240.0 ± 18.0	220.0 ± 15.0	7.6 ± 0.7	6.7 ± 0.5	6.9 ± 0.4	6.9 ± 0.6	7.7 ± 0.2	460.0 ± 30.0	2.9 ± 0.18	10.5 ± 0.65
B	L_1H	150.0 ± 15.0	140.0 ± 10.0	128.0 ± 10.0	115.0 ± 12.0	3.8 ± 0.1	3.5 ± 0.1	3.6 ± 0.1	3.7 ± 0.1	12.0 ± 0.7	200.0 ± 13.0	4.8 ± 0.10	17.0 ± 0.60
C	Me_3Ge (L_1)	140.0 ± 10.5	130.0 ± 15.0	118.0 ± 12.0	105.0 ± 11.0	3.0 ± 0.5	3.1 ± 0.1	3.0 ± 0.2	3.0 ± 0.3	12.5 ± 0.8	180.0 ± 15.0	5.2 ± 0.80	18.0 ± 0.90
D	L_2H	145.0 ± 10.8	135.0 ± 13.0	130.0 ± 12.0	150.0 ± 12.0	4.2 ± 0.1	4.1 ± 0.3	4.0 ± 0.1	3.9 ± 0.2	11.7 ± 0.3	260.0 ± 12.0	4.5 ± 0.11	15.1 ± 0.60
E	Me_3Ge (L_2)	130.0 ± 9.5	127.0 ± 13.0	131.0 ± 15.0	140.0 ± 12.0	4.0 ± 0.2	3.7 ± 0.2	3.9 ± 0.1	3.7 ± 0.1	11.9 ± 0.2	240.0 ± 15.0	4.3 ± 0.10	15.8 ± 0.65
F	L_3H	210.0 ± 15.0	180.0 ± 10.0	190.0 ± 10.0	170.0 ± 10.0	6.6 ± 0.3	5.1 ± 0.2	5.2 ± 0.3	5.1 ± 0.5	11.0 ± 0.2	400.0 ± 10.0	3.5 ± 0.10	13.0 ± 0.50
G	Me_3Ge (L_3)	150.0 ± 15.0	135.0 ± 10.0	170.0 ± 10.0	150.0 ± 12.0	4.2 ± 0.1	4.0 ± 0.2	4.2 ± 0.3	4.9 ± 0.2	11.5 ± 0.3	350.0 ± 10.0	4.0 ± 0.11	15.0 ± 0.60

than the bases themselves in inhibiting the fertility in male rats. Thus, these compounds may be good antiandrogen agents.

CONCLUSION

The present study explained the formation of penta-coordinated complexes of germanium and which are scanty in the literature. The new findings of these studies are the biological activity of the present germanium complexes. These complexes show good antiandrogen activity. Further deep studies in the field can open the door for new contraceptives for male in the form of coordination compounds.

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