Spectroscopic Characterization and *in vitro* and *in vivo* Screening of Difluoro-Boron Complexes of NO and NS Donor Ligands

Chitra SAXENA, Ran Vir SINGH,* and Suresh Chand JOSHI†
Department of Chemistry, University of Rajasthan, Jaipur-302004, India
† Reproduction Physiology Section, Department of Zoology, University of Rajasthan, Jaipur-302004, India
(Received August 23, 1993)

Stereochemical and biochemical aspects of some difluoroboron complexes of the types BF_2(NS) and BF_2(NO) with ligands having (NS) and (NO) donor systems have been described. Based on IR, ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and ^{11}B NMR spectral studies, a tetracoordinated state of boron has been established. In order to assess their growth inhibiting potency the ligands and their fluoroboron complexes have been tested *in vitro* against a number of pathogenic fungi and bacteria at different concentrations and were found to possess remarkable fungicidal and bactericidal properties. The testicular morphology, testicular sperm density, sperm motility, density of cauda epididymal spermatozoa, and fertility in mating trails and biochemical parameters of reproductive organs with 2-acetylthiophene thiosemicarbazone, 2-acetylnaphthalene semicarbazone, and their fluoro complexes *in vivo* have also been examined and discussed.

Semicarbazones and thiosemicarbazones are probably the most intriguing nitrogen and oxygen or sulfur donor ligands.[1,2] Depending on reaction conditions, these compounds may act as neutral or charged ligand moieties.[3,4] Several references are available for their anticarcinogenic,[5] tuberculostatic[6] antibacterial[7] and antifungal[8] activities. Boron complexes of these ligands have been found to possess conspicuous biocidal activity.[9] It is however, interesting that the biological activity gets enhanced on undergoing complexation with the metal ions.[10,11] As a part of our continuing interest in the synthesis of fluoroboron complexes of biologically active ligands, we now report the synthesis and characterization of such complexes by the reactions of boron trifluoride–acetic acid (1/2) with semicarbazones and thiosemicarbazones of heterocyclic ketones. Some ligands and corresponding fluoro complexes have been screened for their antifungal, antibacterial and antifertility behavior and a comparative account of these activities (ligand vs. complex) and structure–activity relationship have been incorporatd in the results.

Experimental

The experimental procedures and method for the preparation of ligands are same as reported elsewhere.[9,10]

Synthesis of Difluoroborn Complexes. The fluoroboron complexes were prepared by the reactions of boron trifluoride–acetic acid (1/2) with the ligands in 1:1 molar ratio in presence of dry acetic anhydride. The reaction proceeded smoothly with the elimination of HF and AcOH. The resulting products were recrystallized from methanol–ether (1:1) mixture and finally dried in vacuo. The important physical properties and analytical data of the difluoroboron complexes are given in Table 1.

Biological Screening. Some of the synthesized ligands and their corresponding boron complexes were tested for the *in vitro* growth inhibitory activity against pathogenic fungi, viz., *Macrophomina phaseolina*, *Fusarium oxysporum* and bacteria, viz., *Pseudomonas cepacicola*, *Escherichia coli*, and *Klebsiella aerogenous*. Proper temperature, necessary nutrients and growth media free from other microorganisms were empolyed for the preparation of cultures of fungi and bacteria using aseptic techniques.[12]

Antifungal Activity. The fungi were grown in agar medium (glucose starch, agar-agar and 1000 ml of water) at 25±2°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 colony in petriplates after four days and the percentage inhibition was calculated by the following relationship, % inhibition$=(C-T)\times 100\times C^{-1}$, C and T are the diameters of the fungus colony in control and test plate, respectively.

Antibacterial Activity. The bactericidal activity was evaluated by the paper-disc plate method. The nutrient agar medium (peptone, beef extract, NaCl and agar agar) and 5 mm diameter paper discs of Whatman No. 1 were used. 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 petriplates previously seeded with the test organism. The plates were incubated for 24—30 h at 28±2°C and the inhibition zone around each disc was measured.

Results and Discussion

Reactions of boron trifluoride–acetic acid (1/2) with these ligands have been carried out in 1:1 molar ratio in dry acetic anhydride. These reactions proceed with the liberation of HF and AcOH.

$$BF_3\cdot 2AcOH + SCZH \longrightarrow BF_2(SCZ) + HF + 2AcOH$$
$$BF_3\cdot 2AcOH + TSCZH \longrightarrow BF_2(TSCZ) + HF + 2AcOH$$

These reactions are quite facile and can be completed in 8—10 h of refluxing. The resulting difluorosemicarbazonato and thiosemicarbazonato complexes of boron are slightly soluble in methanol and chloroform and soluble in DMSO. The complexes are monomeric in nature as indicated by the molecular weight determinations. The low molar conductance values (7—15

Table 1. Analyses and Physical Properties of Difluoroboron Complexes

Product and Color	Mp °C	Yield %	Analyses(%)Found(Calcd) B	N	S	Mol. Wt. Found (Calcd)
BF_2(AcFuran·TSCZ)	96	68	4.36	18.24	13.54	204
Brown			(4.68)	(18.19)	(13.88)	(231)
BF_2(AcFuran·SCZ)	103	74	5.18	19.48	—	267
Dark yellow			(5.03)	(19.55)		(215)
BF_2(AcThiop·TSCZ)	124	86	4.16	17.15	25.68	218
Brown			(4.37)	(17.00)	(25.95)	(247)
BF_2(AcThiop·SCZ)	109	88	4.52	18.05	13.79	268
Brown			(4.68)	(18.19)	(13.88)	(231)
BF_2(AcPyd·TSCZ)	128d	79	4.34	22.98	13.31	278
Dark brown			(4.47)	(23.15)	(13.25)	(242)
BF_2(AcPyd·SCZ)	112d	82	4.49	24.87	—	248
Dark brown			(4.78)	(24.79)		(226)
BF_2(AcNaph·TSCZ)	152	75	3.56	14.55	11.07	310
Dark brown			(3.71)	(14.43)	(11.01)	(291)
BF_2(AcNaph·SCZ)	128	80	3.79	15.39	—	298
Brown			(3.93)	(15.28)		(275)

$ohm^{-1}\,cm^2\,mol^{-1}$) reveal the nonelectrolytic nature of the synthesized complexes.

In the IR spectra of ligands a sharp band in the region 1610—1595 cm^{-1} due to >C=N group[13] shifts slightly towards higher frequency in the difluoroboron complexes indicating the coordination of the azomethine nitrogen to the boron atom. This is further supported by the presence of a new band[14] at 1570—1540 cm^{-1} due to B←N. New bands in the spectra of fluoro derivatives at 1350—1330, 1240—1210, and 780—755 cm^{-1} can be assigned to ν_{B-O},[15] ν_{B-F},[16] and ν_{B-S}[17] vibrations, respectivley. The medium intensity bands exhibited in the region 3250—3100 cm^{-1} can be assigned to ν_{NH}[18] of the free ligands, which disappear in the boron complexes suggesting the possible loss of a proton on the α-nitrogen.

The ^1H NMR spectra of some of the ligands and their difluoro boron complexes have been recorded in DMSO-d_6 (Table 2). The following structural inferences have been drawn by comparing the spectra of the ligands with those of the corresponding difluoro boron derivatives.

The disappearance of the –NH resonance signals of the ligands in the case of fluoroboron complexes provide evidence for the complexation through this functional group. In the spectra of complexes, the downfield shift in the position of $H_3C-\underset{|}{C}=N$ protons also indicates the coordination of azomethine nitrogen to the boron atom. The aromatic proton resonance signals of the ligands are also observed at a slightly downfield shifted position in the case of the corresponding boron derivatives.

The ^{13}C NMR spectra of AcThiop·SCZH and AcPyd·TSCZH and their difluoroboron complexes were recorded in DMSO (Table 3). A considerable change in the chemical shifts of both the C=O/C=S carbon and the azomethine carbon clearly indicates the bonding of oxygen or sulfur and nitrogen to the boron atom.

The ^{11}B and ^{19}F NMR spectra of all the difluoroboron complexes, recorded in DMSO-d_6 using BF_3·Et_2O and C_6F_6 as external standards for boron and fluorine, respectively, are listed in Table 4.

The ^{11}B NMR spectra give signals which range between δ=1.58—7.47 and the ^{19}F shifts of the BF_2 entity are found in the range between δ=−142.25 to −152.15. Both the values are in good agreement with the previously reported[19,20] values, indicating coordination number four in these complexes around the boron atom. Nöth and co-workers have also reported similar data for a number of boron complexes with N and S donor ligands.[21]

On the basis of the foregoing studies, it can be inferred that the imines behave as monobasic bidentate ligands and accordingly the difluoroboron complex with tetracoordinated environment around boron atom with 2-acetylthiophene thiosemicrabazone as the ligand may have the following structure (Chart 1):

Microbial Assay. Fungicidal and bactericidal activities of various heterocyclic ligands and their corresponding difluoroboron complexes against different fungi and bacteria have been recorded in Tables 5 and 6.

It is clear from the fungicidal and bactericidal screening data that the non-metal complexes were more toxic in comparison to their parent ligand itself.

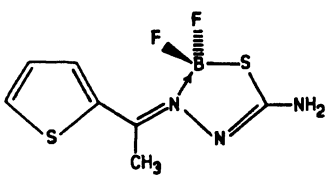

Chart 1.

Table 2. ^{1}H NMR Spectal Data (δ/ppm) of Ligands and Their Difluoro Boron Derivatives

Compound	–NH(b)	$-NH_2$(b)	Aromatic(m)	$-CH_3$(s)
AcFuran·TSCZH	9.90	2.83	7.80—6.60	1.80
BF_2(AcFuran·TSCZ)	—	2.80	8.48—7.24	2.12
AcFuran·SCZH	10.90	2.32	7.68—6.64	1.72
BF_2(AcFuran·SCZ)	—	2.36	7.96—7.08	2.08
AcThiop·TSCZH	10.68	2.81	8.68—7.16	1.68
BF_2(AcThiop·TSCZ)	—	2.84	8.92—7.48	1.96
AcThiop·SCZH	9.68	2.80	7.84—7.20	2.32
BF_2(AcThiop·SCZ)	—	2.84	8.56—7.80	2.40
AcPyd·TSCZH	10.64	2.84	8.92—7.48	1.82
BF_2(AcPyd·TSCZ)	—	2.88	9.24—7.92	2.08
AcPyd·SCZH	9.83	2.12	7.93—7.34	1.80
BF_2(AcPyd·SCZ)	—	2.10	8.32—7.64	2.12
AcNaph·TSCZH	10.65	2.90	8.93—7.55	1.91
BF_2(AcNaph·TSCZ)	—	2.92	9.08—7.96	2.16
AcNaph·SCZH	10.60	2.88	8.64—7.56	1.88
BF_2(AcNaph·SCZ)	—	2.92	8.80—7.92	2.40

Table 3. ^{13}C NMR Spectral Data (δ/ppm) of Ligands and Their Corresponding Difluoroboron Complexes

Compound	Amido/Thiolo carbon	Azomethine carbon	Methyl carbon	Aromatic carbons				
AcThiop·SCZH	178.62	145.35	13.17	140.31	125.37	126.45	126.70	
BF_2(AcThiop·SCZ)	170.16	141.96	14.30	140.26	126.55	128.48	128.90	
AcPyd·TSCZH	179.19	156.20	11.33	147.52	123.04	119.89	135.50	146.88
BF_2(AcPyd·TSCZ)	172.64	149.53	13.56	147.68	123.44	120.12	135.48	146.82

Table 4. ^{11}B and ^{19}F NMR Spectral Data (δ/ppm) of BF_3·2AcOH and Its Difluoroboron Derivatives

Compound	^{11}B	^{19}F
BF_3·2AcOH	1.19	−144.21
BF_2(AcFuran·TSCZ)	2.28	−144.35
BF_2(AcFuran·SCZ)	1.58	−152.15
BF_2(AcThiop·TSCZ)	5.24	−147.49
BF_2(AcThiop·SCZ)	7.47	−145.41
BF_2(AcPyd·TSCZ)	2.18	−146.25
BF_2(AcPyd·SCZ)	2.26	−146.38
BF_2(AcNaph·TSCZ)	2.52	−150.25
BF_2(AcNaph·SCZ)	2.20	−148.56

Mode of Action: It is seen that the complexes are inhibiting the growth of fungi and bacteria to a greater extent as the concentration is being increased. Potato dextrose agar media(PDA) rich in carbohydrates is serving as the major nutrient source, is utilized by the fungus or bacteria with the help of various enzymes (viz. amylase, pectinase, cellulase etc.). These extracellular enzymes secreted by these microorganisms ooze out from the membrane of fungus or bacteria into the medium and lead to the breakdown of complex polysaccharides into simpler monosaccharides. Further, these enzymes turn complex proteins to simpler proteins. These are then untilized by the respective bacteria or fungus.

Since, the complexes are inhibiting the growth of microorganisms it is assumed that the complexes are affecting the production of these enzymes, as a result of it the fungus or bacteria is unable to draw some nutrition for itself or the intake of food is decreased and consequently the growth is ceased. At lower concentrations, when the enzyme leaches out, the growth of microorganisms is arrested. Though the enzyme production is being affected, but that little amount produced is sufficient to suffice the need of the microorganisms to grow, whilst higher concentration proves fatal/toxic to microorganisms. It destroys the enzyme mechanism by blocking any of the metabolic pathway (viz. lipid, carbohydrate, amino acid) and hence due to lack of availability of proper food the microorganism dies.

The mechanism of toxicity of these non-metal complexes to micro-organisms may also be due to inhibition of respiration or by uncoupling of oxidative phosphorylation and the disruption of cell structure or the permeability of the affected cell membrane resulting in leakage of cell contents/enzymes.

Though, these compounds are stable in open atmosphere and sparingly soluble in H_2O but on prolong keeping in H_2O they occupy $[BF_2\cdot L(OH)]^-$ (LH= ligand molecule) type of structure and which is later on accumulated by the fungal cells. These ions are denaturing the proteins. Enzymes are proteins and it is expected that nonmetal inactivate these catalysts. However, not all enzymes are equally inactivated by low concentrations of these non-metallic complexes, there-

Table 5. Fungicidal Screening Data of Ligands and Their Difluoroboron Complexes

Compound	Average percentage inhibition after 96 h					
	Macrophomina phaseolina			*Fusarium oxysporum*		
	Concn in ppm					
	50	100	200	50	100	200
AcFuran·TSCZH	30	41	47	32	44	52
BF_2(AcFuran·TSCZ)	38	54	69	41	56	72
AcFuran·SCZH	15	28	42	12	30	32
BF_2(AcFuran·SCZ)	27	35	57	29	41	47
AcThiop·TSCZH	35	45	50	34	56	60
BF_2(AcThiop·TSCZ)	42	68	88	46	64	84
AcThiop·SCZH	6	17	38	7	16	29
BF_2(AcThiop·SCZ)	18	47	71	41	56	74
AcPyd·TSCZH	33	47	52	30	55	61
BF_2(AcPyd·TSCZ)	40	58	74	37	63	70
AcPyd·SCZH	22	36	44	18	34	46
BF_2(AcPyd·SCZ)	34	52	65	37	49	64
AcNaph·TSCZH	34	45	52	32	54	58
BF_2(AcNaph·TSCZ)	48	60	82	44	63	88
AcNaph·SCZH	27	42	48	20	51	66
BF_2(AcNaph·SCZ)	50	62	87	50	60	94
Bavistin	82	100	100	86	100	100

Table 6. Bactericidal Screening Data of Ligands and Their Difluroboron Complexes

Compound	Diameter of inhibition zone (mm) after 24 h							
	Pseudomonas cepaciola (−)		*Klebsiella aerogenous* (−)		*Escherichia coli* (−)		*Staphylococcus aureus* (+)	
	Concn in ppm							
	500	1000	500	1000	500	1000	500	1000
AcFuran·TSCZH	3	5	4	6	3	5	4	6
BF_2(AcFuran·TSCZ)	4	7	5	8	—	7	6	9
AcFuran·SCZH	2	3	3	5	3	5	3	6
BF_2(AcFuran·SCZ)	—	6	4	7	5	6	4	8
AcThiop·TSCZH	5	10	4	8	4	6	6	11
BF_2(AcThiop·TSCZ)	9	13	8	14	7	11	10	14
AcThiop·SCZH	3	8	4	7	3	5	5	10
BF_2(AcThiop·SCZ)	6	10	8	11	7	9	9	12
AcPyd·TSCZH	3	5	4	7	3	5	4	7
BF_2(AcPyd·TSCZ)	5	8	7	11	6	9	8	13
AcPyd·SCZH	2	4	3	6	3	4	4	6
BF_2(AcPyd·SCZ)	—	7	5	10	5	8	6	11
AcNaph·TSCZH	4	6	4	8	3	5	5	7
BF_2(AcNaph·TSCZ)	9	12	7	13	8	11	9	14
AcNaph·SCZH	4	5	3	6	2	5	4	6
BF_2(AcNaph·SCZ)	8	12	7	11	—	7	8	13
Streptomycin	2	3	3	5	1	2	15	17

fore, low concentration seems to be less effective against growth.

The enzymes which require free mercapto (−SH) groups for activity appear to be especially susceptible to inactivation by ions of the non-metal. Due to greater lipid solubility, the complexes facilitate their diffusion through the spore membrane to the site of action within spores and ultimately killing them by combining with mercapto (−SH) groups of certain enzymes.

It is clear from fungicidal and bactericidal screening data that under identical experimental conditions all the boron complexes are more toxic than their parent ligands against the same microorganism. However, none of the ligands or boron compounds possessed better inhibitory action than the conventional fungicide, 2-(methoxycarbomoly)-benzimidazide which was utilized for comparing the results. On the other hand all the boron compounds are more active against gram negative strain bacteria than the conventional bactericide, streptomycin used as standard. Over all the boron compounds are superior than the parent ligands and the superiority varied from 7—30%.

Antifertility Activity. Experimental Design: Forty adult male albino rats of inbred colony housed

Table 7. Changes in the Body Weights and Organs Weights of Reproductive Organs after Treatment with Ligands and Their Complexes

Treatment	Body weight (g)		Organ weight mg/100 g body weight			
	Initial	Final	*Testes*	*Epididymis*	*Seminal vesicle*	*Ventral prostate*
Control	190.0± 12.0	220.0± 9.50	1050.00± 70.50	400.00± 28.50	340.00± 27.80	250.75± 30.50
AcThiop·TSCZH	180.0± 15.0	215.0± 10.5[c]	805.0± 50.0[a]	345.0± 20.5[a]	300.0± 10.0[a]	200.0± 10.7[a]
BF_2(AcThiop·TSCZ)	193.0± 17.0	228.0± 10.5[c]	710.0± 30.0[b]	280.0± 20.7[b]	270.0± 10.0[b]	170.0± 10.2[b]
AcNaph·SCZH	187.0± 15.0	221.0± 8.5[c]	705.0± 15.3[b]	255.0± 21.3[b]	275.0± 8.9[b]	159.0± 13.0[b]
BF_2(AcNaph·SCZ)	185.0± 15.0	220.0± 7.3[c]	650.0± 20.5[b]	190.0± 10.3[b]	270.0± 10.8	150.0± 10.3[a]

a) $p \leq 0.05$, b) $p \leq 0.001$, c) Non significant. Values means ± SE of six determinations.

Table 8. Altered Sperm Dynamics and Fertility Test after Treatment with Ligands and Their Boron Complexes

Treatment	Sperm density (million/ml)		Sperm motility	Fertility test
	Testes	*Epididymis*	*Cauda epididymis*	%
Control	1.75±0.09	45.52±1.50	72.0±5.21	95(+ve)
AcThiop·TSCZH	0.93±0.10[b]	35.0±0.5[a]	51.0±3.7[b]	70(−ve)
BF_2(AcThiop·TSCZ)	0.80±0.15[b]	29.0±0.5[b]	45.0±3.4[b]	80(−ve)
AcNaph·SCZH	0.83±0.13[a]	30.3±0.3[b]	49.0±3.2	75(−ve)
BF_2(AcNaph·SCZ)	0.61±0.15[b]	20.0±0.3[b]	41.0±2.1	95(−ve)

a) $p \leq 0.05$, b) $p \leq 0.001$. Values means ± SE of six determinations.

Table 9. Effects of Ligands and Boron Complexes on Various Biochemical Parameters of Reproductive Organs

Treatment	Fructose (mg/g)	Total cholesterol (mg/g)	Total protein (mg/g)				Sialic acid (mg/g)			
	Seminal vesicle	*Testes*	*Testes*	*Epididymis*	*Seminal vesicle*	*Ventral prostate*	*Testes*	*Epididymis*	*Seminal vesicle*	*Ventral prostate*
Control	450.0± 30.0	7.30± 0.52	225.0± 17.0	205.0± 19.3	250.0± 10.8	230.0± 20.5	7.30± 0.9	6.30± 1.2	6.80± 1.3	6.90± 0.5
AcThiop·TSCZH	360.0± 40.0[a]	8.1± 0.20[a]	150.0± 13.0[a]	170.0± 11.3[a]	190.0± 15.35[a]	185.0± 15.35[a]	5.80± 0.7[a]	4.90± 1.3[b]	5.0± 0.8[a]	5.1± 0.3[a]
BF_2(AcThiop·TSCZ)	320.0± 21.5[b]	8.4± 0.30[b]	130.0± 10.5[b]	155.0± 10.5[b]	147.5± 13.8[b]	150.0± 17.3[b]	4.30± 0.8[b]	4.1± 1.5[b]	4.0± 1.3[b]	4.20± 0.4[b]
AcNaph·SCZH	330.0± 32.0[b]	8.6± 0.25[b]	135.0± 10.3[b]	160.0± 10.1[b]	160.0± 11.7[b]	156.0± 11.5[b]	4.90± 0.3[b]	4.6± 1.3[b]	4.2± 1.5[b]	4.7± 0.7[b]
BF_2(AcNaph·SCZ)	290.0 15.0[b]	9.1± 0.35[b]	120.0± 10.5[b]	120.0± 7.9[b]	140.0± 13.5	115.0± 10.1[b]	3.50± 0.6[b]	3.4± 1.1[b]	3.0± 0.8[b]	3.20± 0.6[b]

a) $p \leq 0.05$, b) $p \leq 0.001$. Values means ± SE of six detrminations.

in air conditioned animal room at 24±2°C with 14 h light. Water and food was given *ad libitum*. They were divided into five groups containing eight animals each. The first group served as vehicle (olive oil) treated control. In the second group ligand (AcThiop·TSCZH) 50 mg kg^{-1} body weight suspended in 0.2 ml olive oil, was given orally for a period of 60 d. The animals of groups, third, fourth and fifth, received same dose of compounds, BF_2(AcThiop·TSCZ), AcNaph·SCZH and BF_2(AcNaph·SCZ), respectively, for the similar period. The animals were screened for fertility test and autopsized for determination of detailed biochemical studies.

Reproductive organs were excised, bloted free of blood, weighed and were frozen for biochemical estimations. The sperm motility and density of cauda epididymal spermatozoa, the total cholesterol, total protein, sialic acid, and fructose were determined by standard laboratory techniques.

Results

Body and Organ Weight. No significant change in the body weight were observed in any experimental group when compared with their initial body weights. The weight of testes, epidiymis, seminal vesicle and vertral prostate were decreased significantly in ligand ($p<0.05$), AcNapH·SCZH, BF_2(AcThiop·TSCZ) and BF_2(AcNaph·SCZ) ($p<0.001$) treated rats (Table 7).

Sperm Motility and Sperm Density. A significant ($p<0.001$) decline in cauda epididymis were observed in animals treated with ligands and their complexes. Sperm density in testes and cauda epididymis were also reduced (Table 8).

Biochemical Parameters of Reproductive Organs. Fructose: A significant reduction in fructose contents of seminal vesicle was observed in ligands ($p<0.05$), and their complexes ($p<0.001$) treated animals.

Total Cholesterol: The total cholesterol contents of testes were increased in all experimental groups when compared with controls (both ligands, $p<0.05$; both compounds, $p<0.001$).

Total Protein and Sialic Acid. Ligands and their boron complexes resulted in a significant reduction in total protein and sialic acid contents of testes, epididymis, ventral prostate and seminal vesicle (ligands, $p<0.05$; complexes, $p<0.001$) (Table 9).

Discussion

The most important findings in the present study is a significant reduction in both, in sperm density and motility of epididymal spermatozoa. The exposure of the ligands and their boron complexes to rats hampers the fertility because a number of normal fast growing spermatozoa are necessary for fertilizing an ovum.[22] Since a number of androgensensitive parameters (protein, sialic acid, fructose, total cholesterol) in target organs were found to be altered by these compounds, it is probable that the structure and function of the epididymis and other sex organs are changed.

Our findings are in parallel with the work of Kroasovskii et al.,[23] who observed that boron exposure results in infertility, oligospermia and decreased libido in occupationally exposed men. Boron accumulates slowly and persists in the testes which could delay recovery.[24] Chinoy and Sequeria[25] reported that fluoride may be essential for some physiological process and reported progressive development of infertility.

The authors are thankful to D.S.T., Rajasthan State, Jaipur for financial assistance and to Dr. S. N. Sharma, Seed Technologist, Durgapura Agricultrural Research Institute, Jaipur, for providing facilities for recording the antifungal and antibacterial activities.

References

1) B. A. Gingras, R. W. Hornal, and C. H. Baylay, *Can. J. Chem.*, **38**, 712 (1960).
2) A. Saxena and J. P. Tandon, *Polyhedron*, **3**, 681 (1984).
3) M. Das and S. E. Livingstone, *Coord. Chem. Rev.*, **13**, 101 (1974).
4) A. Saxena, A. J. Crowe, and J. P. Tandon, *Inorg. Chim. Acta*, **84**, 9 (1983).
5) B. L. Feedlander and A.Fraust, *J. Am. Chem. Soc.*, **81**, 638 (1952).
6) R. Dovnick, F. Pansy, G. Stryker, and J. Bornstein, *J. Bacteriol.*, **59**, 667 (1950).
7) N. P. Buu-Hoi, T. B. Voc, and N. D. Xuong, *Bull. Soc. Chim. Fr.*, **1955**, 684.
8) B. G. Benns, B. A. Gingras, and C. H. Baylay, *Appl. Microbiol.*, **8**, 353 (1960).
9) L. Bhal, J. P. Tandon, and S. K. Sinha, *Curr. Sci.*, **53**, 566 (1984).
10) D. Singh and R. V. Singh, *J. Inorg. Biochem.*, **50**, 227 (1993).
11) P. N. Saxena and A. K. Saxena, *Appl. Organomet. Chem.*, **3**, 349 (1989).
12) E. R. Rawlins, "Bentray's Text Book of Pharmaceuticals," 8th ed, Boilliere Tindall, London (1977).
13) V. P. Singh, R. V. Singh, and J. P. Tandon, *Main Group Met. Chem.*, **13**, 135 (1990).
14) C. Saxena and R. V. Singh, *Main Group Met. Chem.*, **15**, 31 (1992).
15) K. K. Chaturvedi, R. V. Singh, and J. P. Tandon, *J. Prakt. Chem.*, **327**, 144 (1985).
16) D. Mukhopadhyay, B. Sur, and R. G. Bhattacharya, *Indian J. Chem., Sect. A*, **24A**, 425 (1985).
17) V. P. Singh, R. V. Singh, and J. P. Tandon, *J. Inorg. Biochem.*, **39**, 237 (1990).
18) R. K. Sharma, R. V. Singh, and J. P. Tandon, *J. Inorg. Nucl. Chem.*, **42**, 1267 (1980).
19) C. Saxena, N. Fahmi, and R. V. Singh, *Indian J. Chem., Sect. A*, **31A**, 963 (1992).
20) K. Jones and E. F. Mooney, *Annu. Rep. NMR Spectrosc.*, **3**, 371 (1970).
21) H. Nöth, *Z. Anorg. Allg. Chem.*, **554**, 113 (1987).
22) P. D. Waller, A. Martin, B. H. Vickery, and L. J. D. Zaneveld, *Contraception*, **41**, 411 (1990).
23) G. N. Kroasovskii, S. P. Varshavskaya, and A. I. Barisov, *Environ. Health Perspect.*, **13**, 69 (1976).
24) S. D. Schrag and R. L. Dixon, "Reproductive Toxicology," ed by R. L. Dixon, Raven Press, New York (1985), p. 301.
25) N. J. Chinoy and E. Sequeria, *Reprod. Toxicol.*, **3**, 261 (1989).