Biologically Active Sulfonamide Schiff Base Complexes of Selenium(IV) and Tellurium(IV)

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Several sulfonamide-Schiff base complexes of selenium(IV) and tellurium(IV) were prepared and characterized using conductivity measurements, and infrared and proton magnetic resonance spectra. Elemental analyses confirmed a 1:2 (metal:sulfonamide-Schiff base) stoichiometry. Most of the complexes proved to be biologically active as evidenced by pharmacological tests.

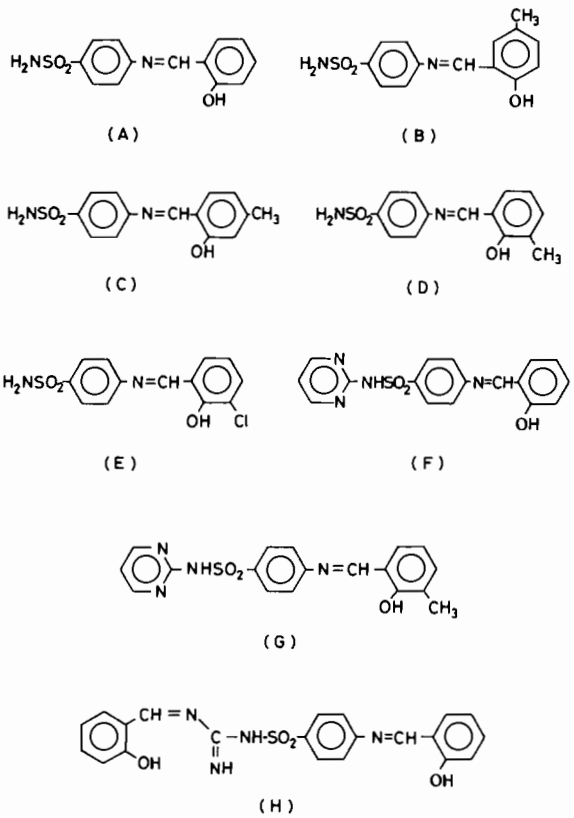
Introduction

Studies have shown that the metal complexes involving sulfonamide-Schiff bases are of tremendous therapeutic importance [1–3]. A study was undertaken in order to synthesize, characterize and determine the biological activity of a number of selenium(IV) and tellurium(IV) complexes of sulfonamide-Schiff bases. The complexes were characterized using infrared and proton magnetic resonance spectra as well as by conductance measurements. Biological activity was studied by using bacteriostatic, anti-inflammatory and hypoglycemic tests.

Experimental

All the chemicals used in this work were of reagent grade. Sulfonamide-Schiff bases were prepared by the reaction of the corresponding (parasulfonamido) aniline with substituted (1-hydroxy) benzaldehyde in equimolar proportions. The reagents were dissolved in ethanol and the mixture was maintained at constant temperature (25 °C) in a water bath for one hour.

The following sulfonamide-Schiff bases were prepared:



The selenium(IV) and tellurium(IV) complexes were prepared by mixing the respective metal tetrachloride with the sulfonamide-Schiff base chelate in dry benzene in the molar ratio of 1:2.

The resulting complex was then filtered, washed repeatedly with anhydrous benzene using a Soxhlet extractor, and finally dried under vacuum over P_2O_5.

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TABLE I. Analytical and Physical Data for Sulfonamide-Schiff Base Complexes of Selenium(IV).

Ligand	Complex Number	Empirical Formula of the complex	M.P. °C	%Se[a]	%N[a]	%Cl[a]	%S[a]	Molar Cond. (ohm^{-1} cm^2 mol^{-1})
A	1.	$(C_{13}H_{11}N_2O_3S)_2SeCl_2$	205	11.24 (11.28)	8.01 (8.00)	10.12 (10.14)	9.05 (9.14)	65.00
B	2	$(C_{14}H_{13}N_2O_3S)_2SeCl_2$	220	10.82 (10.85)	7.66 (7.69)	9.70 (9.75)	8.81 (8.79)	60.80
C	3.	$(C_{14}H_{13}N_2O_3S)_2SeCl_2$	210	10.86 (10.85)	7.65 (7.69)	9.80 (9.75)	8.88 (8.79)	68.00
D	4.	$(C_{14}H_{13}N_2O_3S)_2SeCl_2$	210	10.84 (10.85)	7.65 (7.69)	9.79 (9.75)	8.80 (8.79)	72.60
E	5.	$(C_{13}H_{10}N_2O_3SCl)_2SeCl_2$	190	10.25 (10.27)	7.30 (7.28)	9.25 (9.23)	8.30 (8 32)	69.43
G	6.	$(C_{18}H_{15}N_4O_3S)_2SeCl_2$	300	8.97 (8.93)	12.65 (12.67)	8.01 (8.03)	7.21 (7 24)	66.00

[a]Figures in the parentheses are theoretical yields.

Due to the toxic nature of these complexes, every precaution was taken while handling them.

Elemental analyses were carried out by a procedure discussed elsewhere [4]. Selenium and tellurium were determined as their respective metals. Chlorine was determined as the silver chloride precipitate, while sulfur was determined as the barium sulfate salt. The method of Kjeldahl was used to determine the nitrogen content of the complexes.

Conductivities were measured in dimethylformamide (DMF) using an Elico-CM-82 conductivity bridge with a cell having a cell constant of 0.829 cm^{-1}. All conductivity measurements were performed at room temperature using 10^{-3} *M* solutions of complex.

The infrared spectra (IR) from 4000 to 200 cm^{-1} were obtained using a Perkin-Elmer 180 spectrophotometer. Samples were prepared as KBr pellets. Proton magnetic resonance (PMR) spectra were recorded using a S-60C PMR instrument. All PMR samples were dissolved in deuterated dimethylsulfoxide (d_6-DMSO), and tetramethylsilane (TMS) was used as the internal standard

Pharmacological Tests

The antibacterial activity test was adapted from a method used by Chaturvedi *et al.* [5] The test compounds were dissolved in dimethylformamide, then added to a nutrient agar for bacteria giving a final concentration of 200 μg/ml. The extent of inhibition was measured in millimeters using the zone of inhibition produced after 24 hours. The bacteriostatic properties of sulfonamide-Schiff base complexes of selenium(IV) and tellurium(IV) were compared with those of the parent compounds.

The hypoglycemic activity tests were carried out using albino rats which had been fasting for 48 hours prior to dosage. 50 mg/kg body weight (selenium complexes) and 100 mg/kg body weight (tellurium complexes) were administered to the rats. Blood samples were retrieved by cardiac puncture four hours after the administration of the test compounds. The sugar content was determined by the Nelson-Somogyi method. Tolbutamide was used as a reference compound in order to assess the pharmacological activity of the sulfonamide-Schiff bases and their complexes.

The anti-inflammatory activity test was carried out by using the carrageenan induced rat paw edema assay of Winter *et al.* [6]. 50 mg/kg body weight was found to be a safe dose level for sulfonamide-Schiff base complexes of selenium(IV) in acute toxicity studies.

Results and Discussion

Analytical Data

All the complexes are colored and amorphous in nature. They are insoluble in common organic solvents but soluble in DMF and DMSO. The elemental analyses (see Tables I and II) agree well with 1.2 stoichiometry (metal:sulfonamide-Schiff base). For selenium(IV) complexes, the molar conductivities are in the range of 60–73 ohm^{-1} cm^2 $mole^{-1}$. These values approach those expected for 1:1 electrolyte [7] in DMF. Tellurium(IV) complexes on the other hand, behave as 1:2 electrolytes in DMF as indicated by the molar conductivities which fall in the range of 103–174 ohm^{-1} cm^2 mol^{-1}.

Infrared Spectra

When the spectra of the selenium and tellurium complexes are compared with those of the uncom-

TABLE II. Analytical and Physical Data for Sulfonamide-Schiff Base Complexes of Tellurium(IV).

Ligand	Complex Number	Empirical Formula of the complex	M.P °C	%Te[a]	%N[a]	%Cl[a]	%S[a]	Molar Cond. (ohm^{-1} cm^2 mol^{-1})
A	7.	$(C_{13}H_{12}N_2O_3S)_2TeCl_4$	195	15.56 (15.53)	6.88 (6.82)	17.30 (17.29)	7.80 (7.79)	133.23
B	8.	$(C_{14}H_{14}N_2O_3S)_2TeCl_4$	160	15.00 (15.02)	6.60 (6.59)	16.73 (16.72)	7.52 (7.53)	154.27
C	9.	$(C_{14}H_{14}N_2O_3S)_2TeCl_4$	167	15.03 (15.02)	6,49 (6.59)	16.70 (16.72)	7.54 (7.53)	138.56
D	10.	$(C_{14}H_{14}N_2O_3S)_2TeCl_4$	168	15.00 (15.02)	6.58 (6.59)	16.70 (16.72)	7.55 (7.53)	140.90
E	11.	$(C_{14}H_{11}N_2O_3SCl)_2TeCl_4$	158	13.89 (13.95)	6.14 (6.12)	15.52 (15.53)	7.10 (7.00)	173.87
F	12.	$(C_{17}H_{14}N_4O_3S)_2TeCl_4$	185	13.00 (13.05)	11.44 (11.46)	14.54 (14.53)	6.63 (6.55)	173.13
G	13.	$(C_{18}H_{16}N_4O_3S)_2TeCl_4$	180	12.61 (12.69)	11.16 (11.14)	14.10 (14.12)	6.30 (6.37)	103 20
H	14.	$(C_{21}H_{18}N_4O_4S)_2TeCl_4$	170	11.98 (11.46)	10.10 (10.06)	12.80 (12.75)	5.85 (5.75)	173.99

[a]Figures in the parentheses are theoretical yields.

TABLE III. Infrared Data and Assignments for Sulfonamide-Schiff Bases and Their Complexes.

Frequency Ranges (cm^{-1})			Assignments
I[a]	II[b]	III[c]	
3360–3370	3360–3370	3360–3380	ν_{as} (N–H)
3240–3255	3250–3275	3250–3260	ν_{sym} (N–H)
3070–3085	3070–3075	3075–3080	ν(N–H) + ν(C–H)
2600	–	2600	ν(O–H)
1615–1620	1650	1650–1655	ν(C=N)
1595–1605	1620	1620	ν(C=C)
1575–1585	1580	1575–1590	NH_2 deformation and ν(C=C)
1500–1505	1495–1520	1500–1520	ν (C=C)
1350–1360	1330–1360	1380–1390	ν_{as} (S=O)
1320	1318–1330	1320	ν_{as} (S–O)
1280–1290	1260–1280	1290	ν (C–O)
1155–1165	1160–1170	1160–1170	ν_{sym} (S=O)
915–925	920	920–925	ν (S–N)
520–525	520	520–548	S–O symmetric deformation

[a]I Sulfonamide-Schiff Bases (A–E). [b]II Sulfonamide-Schiff Base Complexes of Se(IV) (1–5). [c]III Sulfonamide-Schiff Base Complexes of Te(IV) (7–11).

plexed sulfonamide-Schiff base chelates, the bands at 3360 cm^{-1}, 3250 cm^{-1}, 3075 cm^{-1}, 1580 cm^{-1}, and 920 cm^{-1} are unchanged. This indicates that the sulfonamido group does not coordinate with selenium and tellurium in these complexes. See Table III.

The band at 2600 cm^{-1} in the sulfonamide-Schiff base chelates disappears on coordination with selenium but remains unchanged on coordination with tellurium. These results indicate that the hydroxy group of the salicylaldehyde moiety has reacted with selenium tetrachloride to establish an Se–O bond [8–10] but not with tellurium [11].

The vibrations due to the azomethine group in some of the complexes (3–5) are shifted to a higher region (1650–1655 cm^{-1}) substantiating coordina-

TABLE IV. Proton Magnetic Resonance Chemical Shifts[a] of Sulphonamide-Schiff Bases and their Complexes with Selenium(IV) and Tellurium(IV).

C	3	9	G	6	13	H	14	Assignments
12.67	–	9.76	11.47	–	10.13	12.66	10.27	Hydroxy proton of sulphonamido-Schiff base
8.68	8.70	8.77	–	8.83	8.83	8.70	9.00	Methine protons
6.55 to 8.25	6.60 to 8.00	6.70 to 8.00	6.30 to 8.57	6.40 to 8.67	6.60 to 8.60	6.47 to 8.10	6.30 to 7.73	Phenyl protons
3.27	3.50	3.65	3.33	–	–	3.25	3.67	Nitrogen protons
2.37	2.30	2.35	2.27	2.27	2.27	–	–	CH_3 protons

[a]In ppm (δ) relative to TMS.

TABLE V. Antibacterial Activity of Sulphonamide-Schiff Bases and their Selenium and Tellurium Complexes.

Chelate/Complex	Zone of Inhibition in mm – Organisms		
	E. coli	*B. subtilis*	*S. Aureus*
B. 3-methyl-salicylidene-(*p*-sulfonamido)aniline	21	19	24
2. Dichlorobis[3-methyl-salicylidene-(*p*-sulfonamido)-aniline]selenium(IV)	15	30	26
8. Tetrachlorobis[3-methyl-salicylidene-(*p*-sulfonamido)-aniline]tellurium(IV)	24	22	20
C. 4-methyl-salicylidene-(*p*-sulfonamido)aniline	20	16	19
9. Tetrachlorobis[4-methyl-salicylidene)-(*p*-sulfon-amido)aniline]tellurium(IV)	20	20	16
D. 5-methyl-salicylidene-(*p*-sulfonamido)aniline	20	18	19
4. Dichlorobis[5-methyl-salicylidene-(*p*-sulfonamido)-aniline]selenium(IV)	20	15	17
10. Tetrachlorobis[5-methyl-salicylidene-(*p*-sulfon-amido)aniline]tellurium(IV)	36	–	27
E. 5-chloro-salicylidene-(*p*-sulfonamido) aniline	20	22	23
5. Dichlorobis[5-chloro-salicylidene-(*p*-sulfon-amido)aniline]selenium(IV)	26	18	24
11. Tetrachlorobis[5-chloro-salicylidene-(*p*-sulfonamido)aniline]tellurium(IV)	12	22	20
A. Salicylidene-(*p*-sulfonamido)aniline	18	20	16
7. Tetrachlorobis[salicylidene-(*p*-sulfonamido) aniline]tellurium(IV)	40	18	26

tion through the azomethine nitrogen [12–13]. This coordination has affected the aromatic C=C stretching frequency which is now shifted to 1620 cm^{-1} in these same complexes. A comparison of the spectra of the ligands F–H with that of the complexes (12–14) reveals the same shift from 1612 cm^{-1} in the ligands to 1620–1640 cm^{-1} in the complexes.

The band observed at 1290 cm^{-1} is ascribed to the phenolic C–O stretch in the sulfonamide-Schiff base ligands. The band shifts down to around 1260 cm^{-1} in the selenium complexes, but does not move in the tellurium complexes. This further substantiates the coordination between the hydroxy group of the sulfonamide-Schiff base and selenium [14].

In the region 900–300 cm^{-1} one can observe the bands due to selenium–nitrogen, tellurium–nitrogen, selenium–chloride and tellurium–chloride vibrations. Considering the complexity of the spectra in this region, the assignments made are only tentative. Selenium–nitrogen and tellurium–nitrogen bands have been observed [15] around 550 cm^{-1}, while tellurium chloride stretches have been reported in the region 330–300 cm^{-1} [16, 17]. In this work,

TABLE VI. Effect of Sulfonamide-Schiff Bases and Their Selenium and Tellurium Complexes on the Blood Glucose Level of Rats.

Chelate/Complex	Mg of Glucose per 100 ml of blood	Percentage Change
1. 3-methylsalicylidene-(*p*-sulfonamido) aniline	109.5	−24.3
2. Dichloro bis[3-methylsalicylidene (*p*-sulfonamido)aniline] selenium(IV)	108.0	−25.4
3. Tetrachloro bis[3-methylsalicylidene-(*p*-sulfonamido)aniline] tellurium(IV)	219 2	+51.5
4. Salicylidene-sulphadiazine	200.0	+38.2
5. Tetrachloro bis[salicylidene-sulphadiazine] tellurium(IV)	98.1	−32.2
6. Tolbutamide (reference)	80.0	−44.7
7. Control	144.7	–

the bands around 550 cm^{-1} and 320 cm^{-1} have been assigned to ν(Se–N) or ν(Te–N) and ν(Te–Cl) respectively.

Proton Magnetic Resonance Spectra

The PMR chemical shifts of sulfonamide-Schiff base chelates and their complexes with selenium(IV) and tellurium(IV) are reported in Table IV. The chelate spectra possess four characteristic absorptions. The sharp signal due to the methine proton is observed around 8.8 ppm. Previous researchers [18–20] have demonstrated that the methine proton in some Schiff bases is labile and can bond to the azomethine nitrogen. The splitting of the methine proton signal has substantiated the existence of this tautomeric equilibrium [21, 22]. However, in the sulfonamide-Schiff bases under consideration, the methine proton signal is a singlet, and there appears to be no tautomeric equilibrium. The multiplet signals of the phenyl protons are located in the region 6.3 to 8.7 ppm. The characteristic signal associated with the nitrogen protons can be found between 3.3 and 3.7 ppm. The resonance due to the proton of the orthohydroxy group (11.5–12.7 ppm) of the chelate disappears in the selenium(IV) complexes indicating that coordination has taken place through the OH of the Schiff base. Finally, in those ligands and complexes where methyl groups have been substituted on the phenyl ring of the sulfonamide-Schiff base, additional absorptions are observed around 2.27–2.37 ppm.

Pharmacological Tests

The antibacterial activity of sulfonamide-Schiff bases and their complexes is summarized in Table V. The compounds were screened for their antibacterial activity using three microorganisms; namely, *E. Coli* (gram negative), *B. Subtilis* and *S. Aureus* (gram positive). These bacterial strains were chosen since they are known commensals and pathogens of human beings. The results show that all compounds exhibit antibacterial activity against at least one type of bacteria. Furthermore, in many cases the selenium and tellurium complexes were found to be more potent than the original chelate in their inhibition properties. This has been explained in terms of the greater lipid solubility and cellular penetration of the complexes [23].

The hypoglycemic activity of sulfonamide-Schiff bases and their corresponding complexes with selenium(IV) and tellurium(IV) are listed in Table VI. Tolbutamide at a dosage level of 200 mg/kg body weight, lowered the blood glucose level in this system by 44.7%. The results were expressed as a percentage difference between the mean change in the control and the mean change in the treated groups, four hours after administration.

3-methylsalicylidene-(*p*-sulfonamido) aniline shows some hypoglycemic activity when compared with tolbutamide. The selenium complex of 3-methylsalicylidene-(*p*-sulfonamido) aniline shows identical behavior as the chelate, whereas the tellurium complex exhibits hyperglycemic activity. Significant hypoglycemic effects were produced by the tellurium(IV) complex of salicylidene-sulphadiazine, whereas salicylidene-sulphadiazine has no positive hypoglycemic activity.

The anti-inflammatory activity of sulfonamide-Schiff base complexes of selenium are listed in Table VII, along with the activity of the standard phenylbutazone. The results indicate that the selenium complexes show mild anti-inflammatory activity when compared with that of phenylbutazone.

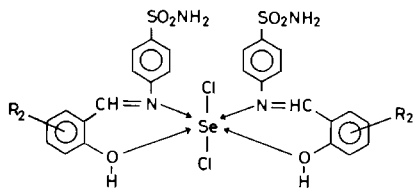
TABLE VII Anti-inflammatory Activity of Sulphonamide Schiff Base Complexes of Selenium(IV).

Chelate/Complex	Dose level	Dose level in mg	Initial reading	Reading after 3 hrs	Edema formed	% Inhibition
1. Dichloro-3-methylsalicylidene-(*p*-sulfonamido)-aniline selenium (IV)	50 mg/kg	08.25	5.90	8.60	2.70	22.88
2. Dichloro-5-methyl-(*p*-sulfonamido)-aniline selenium(IV)	50 mg/kg	10.00	5.70	7.90	2.20	37.14
3. Dichloro-5-methylsalicylidene-sulphadiazine selenium(IV)	50 mg/kg	10.00	6.50	8 93	2.43	30.57
4. Phenylbutazone (standard)	50 mg/kg	10.00	4.40	4.85	0.45	87.14
5. Control	4% Gumacia	16.20	6.20	9.70	3.50	–

Conclusions

A few complexes of selenium(IV) and tellurium-(IV) with sulphonamide-Schiff bases obtained by the condensation of substituted salicylaldehyde and (*p*-sulfphonamido)aniline have been prepared The elemental analyses show that these complexes have 1:2 stoichiometry. The conductance data of selenium (IV) and tellurium(IV) complexes indicate that these are 1.1 and 1:2 electrolytes respectively. The coordination of the azomethine nitrogen to selenium and tellurium, through the azomethine nitrogen is substantiated by infrared and PMR spectral data. These results also confirm the non-reactivity of the $-SO_2-NH_2$ group in coordination. On the basis of the above information the selenium or tellurium complexes under investigation exhibit a coordination number of six and remain in an octahedral environment. The following tentative structures may be proposed for these complexes.

1



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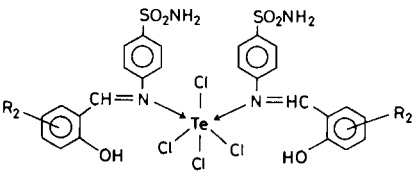

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References

1 D. B. Clayson, J. A. Pringle and G. M. Ronser, *Biochem. Pharmacol*, *16*, 614 (1967).
2 W. N. Beeslay, W. Peters and K. Mager, *Ann Trop Med. Parasital.*, *62*, 288 (1960).
3 E. Goeres and B. Lange, *Acta Biol. Med*, *21*, 193 (1968).
4 A I. Vogel, 'Textbook of Quantitative Inorganic Analysis', 3rd ed., Longmans, Green and Co., New York, N.Y., (1969).
5 K. K. Chaturvedi, S. Siddiqui, B. K. Agrawal and R. Naushal, *Ind J Pharm.*, *37*, 85 (1975).
6 C. A. Winter, E. A. Risley and C. W. Nuss, *Proc. Soc. Exp. Biol. Med*, *111*, 544 (1962).
7 D. A. Couch, P. S. Elmes, J. E. Fergusson, M. L. Greenfield and C. J. Wilkins, *J. Chem. Soc. (A)*, 1813 (1967).
8 V. N. Shafranskii and I. L. Fusu, *Russ. J Inorg. Chem.*, *18*, 1416 (1973).
9 *Ibid.*, *19*, 415 (1974).
10 V. N Shafranskii, I. V. Dranka, I. L. Fusu, D. D. Buburuz and A. E. Raiskaya, *Russ. J. Inorg Chem.*, *21*, 1685 (1976).
11 N. S Biradar and V. B. Mahale, *Z. Anorg. Allg Chem.*, *388*, 277 (1972).
12 P. Teyssie and J. J. Charetee, *Spectrochim Acta*, *19*, 1407 (1963).
13 L. E. Clougherty, J. A. Sousa and G. M. Wyman, *J Org. Chem.*, *22*, 462 (1957).
14 J. A. Faniran, K. S. Patel and J. C. Bailar, Jr., *J Inorg Nucl. Chem.*, *36*, 1547 (1974).
15 U. Klingebiel, D. Werner and A. Meller, *Monats. Chem.*, *107*, 939 (1976).
16 W R. McWhinnie and P. Thavornyutikarn, *J Chem. Soc., Dalton*, 551 (1972).
17 E. R. Clark, A. J. Collett and D. G. Naik, *J Chem. Soc., Dalton*, 1961 (1973).
18 G. O. Dudek and G P. Volpp, *J Am. Chem. Soc.*, *85*, 2697 (1963).
19 G. O. Dudek and E. P. Dudek, *J. Am. Chem. Soc.*, *86*, 4283 (1964).
20 G. O. Dudek and E P. Dudek, *J Chem Soc (B)*, 1356 (1971)
21 J. J. Charette, *Spectrochim. Acta*, *19*, 1275 (1963).
22 N. M. D. Brown and D. C. Nonhebel, *Tetrahedron*, *24*, 5655 (1968).
23 P. Jain and K. K. Chaturvedi, *J Inorg. Nucl. Chem.*, *38*, 799 (1976);
ibid., *39*, 901 (1977).