NOTE

Studies on Furosemide Salicylaldehyde Schiff Base Complex with Copper(II) and Zinc(II)

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The synthesis and characterization of metal complexes of Zn(II) and Cu(II) using Schiff base ligand salicylaldehyde-furosemide is reported. Furosemide is a diuretic drug and it is used to increase the rate of urination through kidneys. Analytical data and stoichiometry suggest ligand-metal ratio as 2 : 1. The structure assigned to the complexes, synthesized *via* Schiff base formation is supported by infrared spectral studies.

Key Words: Furosemide, Schiff base, Metal Complexes.

Schiff base metal chelates are widely applicable because of their industrial and biological importance and hence have well been studied in the past[1-4]. In continuation of our previous work on metal complexes of established drugs[5-10], herein, the synthesis and structural studies of furosemide-Cu and furosemide-Zn complexes are described.

All the chemical used were of analytical grade. Pure sample of furosemide (FSD) (m.f. $C_{12}H_{11}N_2O_5S$, m.w. 330.75) was obtained from Geno Pharmaceuticals Pvt. Ltd., Goa. Metal salts $CuCl_2 \cdot 2H_2O$ and $ZnCl_2$ used were of Qualigen Chemicls. Solvents used were methyl alcohol and acetone.

Equimolar solutions of pure drug (0.01 M) and salicylaldehyde (0.01 M) were taken in methanol-water mixture (1 : 1 ratio). Both the solutions were mixed and refluxed for 3 h. The reaction mixture was kept overnight. Light yellow crystals of furosemide-Schiff base were formed in the reaction mixture, which were washed with 50% methanol, filtered, dried and weighed.

Ligand-Metal ratio and stoichiometry

To confirm the ligand-metal ratio, conductometric titrations using monovariation method were carried out on Systronics conductometer and dip type electrode. Titrations were carried out at 21°C and 20°C respectively for $CuCl_2 \cdot 2H_2O$ and $ZnCl_2$.

0.01 M solution of furosemide-Schiff base was prepared in 60% acetone and diluted to 200 mL with same solvent. This Schiff base solution was titrated against

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0.02 M metal solutions using monovariation method. After making volume corrections the results were plotted in the form of a graph which shows the ligand- metal ratio for Cu and Zn as 2 : 1. Formation of 2 : 1 complex was further confirmed by Job's method[10] of continuous variation, modified by Turner and Anderson[11]. The stability constants and free energy changes were also calculated (Table-1).
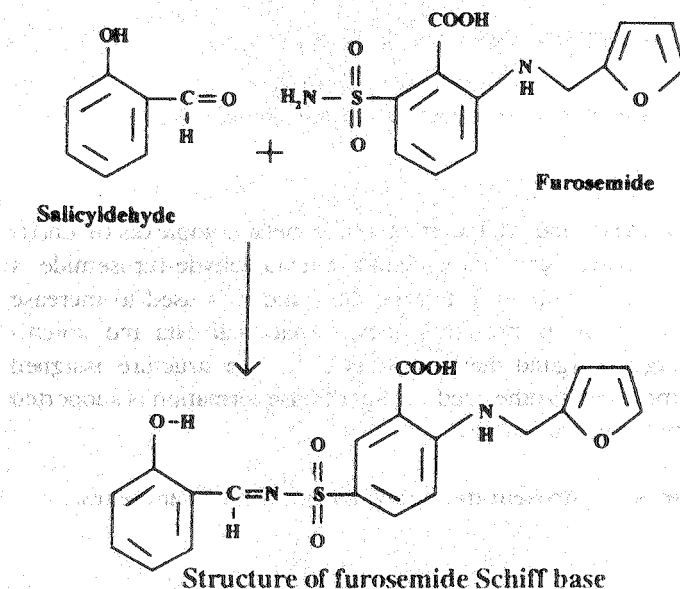

Structure of furosemide Schiff base

TABLE-I
SYNTHESIS AND PHYSICOCHEMICAL CHARACTERISTICS OF COMPLEXES

	Ligand/metal ratio	Colour	Yield (%)	Stability constant log K (L/mol)	Free energy change ΔF (Kcal/mol)
FSD-SB	—	Pale yellow crystals	65	—	—
(FSD)$_2$Cu	2 : 1	Green crystals	40	9.59	−11.680
(FSD)$_2$Zn	2 : 1	Yellow crystals	32	9.32	−11.456

Synthesis of complexes

For the synthesis of complexes of furosemide-Cu and furosemide-Zn, 0.006 M ligand solution was prepared in 60% acetone and refluxed for 4 h with 0.003 M solution of $CuCl_2 \cdot 2H_2O$ and $ZnCl_2$ separately. The refluxed solutions were kept for two days. Solid crystalline compounds appeared in the solutions. Complexes of furosemide-Cu and furosemide-Zn were washed with 60% acetone, filtered, dried and weighed.

TABLE-II
ANALYICAL DATA OF COMPLEXES

Complex (m.w.)	Elemental analysis (%) Found (Calcd.)					m.p. (°C)
	C	H	N	S	Metal	
$(C_{19}H_{13}ClN_2O_6S)_2Cu$ (927.6)	36.98 (36.00)	2.5 (2.91)	15.69 (16.67)	17.93 (17.50)	8.86 (8.91)	245
$(C_{11}H_9N_4O_4S_2)_2Zn$ (928.6)	36.86 (36.89)	2.57 (2.51)	15.60 (16.17)	17.63 (17.50)	8.51 (8.61)	150

Structure of furosemide Schiff base metal complex

Proposed structure was further confirmed by IR spectral data[12–16]. Bands observed at 1157.6 and 1164.76 cm^{-1} are characteristic of SO_2—N group. Absorption band at 1410 and 1440 cm^{-1} shows the presence of chelate ring. Frequency at 680 and 690 cm^{-1} is characteristic of M—O linkage. Bands at 583 and 586 cm^{-1} are attributed to M—N linkage while frequencies at 1362 and 1212 cm^{-1} indicate the S—N linkage.The disappearance of frequencies of phenolic —OH in complex supports its involvement in complexation.

REFERENCES

1. A. Kumar, G. Singh and R.N. Handa, *Indian J. Chem.*, **38**, 617 (1999).

2. J. Mohan and S. Kataria, *Indian J. Heterocycl. Chem.*, **6**, 317 (1997).

3. R. Qureshi and S.A. Iqbal, *Asian J. Chem.*, **2**, 321 (1990).

4. S.F. Tan and K.P. Ang, *Transition Met. Chem.*, **9**, 390 (1984); **13**, 64 (1988).

5. C.N.R. Rao and M.C. Ganorkar, *Indian J. Chem.*, **24A**, 877 (1985); **26A**, 887 (1987); **27A**, 52 (1988).

6. S.A. Iqbal and R. Qureshi, *Asian J. Exp. Sci.*, **1**, 68 (1985).

7. S.A. Iqbal, S. Siddiqui, R. Qureshi and A. Desnavi, *Orient. J. Chem.*, **1**, 32 (1985).

8. R. Qureshi and S.A. Iqbal, *Orient. J. Chem.*, **13** (1997).

9. S. Nadkarni, Indian Meteria Medica, Vol. II, p. 51 (1976).

10. P. Job, *Ann Chim.*, **10**, 113 (1928).

11. S.E. Turner and R.C. Anderson, *J. Am. Chem. Soc.*, **71**, 912 (1949).

12. A.I. Vogel, Quantitative Inorganic Analysis, Longman, Green & Co., London, p. 455 (1954).

13. L.J. Bellamy, Chemical Applications of Spectroscopy, Interscience, New York (1956).

14. K. Nakamoto, Infrared Spectra of Inorganic and Co-ordination Compounds, John Wiley, New York (1956).

15. A. Weissberger, Chemical Applications of Spectroscopy, Interscience, New York (1956).

16. C.N.R. Rao, Chemical Applications of IR Spectroscopy, Academic Press, New York (1963).