ISSN 0975-6299 Vol 2/Issue 1/ Jan-Mar 2011

International Journal of Pharma and Bio Sciences

RESEARCH ARTICLE

MEDICINAL CHEMISTRY

SYNTHESIS AND BIOLOGICAL STUDIES OF MN (II), CO (II), ZN (II) AND NI (II) COMPLEXES DERIVED FROM O, N DONOR SCHIFF BASE OF SULPHAMETHOXAZOLE.

Corresponding Author

V.UMA

Synthetic Lab, P. G. Department of Chemistry, Faculty of Science, Government College Ajmer, Rajasthan (INDIA).

Co Authors

SUNIL JOSHI AND VATSALA PAWAR

Synthetic Lab, P. G. Department of Chemistry, Faculty of Science, Government College Ajmer, Rajasthan (INDIA).

ABSTRACT

Two new respectively Schiff bases were prepared by taking *p*-Chlorobenzaldehyde and Vanillin with Sulphamethoxazole.The complexes of the type MPbS, MVS were prepared further and all were characterized on the basis of elemental analysis, IR spectra, ^{1}HNMR spectra, conductivity, Melting Point and Molecular Weight determination. Comparative biocidal behavior of Schiff bases and their metal complexes have also been studied against Gram (-) like *E. coli* and Gram (+) like *S. aureus, M. luteus and B. lichenformis* (ATCC).

KEY WORDS

Antibacterial activity, Schiff bases

INTRODUCTION

The introduction of nitrogen atom in the structure of organic compounds has often resulted in important consequences in their behaviors towards metal ions.[1-3]

The present study deals initially with the synthesis and characterization of Schiff bases of *p*-chlorobenzaldehyde and vanillin with Sulphamethoxazole[4,10] respectively and further their biological activities. Sulphamethoxazole is a very well known drug.[5,9] Its activity was found to be more when attached with vanllin and *p*-chlorobenzaldehyde and further binded with metal complexes like Zn (II), Co (II), Ni (II), and Mn(II). They also showed anticancer[11], anti-tumor[12], antidiabetic activities.[6-8]

Thus they are found to be very important from the biological point of view.

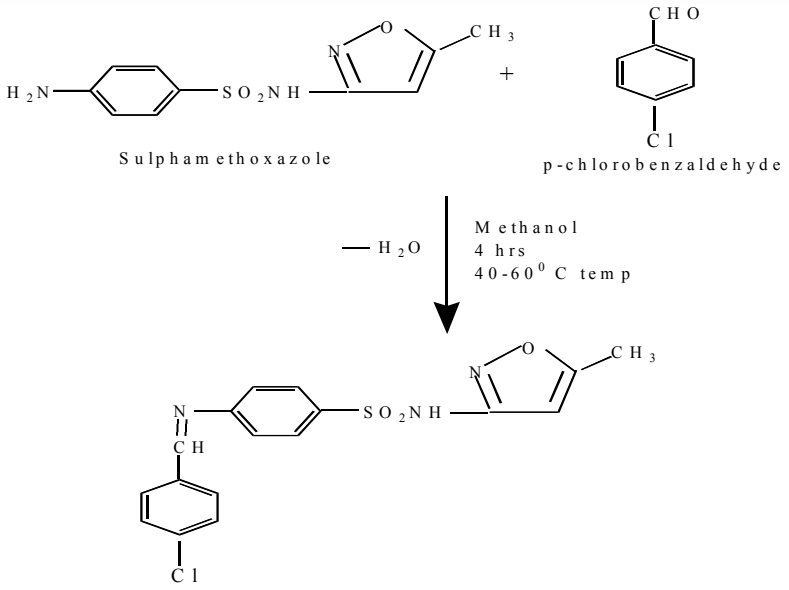
MATERIAL AND METHOD

All chemicals and solvent used were of analytical grade. UV-VIS spectra were obtained on digital spectrophotometer in the range 300-900nm in DMF.

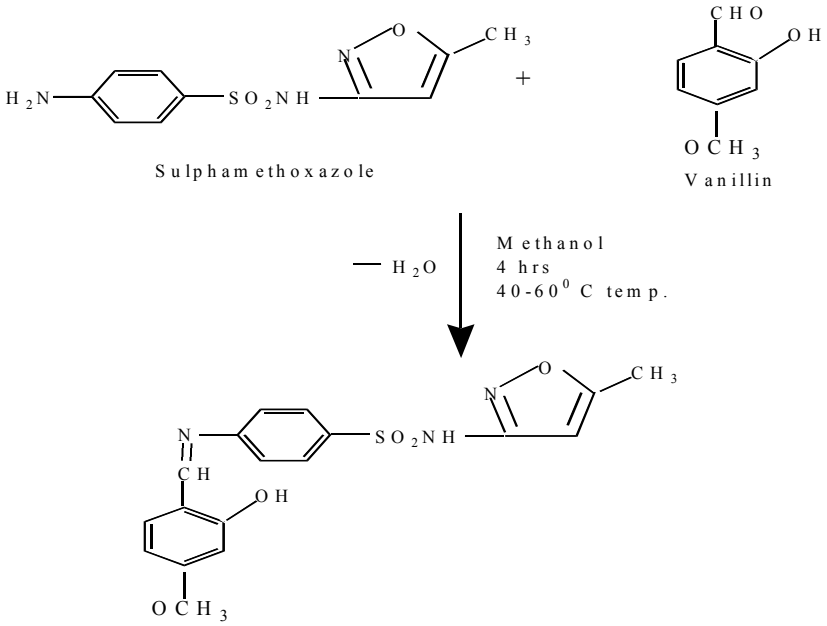
IR spectra were recorded using KBr disc on shimadzu 8201PC FT-IR spectrophotometer, in the range 4000-400cm^{-1}. ^{1}HNMR spectra were recorded in MeOD. Elemental analysis was carried out on a Elementar Vario ELIII. Conductance measurement of 10^{-3} M solution of the complexes in DMF was carried out on an Equiptronic model no. Eq-660A. Melting point of the ligands and metal complexes were determined by open capillary method using sunsim electric melting point apparatus and are uncorrected. Molecular weight of ligands and their metal complexes were determined by Rast Camphor method. *In vitro* screening for antibacterial activities were done by paper disc diffusion method.

Synthesis of the organic ligands (PbS, VS):-

Sulphamethoxazole (1 mol,1.265gm.) was dissolved in methanol (10 ml) and then added to methanolic solution of the *p*-Chlorobenzalehyde (1 mol,0 .702gm.) Vanillin (1 mol, 0.760 gm.) to this KOH (0.1 % in methanol)was added to adjust the pH of the solution between 7-8. The reaction mixture was refluxed for 4 hrs. After complete refluxation clear yellow and brown colored solution was obtained, the Schiff base was isolated by crystallization after volume reduction by evaporation. The crystalline product was dried under vacuum and kept in a desicator..



Scheme I Synthesis of (Ligand PbS)



Scheme II Synthesis (Ligand VS)

Synthesis of metal complex:- (PbSM, VSM)

Sulphamethoxazole (0.2mol, 0.253gm.) *p*-Chlorobenzalehyde (0.2mol, 0.140gm.), Vanilline (0.2mol, 0.152gm.) and (0.1mol.) metal M= Zn (II) (0.199 gm.), Ni (II) (0.136 gm.), Mn (II) (0.197gm) and Co (II) (0.237gm), were dissolved in methanol (10 ml) separately. To this KOH (0.1 % in methanol) was added to

adjust the pH of the solution between 7-8 and then the mixture was refluxed for 5-6 hrs. A dark brown colored product was isolated after reduction of solvent volume by evaporation, then filtered, washed with methanol and then dried over vacuum.

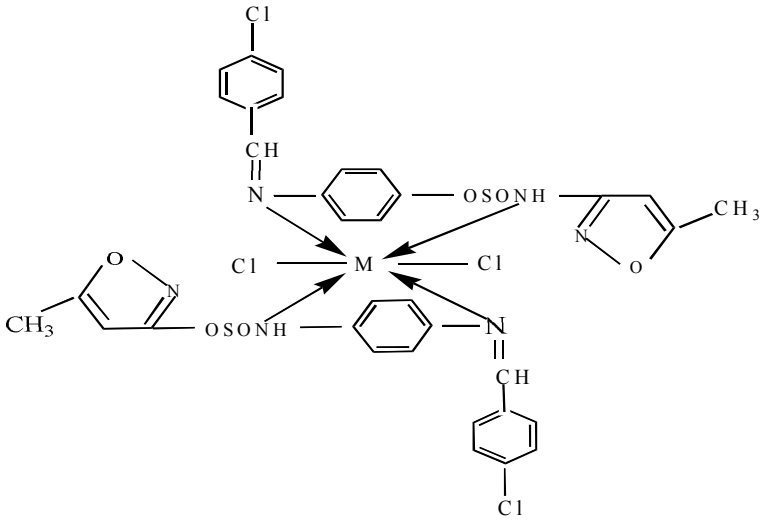


Fig. 1
Metal complex PbSM

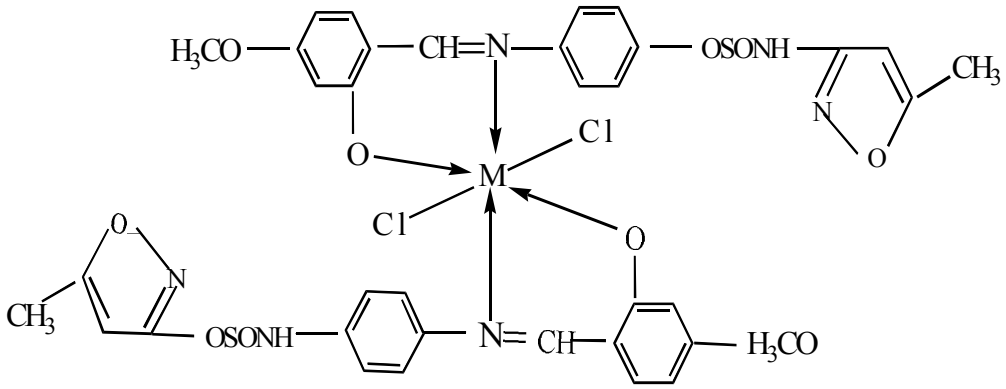


Fig. 2
Metal Complex VSM

RESULT AND DISCUSSION

Characterization of the compounds

All the synthesis all compounds are air and moisture stable, intensely colored amorphous solid which decomposes above 240^0 C. They ligands are soluble in methanol, DMF and DMSO and metal complexes are soluble in DMF and DMSO and they are insoluble in common organic solvent like chloroform, acetone, ether, ethanol and carbon tetra chloride.

The molar conductance of the ranges between (0.22 to 0.48 $ohm^{-1}cm^2mol^{-1}$) which was carried out in DMF solvent indicates that the under study are non-electrolytic in nature. Insolubility of these complexes in water and there non-electrolytic nature provid sufficient evidence for covalance of the compound. Purity of

compounds was confirmed by Thin layer chromatography as both ligands and complexes moves as a single spot indicating the presence of only one component. Molecular weight determined by Rast Camphor method and were found in accordance with calculated value the range of ligands (375-387) and metal complexes (837-867) , confirming the monomeric nature of the compounds. The yield of compounds found in the range of (70-80 %) as shown in **table 1.**

Table 1
Micro analytical datas of ligand and their metal complexes

S. No.	Name of compound	Carbon found (calc.)	Hydrogen found (calc.)	Oxygen found (calc.)	Nitrogen found (calc.)	Conductivity	M.P. (°C)	M.W. found (calc.)	Colour	Yeild %
1.	PbS	54.31 (54.28)	3.72 (3.60)	12.77 (12.65)	11.18 (11.2)	0.48	240	375.6 (372.56)	yellow	72
2.	PbS - Zn^{+2}	50.07 (49.85)	3.45 (3.25)	11.78 (11.69)	10.31 (10.2)	0.30	320	850.7 (848.25)	light brown	74
3.	PbS - Co^{+2}	50.36 (50.20)	3.45 (3.25)	11.85 (11.56)	10.36 (10.2)	0.36	308	834.1 (833.26)	black	70
4.	PbS - Mn^{+2}	50.67 (50.40)	3.47 (3.25)	11.92 (11.65)	10.43 (10.3)	0.22	348	839.2 (837.26)	black	78
5.	PbS - Ni^{+2}	49.95 (49.84)	3.42 (3.34)	11.75 (11.62)	10.28 (10.1)	0.24	358	0 843.9 (841.32)	brown	75
6.	VS	52.68 (52.56)	4.39 (4.20)	20.66 (20.46)	10.84 (10.6)	0.43	242	387.18 (378.9)	light brown	74
7.	VS -Co^{+2}	48.96 (48.92)	3.84 (3.78)	11.52 (11.45)	10.08 (10.1)	0.26	358	867.26 (866.36)	brown	76
8.	VS -Zn^{+2}	48.69 (48.49)	3.81 (3.74)	11.45 (11.32)	10.02 (9.76)	0.38	368	837.86 (826.56)	black	80
9.	VS -Mn^{+2}	49.25 (49.20)	3.86 (3.76)	19.31 (19.26)	10.14 (9.86)	0.42	374	862.36 (860.62)	brownish yellow	72
10.	VS - Ni^{+2}	48.57 (48.42)	3.81 (3.75)	11.43 (11.38)	10.00 (9.86)	0.40	346	867.86 (866.63)	brown	71

All the spectral datas were consistent with the assigned structure of the compounds. The ligands show strong band in the regin 1590-1620 cm^{-1} it however confirmed that the amino and aldehydes moieties of the starting reagents were converted into the Schiff base showing the azomethine linkage. The comparison of the IR spectra of the Schiff base and its metal complexes, further indicated that the Schiff base were coordination to the metal atom from mainly tetra donor sites hence, acting as a tetradentate ligand, the band originally appearing at 1565-1590 cm^{-1} in the spectra of ligands due to the azomethine shifted to lower frequency by 20-25 cm^{-1} suggesting the participation of the azomethine nitrogen in the complexes. It is found from the IR spectra of the complexes that there are wide and strong band at 530 – 580 cm^{-1} for (M-N) bonding and the band the v(Ar-OH) observed at 3518 cm^{-1} in the ligand (VS) and disapiared in metal complexes showing the participation of the O-M group in coordnation. 440-470 cm^{-1} for (M-O) which are assigned to metal stretching vibration. The ^{1}HNMR spectral data of ligands (PbS) and **(**VS) shows signal between δ7.40-7.60 and δ6.77-6.77 respectively due to aromatic ring which gets shifted downfield in their metal complexes. The VU-VIS spectra of ligands (PbS and VS) showed two bands between 300-340 nm and 320-370 nm. The first band may be due to Π – Π* transition with in the aromatic ring. The second band would be due to n- Π * transition within –C=N group. Shown in **table 2.**

Table 2

Characteristic IR and ^{1}HNMR spectral data of the ligands and their metal complexes

S No	Compd. Name	IR spectra cm^{-1}				^{1}HNMR Spectra ppm			U.V. Visible	
		v (Ar-OH)	v (O-M)	v (N-M)	v (C=N)	δ(CH=CH)	δ(Ar-H)	(N=H)	(C=C)	(C=N)
1.	PbS	-	-	-	1590	4.80	6.77-7.3	7.55	300	350
2.	PbS -Zn^{+2}	-	-	530	1572	4.38	6.17-7.2	7.45	306	320
3.	PbS - Co^{+2}	-	-	577	1565	4.78	6.44-7.1	7.42	304	318
4.	PbS - Mn^{+2}	-	-	560	1580	4.58	6.12-6.28	7.48	309	340
5.	PbS - Ni^{+2}	-	-	560	1584	4.59	6.15-7.02	7.50	312	340
6.	VS	3518	-	-	1620	5.27	6.79-7.30	7.58	310	365
7.	VS -Co^{+2}	-	448	538	1582	5.15	6.45-7.15	7.44	340	345
8.	VS -Zn^{+2}	-	450	548	1584	4.84	6.23-7.14	7.49	320	346
9.	VS -Mn^{+2}	-	470	559	1572	4.24	6.77-6.72	7.47	320	336
10	VS - Ni^{+2}	-	440	580	1578	4.36	6.42-7.32	7.46	320	348

Antimicrobial Activity

Schiff base and their metal chelates were evaluated for their antibacterial activities against bacteria Gram (-) like *E. coli* and Gram (+) like *S. aureus, M. luteus* and *B. lichenformis.* The compounds were tested at a three different concentration of 100ppm 500ppm 1000ppm in DMF solution using the paper disc diffusion method. The susceptibility zones measured in diameter (mm) were the zones around the discs killing the active bacteria. The Schiff base ligand and their complexes individually exhibited varying degree of inhibitory effect on the growth of the tested bacterial. Significance level of all compounds (P<.001) (P<.01*). The mean ± SEM values are also shown in **table 4**. The antimicrobial results are evaluated as MIC values shown in **table 3**.

Table 3
MIC of the ligand and their metal complexes

S. No.	**Name of Compound**	***E. Coli* (-)**	***S. Aureus* (+)**	***M. Luteus*(+)**	***B. Lichenformis*(+)**
		mg/ml	mg/ml	mg/ml	mg/ml
1.	PbS	0.50	0.50	0.56	0.50
2.	PbS -Zn^{+2}	0.35	0.40	0.36	0.29
3.	PbS -Co^{+2}	0.35	0.27	0.27	0.21
4.	PbS -Mn^{+2}	0.34	0.34	0.19	0.26
5.	PbS - Ni^{+2}	0.26	0.27	0.24	0.22
6.	VS	0.50	0.48	0.47	0.41
7.	VS -Co^{+2}	0.34	0.40	0.27	0.29
8.	VS -Zn^{+2}	0.25	0.33	0.18	0.18
9.	VS -Mn^{+2}	0.31	0.27	0.27	0.29
10.	VS - Ni^{+2}	0.21	0.40	0.27	0.29

Table 4
Antimicrobial activity of ligands and their metal complexes.

S.No.	*E. Coli* (-)				*S. aureus* (+)		*M. luteus*(+)			*B. lichenformis*(+)		
	100 ppm	500 ppm	1000 ppm	100 ppm	500 ppm	1000 ppm	100 ppm	500 ppm	1000 ppm	100 ppm	500 ppm	1000 ppm
PbS	19(±.415)	24(±305)	30(±.465)	20(±.278)	26(±.275)	36(±304)	18(±.411)	23(±.627)	26(±.968)*	18(±.200)	24(±.276)	26(±.305)
PbS $_{Zn}^{+2}$	21(±.411)	27(±095)	34(±.305)	22(±.208)	27(±.304)	38(±424)	19(±.557)	25(±.578)	29(±.161)	20(±.197)	26(±.274)	32(±.329)
PbS $_{Co}^{+2}$	21(±.200)	25(±421)	34(±.265)	23(±.562)	28(±.627)	39(±429)	20(±.629)	26(±.720)	30(±.410)	21(±.520)	26(±.999)*	32(±.200)
PbS $_{Ni}^{+2}$	20(±.305)	26(±264)	36(±.495)	22(±.307)	28(±.404)	39(±562)	21(±.604)	26(±.542)	30(±.172)	20(±.182)	27(±.189)	30(±.162)
PbS $_{Mn}^{+2}$	21(±.578)	28(±598)	36(±.528)	23(±.402)	28(±.208)	38(±211)	20(±.444)	27(±.208)	32(±.127)	20(±.203)	28(±.551)	29(±.567)
VS	19(±.424)	24(±200)	31(±.578)	21(±.224)	26(±.994)*	35(±558)	18(±.629)	24(±.548)	27(±.547)	19(±.208)	25(±.304)	26(±.424)
VS $_{Zn}^{+2}$	20(±.304)	26(±.129)	32(±.425)	22(±.598)	27(±.502)	38(±455)	20(±.429)	26(±.547)	29(±.128)	20(±.181)	26(±.195)	28(±.209)
VS $_{Co}^{+2}$	21(±.416)	27(±493)	34(±.162)	23(±.161)	27(±.494)	36(±304)	21(±.330)	27(±.320)	32(±.429)	219±.305)	27(±.161)	30(±.265)
VS $_{Ni}^{+2}$	21(±.465)	26(±402)	35(±.122)	23(±.208)	28(±.305)	38(±551)	19(±.578)	28(±.203)	30(±.120)	20(±.094)	26(±.204)	32(±.365)
VS $_{Mn}^{+2}$	20(±.365)	28(±320)	36(±.182)	22(±.302)	27(±.122)	37(±162)	19(±.560)	28(±.512)	30(±.495)	20(±.611)	26(±.712)	30(±.182)
Ofloxacin	21±.325	24±.369	28±.458	25±.458	28±.658	32±.259	19±.264	23±.265	25±.359	19±.458	24±.501	25±.650

Significance level (P<.001), (P<.01).*

CONCLUSION

The result of this investigation supports the suggested structure of the metal complexes. A square planner structure was suggested for all the complexes, the Schiff base ligands were found to be biologically active and their metal complexes display enhanced antimicrobial activity against one or more strains, chelation tends to make the ligands act as more powerful and potent bactericidal agent. .

ACKNOWLEDGMENT

We are thankful to the Principal, Head chemistry department, Govt. College Ajmer for providing research facilities and Central Drug Research Institute, Lucknow, for spectral studies.

REFERENCES

1. Mohammad I H B and Mohammad A, *Applied Organometallic Chemistry,* 19, 864-869, (2005).
2. Sheela C D, Gomathi A and Chandran S R, *Tharmaras P. Polish J. Chem*., 80, 1781, (2006).
3. Sidoappa K, Reddy T, Malukarjun M and Reddy C V, *E-Journal of Chemistry*, 5 (1): 155, (2008).
4. Elzahany E A, Hegab E A, Khalil S K H and Youssef N S, *Australian journal Of Basic and Applied Sciences*, 2 (2): 210, (2008).
5. Prasad Y R, Kumar P P, Kumar P R and Rao S S, *E-Journal of Chemistry*, 5 (1): 144, (2008).
6. Sathisha M P, Revankar V K and Pai K S R, *"Metal Based Drugs"* 2008, Article ID 362105, DOI 10.1155/2008/362105.
7. Chandra S, Raizada S, Tyagi M and Gautam A, "*Bioinorganic Chemistry and Applications*, 2007, Article ID 51483 DOI 10.1155/2007/51483.
8. Gudasi K B, Havanur V C, Patil S A and patil B R, *"Metal Based Drugs"*, 2007, DOI 10.1155/2007/37348.
9. Vidyavati R, Nirdosh P and Angadi S D, *Journal of Chem.*, 5 (3): 577, (2008).
10. Nair R, Shah A, Baluja S and Chanda S, *J. Serb. Chem. Soc.*, , 71 (7): 733, (2006).
11. Spinu C, Pleniceanu M and Tigae C, *Turk J. Chem.*, 32, 487, (2008).
12. Revanasidappa M, Swesh T, Khasim S, Raghavendra S C, Basavaraja C and Angadi S D, *E-Journal of Chemistry,* 5 (2): 395, (2008).
13. Panchal P K, Pansuriya P B and Patel M N, *Journal of enzyme Inhibition and Medicine Chemistry,* 21, (4): 453-458, (2006).