Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2010, 2(5): 329-336
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X

Antibacterial Properties of Mn (II), Co (II), Ni (II) and Zn (II) Complex of derived from Schiff base Trimethoprim

Sunil Joshi, Vatsala Pawar and V.Uma*

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

ABSTRACT

In the present study, Schiff bases have been synthesized by the condensation of Trimethoprim with p-Chlorobenzaldehyde and Vanillin respectively in methanol. Further their metal complexes have been synthesized by metal salts of Mn (II), Co (II), Ni (II) and Zn (II). Structural assignment of these compounds has been made on the basis of molecular weight, molar conductivities, elemental analysis, UV, IR and ^{1}HNMR spectral data. Synthesized compounds were screened for their in vitro growth inhibiting activity against different strains of bacteria viz., gram positive Staphylococcus aureus, Bacillus licheniformis, Micrococcus luteus and gram negetive Escherichia coli and were compared with the standard antibiotic oflaxocin

Key word:- antibacterial activity of drug and aldehydes.

INTRODUCTION

There is a considerable interest in the coordination chemistry of Schiff bases with various metal ions, [1-6] partially due to their capability of acting as multidentate N-N and N-O donors with the formation of mono or polynuclear complexes. [8, 9] Metal complexes of Schiff bases have been extensively studied due to their synthetic flexibility, [7, 10] selectivity and sensitivity towards the central metal atom. The chemistry of Schiff base complexes continues to attract many researchers because of their applications in various fields like food and dyes industry, analytical chemistry, catalysis and biological studies. [11-15] It was therefore, proposed to investigate the ligation properties of Schiff bases derived from trimethoprim with p-chlorobenzaldehyde and vanillin and their complexes with metals ion [16, 17].

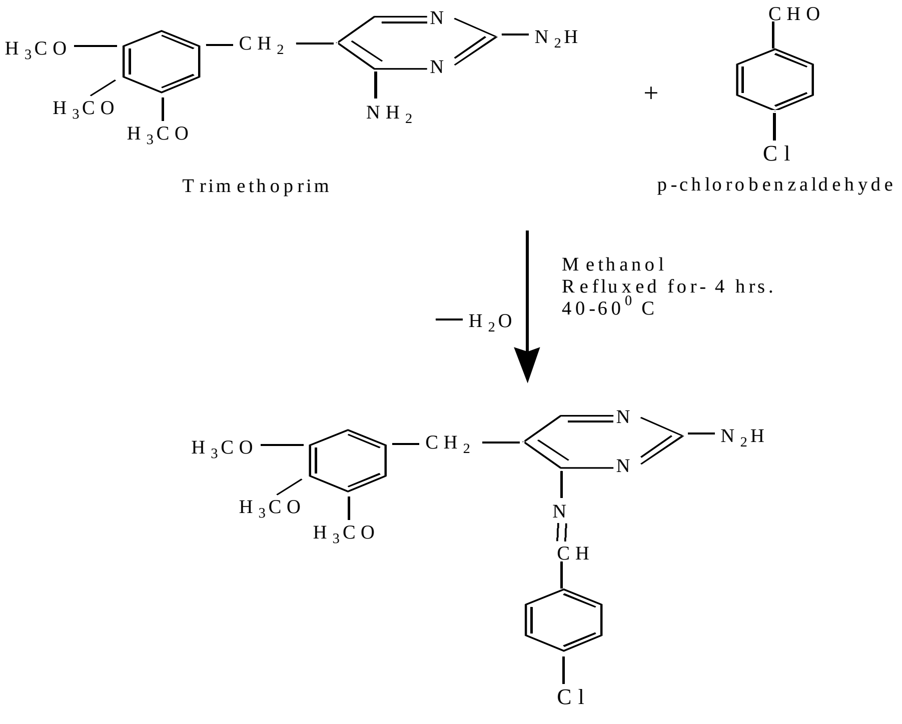
MATERIALS AND METHODS

All chemicals and solvent used were of analytical grade **.** All metal (II) salts were used as chloride. UV-VIS spectra were obtained on a Perkins Elmer spectrophotometer in the 300-900nm range in DMF.

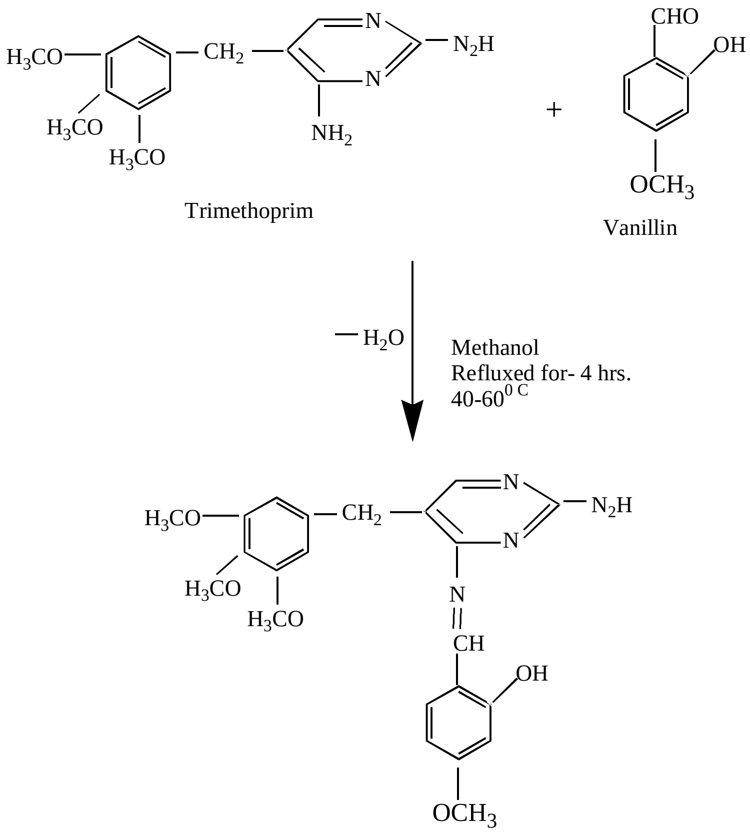
IR spectra were recorded using KBR disc on a FT-IR spectrophotometer, Shimadzu 8201PC in the range of 4000-400cm^{-1}. ^{1}HNMR spectra were recorded in MeOD at room temperature. Elemental analysis was carried out on a vario EL III Elementar Carlo- Erba 1108. Conductance measurement of 10^{-3} M solution of the complexes in DMF was carried out on an Equiptronic model no. Eq-660A. Melting point of the ligands and their 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 [11, 15].

Synthesis of the ligands- (PbT, VT)

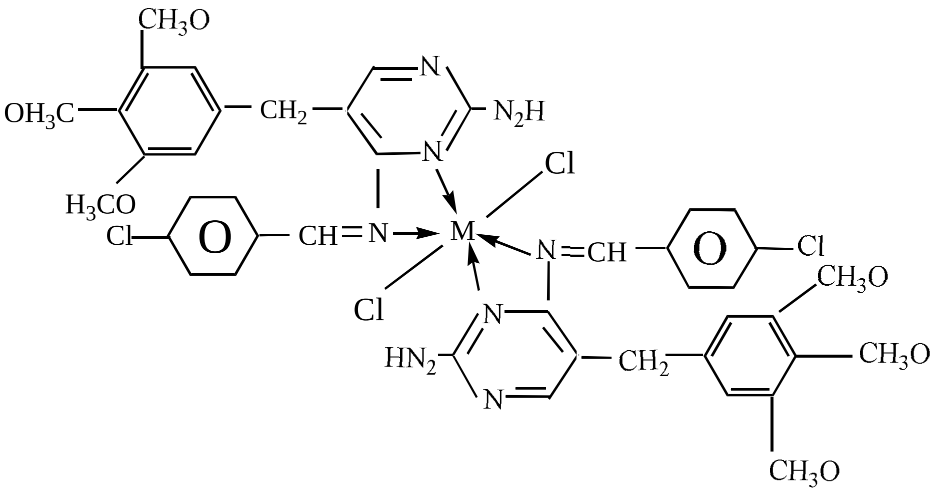
Trimethoprim (1.827 gm, 1 mol.) was dissolved in methanol (10 ml) was added to the *p*-Chlorobenzalehyde (0.702gm, 1 mol.) and Vanillin (0.7607 gm, 1 mol) respectivily dissolved in methanol (10 ml). To this few drops of KOH (0.1 % in methanol) was added to adjust the pH 7-8 and the mixture was refluxed for 4 hrs. After complete refluxation yellow and brown coloured precipitate was separated after removal of the solvent at room temp. The precipitate was recrystallised at room temperature with some solvent like as petroleum ether and it was dried under vacuum.



Ligand PbT



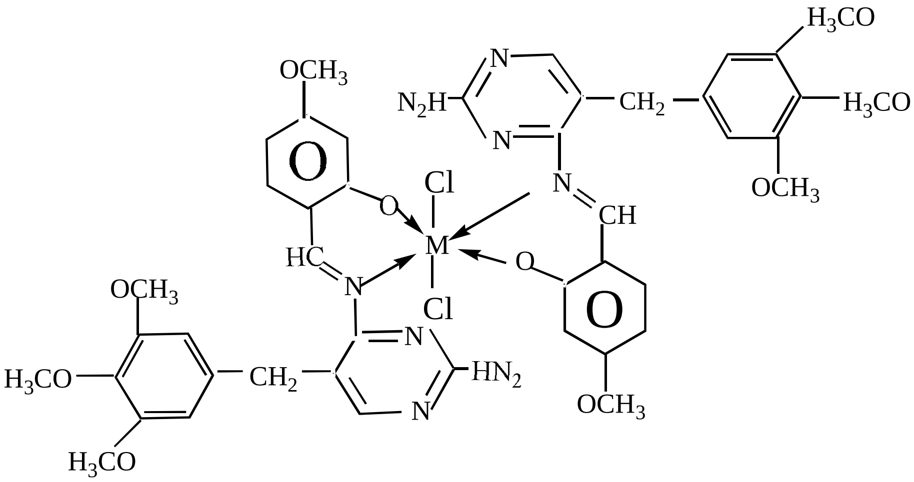
Ligand VT



Metal Complex PbTM

Synthesis of metal complexes- (PbTM, VTM)
Trimethoprim (0.2 mol.), *p*-Chlorobenzalehyde (0.2 mol.) Vanillin (0.2 mol) and (0.1 mol.) metal chlorides of Ni (II), Zn (II), Mn (II), and Co (II), were dissolved in methanol (10 ml)

separately. To this few drops of KOH (0.1 % in methanol) was added to adjust the pH of the solution between 7-8 and the mixture was refluxed for 4-5 hrs. A green and dark brown colored product was isolated after reduction of solvent volume by evaporation, which was filtered, washed with methanol and then recrystallised with methanol and dried over vacuum.



Metal Complex VTM

Antibacterial Studies

The synthesised metal complexes and Schiff base ligands were screened for their antibacterial activity against pathogenic bacteria species like gram (-) *E. coli* and gram (+) *S. aureus, M. luteus and B. lichenformis* (ATCC), which were grow in nutrient agar medium at 37 ^{0} C for 24 hrs. The paper disc diffusion method was adopted for the determination of antibacterial activity. Antibiotics ofloxacin was used as positive control.

Antibacterial activities of the compounds were tested against using Muller Hinton agar medium. The sterilized (autoclaved at 121°C for 15 min) medium (40-50°C) was poured into the Petri dishes to give a depth of 3-4 mm and allowed to solidify. The suspension of the microorganism then streaked on plates. The paper discs impregnated with the test compounds was placed on the solidified medium. The plates were pre-incubated for 1 h at room temperature and incubated at 37°C for 24 h. Ofloxacin was used as standard. The observed zone of inhibition is presented as mean ±SEM in table (IV), and also the MIC values are shown in table (III).

RESULT AND DISCUSSION

Characterization of the compound

All the synthesis compounds are air and moisture stable, intensely colored amorphous solid. The of ligands decomposes between range 140-200^{0}C and metal complexes range between 210-350^{0}C. There ligands are soluble in methanol, DMF and DMSO and metal complexes are soluble in DMF and DMSO, but they insoluble in common organic solvent like chloroform, acetone, ether, ethanol and carbon tetra chloride.

The molar conductance of the complexes ranges between (0.22-0.46 ohm^{-1} cm^2 mol^{-1}) which was carried out in DMF solvent indicates that the complexes 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 ligand was confirmed 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 in the range (412-424) ligands and (910-930) metal complexes, confirming the monomeric nature of the compounds. The yield of compounds found in the range of (60-80 %). All microanalytical datas show in table (I).

All the spectral data was consistent with the assigned structure of the compounds. In the bands IR spectraum, the (Ar-OH) observed at 3428 cm^{-1} in the ligand (VT) and disapiared in metal complexes showing the participation of the O-M group in coordnation. The ligands show strong band in the regin1610-1614 cm-1 due to C=N which is assignable to the Schiff bases, which appeared in both synthesized ligands. This band gets shifted to lower frequency in the complexes , indicating the coordination through azomethine nitrogen. 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 440-470 cm^{-1} for (M-O) which are assigned to metal stretching vibration. The ^{1}HNMR spectral data of ligands (PbT) and **(**VT) shows signal between δ7.54-7.61 and δ7.48-7.57 respectively due to aromatic ring which gets shifted downfield in their metal complexes. The VU-VIS spectra of ligands (PbT and VT) showed two bands between 320-335 nm and 350-370 nm. The first band may be due to Π – Π* transition within the arometic ring. The second band would be due to n- Π * transition within –C=N group. As shown in table (II).

Table I: Micro analytical data of their ligand and metal complexes

S. No.	**Name of compound**	**Carbon Found (calc.)**	**Hydrogen Found (calc.)**	**Oxygen Found (calc.)**	**Nitrogen Found (calc.)**	**Conductivity ohm^{-1} cm^{2} mol^{-1}**	**M.P. (°C)**	**M.W. found (calc.)**	**Colour**	**Yield in %**
1.	PbT	53.36 (53.39)	3.58 (3.78)	12.45 (12.78)	11.16 (11.29)	0.42	182	410.6 (412.8)	Orange	62
2.	PbT -Ni^{+2}	49.02 (49.42)	3.21 (3.48)	11.24 (11.69)	10.31 (10.48)	0.31	240	914.8 (918.4)	Light green	70
3.	PbT -Co^{+2}	50.32 (50.58)	3.40 (3.48)	11.22 (11.86)	10.12 (10.29)	0.34	280	915.8 (918.6)	Dark green	78
4.	PbT -Mn^{+2}	50.12 (50.41)	3.15 (3.46)	11.29 (11.48)	10.08 (10.46)	0.22	290	912.8 (913.7)	Yellow	75
5.	PbT -Zn^{+2}	49.42 (49.88)	3.12 (3.54)	11.77 (12.05)	10.02 (10.28)	0.28	308	922.5 (925.2)	Cream	73
6.	VT	52.16 (52.58)	4.25 (4.38)	20.64 (20.86)	10.62 (10.85)	0.46	198	422.6 (424.4)	brown	74
7.	VT -Co^{+2}	48.89 (50.12)	3.45 (3.75)	11.89 (12.08)	10.03 (10.09)	0.24	320	939.5 (941.8)	brown	68
8.	VT -Ni^{+2}	48.68 (48.83)	3.48 (3.64)	11.42 (11.89)	10.02 (10.24)	0.39	348	912.6 (914.6)	Light brown	70
9.	VT -Mn^{+2}	49.06 (49.22)	3.70 (3.84)	19.11 (19.38)	10.14 (10.20)	0.41	294	935.6 (936.1)	yellow	69
10.	VT -Zn^{+2}	48.19 (48.46)	3.63 (3.82)	11.44 (11.84)	10.00 (10.16)	0.37	346	946.2 (948.4)	Light brown	72

All the compounds were evaluated for their antibacterial activity *in vitro* by using zone inhibition technique against *E.coli*(-) *S.aureus*(+) *M.luteus*(+) and *B.licheniformis* (+) at different concentration (100, 500 and 1000ppm). Experiments were repeated three times and the results were expressed as (Mean±SEM) values in table (IV). The results obtained were compared with the standard drug Ofloxacin. PbT .38 mg/ml shows is most active against *E. coli* and VT is .37 mg/ml shows is most active against *S.aureus*. The metal complexes screaned an increased in activity in comparision with ligands. The MIC values are also shown in table (III).

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

S.No	**Comp.**	**IR spectra cm^{-1}**					**^{1}HNMR Spectra ppm**			**U.V. Visible**	
		(O-M)	(Ar-OH)	(N-M)	(C=N)	(Ar-CH)	δ(CH=CH)	δ(Ar-H)	(N=H)	(C=C)	(C=N)
1.	PbT	-	-	-	1610	3028	4.81	6.78-7.4	7.61	320	350
2.	PbT -Ni^{+2}	-	-	542	1590	3012	4.32	6.17-7.1	7.52	321	330
3.	PbT -Co^{+2}	-	-	541	1585	3015	4.79	6.44-7.2	7.48	321	338
4.	PbT -Mn^{+2}	-	-	568	1592	3018	4.55	6.12-6.26	7.49	322	340
5.	PbT -Zn^{+2}	-	-	558	1588	3016	4.56	6.15-7.01	7.54	320	342
6.	VT	-	3428	-	1614	3030	5.24	6.79-7.32	7.57	330	370
7.	VT -Co^{+2}	440	-	530	1598	3014	5.18	6.45-7.18	7.39	328	340
8.	VT -Ni^{+2}	458	-	557	1592	3016	4.89	6.23-7.16	7.42	332	352
9.	VT -Mn^{+2}	448	-	578	1589	3020	4.74	6.77-6.75	7.40	329	348
10.	VT -Zn^{+2}	470	-	572	1584	3019	4.82	6.42-7.18	7.45	331	358

Table III:- MIC of the ligand and their metal complexes.

Name of Compound	***E. Coli* (-)**	***S.Aureusi*(+)**	***M. Luteus*(+)**	***B. Lichenformis*(+)**
	mg/ml	**mg/ml**	**mg/ml**	**mg/ml**
PbT	0.38	0.41	0.43	0.42
PbT $_-$Ni^{+2}	0.29	0.30	0.29	0.30
PbT $_-$Co^{+2}	0.30	0.31	0.32	0.31
PbT $_-$Zn^{+2}	0.28	0.29	0.30	0.31
PbT $_-$Mn^{+2}	0.27	0.28	0.28	0.29
VT	0.42	0.37	0.48	0.43
VT -Ni^{+2}	0.32	0.28	0.29	0.30
VT -Zn^{+2}	0.30	0.29	0.31	0.31
VT –Co^{+2}	0.30	0.29	0.30	0.30
VT -Mn^{+2}	0.28	0.27	0.29	0.28

Table IV:- Antimicrobial activity of ligands and their metal complexes.

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

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
PbT	19±.526	26±.574	35±.303	15±.027	25±.424	32±.372	17±.994*	23±.096	33±.304	16±.502	25±.305	33±.155
PbT _Ni^{+2}	20±.306	29±.304	36±.502	19±.434	28±.26	34±.300	18±.304	26±.305	34±.094	19±.265	27±.557	34±.304
PbT _Co^{+2}	20±.418	28±.584	36±.491	19±.155	27±.674	35±.304	18±.614	27±.960*	36±.494	17±.301	27±.465	35±.306
PbT _zn^{+2}	21±.310	29±.294	38±.370	18±.495	26±.354	34±1.05	19±.206	27±.712	35±.059	18±.680*	26±.156	36±.305
PbT _Mn^{+2}	20±.209	28±.304	37±.759	17±.255	27±.582	35±.154	19±.405	28±.416	37±.205	20±.304	27±.304	34±.208
VT	18±.208	24±.870*	35±.328	19±.152	27±.960*	37±.261	16±.234	25±.251	34±.054	17±.105	25±.308	35±.269
VT _Ni^{+2}	20±.309	28±.260	37±.207	20±.402	29±.400	38±.153	19±.584	26±.416	35±.155	18±.302	27±.204	37±.308
VT _Zn^{+2}	19±.251	27±.208	38±.466	20±.090	28±.208	39±.175	20±.114	26±.416	37±.201	20±.232	26±.106	38±.374
VT _Co^{+2}	19±.116	28±.232	38±.204	20±.058	28±.379	38±.205	18±.496	26±.208	36±.502	19±.236	28±.498	37±.466
VT _Mn^{+2}	20±.419	29±.344	37±.394	22±.494	29±.208	39±.266	19±.559	27±.379	38±.262	20±.438	27±.347	36±.615
Ofloxacin	24±.452	29±.652	33±.326	25±.254	30±.546	34±.125	24±.245	28±.154	32±.258	20±.298	25±.499	30±.356

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 show 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 principal and head govt. college Ajmer for providing facilities. SAIF , central drug research institute , Lucknow, for spectral studies.

REFERENCES

[1] K. Sharma, R. Mishra and S. Sharma, *Asian J. Chem.*, **2010**, 14, 1453.
[2] V.I. Pekhnyo, S.P. Orysyk, V.V. Bon and V.V. Orysyk, *Polish J. Chem.,2006*, 80, 1789.
[3] Z.H. Chohan, M.A. Mohammad, A. Akhtar, *Bio- Inorganic Chem. and Application*, **2006**, 83**,** 131.
[4] Z.H. Chohan, *Applied Organometalic Chemistry*, **2006**, 20, 2, 112.
[5] A.A. Chavan and N.R. Pai, *Molecules*, **2007**, 12, 2467-77.
[6] Z.H. Chohan, M. Hassan, K.M. Khan and C.T. Supuran, *J. Enz. Inhib. Med. Chem.*, **2005**, 20, 183-88.
[7] Muthukumaran, *Spectrochim Acta A Mol Biomol Spectrosc*, **2008**, 71, 628-35.
[8] M.A. Neelakantan, F. Rusalraj, J. Dharmaraja, S. Johnsonraja, T. Jeyakumar and M.S. Pillai, *Spectrochim Acta A Mol. Biomol. Spectrosc.*, **2008**, **7**, 1599-609.
[9] P.D. Mehata, *Indian J. Pharm. Sci.*, **2006**, 68, 101-103.
[10] S.J. Wadher, *Int.J. PharmTech Res.*, **2009**, 1,(1), 33.
[11] P. Mittal and V. Uma, *Int. J. Chem. Sci.*, **2008**, 6, 2, 1050-1060.
[12] R. Rajavel and C.N. Krishnan, *Orient. J. Chem.*, **1998**, 14(2), 313.
[13] C. Erdal and K. Mehmet, *J. Coord. Chem.*, **2004**, 57(14), 1217- 1223.
[14] L.I.V. Jian-ning, W.U. Bo-wan, B. Zhang and L.I.U. Yongchun, *Turk. J. Chem.*, **2006**, 30, 41-48.
[15] P. Mittal and V. Uma, *Asian Journal of Chemistry*, **2009**, 21**,** 2, 1230-1238.
[16] R. Nair, A. Shah, S. Baluja and J. Chanda, *Serbi, Chem. Soc.*, **2006**, 71(7)**,** 733-744.
[17] Z.A. Filmwala, S.M. Nandavadekar and R.M. Patil, *Asian Joural of Chemistry*, **2007**, 19 (6)**,** 4697-4703.