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SYNTHESIS AND ANTIMICROBIAL ACTIVITIES OF N-S DONOR LIGAND AND ITS TRANSITION METAL COMPLEXES

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ABSTRACT

Mn (II), Co (II), Ni (II), Pd (II) and Pt (II) complexes having the general composition $M(L)_2Cl_2$ [where L = p-Vanillin thiosemicarbazone, M= Mn (II), Co (II), Ni (II), Pd (II) and Pt (II) have been synthesized. All these compounds were characterized by elemental analysis, IR, ^1H NMR and electronic spectral studies. On the basis of spectral studies, an octahedral geometry has been assigned for Mn (II) and Co (II) complexes whereas square planar geometry have been assigned for Ni (II), Pd (II) and Pt (II) complexes. The free ligand and its metal complexes have been tested *in vitro* against a number of microorganisms in order to assess their antimicrobial properties. The antimicrobial data reveals that the metal complexes act as more active antibacterial agents than the uncomplexed ligand from which they are derived.

Key words : Thiosemicarbazone, Transition metal complexes, Synthesis, Antimicrobial

INTRODUCTION

For many years, thiosemicarbazones and their metal complexes have been the subject of most structural and medicinal studies because of their biological potential[1-3]. It has been believed that the thiosemicarbazones are efficient in certain biological mechanisms because of their chelating ability towards trace metal ions. The bacterial and fungicidal activities of transition metal complexes are due to their ability to form chelates with the essential metal ions bonding through nitrogen as well as sulphur donor atom of ligand. In addition to antitumor effect of transition metal complexes of thiosemicarbazones[4-6], it is well known that they are also antiviral and even anti-HIV chemicals[7, 8]. Further, it can be mentioned that the thiosemicarbazones have anticonvulsant,

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antimalarial, antiamoebic and antioxidant properties as other biological activities[9-15]. In the present paper, we report the synthesis and biological studies of Mn (II), Co (II), Ni (II), Pd (II) and Pt (II) complexes with a bidentate ligand (Fig. 1).

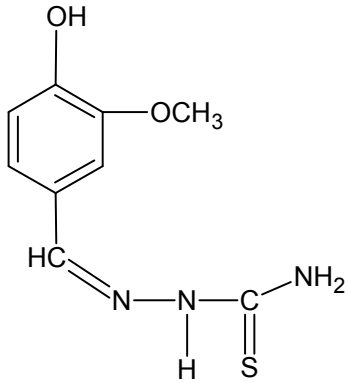


Fig. 1. Structure of ligand (L)

EXPERIMENTAL

All the chemicals used were of AnalaR grade and procured from Sigma-Aldrich and Fluka. Metal salts were purchased from E. Merck and were used as received.

Synthesis of ligand

Hot ethanolic solution of thiosemicarbazide (1.82 g, 0.02 mol) and ethanolic solution of p-vanillin (3.04 g, 0.02 mol) were mixed slowly with constant stirring. This mixture was refluxed at 70-80 ^{0} C for 3 hrs. The completion of the reaction was confirmed by the TLC. The reaction mass degassed on a rotatory –evaporator, over a water bath. The degassed reaction mass, on cooling gives white colored crystals. They were filtered, washed with cold EtOH and dried under vacuum over $P_4O_{10.}$

Synthesis of complexes

Hot ethanolic solution (20 mL) of corresponding metal salts (0.01 mol) were mixed with hot ethanolic solution of the respective ligand (0.01 mol) and refluxed for 3-4 h at 70-80^{0}C. On cooling the contents, the colored complex separated out in each case. It was filtered, washed and recrystalized with 50% ethanol and dried under vacuum over $P_4O_{10.}$ Purity of the complexes were checked by TLC.

Physical measurements

The C, H and N were analyzed on Carlo-Erba 1106 elemental analyzer. The nitrogen content of the complexes was determined using Kjeldahl's method. Molar conductance was measured on the ELICO (CM 82T) conductivity bridge. Magnetic susceptibility was measured at room temperature using $CuSO_4.5H_2O$ as calibrant. ^1H NMR spectra were recorded at room temperature on a Brucker Advance DPX-300 spectrometer using DMSO-d_6 as a solvent. IR spectra (KBr) were recorded on FTIR spectrum BX-II spectrophotometer. The electronic spectra were recorded in DMSO on Shimadzu UV mini-1240 spectrophotometer.

Antibacterial screening

The antibacterial activitity of the ligand and its metal complexes were tested by using paper disc diffusion method [16, 17] against *S. aureus* and *E. coli.* The test compounds in measured quantities were dissolved in DMF to get a concentrations of 250 and 125 ppm of compounds. 25 mL nutrient agar media (NA) was poured in each petriplates. After solidification, 0.1 mL of test bacteria was spread over the medium using a spreader. The disc of Whatmann No. 1 filter paper having the diameter 5.00 mm each containing (1.5 mg cm^{-1}) of compounds were placed at 4 equidistant places at a distance of 2 cm from the center in the inoculated petriplates. Filter paper disc treated with DMF served as control and streptomycin was used as a standard drug. All determinations were made in duplicate for each of the compounds. Average of two independent readings for each compounds was recorded. These petriplates were kept in refrigerator for 24 hrs for pre-diffusion. Finally, petriplates were incubated for 26-30 hours 28 ± 2ºC. The zone of inhibition was calculated in mm carefully.

Antifungal screening

The preliminary fungitoxicity screening of the compounds were performed against the test fungi, *R. bataticola* and *A. niger* by the food poision technique[18-20]. Stock solutions of compounds were prepared by dissolving the compounds in DMF. Chlorothalonil has been used as commercial fungicide and DMF served as a control. Appropriate quantities of the compounds in DMF was added to potato dextrose agar medium in order to get a concentrations of 250 and 125 ppm of compound in the medium. The medium was poured into a set of two petriplates under aseptic conditions in a laminar flow hood. When the medium in the plates was solidified, a mycelial discs of 0.5 cm in diameter was cut from the periphery of the 7 days old culture and it was aseptically inoculated upside down in the centre of the petriplates. These treated petriplates were incubated at 26 ± 1ºC until fungal

growth in the control petriplates was almost complete.

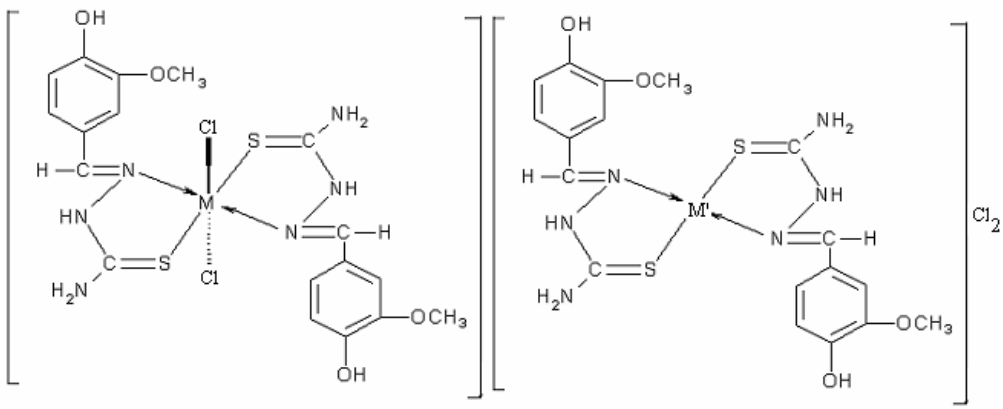
The mycelial growth of fungi (mm) in each petriplates was measured diametrically and growth inhibition (I) were calculated by using the formula :

$$I\ (\%) = (C\text{-}T)/C \times 100$$

Where C and T is the growth of control and test compounds (mm), respectively.

RESULTS AND DISCUSSION

On the basis of elemental analysis, the complexes were assigned to possess the compositions as shown in Table 1.The molar conductance data of the Mn (II) and Co (II) complexes in DMSO lies in the range 9.2 -10 $\Omega^{-1}cm^2mol^{-1}$ indicating non-electrolytic nature. However, Ni (II) Pd (II) and Pt (II) complexes are 1 : 2 electolytes with conductance values of 208-217 $\Omega^{-1}cm^2mol^{-1}$. Thus these complexes may be formulated as $[M\ (L)_2Cl_2]$ and $[M'\ (L)_2]Cl_2$ [M= Mn (II), Co (II), M'= Ni (II), Pd (II) and Pt (II)]. On the basis of above spectral studies, the following structures may be suggested for the complexes (Fig. 2).



[where M=Mn (II), Co (II) and M'= Ni (II), Pd (II) and Pt (II)]

Fig. 2: Structure of complexes

The antimicrobial data (Table 3 and 4) indicate that most of the complexes have higher antimicrobial activity than the free ligand. Such increased activity of the metal chelates can be explained on the basis of chelation theory. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups.

Table 1. Molar conductance and elemental analysis data of the complexes

Compound	Molar conductance ($\Omega^{-1}cm^2mol^{-1}$)	Colour	M. P. (°C)	Yield (%)	Elemental analysis found (calculated) (%)			
					Metal	C	H	N
Ligand ($C_9H_{11}N_3O_2S$)	-	White	195	65	-	47.97 (48.00)	4.86 (4.89)	18.62 (18.67)
$[Mn(L)_2Cl_2]$ $MnC1_8H_{22}N_6O_4S_2Cl_2$	10	Light Pink	260	62	10.1 (9.55)	37.51 (37.50)	3.86 (3.82)	14.64 (14.58)
$[Co(L)_2(NO_3)_2]$ $CoC1_8H_{22}N_6O_4S_2Cl_2$	9.2	Pink	230	64	10.18 (10.15)	37.2 (37.24)	3.84 (3.79)	14.43 (14.48)
$[Ni(L)_2]Cl_2$ $NiC1_8H_{22}N_6O_4S_2Cl_2$	212	Brick red	245	70	10.13 (10.15)	37.22 (37.24)	3.76 (3.79)	14.45 (14.48)
$[Pd(L)_2]Cl_2$ $PdC1_8H_{22}N_6O_4S_2Cl_2$	217	Yellow	272	66	16.93 (16.90)	34.47 (34.45)	3.57 (3.51)	13.42 (13.39)
$[Pt(L)_2]Cl_2$ $PtC1_8H_{22}N_6O_4S_2Cl_2$	208	Yellow	287	62	27.2 (27.23)	30.21 (30.16)	3.1 (3.07)	11.76 (11.73)

Table 2 (a). ^{1}H NMR and IR spectral data of the ligand (L) and its complexes

Compounds	^{1}H NMR (δ ppm)			IR data (cm^{-1})					
	HC=N	N-H	OCH_3	ν(N-H)	ν(N-N)	ν(C=N)	ν(C=S)	ν(M-S)	ν(M-N)
Ligand(L)	8.02	10.9	3.62	3245	1104	1585	765	-	-
$[Mn(L)_2Cl_2]$	-	-	-	3252	1120	1548	752	312	432
$[Co(L)_2Cl_2]$	-	-	-	3258	1125	1559	746	309	450
$[Ni(L)_2]Cl_2$	8.18	10.6	3.6	3240	1118	1556	744	315	442
$[Pd(L)_2]Cl_2$	8.22	10.8	3.61	3260	1122	1562	758	310	455
$[Pt(L)_2]Cl_2$	8.24	10.9	3.6	3267	1116	1545	740	318	447

Table 2(b). Magnetic moments and electronic spectral data of the complexes

Complexes	μ_{eff} (BM)	λ_{max} (cm^{-1})
$[Mn(L)_2Cl_2]$	5.85	18500, 23310, 24440, 27932
$[Co(L)_2Cl_2]$	5.08	9727, 15438, 18975
$[Ni(L)_2]Cl_2$	Diamagnetic	14492, 21645, 29062
$[Pd(L)_2]Cl_2$	Diamagnetic	20746, 22321, 25510
$[Pt(L)_2]Cl_2$	Diamagnetic	18867, 24271, 27778

Table 3. Antibacterial screening data of the ligand and its metal complexes

Compounds	Diameter of inhibition zone (mm) (conc. in μgmL^{-1})			
	S. aureus		*E. coli*	
	250	**500**	**250**	**500**
Ligand (L)	8	10	12	15
$[Mn(L)_2Cl_2]$	11	14	14	20
$[Co(L)_2Cl_2]$	14	19	17	24
$[Ni(L)_2]Cl_2$	17	21	18	22
$[Pd(L)_2]Cl_2$	22	26	25	31
$[Pt(L)_2]Cl_2$	24	30	28	33
Streptomycin (control)	28	32	32	36

Table 4. Antifungal screening data of the ligand and its metal complexes

Compounds	Fungal inhibition (%) (conc. in μgmL^{-1})			
	R. bataticola		*A. niger*	
	250	**500**	**250**	**500**
Ligand(L)	29	34	25	36
$[Mn(L)_2Cl_2]$	32	40	35	43
$[Co(L)_2Cl_2]$	39	59	42	56
$[Ni(L)_2]Cl_2$	48	62	50	65
$[Pd(L)_2]Cl_2$	57	70	60	74
$[Pt(L)_2]Cl_2$	61	75	63	78
Chlorothalonil (standard)	62	78	66	85

Further, it increases the delocalization of π-electrons over the whole chelating ring and enhances the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration of the cell and thus, blocks the synthesis of proteins, which restricts further

growth of the organism.

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REFERENCES

1. N. K. Singh, S. B. Singh, A. Shrivastav and S. M. Singh, Proc. Ind. Acad. Sci. (Chem. Sci.), **113**, 257 (2001).
2. I. Kizilcikh, B. Ulkuseven, Y. Dasdemir and B. Akkurt, Synth. React. Inorg. Met-Org. Chem., **34**, 653 (2004).
3. D. S. Mishra, M. Naskar, G. B. Drew and S. K. Chattopadhyay, Inorg. Chim. Acta, **359**, 385 (2006).
4. O. E. Offiong and S. Martelli, Trans. Met. Chem., **22**, 263 (1997).
5. M. C. Rodríguez-Argüelles, E. C. López-Silva, J. Sanmartín, P. Pelagatti, F. Zani, J. Inorg. Biochem., **9**, 2231 (2005).
6. E. M. Jouad, G. Larcher, M. Allain, A. Riou, G. M. Bouet, M. A. Khan and X. D. Thanh, J. Inorg. Biochem., **86**, 565 (2001).
7. D. C. Quenelle, K. A. Keith and E. R. Kern, Antiviral Research, **71**, 24 (2006).
8. J. Vamecq, K. V. Deproorten, J. H. Poupaert, J. Balzarini, E. De clercq and J. P. Stables, Life Sci., **63**, 267 (1998).
9. S. Sharma, F. Athar, M. R. Maurya, F. Naqvi and A. Azam, European J. Med. Chem., **40**, 557 (2005).
10. E. Labisbal, K. D. Haslow, A. S. Pedrares, I. V. Martinez, S. H. Ortega and D. X. West, Polyhedron, **22**, 2831 (2003).
11. R. K. Agarwal, L. Singh and D. K. Sharma, Bioinorg. Chem. Appli., (2006), 1D 59509, 10 pages (2006).
12. J. A. B. Jeragh and E. I. Dissouky, J. Coord. Chem., **58**, 1029 (2005).
13. G. Aguirre, L. Boiani, H. Cerecetto, M. Fernández, M. González, A. Denicola, L. Otero, D. Gambino, C. Rigol and C. Olea-Azarl, Bioorg. Med. Chem., **12**, 4885 (2004).
14. N. Bharti, F. Athar, M. R. Maurya and A. Azam, Bioorg. Med. Chem., **12**, 4679 (2004).

15. M. Karatep and F. Karatas, Cell Biochem. Funct., **24**, 547 ((2006).
16. H. A. Tang, L. F. Wang and R. D. Yang, Transition Met. Chem., **28**, 395 (2003).
17. S. Chandra, S. Raizada, M. Tyagi and A. Gautam, Bioinorg. Chem. Appl., 7 (2007).
18. N. K. Singh and A. Srivastava, Transition Met. Chem., **25**, 133 (2000).
19. S. Chandra, S. Raizada, M. Tyagi and P. K. Sharma, Spectrochim. Acta, **69A**, 816 (2008).
20. S. Chandra and M. Tyagi, J. Indian Chem. Soc., **85**, 42 (2008).

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