Available online at www.joac.info

ISSN: 2278-1862

Journal of Applicable Chemistry

2015, 4 (2): 609-614

(International Peer Reviewed Journal)

Study of Schiff Base Complexes of Mn(II), Co(II), Ni(II), Cr(III), Cu(II), Zn(II) and Cd(II) as Microbial Growth Inhibitors

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Accepted on 17th March 2015

ABSTRACT

The amino acid ligand [1-(2,4-dihydroxy-phenyl)-ethanone-(S)-alpha-amino-4-hydroxybenzenepropanoic acid] (DHPEAHP) was prepared by the reaction of 1-(2,4-dihydroxy-phenyl)-ethanone (DHPE) with (S)-alpha-amino-4-hydroxybenzene propanoic acid (AHP). The complexes of this ligand have been prepared using metal acetates of Mn(II), Co(II), Ni(II), Cr(III), Cu(II), Zn(II) and Cd(II) under reflux in methanol. The products were found to be crystalline solid. The complexes have been characterized by analytical, FT-IR, diffused reflectance, magnetic susceptibility measurements and Thermogravimetric analysis. All the compounds were screened for antibacterial activity against some clinically important bacteria, such as E. coli, S. typhy, S. aureus, P. aeruginosa and K. pneumonie by using nutrient agar medium and antifungal activity against C. albicans and A. niger species by using potato dextrose agar medium. The MIC values of the complexes were determined by the serial dilution techniques.

Keywords: Amino acid, DHPEAHP, antibacterial, antifungal, *MIC* value.

INTRODUCTION

Day by day Schiff bases are more frequently applied for the betterment of human welfare. The importance of the Schiff base is due its versatile nature. Literature survey shows that many Schiff bases exhibit biological activities [1-4] such as antifungal, antibacterial, antitumor, anti-inflammatory, and antipyretic, among others. Some of them have been used as complexing agents [5-6] and powerful corrosion inhibitors [7] They are synthesised from various compounds [8-11] Recently there has been a considerable interest in the chemistry of compounds of amino acid because of their potential pharmacological applications [12] .

Extensive investigations have been made on acetophenone amino acid Schiff bases and their metal complexes because of their possible use as potential N-pyridoxylidene amino acid systems [13]. Metal chelates of the Schiff bases derived from acetophenone and amino acids have been shown to be important class of compounds in elucidating the mechanism of transamination reaction in biological systems [14]. Amino acid Schiff bases are sensitive to moisture and decompose when exposed to air, hence they are usually generated immediately prior to use for complexation. This is because only a small number of crystalline Schiff bases derived from amino acids and acetophenone can be isolated [15].

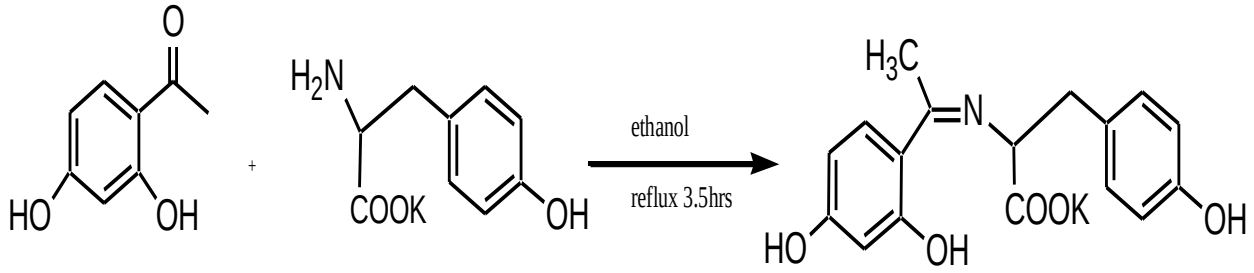
In the last decade, various electrically conductive substances have been studied extensively including polymers also [16]. Conducting substances have attracted much attention from both fundamental and

practical viewpoints. The study of aromatic substances that have a molecular structure containing π -bonds in chains is an active research area in the field of conducting substances [17]. Conductive substances have a number of potential technological applications in the areas of chemical transistors, including rechargeable batteries, electrochromic display devices and biochemical analyses [18]. in this work we report the synthesis and characterization of Schiff base derived from the condensation of (S)-alpha-amino-4-hydroxybenzenepropanoic with [1-(2,4-dihydroxy-phenyl)-ethanone] and their metal complexes with Mn(II), Co(II), Ni(II), Cr(III), Cu(II), Zn(II) and Cd(II) ions.

MATERIALS AND METHODS

All the chemicals were of A.R. grade and used as received. 1-(2,4-dihydroxy-phenyl)-ethanone was prepared by known methods. The solvents were purified by standard methods. IR spectra of the compounds were recorded on Perkin Elmer 842 spectrophotometer in the region 400-4000cm^{-1}. The diffuse reflectance spectra of the complexes were recorded on Varian Cary-5000 UV-visible spectrophotometer. The thermogravimetric analysis was performed in air atmosphere at 10^0 C min^{-1} heating rate. ^{1}H-NMR were acquired with BRUKER-400 spectrometer in DMSO-d^6. Elemental microanalysis was performed on a (C.H.N) analyser from heraeus (Vario EL). The magnetic moment measurement were made on a Gouy balance at room temperature using [$HgCo(SCN)_4$] as the calibrant.

Synthesis of [1-(2,4-Dihydroxy-phenyl)-ethanone-(S)-Alpha-amino-4-hydroxybenzene -propanoic acid] [DHPEAHP] : [1-(2,4-Dihydroxy-phenyl)-ethanone] (1.52 g, 0.01mmol) and (S)-Alpha-amino-4-hydroxybenzenepropanoic acid (1.81g, 0.01mmol) were placed in round bottomed flask in distilled methanolic medium, and few drops of acetic acid were added as a catalyst. The reaction mixture was refluxed on water bath for 3.5 h, precipitated crystals of Schiff base were obtained, filtered and recrystalised with ethanol and dried. The yield was found to be 69.34%. Following Scheme represents synthesis of ligand.



1-(2,4-Dihydroxy-phenyl)-ethanone

Potassium salt of (S)-Alpha-amino-4-hydroxybenzenepropanoic acid

DHPEAHP

Preparation of metal complexes: All the complexes were prepared by mixing a ethanolic solution of $M(CH_3CO)_n$ nH_2O with the methanolic solution of Schiff base DHPEAHP in a 1:1 molar ratio. The resulting mixture was refluxed on a water bath for 8–9 h. The colored product appeared on standing and cooling the solution. The precipitated complex was then filtered under suction and washed successively with hot water and methanol to remove unreacted ligand and metal acetate if any present and then dried.

RESULTS AND DISCUSSION

The ligand DHEPEAHP and its complexes have been characterized on the basis of ^{1}H NMR, IR spectral data, elemental analysis, diffused reflectance spectra, magnetic susceptibility measurements and Thermo gravimetric analysis data.

The tridentate *ONO* donor hydrazone ligand used in the present work was derived from the condensation of [1-(2,4-Dihydroxy-phenyl)-ethanone with (S)-Alpha-amino-4-hydroxybenzenepropanoic acid in

ethanol. The isolated complexes are bright in colour, quite air stable and can be stored for long periods. All the complexes are insoluble in water, soluble to very limited extent in common organic solvents but considerable extent in DMSO. The elemental analyses (Table 1) indicate that all these complexes have 1:1 metal: ligand stoichiometry.

Table 1: Analytical data, color and synthetic conditions of complexes of DHPEAHP

S.N0	Compounds	Color	Solvent used	Time of Reflux	Elemental analyses % found (calcd.)			
					M	C	H	N
1.	DHPEAHP	Yellow-orange	MeOH-EtOH	3.5 h.	--	57.32 (57.77)	4.21 (4.56)	3.41 (3.96)
2.	[Mn(DHPEAHP)(H_2O)$_3$]	Light brown	EtOH	6.0 h.	13.21 (13.02)	48.53 (48.35)	5.23 (5.00)	3.12 (3.33)
3.	[Co(DHPEAHP)(H_2O)]	Pink	EtOH	6.0 h.	15.28 (15.10)	54.12 (52.32)	4.21 (4.40)	4.22 (4.00)
4.	[Ni(DHPEAHP)(H_2O)$_3$]	Pista	DMF- EtOH	5.0 h.	14.00 (13.78)	47.66 (47.93)	4.78 (4.98)	3.30 (3.42)
5.	[Cr(DHPEAHP)(H_2O)$_3$]. (H_2O)	Green	DMF- EtOH	8.0 h.	12.05 (11.89)	46.47 (46.68)	5.18 (5.30)	3.47 (3.29)
6.	[Cu(DHPEAHP)(H_2O)]. 2(H_2O)	Pale green	DMF- EtOH	10.0 h	14.54 (14.75)	47.70 (47.39)	4.61 (4.92)	3.42 (3.25)
7.	[Zn(DHPEAHP)(H_2O)]	Pale orange	EtOH	8.0 h.	16.30 (16.48)	51.60 (51.47)	4.14 (4.32)	3.45 (3.53)
8.	[Cd(DHPEAHP)(H_2O)].(H_2O)	Light brown	EtOH	8.0 h	24.15 (24.35)	44.04 (44.22)	4.25 (4.15)	3.28 (3.03)

^{1}HNMR spectrum of DHPEAHP (300MHz, $CDCl_3$, δ in ppm) [19-21]: The ^{1}H NMR spectrum of ligand DHPEAHP has been recorded in $CDCl_3$, which indicated that different non- equivalent proton(s), resonates at different values of applied field. The δ-values in ppm are- 12.67 (1H, broad, s, phenolic -OH), 11.85 (1H, s, -NH), 7.65-6.37 (7H, m, Ar-H), 4.82 (1H, t, -CH), 2.56 (2H, d,-CH_2), 1.602 (3H, s, -CH_3).

Infrared Spectra: Results are presented in table 2.

Table 2: Infrared spectral data (cm^{-1}) of DHPEAHP and its metal complexes.

S.N.	Compounds	*ν*(O-H) /*ν*(OH--N)	*ν*(COO) assy	*ν*(COO) sym	*ν*(C-O)	*ν*(C=N)	*ν*(M-O)	*ν*(M-N)	*ν*(H_2O)
1.	DHPEAHP	3398	1678	1428	1300	1632	--	--	--
2.	[Mn(DHPEAHP)(H_2O)$_3$]	--	1610	1414	1310	1600	465	536	3226, 1516, 848
3.	[Co(DHPEAHP)(H_2O)]	--	1614	1400	1302	1608	470	534	3420, 1524, 864
4.	[Ni(DHPEAHP)(H_2O)$_3$]	--	1623	1396	1312	1604	468	524	3258, 1514, 806
5.	[Cr(DHPEAHP)(H_2O)$_3$] (H_2O)	--	1598	1394	1312	1598	480	512	3346, 1544, 804
6.	[Cu(DHPEAHP)(H_2O)] 2(H_2O)	--	1604	1398	1308	1602	478	546	3214, 1530, 826

7.	[Zn(DHPEAHP)(H_2O)]	--	1615	1394	1306	1604	472	525	3326, 1522, 810
8.	[Cd(DHPEAHP)(H_2O)] (H_2O)	--	1600	1390	1318	1614	477	538	3344, 1526, 804

APPLICATIONS

Antimicrobial Activity: The minimum inhibitory concentration (MIC) is the lowest concentration of an antimicrobial compound that inhibits the visible growth of a microorganism after overnight incubation. MIC of the various compounds against bacterial and yeast strains was tested through a modified agar well diffusion method [28].In this method, a two-fold serial dilution of each compound was prepared by first reconstituting the compound in DMSO followed by dilution in sterile distilled water to achieve a decreasing concentration range of 512 to 1 μg mL^{-1}. 100 μL of each dilution was introduced into wells (in triplicate) in the agar plates already seeded with 100 μL of standardized inoculums (10^6 cfu mL^{-1}) of the test microbial strain. All test plates were incubated aerobically at 37^{o}C for 24 h, and the inhibition zones were observed. MIC was recorded for each test organism.

To access the antibacterial activity of obtained compound Agar Well Diffusion method was used. This activity was determined by using Mullar Hinton Agar [29]. A loop full culture of each test organism were inoculated in sterilized nutrient agar and incubated overnight to obtain the broth culture. All the culture were inoculated on Mullar Hinton Agar plate by using sterile cotton swab after swabbing well was punched on media and the different dilutions of the compounds were added in to the well with the help of dropper. After addition of sample the plate were incubated at 37^{0}C for 24 h. After incubation period plates were examined and zone of inhibition were measured.

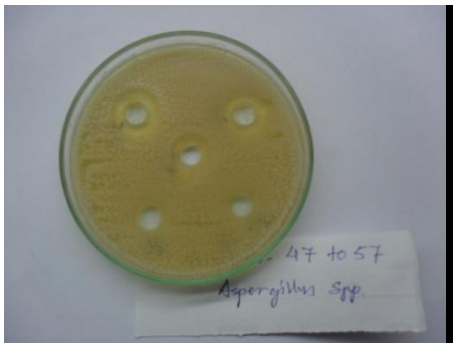
Antifungal activity: The *in vitro* antifungal assay was performed by the disc diffusion method [30]. The complexes and ligand were tested against the fungi *Aspergillus niger*, and *Candida albicans*, cultured on potato dextrose agar as the medium. In a typical procedure, a well was created on the agar medium and nystatin as the control was inoculated with the fungi. The well was filled with the test solution, which diffuses and the growth of the inoculated fungi is affected. The inhibition zone which developed on the plate was measured. The antimicrobial activity of ligand DHPEAHP and its complexes are shown in table 3.

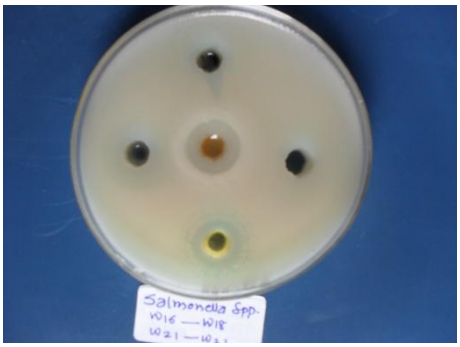
Table 3: Antimicrobial activities of ligand DHPEAHP and its metal complexes

Compounds	Antibacterial					Antifungal	
	E. coli	*S. typhi*	*S. aureus*	*P. auruginosa*	*K. pneumonie*	*A. niger*	*C. albicans*
DHPEAHP	06	20	19	16	18	17	20
Mn-DHPEAHP	25	26	26	22	10	25	08
Co-DHPEAHP	26	26	22	24	12	27	06
Ni- DHPEAHP	27	28	04	20	18	19	22
Cr- DHPEAHP	25	22	20	22	07	24	10
Cu-DHPEAHP	26	28	23	25	14	22	24
Zn- DHPEAHP	28	24	22	20	24	20	18
Cd-DHPEAHP	27	25	22	22	25	20	19
Amikacin	28	28	23	25	22	--	--
Fluconazole	-	-	-	-	-	25	24

The ligand DHPEAHP is active towards all strains except *E. coli*. Mn(II), Co(II), Cr(III) complexes shows high activity against *E. coli, S. typhi, P. auruginosa, A. Niger* and low activity against *K. pneumonie and C. albicans.* Complexes of Ni(II) and Cu(II) shows more active towards *E. coli, S. typhi* but inactive towards *S. aureus.* Zn(II) and Cd(II) complexes are found strongly reactive towards *K. pneumonie* and *E. coli* and shows moderate to low active against remaining microorganisms.

The increased toxicity of metal complexes may be due to the effect of the metal ion configuration and charge on the normal cell. A possible mode of toxicity may be specified by the chelation theory. Chelation reduces considerably the polarity of the metal ion mainly because of partial sharing of its π electrons and delocalization over the whole chelate ring. Such chelation increases the lipophilic character of the metal chelate, which probably tends to break down the permeability barrier of cells, resulting in interference with the normal cell process [31-32]. Thus, the results suggest that the variation in structure affects the growth of microorganisms and may result in an inhibitory effect, stimulatory effect or reduction in the toxicity of metal ions toward some microorganisms. Amikacin (100µg mL^{-1}) was used as a standard for antibacterial activity and Fluconazole (100µg mL^{-1}) was used as a standard for antifungal activity.





CONCLUSIONS

From the data of antimicrobial activity it was found that there was enhancement of activity after complexation also he activity increases with increase in concentration of the test solution.

ACKNOWLEDGMENTS

The authors are greatly thankful to SAIF, CDRI Lucknow and SAIF Cochin (Kerala) for providing spectral data, Head, Department of Microbiology for microbial activity and the Principal, Shri Shivaji college of Arts, Commerce and Science, Akola for providing necessary facilities.

REFERENCES

[1] S. Shah, R. Vyas, R. H. Mehta, *J. Ind. Chem. Soc.*, **1992,** 69, 590.
[2] S. N. Pandeya, D. Sriram, G. Nath, E. De. Clercq, *Eur. J. Pharma. Soc.*, **1999,** 9, 25.
[3] P. G. More, R. B. Bhalvankar, S.C. Patter, *J. Ind. Chem. Soc.*, **2001**, 78, 474.
[4] V. E. Kuzmin, A. G. Artemenko, R. N. Lozytska, A. S. Fedtchouk, V.P. Lozitsky, E.N. Muratov, A.K. Mescheriakov, *SAR & QSAR Environ. Res.*, **2005**, 16, 219.
[5] W. Sawodny, M. Riederer, E. Urban, *Inorg. Chim. Acta*, **1978**, 29, 63.
[6] S. Oshima, N. Hirayama, K. Kubono, H. Kokusen, T. Honjo, *Anal. Sci.*, **2002**, 18, 1351.

[7] K. Agarwal, Synthetic Lubricating Oil Greases Containing Metal Chelates of Schiff Bases, United States Patent, **1992**, 5147567.
[8] A. I. Krylov, B.V. Stolyarov, *Zh. Org. Khim*., **1978,** 14, 2224.
[9] S. N. Pandeya, D. Sriram, *Acta Pharm. Turc*., **1998,** 40, 33.
[10] I. A. Mustafa, B. K. Al-Asa'ady, T.A.K. Al-Allaf, *Asian J. Chem.*, **2002,** 14, 753.
[11] H. S. Abbo, J. J. Salam, T. R. Prasad, S. Chand, *J. Mol. Catalysis*, **2005,** 225.
[12] Z. H. Chohan, S. K. A Sherazi, *Metal-Based Drugs*. **1997**, 4(6), 327.
[13] P. K. Sharma, S. N. Dubey, *Ind. Chem. Soc*., **1995, 72**, 577.
[14] A. S. Demir, O. Reis, M. Emrullahoglu, Tetrahedron, **2002,** 58, 8055.
[15] E. Leporati, J. Coord. Chem., **1994,** 33, 179.
[16] E. T. G. Cavalheiro, M. Ionashiro, G. Marino, S. T. Breviglieri, G. O. Chierice, *Trans. Met. Chem*., **2000,** 25, 69.
[17] B. Sarı, M. Talu, *Turk. J. Chem.*, **1998**, 22, 301.
[18] S. Naitoh, K. Sanui, N. Ogata, *J. Electroanal. Chem. Commun*., **1986**, 1349.
[19] J. R. Dyer, Application of Absorption Spectroscopy of Organic Compounds, **1991**, 8th ed., Prentice Hall, 36-38.
[20] R. M. Silverstein and F. X. Webster, Spectrometric Identification of Organic Compounds, John Wiley and Sons, Inc. New York**, 2004**, 6th ed., 83-86, 104-106.
[21] L. H. Cai, P. Z. Hu, X. L. Du, L. X. Zhang, Y. Liu, *Indian J. Chem.*, **2007**, 46B, 523.
[22] K. Nakamoto, Infrared and Raman Spectra of Inorganicn and Coordination Compounds, 4th ed., Wiley, New York (1986).
[23] P. Choubey P. and P. Singh, *J Ind. Chem. Soc.*, **2003**, 80, 40.
[24] H. S. Lucia, A. Terra, M. Guekezian, I Gaubeur, J. R. Matos, E. Maria and V. Suarez-Iha, *Polyhedron*, **2002**, 21, 2375.
[25] V. N. Potange, P. S. Mane, V. G. Mane and B. R. Arbad, *J Indian Chem Soc*., **2008**, 5, 792.
[26] A. P. Mishra and L. R. Pandey, *Indian J. Chem*., **2005**, *44A*, 94.
[27] M. Koca, F. Dagdelen and Y. Aydedu, *Mater. Lect*., **2004**, *58*, 2901.
[28] British pharmacopoeia-II, Biological assay and Tests, the Stationary Office Ltd., London; **1998,** A-205.
[29] J. H. Mueller and J. Hinton, *Proc. Soc. Exp. Biol. Med.*,**1941**, 48, 330.
[30] S. C. Prescott, C. G. Duan, Industrial Microbiology, McGraw Hill, Koyakesha, **1949**, 3rd ed., 519.
[31] L. Mishra, V. K. Singh, *Ind. J. Chem*. **1993**, 32A, 446.
[32] S. Baluja, A. Solanki and N. Kachhadia, *J Iranian Chem. Soc.*,**2006**, 3(4), 312-317.