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Synthesis, Characterization, Spectral Studies, Biocidal Activities of Fe(III), Co(II), Zn(II), Cd(II), Y(III), and In(III) Complexes of Schiff base derived from L-Phenylalanine

M.H. SALUNKE, Z.A. FILMWALA* and A.D. KAMBLE

Bhausaheb Nene ASC College, Pen, Raigad - 402 107 (India).
*N.S. Research Laboratory, St. Xavier's College, Mumbai - 400 001 (India).

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ABSTRACT

2-Amino-3-phenyl-propionic acid hydrazide (APPAH) (1) has been prepared by reacting earlier reported compound 2-amino-3-phenyl-propionic acid methyl ester (APPAME) with hydrazine hydrate. Schiff base 2[(4-methoxy-bezylidene)-amino]-3-phenyl-propionic acid (4-methoxy-benzylidene)-hydrazide (MBAPPAMBH) (2) has been synthesized by reacting (1) with 4-methoxy benzaldehyde and its metal complexes with Fe(III), Co(II), Zn(II), Cd(II), Y(III), and In(III) have been prepared. The ligand and metal complexes were characterized on the basis of elemental analysis, IR, NMR spectral data, molar conductance, magnetic susceptibility measurement, thermal analysis (TGA/DTA). In vitro antibacterial and antifungal activities of all compounds were tested.

Key words: Synthesis, Schiff base, Fe(III), Co(II), Zn(II), Cd(II), Y(III), and In (III) complexes, Antibacterial and antifungal activities.

INTRODUCTION

Amino acids are the building units of all proteins and enzymes[1] and associated with metal ions in biological system[2]. These acids are being converted to acid hydrazide having two amino groups, these diamine are able to form Schiff bases with condensation of aromatic aldehydes. Metal complexes prepared from Schiff bases of derivative of amino acids posses biological activities[3-4]. Coordination behavior of this ligand with several metal ions is found in biological systems. Preparation of heterocyclic ligands containing Carbonyl and azomethine groups with potential binding ability has drawn a lot of attention because of their antibacterial[5,6] fungicidal[7], herbicidal[8], and anti-inflammatory[9] properties.

In the present work, synthesis, characterization of asymmetric Schiff base (MBAPPAMBH)(2) and its metal complexes with some paramagnetic, diamagnetic and rare earth metal ions, their elemental analysis, IR, ^{1}HNMR spectral data, molar conductance, magnetic

susceptibility measurement, thermal analysis (TGA / DTA) and their antimicrobial and antifungal activities are described. The Schiff base (MBAPPAMBH) (2) is prepared by refluxing 4-methoxy-benzaldehyde with (APPAH) (1) in 2:1 molar ratio in ethanol. Metal complexes of Fe(III), Co(II), Zn(II), Cd(II), Y(III), and In(III) are prepared by condensation with (MBAPPAMBH)(2). The Schiff base ligand and Co(II), Zn(II), Cd(II) complexes were found to be more active antibacterial and antifungal as compared to Fe(III), Y(III), and In(III) complexes.

EXPERIMENTAL

All chemicals and solvents used in present investigation were of E-Merck, Sigma -Aldrich Company and solutions were prepared in doubled distilled water, all the metal salts were used as chlorides. The melting points were recorded by capillary tube method using Toshniwal melting point apparatus and are uncorrected. The molar conductance of ligand and metal complexes was measured by digital conductometer model no. Eq-660A in DMF, 10^{-3}mol at 25°C. The magnetic susceptibility of these complexes were measured by Gouy's method at room temperature using Hg [Co $(NCS)_4$] as Celibrant. The elemental analysis were carried out on a vario EL III Elementar Carlo-Erba 1108. IR spectra were recorded using KBr disks on Perkin Elmer Spectrum RX-1 FT-IR spectrometer, in the range of 4000-400 cm^{-1} at Institute of Chemical Technology, Matunga, Mumbai. Thermal analysis (TGA / DTA) were carried out in nitrogen atmosphere with a heating rate of 10^0C/ min., using Rijaku Thermo plus TG- 8120 thermoanalyser. ^{1}HNMR spectra were recorded in DMSO-d_6 using TMS as internal standard on a Jeol Japan 300 MHz FT NMR at Institute Of Science, Mumbai. Purity of compounds was checked by TLC on silica gel plates (60F254) and visualized under UV light.

Synthesis of ligand (Schiff base)

2-amino-3-phenyl-propionic acid methyl ester was prepared by earlier reported method[10] and purity of compound was checked by TLC.

Synthesis of 2-Amino-3-phenyl-propionic acid hydrazide (APPAH) (1)

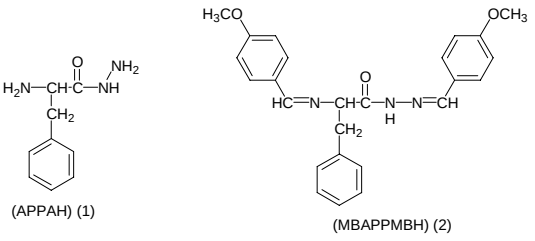
2-Amino-3-phenyl-propionic acid methyl ester (0.1 mol) was refluxed on water bath with excess of hydrazine hydrate (99%, (0.2 mol) in 25ml of ethanol for 6-7h. The resulting product was poured in ice-cold water and kept overnight, light brown solid was crystallized out [11-12]. The product washed with ice-cold alcohol and dried in air. The yield of almost pure Phenylalanine hydrazide was 91%, m.p.167ºC.

Synthesis of 2[(4-methoxy-bezylidene)-amino]-3-phenyl-propionic acid (4-methoxy-benzylidene)-hydrazide (MBAPPAMBH) (2)

Prepared by mixing an ethanoic solution (50 ml) of (1) (0.01 mol) with 4-methoxy benzaldehyde (0.02 mol) and catalytic amount of conc. H_2SO_4 in the same volume of ethanol and mixture was reflux with stirring for 8 h. The obtained precipitate was collected by filtration through Buchner funnel, washed and re-crystallized from absolute ethanol then dried at room temperature in desicator over anhydrous calcium chloride; yield was 90%, m.p.198 ºC-199 ºC.

Preparation of complexes (3-a to 3-f) with MBAPPAMBH (2)

Purified Schiff base (MBAPPAMBH) (0.003 mol) was dissolved in ethanol (50 ml) while metal chlorides (0.003 mol) was dissolved in methanol (5 ml) were mixed, one drop of piperidine was added as a catalyst and mixture was reflux with stirring for 7-8 h. The solution was cooled and pH was measured by combine electrode and it was recorded as 6.8, few drops of ammonium hydroxide was added until pH 8.5-9.5, during which colored complexes precipitate out[13] were filtered and washed with water (15 ml x 3) & ethanol (25 ml x 3) to remove any unreactive ligand & metal ions, after the complexes are dried in vacuum over anhydrous calcium chloride in a desicator. These complexes were used for further study.



Scheme 1:

RESULTS AND DISCUSSION

Physical properties

These complexes are air stable, colored, solids which decompose above> 300°C. They are insoluble in common organic solvents but soluble in ethanol, DMSO, DMF. The molar conductance of ligand and complexes dissolved in DMF fall into the range 7-24 S cm^2mol^{-1} of 10^{-3} mol dm^{-3} solution indicating their non electrolytic nature[14] in DMF. The analytical data and magnetic moments of complexes are presented in Table -1. The magnetic moment of Fe (III) complex has value 5.94 B.M. indicating good agreement with that reported for high spin complex with d^5 system (t_2g^3 eg^2) and octahedral geometry[15]. The magnetic moment value for the Co (II) complex is 4.99 B.M. expected for octahedral geometry[16] with high spin paramagnetic d^7 system (t_2g^5 eg^2) and 3 unpaired electrons. Zn(II) and Cd(II) complexes have not ligand field stabilization effect owing to complete d-sub shell , therefore Zn(II) and Cd(II) complexes should be diamagnetic spin free tetrahedral complexes[17] with d^{10} system. Y(III) and In(III) are also diamagnetic with d^{10} system and octahedral stereochemistry[18-19]. The elemental analysis of carbon, hydrogen, nitrogen and gravimetric percentage estimation of metals indicated that Fe (III) Zn(II) Cd (II) and Y(III) complexes are 1:1 metal ligand stoichiometry where as In(III) has 1:2 metal ligand stoichiometry.

IR spectral data (KBr) (cm^{-1}) - (APPAH) Compound (1)

3349.82 -(-NH-NH_2), 3035.52 -(-NH_2 group of primary ammonium salt), 3300-2880- broad band due to [(i)-(C-H stretching, aromatic) (ii) (C-H stretching, aliphatic)] , 1615-(-CONH-) 1562.93 -(Ar-ring),1495 -(-N-N-stretch), 1225.83- (-C-N stretch).

(MBAPPAMBH) Compound (2)

3410-(N-H stretching), 3307.69-(-CONH-asymmetric vibration of-N-H), 3003.36 ?(Ar-H), 2815.00 -(-OCH_3) 1653.39 -(>C=O),1602.21 - (-CH=N-azomethine), 1563.80 (C_6H_5-conjugation), 1493.11 -(N-N stretching), 1248.38 - (C-N stretching), 827.03 (P-substituted- C_6H_5).

The IR spectrum of the ligand MBAPPAMBH shows a band of medium intensity at 1602.21 cm^{-1} which can be assigned to -(-CH=N-)[20-21], In the spectra of complexes this band shows a negative shift 28-61 cm^{-1} and appeared in the region 1508-1575 cm^{-1} indicating the coordination of nitrogen atom of azomethine group[22]. The coordination through azomethine nitrogen is further confirmed by the appearance of a band at 457-490 cm^{-1} in complex may be assignable[23] to (M-N). Other significant IR band of ligand appears at 1653.39 cm^{-1}, this band is sharp and strong may be assigned to (C=O) [24-25]. The position of this band in all complexes shows a negative shift 20-41 cm^{-1} and appeared at the region 1616-1633 cm^{-1} This shift is due to coordination of oxygen atom of a carbonyl group to the metal ion .The coordination through oxygen atom is further confirmed by the appearance of the band at 530-608 cm^{-1} in the complex may be assignable to -(M-O) [26-27]. The broad band in 3000-3300 cm^{-1} region in Fe(III),Co(II), Zn(II), Cd(II) and Y(III) complexes attributed to the presence of coordinated water molecules[28-29], this have also been confirmed by TGA/DTA analysis . The IR spectra of these complexes exhibited a new band in range of 3500-3550 which may be attributed to -(OH) vibrations of coordinated water. The appearance of band around 860 (cm^{-1}) due to wagging and rocking modes of vibrations of coordinated water molecules[30].

NMR spectral data - ^{1}HNMR (DMSO, 300MHz (ppm)

2-Amino-3-phenyl-propionic acid hydrazide (APPAH)(1)

2.045(s,4H of –NH_2), 3.24(d, 2H of –CH_2), 4.56(t,1H of –CH), 6.87 (d,1H of aryl), 7.82(d, 2H of aryl), 8.05 (d, 2H of aryl), 8.56(s,1H of –NH)

2[(4-methoxy-bezylidene)-amino]-3-phenyl-propionic acid (4-methoxy-benzylidene)-hydrazide (MBAPPAMBH) (2)

3.05(d,2H of –CH_2), 3.73(s, 6H of –OCH_3), 3.46(t, 1H of –CH), 6.63-7.23 (m,13 Ar-H), 8.00 (s, 1H of –NH), 8.11 (s,2H of –CH=N-).

Biological evaluation

Antibacterial and antifungal activities of the ligand and its complexes were carried out against staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis, Escherichia Coli bacteria and

Table 1: Analytical Data, Molar conductance, magnetic moment of MBAPPAMBH and it's metal complexes with Fe(III), Co(II), Zn(II), Cd(II), Y(III), and In(III) ions

S. no.	Compound	Mol.Wt. Calc. (found)	Colour	% Yield	Decomp. temp.	Molar cond. S cm^2mol^{-1}	Magnetic moment per μ_{eff} °C (B.M.)	Elemental Analysis %			
								Metal	C	H	N
1	$C_9H_{13}N_3O$ (APPAH)	179.00	Light Brown	71	167	7.2	-	-	60.33 (59.70)	7.26 (7.03)	23.46 (22.59)
2	$C_{25}H_{25}N_3O_3$(MBAPPAMBH)	415.48	White	87	198-199	10.4	-	-	72.28 (71.87)	6.02 (6.10)	10.12 (10.05)
3	[Fe $(C_{25}H_{25}N_3O_3)(H_2O)_3$]	525.32	Black Brown	88	› 292	18.8	5.94	10.65 (10.44)	57.25 (56.93)	5.91 (5.77)	8.01 (7.85)
4	[Co $(C_{25}H_{25}N_3O_3)$ $(H_2O)_3$]	528.41	Blue Green	90	› 314	15.7	4.99	11.18 (10.96)	56.92 (56.61)	5.88 (5.74)	7.96 (8.26)
5	[Zn $(C_{25}H_{25}N_3O_3)$ (H_2O)]	498.85	Yellowish White	89	› 305	22.1	-	13.12 (12.86)	60.24 (59.91)	5.42 (5.29)	8.43 (8.26)
6	[Cd $(C_{25}H_{25}N_3O_3)$ (H_2O)]	545.88	Light Yellow	84	› 320	23.5	-	21.31 (20.90)	56.88 (57.57)	5.11 (4.99)	7.94 (7.78)
7	[Y $(C_{25}H_{25}N_3O_3)$ $(H_2O)_3$]	558.38	Light Yellow	92	› 298	21.7	-	15.96 (16.82)	53.85 (54.92)	5.56 (5.68)	7.54 (7.64)
8	[In $(C_{25}H_{25}N_3O_3)_2$]	945.78	Dirty Yellow	91	› 311	20.1	-	12.28 (12.48)	64.18 (64.69)	5.34 (6.61)	8.98 (9.61)

Table 2: Antimicrobial activity of ligand and its complexes

Compound	Antibacterial activity								Antifungal activity			
	Gram Positive bacteria				Gram negative bacteria							
	S.aureus		*P.aeruginosa*		*B.Substilis*		*E. Coli*		*A. niger*		*C. albicans*	
	2.0 mg	4.0 mg	2.0 mg	4.0 mg	2.0 mg	4.0 mg	2.0 mg	4.0 mg	2.0 mg	4.0 mg	2.0 mg	4.0 mg
$C_{25}H_{25}N_{25}O_{25}$	-	- -	-	- -	-	-	-	- -	-	-	-	- -
[Fe ($C_{25}H_{25}N_{25}O_{25}$)$(H_2O)_3$]	+	+	+	+	+	+	+	+	+	+	- -	- -
[Co ($C_{25}H_{25}N_{25}O_{25}$)$(H_2O)_3$]	-	- -	- -	- -	+	+	+	+	-	- -	- -	- -
[Zn ($C_{25}H_{25}N_{25}O_{25}$) H_2O]	-	- -	-	- -	-	- -	-	-	-	- -	- -	- -
[Cd ($C_{25}H_{25}N_{25}O_{25}$) H_2O]	-	-	-	- -	-	-	-	- -	- -	- -	- -	- -
[Y ($C_{25}H_{25}N_{25}O_{25}$)$(H_2O)_3$]	+	+	+	+	+	+	+	+	+	+	+	+
[In ($C_{25}H_{25}N_{25}O_{25}$) $_2$]	+	+	+	+	+	+	+	+	+	+	+	+

- - Very Active - Moderately active + Not active

Aspergillus niger, Candida albicans fungi by ditch plate method. 10-15 ml nutrient agar and sabouraud's dextrose agar is used as medium for antibacterial and antifungal activities respectively. The antimicrobial activity was estimated on the basis of size of inhibition zone and the results are shown in table-2. Antibacterial studies shows that the ligand (MBAPPAMBH) and Zn(II), Cd(II) complexes are more active than Co(II) complex whereas Fe(III), Y(III), and In(III) complexes did not showed antibacterial activity against these organisms. Ligand and Co(II), Zn(II), Cd(II) complexes showed significant antifungal activity, Fe(III) complex are very active against Candida albicans and inactive against Aspergillus niger, whereas Y(III) and In(III) did not exhibit any remarkable activity against these fungi.

CONCLUSION

On the basis of above studies it may be concluded that Fe(III), Co(II), Y(III) and In (III) complexes has octahedral geometry with 1:1 metal ligand stoichiometry and Zn(II) and Cd (II) complexes has tetrahedral stereochemistry with 1:2 metal ligand stoichiometry. Antibacterial studies show that the ligand (MBAPPAMBH) and Zn(II), Cd(II) complexes are more active than Co(II) complex. Fe(III), Y(III), and In(III) complex did not showed antibacterial activity against these organisms. Ligand and Co(II), Zn(II), Cd(II) complexes showed significant antifungal activity, Fe(III) complex are very active against Candida albicans and inactive against Aspergillus niger, whereas Y(III) and In(III) did not exhibit any remarkable activity against these fungi.

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