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Journal of Chemical and Pharmaceutical Research

ISSN No: 0975-7384
CODEN(USA): JCPRC5

J. Chem. Pharm. Res., 2010, 2(5):526-533

Antimicrobial evaluation and synthesis of co-ordination polymers

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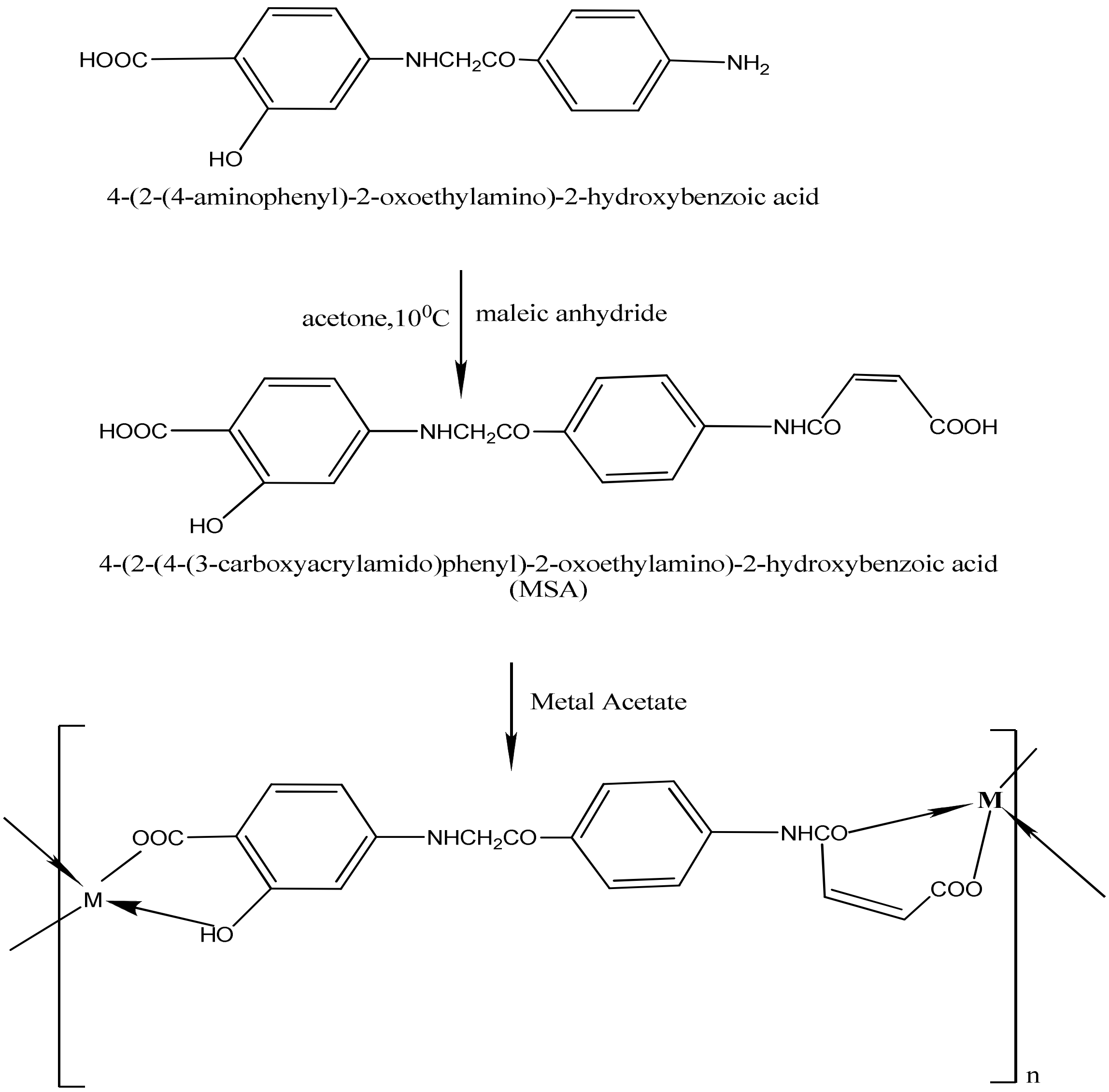
ABSTRACT

The heteronuclear bisligand namely 4-(2-(4-(3-carboxyacrylamido)phenyl)-2-oxoethylamino)-2-hydroxybenzoic acid (MSA) was synthesized and characterized. The bisligand was designated as MSA and its co-ordination polymers with Cu^{+2}, Co^{+2}, Mn^{+2}, Ni^{+2} *and* Zn^{+2} *metal ions were prepared. The co-ordination polymers and parent ligand were characterized by elemental analysis, spectral studies, thermogravimetry, number-average molecular weights* ($\overline{\mathrm{Mn}}$)*, diffuse reflectance spectral studies and magnetic susceptibilities. The samples were also monitored for microbicidal activity.*

Keywords: co-ordination polymer, *antibacterial and antifungal activities.*

INTRODUCTION

The study of co-ordination polymers has made much progress [1]. These polymers are known for their semiconducting catalytic properties, waste water treatment for metal recovery, in protective coating, as antifouling paints, and anti fungal properties [1, 2]. Such co-ordination polymers are mostly derived from bi-chelating ligands in which metal ions and chelating agents are arrayed alternatively. Most of bichelating ligands are derived from well known chelating agents like 8-hydroxy quinoline and salicylic acid etc [3, 6]. The joining segment of these two similar ligands are mainly –N=N-, SO_2, $-CH_2-$, -O- [3-9]. The area in which the co-ordination polymers having bis-azo dye containing ligands has not been developed so far. Such ligand may afford the co-ordination polymer with different properties. Also, 4-amino salicylic acid was an excellent anti-TB drugs and may all are act as a chelating ligand with better microbicidal activity. Hence, it was thought interesting to investigate the field of co-ordination polymers based on hetronuclearting bis ligands having 4-amino salicylic acid and amic acid. Though the amic acid is generally derived by condensation of amines with anhydrides having carboxylic and amide group. Such amic acid may afford metal complex with metal ions. The metal complexation study of various amic acids has been reported recently from our Indian scientist [10-13], so the proposed present work is in connecting with the co-ordination polymers based on hetronuclearting bisligands. The synthetic route is shown in scheme 1.



Co-ordination Polymers of MSA

Where M=Cu^{+2},CO^{+2},Ni^{+2},Mn^{+2} and Zn^{+2}

SCHEME 1

EXPERIMENTAL SECTION

Materials

All the chemicals used were of analytical grade.

Procedure

Synthesis of 4-(2-(4-(3-carboxyacrylamido)phenyl)-2-oxoethylamino)-2-hydroxybenzoic acid(MSA)

The 4-Amino salicylic acid (SA) (i.e. 4-Aminosalicylic acid) was obtained from local dealer. The 4-chloro-acetamido-phenacyl chloride was prepared by reported method [16].

Preparation of 4-(2-(4-aminophenyl)-2-oxoethylamino)-2-hydroxybenzoic acid: This was prepared by following method. The solution of 4-chloro acetamido phenacyl chloride (24.6*g*, 0.1 mole) in acetone was treated with 4-amino salicylic acid (15.3*g*,0.1 mole) in acetone at room temperature. The resultant product was filtered and hydrolyzed by 50:50 HCl: Ethanol mixture.

Preparation of 4-(2-(4-(3-carboxyacrylamido)phenyl)-2-oxoethylamino)-2-hydroxy benzoic acid (MSA): The MSA was prepared by the solution of 4-(2-(4-aminophenyl)-2-oxoethylamino)-2-hydroxybenzoic acid (28.6*g*,0.1mole) in acetone was cooled to 10^{o}C, to this solution the maleic anhydride (19.6*g*,0.2mole) was added with stirring,The resulting product was then filtered and air-dried. The yield of MSA was 76% and m.p.167-169^{0}C (uncorrected). The predicted structure and formation of polymeric ligand is shown in Scheme-1.

Analysis of MSA:

		C%	**H%**	**N%**
Elemental Analysis	Calculated:	59.38	4.20	7.29
$C_{19}H_{16}N_2O_7$ (384)	Found :	59.2	4.1	7.2

Acid Value Theoretical: 193.8 mg KOH/1g. Sample.
Found: 192 mg KOH/1g Sample.

IR Spectral Features (cm^{-1}) : 3030, 1520, 1640 (Aromatic); 1710 (CO);1640(C=C); 3450-3160 (OH); 3400 (Sec.NH);2890,2940(CH_2) ; 1690(COOH); 1650, 1610, 1520 (Amide group)

NMR signals (δ ppm): 8.02-6.40 (m,7H,Ar-H); 4.6 (s,2H,CH_2); 5.9 (1H,s,OH);4.2,9.9 (s,2H, NH) ;11.56 (s,2H, COOH),6.6-6.9(d,2H,CH).

Preparation of Co-ordination Polymers

The Cu^{2+},Co^{2+}, Mn^{+2}, Ni^{2+} and Zn^{2+} metal ion chelates of MSA have been prepared in a similar manner. The procedure is as follows:

To a solution of MSA (43.4 g 0.1 mole) in ethanol-acetone (1:1v/v) mixture (150 ml), 0.1N KOH solution was added dropwise with stirring. The pasty precipitates were obtained at neutral pH. These were dissolved by addition of water up to clear solution. It was diluted to 250 ml. by water and was known as stock solution. 25 ml of the stock solution (which contains 0.01 mole MSA) was added drop wise to the solution of metal salt (0.005 mole for divalent metal ions) in water at room temperature. Sodium acetate or ammonia was added up to complete precipitation. The precipitates were digested on water bath at 80° C for 2h. The digested precipitates of chelates were filtered washed with water and air dried. It was amorphous powder. Yield was almost quantitative. The details are given in Table-1.

Measurements

Elemental analysis of MSA and its co-ordination polymers were carried out on a C,H,N elemental analyzer (Italy). IR spectra of H_2L and the polymeric chelates were scanned on a Nicolet-760D FTIR spectrophotometer in KBr. The metal content analyses of the polymeric chelates were performed by decomposing a weighed amount of each polymeric chelates followed by EDTA (disodium ethylene diamine tetra acetate) titration as reported in the literature [8]. Magnetic susceptibility measurements of all the polymeric chelates were carried out at room temperature by the Gouy method. Mercury tetrathiocynatocobaltate (II), Hg[Co(NCS)], was used as a calibrant. Molar Susceptibilities were corrected for diamagnetism of component atoms using Pascal's constant. The diffuse reflectance spectra of the solid polymeric chelates were recorded on a Beckman DK-2A spectrophotometer with a solid reflectance attachment. MgO was employed as the reference compound.

Table 1: Analytical and spectral data of the co-ordination polymers of MSA (H_2L)

Ligand/ Co-ordination polymers	**Empirical Formula**	**Formula Weight**	**Analyses %Found(Calculated)**				**$\mu_{eff.}$ (B.M.)**	**($\overline{Mn}$) ± 60**	**$\overline{Dp}$**
			%M	**%C**	**%H**	**%N**			
H_2L	$C_{19}H_{16}N_2O_7$	384	-	59.2 (59.38)	4.1 (4.20)	7.2 (7.29)	-	-	-
$[Cu(MSA)(H_2O)_2]_n$	$Cu.\ C_{19}H_{14}N_2O_7.2H_2O$	481.54	12.9 (13.19)	47.3 (47.34)	3.7 (3.73)	5.7 (5.81)	1.99	2952	6
$[Co(MSA)(H_2O)_2]_n$	$Co.\ C_{19}H_{14}N_2O_7.2H_2O$	476.94	12.3 (12.35)	47.3 (47.80)	3.7 (3.77)	5.8 (5.87)	2.83	2439	5
$[Ni(MSA)(H_2O)_2]_n$	$Ni.\ C_{19}H_{14}N_2O_7.2H_2O$	476.71	12.2 (12.31)	47.7 (47.82)	2.7 (3.77)	5.8 (5.87)	3.98	2448	5
$[Mn(MSA)(H_2O)_2]_n$	$Mn.\ C_{19}H_{14}N_2O_7.2H_2O$	472.94	11.5 (11.61)	48.1 (48.20)	3.7 (3.80)	5.8 (5.92)	4.78	2903	6
$[Zn(MSA)(H_2O)_2]_n$	$Zn.\ C_{19}H_{14}N_2O_7.2H_2O$	483.38	13.4 (13.52)	47.0 (47.16)	3.6 (3.72)	5.7 (5.79)	Diamagnetic	2480	5

The number average molecular weight ($\overline{Mn}$) of all the co-ordination polymers were determined by method reported in earlier communications [17].

Thermogravimetric analysis of co-ordination polymers were carried on DuPont 950 TGA analyzer in air at a heating rate of 20°C/min.

Table 2: Thermo gravimetric analysis co-ordination polymers of MSA

Ligand/ Co-ordination polymers	**% weight loss at temperature T(^0C)**					
	100	**200**	**400**	**500**	**600**	**700**
H_2L	-	5.3	10.3	40.3	45.4	48.0
$[CuL(H_2O)_2]_n$	2.5	4.7	12.8	42.5	47.6	53.2
$[CoL(H_2O)_2]_n$	4.5	8.7	16.5	21.7	43.3	59.3
$[NiL(H_2O)_2]_n$	4.6	8.5	14.6	26.8	45.3	59.4
$[MnL(H_2O)_2]_n$	4.7	6.6	9.4	15.5	24.7	36.5
$[ZnL(H_2O)_2]_n$	2.0	3.4	4.8	15.1	23.4	35.6

Antibacterial activities

Antibacterial activity of MSA ligand and its co-ordination polymers were studied against gram-positive bacteria (*Bacillus subtilis and staphylococcus aureus*) and gram-negative bacteria (*E.coli and salmonella typhi*) at a concentration of 50μg/ml by agar cup plate method. Methanol system was used as control in this method. The area of inhibition of zone measured in mm.

Table 3 Antibacterial activities of co-ordination polymers

Zone of Inhibition				
Compounds	**Gram +Ve**		**Gram –Ve**	
	Bacillus subtilis	***Staphylococcus aureus***	***Salmonella typhi***	***E.coli***
$[CuL(H_2O)_2]_n$	64	70	70	71
$[CoL(H_2O)_2]_n$	66	75	65	70
$[NiL(H_2O)_2]_n$	67	72	76	76
$[MnL(H_2O)_2]_n$	65	70	84	78
$[ZnL(H_2O)_2]_n$	71	66	75	72

Antifungal activities

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were *penicillium expansum, Nigrospora Sp., Trichothesium Sp., and Rhizopus nigricum*. The antifungal activity of ligand and its co-ordination polymers was measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200gm,dextrose 20gm,agar 20gm and water one liter. Five days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120° C for 15 min. at 15atm. pressure. These medium were poured into sterile Petri plates and the organisms were inoculated after cooling the petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below:

Percentage of Inhibition = 100(X-Y) / X

Where, X = Area of colony in control plate

Y = Area of colony in test plate

Table 4 Antifungal activities of co-ordination polymers

Zone of Inhibition at 1000 ppm (%)				
Compounds	***Penicillium Expansum***	***Nigrospora Sp.***	***Trichothesium Sp.***	***Rhizopus Nigricum***
$[CuL(H_2O)_2]_n$	75	74	58	56
$[CoL(H_2O)_2]_n$	66	67	63	73
$[NiL(H_2O)_2]_n$	74	79	70	71
$[MnL(H_2O)_2]_n$	72	68	82	75
$[ZnL(H_2O)_2]_n$	61	72	69	72

RESULTS AND DISCUSSION

The synthesis of the bis bidentate ligand**,** 4-(2-(4-(3-carboxyacrylamido)phenyl)-2-oxoethylamino)-2-hydroxybenzoic acid (MSA) has not been reported in the literature. The ligand MSA was isolated in the form of a yellowish powder. It is soluble organic solvents such as in dioxane, DMSO (dimethyl sulfoxide), DMF. The results of elemental analyses of the MSA ligand (Table-1) are agree with those predicted on the basis of formula.

The IR spectrum of MSA features are a broad band extending from 3450-3160cm^{-1} with maximum at 3314 cm^{-1}, attributed to the OH group [3]. The weak bands around 2890and 2940 cm^{-1} may be due to asymmetric and symmetric stretching vibrations of methylene groups($-CH_2-$). The bands at 3400cm^{-1} and at 1710cm^{-1} are respectively due to NH (Sec) and CO group respectively. The band at 1690cm^{-1} due to COOH group. The band around 1650, 1610 and 1520 are attributed to amide group. The others bands are at their respective positions.

The ^{1}H NMR(δ ppm) spectrum of MSA also show the signals 8.02-6.40 (m,7H,Ar-H); 4.6 (s,2H,CH_2); 5.9 (1H,s,OH);4.2,9.9(s,2H, NH) ;11.56 (s,2H, COOH),6.6-6.9(d,2H,CH). These features confirm the proposed structure of ligand MSA. The NMR Data of MSA shown in experimental part are also confirming the structure of MSA.

The co-ordination polymers derived from MSA are insoluble in common organic solvents. Hence it is not possible to characterized the co-ordination polymers by molecular mass using conventional methods like osmometry, viscometry etc. These co-ordination polymers do not melt up to 360°C.

On the basis of the proposed structure shown in Scheme1, the molecular formula of the MSA ligand is $C_{19}H_{16}N_2O_7$, which, upon chelation coordinates with two central metal atom at four co-ordination sites and two water molecules. Therefore, the general molecular formula of the resulting co-ordination polymer is given by [M(MSA).$2H_2O$] as shown in scheme-1. This has been confirmed by the results of elemental analyses of all of the five co-ordination polymers and their parent ligand. The data of elemental analyses reported in Table I are in agreement with the calculated values of C , H and N based on the above mentioned molecular formula of the parent ligand as well as co-ordination polymers. Examination of data of the metal content in each polymer (Table 1) revealed a 1:1 metal: ligand (M/L) stoichiometry in all of the co-ordination polymers.Comparison of the IR spectrum of the ligand MSA and those of the co-ordination polymers reveals certain characteristic differences. The broad band at 3400-3100 cm^{-1} for MSA has almost disappeared for the spectra of polymers. However, the weak bands around 3200 cm^{-1} in the spectra of MSA-Co^{2+},MSA-Ni^{2+},MSA-Mn^{2+} indicate the presence of water molecules which may have been strongly absorbed by the polymer sample. The weak band around 1110cm^{-1} is attributed to the C-O-M stretching frequency [18].The band at 1430 cm^{-1} in the IR spectrum of MSA is attributed to the in-plane OH deformation [18]. The band is shifted towards higher frequency in the spectra of the polymers indicating formation of metal-oxygen bond. These feature suggest that the structure of the co-ordination polymer.

The value of the degree of polymerization of all the co-ordination polymers listed in table 1 suggest that the average Dp for all the polymers in a range of 5 to 6.Magnetic moments (μ_{eff}) of polymeric chelates are given in Table 1.

The diffusion electronic spectrum of MSA-Cu^{2+} co-ordination polymers shows two broad bands around 15,380 cm^{-1} and 22,728 cm^{-1}.The first bands may be due to ${}^2T_{2g} \rightarrow {}^2E_g$ transition, while the second may be due to charge transfer. The first band shows structure suggestion a distorted octahedral structure for the MSA-Co^{2+} polymers. The higher value of μ_{eff} of the MSA-Cu^{2+} polymer support this view [19,20]. The MSA-Ni^{2+} and MSA-Co^{2+} polymers give two absorption bands respectively at 17,249and 23,999 cm^{-1} and at 17,238 and 23727 cm^{-1} which can be assigned respectively to ${}^4T_{1g} \rightarrow {}^2T_{2g}$, ${}^4T_{1g} \rightarrow {}^4T_{1g(P)}$ transitions. These absorption bands and the values of μ_{eff} indicate an octahedral configuration for the MSA-Ni^{2+} and MSA-Co^{2+} polymers [21,22].The spectrum of [MnMSA $(H_2O)_2$] show weak bands at 16,474, 17,690 and 23,164cm^{-1} assigned to the transitions $6_{A1g} \rightarrow\ 4_{T1g}(4G)$, $6_{A1g} \rightarrow\ 4_{T2g}(4G)$ and $6_{A1g} \rightarrow\ 4_{A1g}, 4_{Eg}$ respectively, suggesting an octahedral structure for the [MnMSA$(H_2O)_2$] polymer[22]. As the spectrum of the [ZnMSA $(H_2O)_2$] polymer is not well resolved, it is not interpreted, but its μ_{eff} value shows that it is diamagnetic as expected.

The TGA data for the polymers are presented in Table-2. The weight loss of the polymer samples at different temperatures indicates that the degradation of the polymers is noticeable beyond 300°C. The rate of degradation becomes a maximum at a temperature lying between 400 °C and 500 °C depending upon the nature of the polymers. Each polymer lost about 56% of its weight when heated up to 700 °C. Inspection of the thermograms of MSA-Co^{2+}, MSA-Mn^{2+} and MSA-Ni^{2+} samples revealed that these samples suffered appreciable weight loss in the range 150 to 280°C. This may due to the presence of water strongly absorbed by the polymers. It has also been indicated earlier that the IR spectra of these three polymer samples have OH bands at around 3200 cm^{-1} due to associated water.

On the basis of the relative decomposition (% wt. loss) and the nature of thermograms, the co-ordination polymers may be arranged in order in increasing stability as:

Cu < Ni < Co < Mn

This trend also coincides with the stability order already reported for the metal oxinates [19] and for co-ordination polymers of MSA [3].

The antimicrobial activity of MSA and its co-ordination polymers are presented in Table-3 and 4. The data suggest that all the samples are toxic to bacteria or fungus. The data also suggest that the % age of bacteria or fungus is inhibited in the range of 56 to 78% depending upon the biospecies and co-ordination polymers.

CONCLUSION

The investigation described in the present article revels the following conclusion:
Polycondensation of 4-(2-(4-aminophenyl)-2-oxoethylamino)-2-hydroxybenzoic acid with maleic anhydride in the presence of a base catalyzed yielded a novel 4-(2-(4-(3-carboxyacrylamido)phenyl)-2-oxoethylamino)-2-hydroxybenzoic acid (MSA) polymeric ligand. The applicability of the polymeric ligand was explored by preparing polymeric chelates using different divalent metal ion indicating that the MSA polymeric ligand has good chelating property and high thermal stability.

Further, the polymeric ligand is thermally more stable than its polymeric chelates. Among the five polymeric chelates, M-MSA chelate is least stable, whereas M-MSA polymeric chelates is the most stable having a thermal stability comparable to that of chelates may be used as heat resistant material up to 350^{o}C. The polymeric ligand follows a two steps thermal degradation whereas polymeric chelates follow a single step thermal degradation.

A comparison of the thermal stability of the present polymeric chelates with those of 4-(2-(4-aminophenyl)-2-oxoethylamino)-2-hydroxybenzoic acid with maleic anhydride as a pendent groups of polymeric chelates revels that the MSA polymeric chelates are thermally more stable. Finally, the magnetic susceptibility results indicate that polymeric chelates of Cu^{+2}, Co^{+2}, Mn^{2+} and Ni^{+2} are paramagnetic, whereas that of Zn^{+2} is diamagnetic in nature. All the polymers have good microbicidal activity.

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