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Synthesis and characterization of some organic molecules containing ligand

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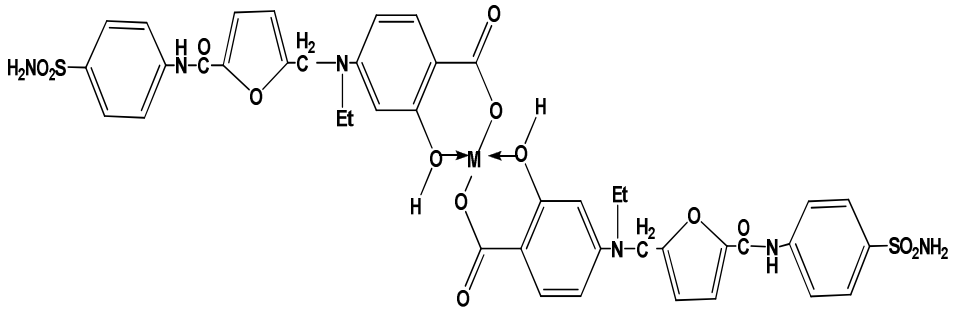
ABSTRACT

*The new ligand 2-hydroxy-4-(methyl((5-(4-sulfamoyl phenyl carbamoyl) furan-2-yl)ethyl amino)benzoic acid (**HMSPCFEAB**) prepared by condensation reaction between 4-(((5-(ethoxy carbonyl)furan-2-yl)methyl)ethyl amino)salicylic acid and Sulphanilamide was give. It was characterized by elemental analysis and spectral studies. The transition metal chelates Cu^{+2},Ni^{+2},Co^{+2},$Mn^{+2}$and Zn^{+2} of HMSPCFEAB were prepared and characterized by metal to ligand ratio, IR spectra and reflectance spectroscopies and magnetic properties. The antifungal activity of HMSPCFEAB and its metal chelates was examined against various fungi.*

Keywords: Sulphanilamide,4-(ethylamino)salicylic acid, Magnetic moment, Spectroscopies study and Antifungal properties.

INTRODUCTION

Organic compounds are most important for mankind. Number of Organic compounds is synthesized daily. The organic compound containing heterocyclic structure shows the pharmaceutical as well as biological activity [1-3]. The furan demonstrate numeral of biological activate be fond of antimicrobial, anthelmintic, anti-inflammatory, diuretic, analgesic [4-7]. Metal ligands are attractive of marketable significance because they maintain the quality of industrial goods analytically [8]. Novel ligands are continuously under investigation, for possible analytical and industrial applications. Salicylic acid and its bi-substituted derivatives is well known complexing agent [9,10]. Water insoluble metal complexes of 4-aminosalicylic acid (PAS) have been reported and investigated for tuberculolstatic effect [11,12]. They also show antibacterial as well as antifungal activity [13]. The reaction of sulfa drug derivatives with Salicylic acid has not been reported so far. Hence, it was thought that sulfa drug and Salicylic acid into one molecule may afford good biological active ligand. In continuous of our previous paper [14], the present work discuss about studies on some organic molecules containing ligand which have sulfa drug moieties **(Scheme-1)**.



metal chelates of 2-hydroxy-4-((5-(4-sulfamoylphenylcarbamoyl)furan-2-yl)ethylamino)benzoic acid (HMSPCFEAB)

Where M=$Cu^{(II)}$, $Co^{(II)}$, $Zn^{(II)}$, $Mn^{(II)}$ and $Ni^{(II)}$

Experimental:
All other chemicals used were of laboratory grade. Chemicals, Ethyl furan-2-carboxylate and 4-(ethylamino) salicylic acid was obtained from local dealer. All other chemicals used were of analytical grade. 5-(chloromethyl)furan-2-yl propionate prepared according to literature [15].

Synthesis of 4-(((5-(ethoxycarbonyl)furan-2-yl)methyl)ethyl)amino salicylic acid:
In a 250 ml RBF, 5-(chloromethyl)furan-2-yl propionate (0.01mole) and K_2CO_3 (0.02mole) were stirred at room temperature in DMF(20 ml) for 1.5hrs and pinch of KI was added. After that 4-(ethylamino)salicylic acid (0.01mole) was added to reaction mixture which was refluxed for 7 hrs. The reaction mixture was poured into water (20 ml) and the mixture was extracted with diethyl ether. The organic extracts were washed with water, dried over anhydrous sodium sulphate and concentrated to obtain crude product. The residue was recrystallized ethyl acetate from to give pure compound. Yield: 62%,m.p.123-125°C,IRvcm^{-1}(KBr):3542(OH)1742(CO),3089(Ar.C-H), 2930 (aliphaticC-H),1330(CN).^{1}HNMR:δ6.51-7.92(3H,s,ArH),6.69-7.11(2H,d,furanCH),4.52(2H,s, CH_2),4.32(2H,q, CH_2), 1.25(3H,t,CH_3),3.15(2H,q,CH_2),1.18(3H,t,CH_3),11.4(1H,s,COOH),5.84(1H,s,OH). Anal. Calcd for $C_{17}H_{19}NO_6$ (333): C, 61.25; H, 5.75; N, 4.20; Found: C, 61.23; H, 5.74; N, 4.18.

Synthesis of 2-hydroxy-4-(methyl((5-(4-sulfamoylphenylcarbamoyl)furan-2-yl)ethylamino)benzoic acid (HMSPCFEAB):
The 4-(((5-(ethoxycarbonyl)furan-2-yl)methyl)ethyl)amino salicylic acid (0.01mole) in ethanol and Sulphanilamide (0.01 mole) in ethanol was refluxed for a period of 9-11 hrs. The excess of solvent was distilled off to get the resulting product. The product was crystallized from 50% ethyl acetate. Yield: 59%, M.P.247-249°C (decompose) uncorrected.

ANALYSIS:
ElementalAnalysis: $C_{21}H_{11}N_3O_7S$ (459)

	C%	H%	N%	S%
Calculated:	53.89	4.61	9.15	6.98
Found :	53.87	4.59	9.14	6.96

IR Spectral Features(cm^{-1}):2940-2870(ArC-C),1685(COOH),3420-3365(NH,OH) and 1210-1170(C-O)
NMR(δppm):6.398.04(m,7H,ArH),11.4(1H,s,COOH),5.84(1H,s,OH),6.687.32(d,2H,CH),8.3(s,1H,NH),3.15(2H,q, CH_2),1.18(3H,t,CH_3),4.52(2H,s,CH_2) and 4.85(s,2H, NH_2)

Synthesis of metal chelates of 2-hydroxy-4-((5-(4-sulfamoylphenylcarbamoyl)furan-2-yl)ethylamino)benzoic acid(HMSPCFEAB):
The metal chelates of HMSPCFEAB with Cu^{+2}, Co^{+2}, Zn^{+2}, Mn^{+2}, and Ni^{+2} metal ions were prepared in two steps. All the metal chelates were prepared in an identical procedure.

(1) Preparation of HMSPCFEAB solution:
HMSPCFEAB (0.05 mol) was taken in 500 ml beaker and formic acid (85% v/v) was added up to slurry formation. To this slurry water was added till the complete dissolution of HMSPCFEAB. It was diluted to 100 ml.

Synthesis of HMSPCFEAB-metal-chelates:
The Cu^{+2}, Co^{+2}, Ni^{+2}, $Mn^{+2}$and Zn^{+2} metal chelates of HMSPCFEAB have been prepared in a similar manner. The general procedure is as follow.

To a solution of HMSPCFEAB (43.1g, 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 PESA) 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 2hrs. 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**.

Table-1: ANALYSIS OF HMSPCFEAB LIGAND AND ITS METAL CHELATES

Empirical Formula	Yield (%)	Elemental Analysis									
		C%		H%		N%		S%		M%	
		Cal.	Found	Cal.	Found	Cal.	Found	Cal.	Found	Cal.	Found
HMSPCFEAB	59	53.89	53.8	4.61	4.5	9.15	9.1	6.98	6.9	-	-
$(HMSPCFEAB)_2$ $Cu^{+2}2H_2O$	63	43.14	43.1	3.60	3.5	12.58	12.5	9.59	9.5	9.52	9.5
$(HMSPCFEAB)_2$ $Co^{+2}2H_2O$	66	43.44	43.4	3.62	3.6	12.67	12.6	9.65	9.6	8.89	8.8
$(HMSPCFEAB)_2$ $Ni^{+2}2H_2O$	64	43.46	43.4	3.62	3.6	12.68	12.6	9.66	9.6	8.86	8.8
$(HMSPCFEAB)_2$ $Mn^{+2}2H_2O$	62	43.71	43.7	3.64	3.6	12.75	12.7	9.71	9.7	8.34	8.3
$(HMSPCFEAB)_2$ $Zn^{+2}2H_2O$	64	43.02	43.0	3.59	3.5	12.55	12.5	9.56	9.5	9.77	9.7

Measurements:
The elemental contents were determined by Thermo Finigen Flash1101 EA (Itally) the metals were determined volumetrically by Vogel's method [16]. To a 100 mg chelate sample, each 1 ml of HCl, H_2SO_4 and $HClO_4$ were added and then 1 g of $NaClO_4$ was added. The mixture was evaporated to dryness and the resulting salt was dissolved in double distilled water and diluted to the mark. From this solution the metal content was determined by titration with standard EDTA solution. Infrared spectra of the synthesized compounds were recorded on Nicolet 760 FT-IR spectrometer. NMR spectrum of HMSPCFEAB was recorded on 60 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathiocynatocobalate (II) $Hg[Co(NCS)_4]$ was used as a calibrant. The electronic spectra of complexes in solid were recorded on at room temperature. MgO was used as reference. Antifungal activity of all the samples was monitored against various fungi, following the method reported in literature [17].

RESULTS AND DISCUSSION

The synthesis of 2-hydroxy-4-((5-(4-sulfamoylphenylcarbamoyl)furan-2-yl)ethylamino)benzoic acid (HMSPCFEAB) was performed by a simple reaction of 4-(((5-(ethoxy carbonyl)furan-2-yl)methyl)ethyl amino)salicylic acid and Sulphanilamide. The resulted HMSPCFEAB ligand was an amorphous brown powder. The C,H,N contents of HMSPCFEAB **(Table-1)** are consistent with the structure predicted **(Scheme-1)**. The IR spectrum of HMSPCFEAB comprises the important bands due to Salicylic acid. The bands were observed at 1676 cm^{-1} for CO of COOH and 3400-3350 cm^{-1} for OH group.

The broad band due to –OH group appeared at 3420-3365cm^{-1}. The NMR spectrum of HMSPCFEAB in DMSO indicates that the singlet of 1 H at 5.43 δ ppm due to –OH group. The aromatic protons are appeared in multiplicity at 6.39-8.04δ. Thus the structure of HMSPCFEAB is confirmed as shown in **Scheme-1**.

The metal and C,H,N contents of metal chelates of HMSPCFEAB **(Table-1)** are also consistent with the predicted structure. The results show that the metal: ligand (M:L) ratio for all divalent metal chelate is 1:2.

The infrared spectra of all the chelates are identical and suggest the formation of the entire metalocyclic compound by the absence of band characteristic of free –OH group of parent HMSPCFEAB. The other bands are almost at their respectable positions as appeared in the spectrum of parent-HMSPCFEAB ligand. However, the band due to (M-O) band could not be detected as it may appear below the range of instrument used. The important IR Spectral data are shown in **Table-2**.

TABLE-2: SPECTRAL FEATRUES AND MAGNETIC MOMENT OF HMSPCFEAB METAL CHELATES

Metal Chelates	μ_{eff} (BM)	Electronic spectral data (cm^{-1})	Transition
HMSPCFEAB-Cu^{+2}	2.52	23431 13193	Charge transfer $^2B_{1g} \rightarrow {}^2A_{1g}$
HMSPCFEAB-Ni^{+2}	3.67	22574 15348	$^3A_{1g} \rightarrow {}^3T_{1g}(P)$ $^3A_{1g} \rightarrow {}^3T_{1g}(F)$
HMSPCFEAB-Co^{+2}	4.70	23714 19083 8904	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$
HMSPCFEAB-Mn^{+2}	5.55	23207 19012 16818	$^6A_{1g} \rightarrow {}^6A_{2g}\ {}^4E_g$ $^6A_{1g} \rightarrow {}^4T_{2g}$ (4G) $^6A_{1g} \rightarrow {}^4T_{1g}$(PG)
HMSPCFEAB-Zn^{+2}	Diamag.		---------

Magnetic moments of metal chelates are given in **Table-2**. The diffuse electronic spectrum of Cu^{+2} chelates shows two broad bands around 13193 and 23431 cm^{-1}. The first band may be due to a $^2B_{1g} \rightarrow {}^1A_{1g}$ transition. While the second band may be due to charge transfer. The first band shows structures suggesting a distorted octahedral structure for the Cu^{+2} metal chelates. The higher value of the magnetic moment of the Cu^{+2} chelate supports the same [18]. The Co^{+2} metal chelate gives rise to two absorption bands at 23714, 19083 and 8904 cm^{-1}, which can be assigned $^4T_{1g} \rightarrow {}^2T_{2g}$, $^4T_{1g} \rightarrow {}^4T_{1g}$(P)transitions, respectively. These absorption bands and the μ_{eff} value indicate an octahedral configuration of the Co^{+2} metal chelate [15]. The spectrum of Mn^{+2} polymeric chelate comprised two bands at 19012 cm^{-1} and 23207cm^{-1}. The latter does not have a very long tail. These bands may be assigned to $^6A_{1g} \rightarrow {}^4T_{2g(G)}$ and $^6A_{1g} \rightarrow {}^4A_{2g(G)}$ transitions, respectively. The high intensity of the bands suggests that they may have some charge transfer character. The electronic spectrum of the Ni^{+2} complex exhibits two bands at 15,359 and 22,584 cm^{-1}, attributed to $^3A_{1g} \rightarrow {}^3T_{1g}(P)$, $^3A_{1g} \rightarrow {}^3T_{1g}(F)$ transitions, respectively, for an octahedral Ni^{+2}complex [19], while Zn^{+2} metal chelate is diamagnetic in nature and its electronic spectra do not furnish any characteristic d-d transitions.

TABLE-3: ANTIFUNGAL ACTIVITY OF HMSPCFEAB LIGAND AND ITS METAL CHELATES

Sample	Zone of inhibition of fungus at 1000 ppm (%)			
	Asperginus Niger	***Botrydeplaia Thiobromine***	***Nigrospora Sp.***	***Rhisopus Nigricans***
HMSPCFEAB	51	60	53	52
HMSPCFEAB-Cu^{+2}	72	74	72	68
HMSPCFEAB-Co^{+2}	71	73	65	61
HMSPCFEAB-Ni^{+2}	70	70	60	64
HMSPCFEAB-Mn^{+2}	66	60	69	60
HMSPCFEAB-Zn^{+2}	58	70	70	67

The magnetic moment is found to be lower than normal range. In the absence of low temperature measurement of magnetic moment it is difficult to attach any significance to this. The observed μ_{eff} values in the range 2.52-5.55 B.M are consistent with the above moiety [20].

The examination of antifungal activity of HMSPCFEAB ligand and its all chelates **(Table-3)** reveals that the ligand is moderately toxic against fungi, while all the chelates are more toxic than ligand. Among all the chelates the Cu^{+2} chelate is more toxic against fungi.

CONCLUSION

In present paper we reported about the synthesis and characterization of new ligand which contain sulfa drug moiety. The new synthesized all compound HMSPCFEAB and its metal chelates was examined for their antifungal

activity against various fungi. They showed that ligand is moderately toxic against fungi, while all the chelates are more toxic than ligand. Among all the chelates the Cu^{+2} chelate is more toxic against fungi.

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