Synthesis, Structure, Spectroscopy and Antimicrobial Activity of Copper (II) Complex of Furfuraldehyde-2-Salisaldehyde Thiosemicarbazide1-(2-ydroxybenzylidene)-4-((4H-pyran-2-yl) methylene) Thiosemicarbazide

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Research Article

Abstract: Cu(II) complexes containing ligand Furfuraldehyde-2-Salisaldehyde thiosemicarbazide 1-(2-hydroxybenzylidene)-4-((4H-pyran-2-yl)methylene) thiosemicarbazidehavebeen synthesised. The ligands were characterised on the basis of Elemental Analyses, Absorption spectra,IR, NMR,X-RD,Massspectalstudy and Antimicrobial Activity. A simple ,sensitive and specific spectrophotometric method for the determination of Cu(II) is developed based on the colour reaction between copper (II) and Furfuraldehyde-2-Salisaldehyde thiosemicarbazide 1-(2-hydroxybenzylidene)-4-((4H-pyran-2-yl)methylene) thiosemicarbazide .Physico-chemical and Analytical characteristic of ofcopper (II) and Furfuraldehyde-2-Salisaldehyde thiosemicarbazide1-(2-hydroxybenzylidene)-4-((4H-pyran-2-yl)methylene) thiosemicarbazidewas studied. Degree of dissociation,Dissociation constant and Stability constant of complex are 0.0476,9.5078x10^{-13} , and 1.0517x10^{12} respectively. The change in free energy of the complex was -68.59 KJ/mole.Composition of the metal and ligand has been determined by job's variation and mole ratio methods. The optimum conditions for complete colour development have been established by studying parameters ike effect of medium,reagent concentration, time period have been studied. Effects of diverse ion have been studied.

Keywords: Copper (II), Furfuraldehyde-2-salisaldehyde thiosemicarbazide, Spectrophotometry,Antimicrobial samples.

Introduction

The biological activity of many drugs can be enhanced upon complexing with metal ions. The biologically active compounds become more effective and bacterio-static upon chelation with metal ions. The biological activity of drug has been shown to be enhanced on complexing with metal ions, hence promoting their use in pharmacology. Thiosemicarbazones and their metal complexes present a wide range of applications that stretch from their use in analytical chemistry through pharmacology to nuclear medicine. Thiosemicarbazone complexes have been stimulated by their biological activity [1-3]. Thiosemicarbazone are biologically active pharmacophores,besides having good complexing ability and their activity enhances on complexation with metal ions [4-7]. Thiosemicarbazone metal chelates have broad applications in biologicaland Industrial fields [8-16]. These complexes are known to be biologically important for antimicrobial [8, 9]. Antibacterial [10, 11], antifungal [12, 13], antitumor [14, 15],fungicides [16], anti-inflammatory [17], antiviral [18], antimalarial [19]. Metal thiosemicarbazone complexes are emerging as new of experimental anticancer chemotherapeutic agents which exhibits clasinhibitory activities against cancerthrough inhibition of a crucial enzyme is obligatory for DNA biosynthesis and cell division vizribonucleotidediphophatereductase (RDR) [20]. Thiosemicarbazone complexes are having imine group (-N=CH-) which imparts the biological activity and chelating properties towards the central metal atom [21-24]. Formylthiosemicarbazone of different heterocyclic system showed that thiosemicarbazone side chain adjacent to the heterocyclic nitrogen and conjugated NNS tridentate ligand system is necessary for anticancer activity [25].I cancer treatment it has been shownthat the active species is not the thiosemicarbazone itself but a metal chelates of the thiosemicarbazones [26]. Complexes of Iron (II), Ruthenium (III), Rhodium (II), Palladium (II), Cobalt (II), Copper (II),Nickel (II),with N-(α-pyridyl)-furfural-2-aldehyde thiosemicarbazone (PFT) and N-(αpyridyl)-thiophene-2-aldehyde thiosemicarbazone (PTT) have been synthesized and characterized by chemical analysis, molar conductance, magnetic susceptibility etc.[27]. The pharmacological

importance of metal complex with heterocyclic thiosemicarbazones[28].Some important medicinal compounds such as thiosemicarbazones, thiadiazolines, 4-thiazolidinones and 5-arylidine derivatives. They act as antibacterial andtuberculostatic agent [29]. Complex of iron (II) with salicylaldehydethiosemicarbazone has been studied spectrophotometrically [30]. The synthesis and biological evaluation of Д-ketoglutaric acid thiosemicarbazone linear and cyclic derivatives and their copper and Zinc complexes. More recently the same group has reported on a series of thiosemicarbazones derived from natural aldehyde and in particular 9-cis-refinal thiosemicarbazone 7 its cobalt (III), nickel (II) and copper (II) complexes [31]. Complexes of transition metal with thiosemicarbazonesandtheirSchiff base have been studied extensively both of the hydrogen atoms of N_4 atom are substituted with alkyl or aryl groups have not been investigated in detail [32].Copper is widely distributed in foods of plants and animal origin. Trace amounts of copper in various substances may be vital, objectionable or perhaps indicative of contamination ormalfunction. Copper traces promote rancidity and off-flavors in foods and beverages. Itsdetermination in biological samples such as blood, liver tissue, hair etc., can be of considerablesignificance in medical diagnosis and biochemical research. Chronic copper poisoning causesgastrointestinal catarrh and haemochromatosis. Copper is also a constituent of severalpharmaceutical preparations. Hence rapid and sensitive methods for its determinations are ingreat demand. A number of spectrophotometric methods have been developed in recent years forthe detetmination of Copper .Among the various organic reagents employed thiosemicarbazones occupy a significant place [33-36].Copper exhibits considerable biochemical action either as an essential trace metal or as a constituent of various exogenously administered compounds in humans. the involvement of copper in human diseases has been described from a medicinal-chemical [37], and a biochemical view [38] focusing on the molecular physiology of Cu transport [39].Much of the current research effort is cited on copper homeostasis [40] and its relation toironmetabolism [41] as well as the role of copper in biological processes related to human physiology and pathology [42, 43]. Current interest in Cu complexes is stemming from their potential use as antimicrobial, antiviral, anti-inflammatory, antitumor agents, enzyme inhibitors, or chemical nucleases Markedly, the biochemical action of Cu complexes with non-steroidal anti-inflammatory drugs (NSAIDs) has been studied [40]. Numerous Cu(II) complexes of NSAIDs showing enhanced anti-inflammatory and antiulcerogenic activity, as well as reduced gastrointestinal toxicity compared to the uncomplexed drug, have been prepared and structurally characterized [44]. The potential chemotherapeutic properties of copper-based compounds [45, 46]. Moreover, several authors have brought to attention the antiviral and antibacterial activity of Cu (II) complexes. For instance, it was shown that the infectivity of influenza a virus is reduced after exposure on copper surfaces [47]. Cu complexes could be helpful in the design and production of antiviral and antibacterial materials, able to deactivate HIV or H1N1 viruses[48] Most copper (II) complexes penetrate into cells while, due to the reducing properties of interacellularthiols, produce the Cu (I) species which activate the molecular oxygen to hydroxyl radicals or superoxide anion .These species attack and break the DNA backbone and damage the cell membrane or interact with proteins.

Materials and Methods

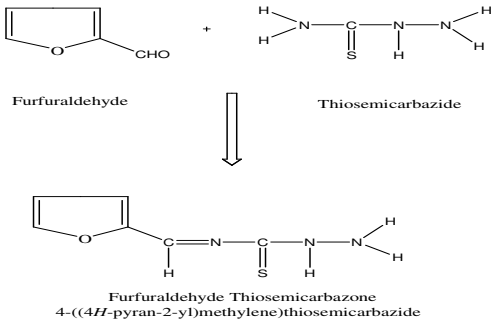
An Elico UV-visible spectrophotometer model UV_SL 164 equipped with 1 cm quartz cell is used for spectrophotometric measurements. An Elico pH meter LI-610 is used for pH measurements. The chemicals used are of analytical reagent grade. Perkin Elmer 221 IR spectrophotometer using KBrpellets techniques is used for IR studies. X-RD was taken on PW 3710 diffract meter using CuK2 radiation has been taken on the instrument BRUKER AC 300F NMR spectrophotometer 300HZ with $CDCl_3$ solvent. Elemental analysis and antimicrobial activity was done in laboratory approved by Central Government for AGMARK.

Synthesis and Characterization ofF2STSC

Synthesis ofF2STSC Furfuraldehyde-2-salisaldehyde thiosemicarbazide(F2STSC)is synthesized in two steps

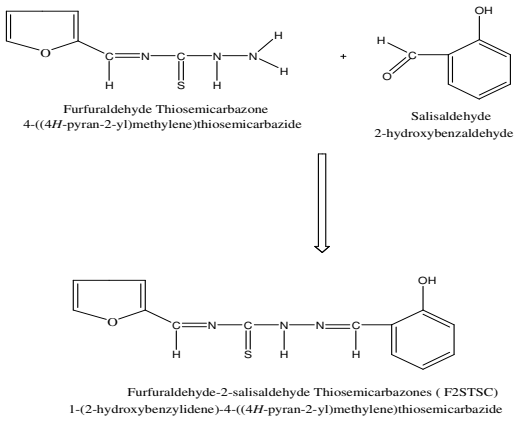
Step I: Furfuraldehydethiosemicarbazide(FTSC)synthesized by refluxing equimolar quantity offurfuraldehyde with thiosemicarbazide in methanol medium for four hours.

Reaction



StepII:Furfuraldehyde-2-salisaldehyde thiosemicarbazide(F2STSC) synthesized by refluxing equimolar quantity of furfuraldehydethiosemicarbazide (FTSC) andSalisaldehydein methanol medium for fourhours.

Reaction



The crude product is crystallized in methanol. The colour is brownish yellow. The recrystallized product has melting point is 280-283^{0}C and molecular weight by formula is 273.00

Characterization ofF2STSC

Elemental Analysis of F2STSC

The elemental analysis of F2STSC was done in laboratory approved by Central Government for AGMARK. It shows the result of elemental analysis in Table 1.

Absorption Spectra of F2STSC The absorption spectra of F2STSC was recorded against a blank solution containing buffer (PH=3) and is shown in Fig 1. Absorption spectra was recorded in the wavelength range 270-420 nm. The complex shows an absorption maximum at 350 nm. At 350 nm wavelength the molar absorptivity of F2STSC is 1.823x10^3 L.mol^{-1}.cm^{-1}.

Infrared spectra of F2STSC

IR spectra of F2STSC was taken in the range of 4000 cm^{-1} to 200 cm^{-1} on perkin Elmer 221 IR Spectrophotometer using KBr pellet technique. The characteristic bands observed are as in

Table 2.Fig 2.Shows IR spectra of F2STSC.

NMR Spectra of F2STSCNMR spectra of F2STSC has been taken from Government of Central Instrumentation Laboratory, Instrument used BRUKER AC 300F NMR spectrophotometer 300HZ with $CDCl_3$ solvent. The characteristic chemical shift and the type of proton given in Table 3. The NMR spectra of F2STSC is an shown in Fig 3. From the NMR spectra and the table it is observed that the aromatic proton tallies with the structure of F2STSC.

X-RD of F2STSCX-RD spectra of F2STSC was taken on PW 3710 diffractometer using CuK_2 radiation(Y=1.54056 A^0). The X-RD diffraction of F2STSC was recorded at angle 2θ from 10.950 to 86.780. The data of X-ray diffraction of F2STSC were presented in Table 4. And x-ray spectrum in Fig. 4 for the determination of structure Hesse-Lipson Procedure is used [49].

Job's method of continuous variation of F2STSC

For Job's method numbers of solutions were prepared by keeping same molar concentration of Cu (II) and furfuraldehyde-2-salisaldehyde thiosemicarbazone constant whilethe ratio varied in different solutions. At 350 nm wavelength absorbance was measured. Fig. 5 indicates that the formation of complexis 1:2.

Antimicrobial Activity of F2STSC Antimicrobial Activity of F2STSC has done in the laboratory approved by Central Government through AGMARK, The result are noted in Table 5.

Physico-chemical Characteristic ofCu (II)-F2STSC

Physico-chemical and Analytical characteristic of Cu (II)-F2STSC was studied and given in Table 6.

Effect of diverse ion of F2STSC

Effect of diverse ion was studied for Cu (II) F2STSC complex using metal copper and F2STSC an error upto 2 % in absorbance was considered to be tolerable Table 7. It concludes that Cu (II) and Mg (II) strongly interfere. While other ions show moderate tolerance for the complex study. EDTA and acetate ion interferes seriously and must be absent.

Table1: Elemental Analysis of F2STSC

Sr.No.	Chemical Analysis	Percentage Found	Percentage Expected
1)	Carbon	47.82	57.12
2)	Hydrogen	05.21	04.05
3)	Sulphur	09.22	11.70
4)	Nitrogen	17.16	15.38
5)	Oxygen	20.59	11.73

Table2: Infrared spectra of F2STSC

Sr.No.	Frequency Wavenumber	Expected Element
1)	740 800 820 920	4 adjacent C-H → 

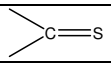
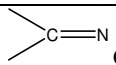
	1030	
2)	1230 1340 1360	CS,-NH.
3)	1430	
4)	1460	 Conjugated cyclic.
5)	1510 1580	Benzens
6)	1580 1660	Unsaturated compoundC=N.
7)	1660 1850	C=S ,StretchSulphur compounds
8)	2000 2280 2505	N=C=N
9)	3700	Free OH, O-H Stretch.

Table 3: NMR data of F2STSC

Sr.No.	Types of proton	Group	Chemicalshift (ppm)
1)	Aromatic	Ar-H	7.6919 7.8638 7.5302 7.4638 7.4186 7.3932 7.3256 7.2754 7.2501 7.2247 6.9325 6.9050 6.8799 6.8549
2)	Primary	R-CH_3	8.3036
3)	Aldehyde	R-CHO	9.6055
4)	Secondary	R_2CH_2	1.2555
5)	Alcohols	HC-OH	3.1239

Table 4: X-RD for F2STSC (Powdermethod)

2 θ	Hkl	Sin^2 Observed	Sin^2 Calculated	d(A^0) Observed	d(A^0) Calculated
12.545	110	0.011937	0.01922	7.0502	5.5555
16.010	110	0.019391	0.01922	5.5313	5.5555
16.150	111	0.019731	0.02752	5.4836	4.6429
18.930	200	0.027032	0.02704	4.6841	4.6840
20.005	200	0.030168	0.02704	4.4348	4.6840
20.535	200	0.031770	0.02704	4.3215	4.6840
22.930	210	0.039509	0.03950	3.8753	3.8752
23.530	210	0.041574	0.03950	3.7778	3.8752
25.260	211	0.047809	0.04780	3.5228	3.5228
26.945	211	0.051158	0.04780	3.4056	3.5228
29.845	220	0.066312	0.07690	2.9912	2.7775
32.705	310	0.079268	0.07337	2.7359	2.8448
32.875	310	0.080071	0.07331	2.7221	2.8448

a=9.3682b= 6.8990C= 8.2502

Structure of Cu(II)-F2STSC

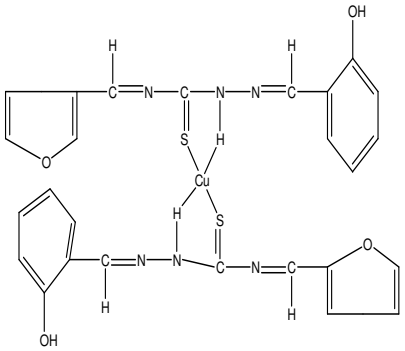


Table5: Antimicrobial Activity of F2STSC

Sr.No.	Antimicrobial	Activity
1)	K.pneumonia	Nil
2)	V. chloerease	Nil
3)	S.typhi	Nil
4)	S. aureus	Nil
5)	E. coli	Nil
6)	B. subtilis	Nil

Table6: Physico-chemical and Analytical Characteristic ofCu (II)-F2STSC

Sr.No.	Characteristics	Result
1)	Absorption spectra	380 nm
2)	Molar extinction coefficient ($L.mol^{-1}.cm^{-1}$.)	$5.034x10^{3}$
3)	pH range (optimum)	2.0
4)	Reagent required for maximum complexation	2.0 ml
5)	Beer's law validity range (ppm)	$9.1575x10^{-6}$M To $9.1577x10^{-5}$ M
6)	Compositon of complex (M:L) obtained in job's and molar ratio method	1:2
7)	Sandell's sensitivity ($\mu g/cm^{-2}$)	0.01262
8)	Degree of dissociation of complex	0.0476
9)	Dissociation constant of complex	$9.5078x10^{-13}$
10)	Stability constant	$1.0517x10^{12}$
11)	Change in free energy	-68.59 KJ/mole

Table 7: Tolerance limit of diverse ions in the determination of Copper(II)

Sr. No.	Metal ion	Metal in added form	Tolerance limitppm
1)	Fe (III)	$FeCl_3$	63.14
2)	Co (II)	$Co(SO_4)$	93.10
3)	Sn (II)	$SnCl_2$	35.01
4)	Mg (II)	$MgCl_2$	12.00
5)	Ni (II)	$NiSO_4.2H_2O$	23.10
6)	EDTA	Na salt of EDTA	None
7)	CH_3COOH	CH_3COOH	None

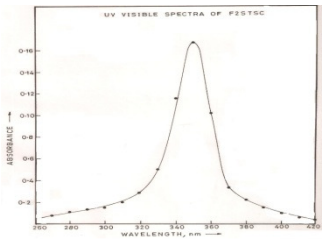


Figure 1: Absorption Spectra of F2STSC

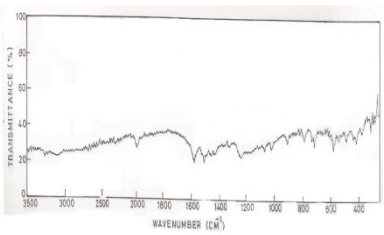


Figure 2:Infrared spectra of F2STSC

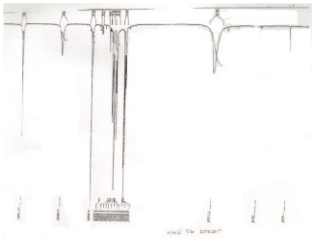


Figure 3:NMR spectra of F2STSC

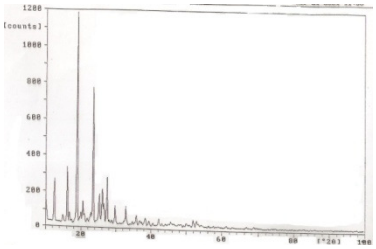


Figure 4:X-RD of F2STSC

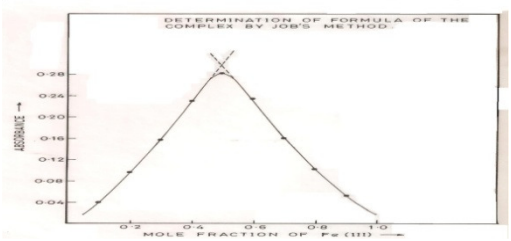


Figure 5: Job's method of continuous variation of F2STSC

Result and Discussion

Cu (II) forms brownishyellow colour complex with Furfuraldehyde-2-salisaldehyde thiosemicarbazide(F2STSC). The complex has melting point is 280-283^{0}C and molecular weight by formula is 273.00. The elemental analysis of F2STSC shows carbon 47.82%, hydrogen 05.21 %, sulphur 09.22 %, nitrogen 17.16 % and oxygen 20.59 %. Complex shows absorption maxima at 350 nm and at 350nm the molar absorptivity of F2STSC is $1.823x10^3$ $L.mol^{-1}.cm^{-1}$.Compositon of complex (M:L) obtained in job's and molar ratio method 1:2 .Sandell's sensitivity is 0.01262 µg/cm^{-2} .Degree of dissociation,dissociation constant and stability constant of the complex are 0.0476,$9.5078x10^{-13}$and $1.0517x10^{12}$. The change in free energy of the comple has-68.59 KJ/mole. Cu (II) and Mg (II) strongly interfere. While other ions show moderate tolerance for the complex study. EDTA and acetate ion interferes seriously and must be absent.

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