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Research Article

TRANSITION METAL COMPLEXES OF SALICYLALDEHYDE NICOTINOYL HYDRAZONE (SANH) SYNTHESIS, CHARACTERIASATION AND ANTIBACTERIAL ACTIVITY

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ABSTRACT
Salicylaldehyde nicotinoyl hydrazone (SANH) has been synthesized. Complexes of Salicylaldehyde nicotinoyl hydrazone with transition metals, Fe (II) & Cu (II) have been synthesized in ethanol medium. The formation of the complexes are endothermic processes. The ligand was characterized by melting point, elemental analysis, absorption spectra, NMR - 1 H prediction and antimicrobial activity while the complexes were characterized by melting point,absorption spectra. A simple & sensitive spectrophotometric method was developed for transition metal complexes of SANH. The optimum condition for complete colour development have been established. The stability constant, dissociation constant & change in free energy of Fe (II) & Cu (II) complexes with SANH are determined. Composition of the metal & ligand has been determined by Job's variation & mole ratio method indicate that the M:L is 2:1. Tolerance limit of diverse ions in the determination of Fe (II) & Cu (II) with Salicylaldehyde nicotinoyl hydrazone are investigated.
Keywords: Salicylaldehyde nicotinoyl hydrazone, Fe (II), Cu (II), Spectrophotometry,Antimicrobial activity.

INTRODUCTION

Hydrazones are present in many of the bioactive heterocyclic compounds that are of wide interest because of their diverse biological and clinical applications. researchers who have The variety of hydrazide derivatives play various biological activities viz. anticancer, anti-HIV[1], anthelmintic[2], antimycobacterial[3], anti-inflammatory[4,5], antidiabetic[6], antimicrobial[7,8,9] , trypanocidal[10] analgesic[11-12] anti-tuberculosis [12-17] antimalarial activities[18-20] antiparasitic activity[21] Hydrazone-based coupling methods are used in medical biotechnology to couple drugs to targeted antibodies e.g. antibodies against a certain type of cancer cell. The hydrazone-based bond is stable at neutral pH (in the blood), but is rapidly destroyed in the acidic environment of lysosomes of the cell.

Iron is essential for cellular growth and division, as Fe-containing proteins catalyze key reactionsinvolving energy metabolism, respiration, and DNA synthesis. In fact, without Fe, cells are unable to proceed from the G, to the **S** phase of the cell cycle[22] . Therefore, all cells require Fe and neoplastic cells have a high Fe requirementrelated to their rapid rate of replication [23-24] Several studies have suggested that limiting Fe uptake by tumor cells may be one strategy to prevent cellular Proliferation[25-27] . A number of reports with the Fe(II1) chelator, desferrioxamine (DFO),have shown that this ligand has a potent cytotoxic effect in vitro and in vivo on the common childhood cancer, neuroblastoma[28-32] In addition to its effects on NB cells, DFO has also been shown to have a favorable antitumor effect on human melanoma cells in culture[32] .on human melanoma cells in culture[33] , on human hepatoma xenografts in nude mice[34] and in hematopoietic tumour[35] when DFO was used in combination with cytotoxic agents in a patient suffering from refractory leukemia, a partial response was obtained[36] a number of other Fe chelators have also been examined for their antitumor effects, including parabactim a-ketohydroxypyridones [37] and pyridoxal isonicotinoyl hydrazone (PIH) [38] In addition to the antineoplastic effect of apochelators, ligand-metal complexes with both nonphysiologic metals platinum physiologic metals copper an also exhibit potent cytotoxicity[39] .

Copper is known to be an essential element in the human body. Copper complexes have shown to have a beneficial effect in the treatment of inflammatory diseases. Copper has been used to successfully treat patients with arthritic and other chronic degenerative diseases. Anti-inflammatory agents (aspirin and ibuprofen, for example) have been shown to be more active than their parent compounds. Copper aspirinate has been shown not only to be more effective in the treatment of rheumatoid arthritis than aspirin alone, but it has been shown to prevent or even cure the ulceration of the stomach often associated with aspirin therapy.

As early as 1912, patients were treated for skin cancer with a mixture of copper chloride and lecithin. Success of such treatment suggested that copper compounds have anticancer activity. In 1930, work in France indicated that injections of colloidal copper expelled tumor tissue. Copper has a direct effect on the control of cholesterol. It is believed that a metabolic imbalance between zinc and copper is a major cause of coronary heart disease. Copper complexes can also have a valuable role in the minimizing damage to the heart muscle following a heart attack. This action is based on the anti-inflammatory action of copper.copper will become an increasingly important component of tomorrow's medical treatments. Copper also displays potent anti-viral activity[39] . Introducing copper into cotton fibers, latex and other polymeric materials enables the production of clothing, bedding and medical devices that possess biocidal properties [40] .Some examples include anti-viral gloves and filters (which deactivate HIV-1 and other viruses), anti-bacterial self-sterilizing fabrics (which kill antibiotic resistant bacteria), anti-fungal socks (which alleviate symptoms of athlete's foot), and anti-dust mite mattress-covers (which reduce mite-related allergies)[41] . Today copper is used as a water purifier, algaecide, fungicide, nematocide, molluscicide, and as an anti-bacterial and anti-fouling agent [42-46] It is considered safe to humans, as demonstrated by the widespread and prolonged use of copper intrauterine devices by women[47-48] .

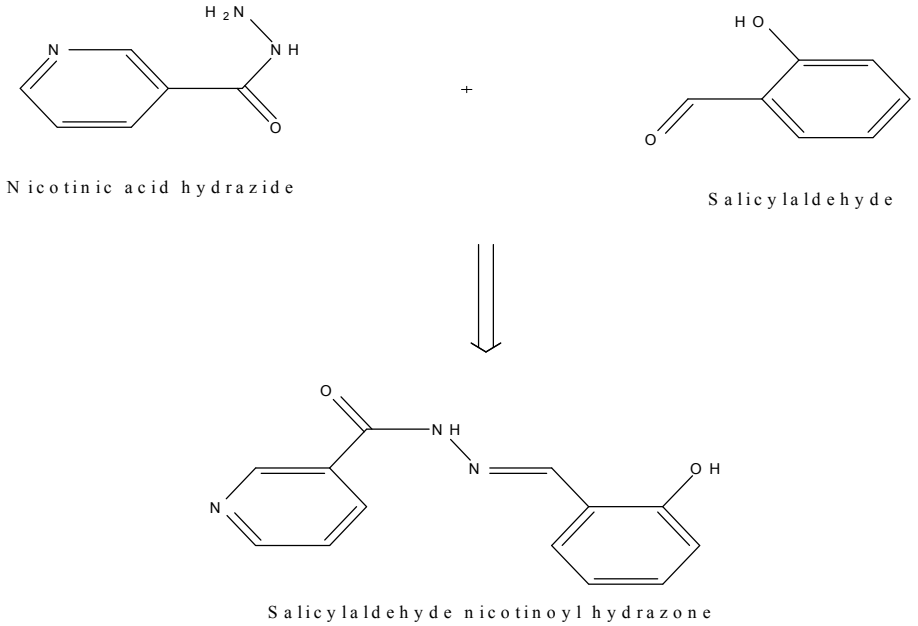
MATERIALS AND METHODS

Melting points were determined by open capillaries method. All chemical and solvents used were of analytical grade .An

Elico pH meter LI-610 is used for the pH measurements. An Elico UV-visible spectrophotometer model UV-SL-164 equipped with 1 cm quartz cell used for spectrophotometeric measurements. Elemental analysis and antimicrobial activity was done in Laboratory approved by Central Government for AGMARK.

SYNTHESIS AND CHARACTERISATION OF SALICYLALDEHYDE NICOTINOYL HYDRAZONE (SANH)

Synthesis of Salicylaldehyde nicotinoyl hydrazone



(E) –N'-(2-Hydroxbenzylidene)nicotinohydrazide

The crude product was crystallized in methanol. The recrystallized product has melting point is 160^0C and molecular weight by formula is 238.00.

Characterization of Salicylaldehyde nicotinoyl hydrazone (SANH)

Absorption Spectra of SANH

Absorption Spectra of SANH was recorded against a blank solution containing buffer (pH 2) . Absorption spectra was recorded in the wave length range 250 nm-430 nm. SANH shows an absorption maximum at 300 nm. At 300 nm wavelength the molar absorptivity of SANH is 0.991×10^3 $L.mol^{-1}.cm^{-1}$. Fig 1.

Elemental Analysis of SANH

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

Antimicrobial Activity of SANH

Antimicrobial Activity of SANH has been done in the Laboratory approved by Central Government for AGMARK. The result are noted in Table 2.

NMR H-1 Prediction

NMR H-1 Prediction of SANH is shown in Table 6 & Fig 2.

Characterisation of SANH Complex with Transition Metal

Absorption Spectra of Fe (II)-SANH & Cu (II)-SANH was recorded against a blank solution containing buffer (pH 2). Absorption spectra was recorded in the wave length range 250 nm-430 nm. The complex shows an absorption maximum at 335 nm & 315 nm. Fig 1.

Effect of Reagent concentration

Effect of Reagent concentration was studied by taking varying amount of reagent and fixed amount of transition metal.

Validity of Beer's Law and Composition of Complex

For the study of Beer's law the solutions were prepared which containing different amounts of Fe (II), & Cu (II) , same amount of SANH & 1 ml of buffer pH 2 .The composition of the Fe (II)-SANH & Cu (II)-SANH complex is found to be 1:2 . It was determined by studying Job's method. The ratio of metal ion to ligand molecule in the coloured complex was found to be 1:2

Experimental result and physical data of SANH complexes with Fe (II) & Cu(II) shown in Table 4

Physico-chemical Characteristic of Fe (II)-SANH & Cu (II)-SANH Complex

Physico-chemical and Analytical characteristic of transition metal complex of SANH was studied and given in Table 4 .

Tolerance limit of diverse ions of transition metal complexes of SANH in Table 5.

Table No. 1.Elemental Analysis of Salicylaldehyde nicotinoyl hydrazone

Sr No.	Chemical Analysis	Percentage Found	Percentage Expected
1)	Carbon	61.32 %	65.55 %
2)	Hydrogen	05.97 %	06.30 %
3)	Oxygen	06.01 %	06.72 %
4)	Nitrogen	19.87 %	21.43 %

Table No. 2. Antimicrobial Activity of Salicylaldehyde nicotinoyl hydrazone

Sr.No.	Antimicrobial	Activity
1)	Klebsiella Pneumoniae	Nil
2)	Vibriae Cholerease	Nil
3)	Bacillus Megaterium	Nil
4)	Salmonalla typhi	Nil
5)	Shigella Flexneri	Nil

Table No.3. Experimental Result & Physical data of Salicylaldehyde nicotinoyl hydrazone & its Complexes

Code No	Compound M.P. (^{0}C)	Colour	Molecular Weight by Formula gm/mole	Yield
SANH	160^{0}C	Yellow	238	89 %
Fe (II)-SANH	137^{0}C	Greenish Yellow	293.845	76 %
Cu (II)-SANH	129^{0}C	Bluish Yellow	301.546	71 %

Table No.4. Physico-Chemical and Analytical Characteristic of Transition Metal Complex of Salicylaldehyde nicotinoyl hydrazone

Sr.No.	Characteristics	Result	
		Fe (II)-SANH	Cu (II)-SANH
1)	Absorption Spectra	335 nm	315 nm
2)	Molar absorptivity	0.9750×10^3 Lit. mol^{-1}. cm^{-1}	0.5243×10^3 Lit. mol^{-1}. cm^{-1}
3)	pH range (optimum)	3.0	4.0
4)	Reagent required for maximum complexation	0.127 ml	0.200ml
5)	pKa	6.004×10^8	4.9014×10^8
6)	Beer's law validity range (ppm)	9 ppm	8.5 ppm
7)	Composition of complex (M : L)	1:2	1:2
8)	Stability Constant	3.85041×10^7	4.05903×10^7
9)	Dissociation Constant	3.00416×10^{-8}	2.96630×10^{-8}
10)	Change in free energy	-40.37 KJ/mole	-52.535KJ/mole
11)	Sandell's Sensitivity (µg /cm^2)	0.003221 µg /cm^2	0.005111 µg /cm^2

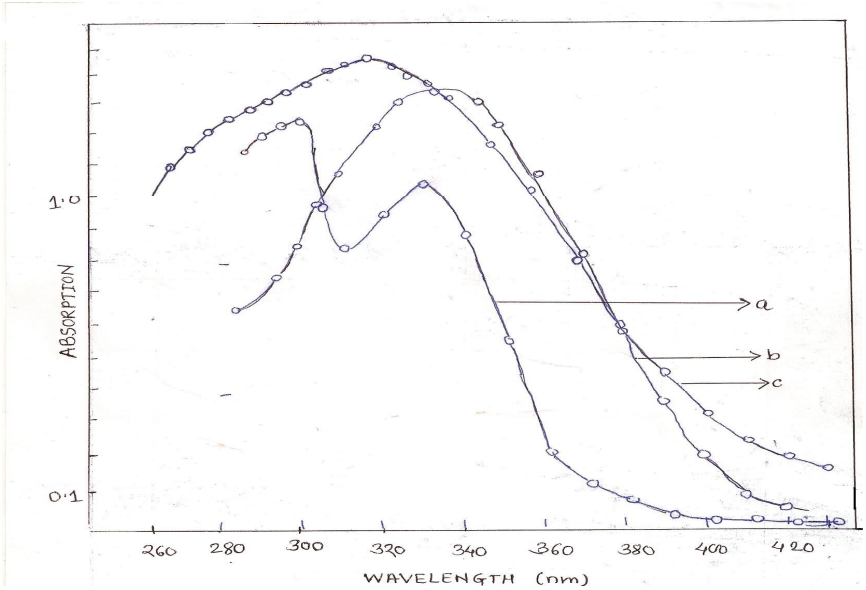
Table No.5. Tolerance limit of diverse ions of Transition Metal Complex of SANH

Sr. No.	Metal ion	Salt	Interference	
			Fe (II)-SANH	Cu (II)-SANH
1)	Mg (II)	$MgSO_4$	140	100
2)	Ca(II)	$CaCl_2.2H_2O$	86	69
3)	Cd (II)	$CdCl_2$	10	08
4)	Mn (II)	$MnCl_2$	50	24
5)	Co (II)	$CoSO_4$	Interferes	04
6)	Ce (IV)	$Ce(SO_4)_2$	10	35
7)	Ba (II)	$BaCl_2$	24	Interfere
8)	Cr (III)	$K_2Cr_2O_7$	25	13
9)	Hg (II)	$HgCl_2$	08	Interfere
10)	Ti (V)	K-titanyl oxalate	19	97
11)	Ni (II)	$NiCl_2$	54	Interfere
12)	Sn (II)	$SnCl_2$	73	19
13)	Na (I)	NaCl	37	50
14)	Pb (II)	$PbSO_4$	70	68
15)	V (v)	V_2O_5	Interferes	Interfere
16)	Zn (II)	$ZnSO_4$	33	24
17)	Al (III)	$AlCl_3$	Interferes	32
18)	Pd (II)	$PdCl_2$	Interferes	69
19)	K(II)	KCl	04	Interfere

Table No .6.NMR H-1 Prediction

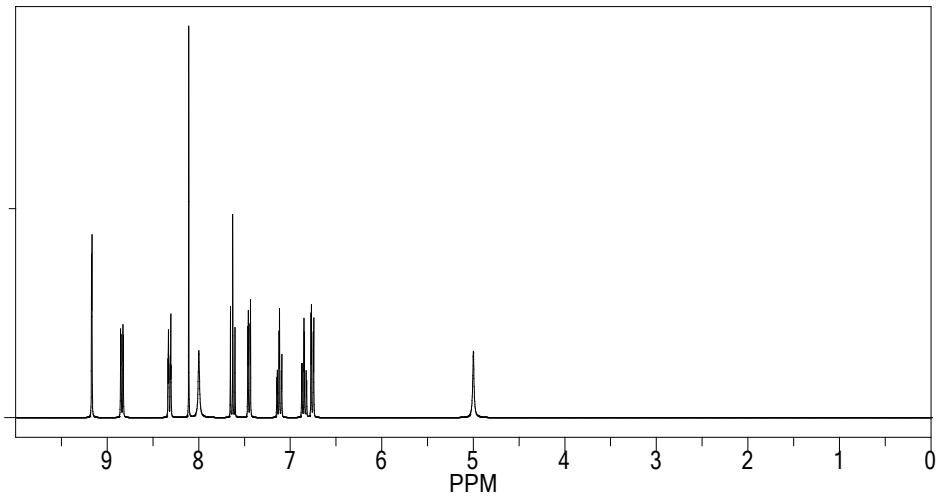
Sr.No.	Types of Proton	Node	Chemical Shift (PPM)
1)	Benzylidenimin	CH	8.11
2)	Aromatic C-OH	OH	5.00
3)	Secondary amide	NH	8.00
4)	3-Pyridine	CH	7.75

Fig No.1.Absorption Spectra of Salicylaldehyde nicotinoyl hydrazone & Complexes



a-------Absorption spectra SANH
b-------Absorption spectra Fe (II)- SANH
c------- Absorption spectra Cu (II)- SANH

Fig No .2 . NMR H-1 Prediction of Salicylaldehyde nicotinoyl hydrazone



RESULT AND DISCUSSION

Salicylaldehyde nicotinoyl hydrazone and its complexes with Fe (II) and Cu (II) was synthesized. Colour of SANH, Fe(II)-SANH & Cu (II) –SANH was yellow, greenish yellow and bluish yellow. Their molecular weight by formula is 238 gm/mole, 293.845 gm/mole & 301.546 gm/mole. The yield of different synthesized compounds were found to be range of 70 -90 % and characterization was done by melting point. SANH shows an absorption maxima at 300 nm, Absorption maxima of Fe (II)-SANH at 335 nm & for Cu (II) –SANH at 315 nm. Elemental analysis of SANH shows that carbon 61.32 %, hydrogen 05.97 %, oxygen 06.01 % and nitrogen 19.87 %. Salicylaldehyde nicotinoyl hydrazone known for their good antimicrobial properties. Antimicrobial activities were carried out by Klebsiella Pneumoniae , Vibriae Cholerease , Bacillus Megaterium , Salmonalla typhi & Shigella Flexneri. Composition of the complexes 1:2.Stability constant, Dissociation constant, Change in free energy of Fe (II)-SANH complex was 3.85041×10^{7}, 3.00416×10^{-8}, - 40.37 KJ/mole & for Cu (II) –SANH complex was 4.05903×10^{7} , 2.96630×10^{-8} , - 52.535KJ/mole respectively.

CONCLUSION

The objective of the present work was to synthesized Salicylaldehyde nicotinoyl hydrazone Fe (II)-Salicylaldehyde nicotinoyl hydrazone & Cu (II)-Salicylaldehyde nicotinoyl hydrazone purity, characterize and evaluate the antimicrobial activity. Fe(II)-SANH & Cu(II)-SANH shows 1:2 complexation.

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