MAR Microbiology

Research Article

Synthesis, Characterization and Antimicrobial Study of 3-nitrobenzaldehyde Thiosemicarbazone and it's Metal Complexes

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Received Date: November 07, 2020
Publication Date: December 01, 2020

Abstract:

*This study was carried out to synthesize and characterize 3-nitrobenzealdhyde thiosemicarbazone ligand and it's transitional metal complexes with Nickel(II), Copper(II), and Cobalt(II) and to evaluate their activity against bacteria and fungi. The synthesized compounds were characterized by FT-IR and UV methods. The results of FT-IR and UV spectra of the ligand and its metal complexes confirm the formation of azomethine group (-C=N-H) accompanied with the absence of carbonyl group (C=O) and formation of (M-N) and (M-S) bonds with all metal ions. The results assign that the ligand is neutral and bidentate species which coordinated via azomethine N and thione S with all three metal ions and the silver nitrate test indicates that the chloride ion was out of coordination sphere. The antimicrobial activity of the ligand and its metal complexes against four types of bacteria (*Bacillus subtilis, Staphylococcus aureus *(Gram +ve)* Escherichia coli *and* Pseudomonas aeruginosa *(Gram –ve) and one fungi* (Candida ablicans) *with different concentrations (75 and 100)mg/ ml was carried out using disc diffusion method. The results showed that the free ligand and Copper (II) complex were inactive against all types of bacteria and fungi and the Nickel(II) and Cobalt(II) complexes exhibited different activities against four types of bacteria and fungi.*

Keywords: *Schiff Bases; Metal Complexes, Antimicrobial Activities.*

Introduction

Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Hugo Schiff in 1864. The common structural feature of these compounds is the azomethine group with a general formula RHC=N-R’ where R and R’ are)alkyl, aryl, cycloalkyl or heterocyclic groups(which may be variously substituted. These compounds are also known as anils, imines or azomethines **[**1**].** Nitrogen analog of both aldehyde and ketone which have the same oxidation level are imines and imine derivatives. In almost every instance these compounds are prepared by an exchange reaction between an imine derivative and a carbonyl compound. For simple imines (R= alkyl, aryl) water removal by either a dehydrating agent (KOH or molecular sieves) or azeotropic distillation is often employed to drive the reaction to completion. Schiff bases that contain aryl substituents are substantially more stable and readily synthesized, while those which contain alkyl substituents are relatively unstable**[**2**]**. Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerizable while those of aromatic aldehydes having effective conjugation are more stable. In general, aldehydes react faster than ketones in condensation reactions, leading to the formation of Schiff bases as the reaction center of aldehydes are sterically less hindered than that of the ketone. Furthermore, the extra carbon of ketone donates electron density to the azomethine carbon and thus makes the ketone less electrophilic compared to aldehydes**[**3**]**. Some semicarbazones, such as nitrofurazone and thiosemicarbazones are known to have anti-viral and anti-cancer activity, usually mediated through binding to copper or iron in cells**[**4**]**. Nitro and halo derivatives of Schiff bases are reported to have antimicrobial and antitumor activities. Some of Schiff base and beta-lactam acts as good antimicrobial agents **[**5**]**. Schiff base ligand and metal complexes of sulfur and nitrogen act as good antibacterial agents**[**6**]**. Certain thiosemicarbazones are relatively specific inhibitors of ribonucleotide reductase which is an important metabolic target for the development of chemotherapeutic agents against cancer**[**7**]**.

The significance of thiosemicarbazone and their metal complexes, apart from their diverse chemical and structural characteristic, stems from not only their potential but also their proven application as biologically active molecules. The wide applications and structural diversity of metal complexes of thiosemicarbazone prompted us to synthesize bidentate NS- donor ligand and their metal complexes. The present work is mainly concerned with the synthesis, characterization and antimicrobial activity of 3-nitrobenzaldehyde thiosemicarbazone ligand and its transition metal complexes.

MATERIALS AND METHODS

Chemical and solvents

Ethanol, Thiosemicarbazide, 3-nitrobenzaldehyde, Nickel(II) Chloride Hydrate, Copper(II) Chloride Hydrate, Cobalt(II) Chloride Hydrate, Silver Nitrate, Potassium Bromide, and Mueller Hinton Agar.

Synthesis of ligand

An equimolar amount of thiosemicarbazide (0.364g, 0.004mole) and 3-nitrobenzaldehyde (0.6g,0.004mol) each one was dissolved in 20ml of ethanol after heating were mixed and refluxed for 6hrs in electrical heater a white precipitate formed was filtered, dried, weighed and kept for further uses **(**Scheme 1**)**.

Synthesis of Metal complexes

A general method used for the synthesis of metal complexes was a 1:2 molar ratio of metal salt (0.0004mole) and prepared ligand (0.0008mole) were dissolved in hot ethanol. The mixture was refluxed for 3hrs in an electrical heater then allowed to cool at room temperature and left for slow solvent evaporation. The colored precipitate was obtained filtered off, washed with cold ethanol, dried, and recrystallized in ethanol **(**Figure 1**)**.

FT-IR Analysis Assay

The sample was mixed with potassium bromide and pressed under high pressure. The KBr melts and seals the sample into a matrix, the result is a KBr pellet that can be inserted into a holder in Perkin-Elmer FT-IR type -1650 spectrophotometer in wavenumber region 4000-200 cm-1.

UV Analysis Assay

0.01g of sample dissolved in 5ml of ethanol thin serial dilution much time was made thin 1ml of solution placed into sample cell of UV spectrometer -1800-Shimadzu.

Disc diffusion method

The paper disc diffusion method was used to screen the antibacterial activity of prepared compounds and performed by using Mueller Hinton agar (MHA). The ligand and its complexes were carried out according to the National Committee for Clinical Laboratory Standards Guidelines. Bacterial suspension was diluted with sterile physiological solution to 108cfu/ml (turbidity = McFarland standard 0.5). One hundred microliters of bacterial suspension were swabbed uniformly on the surface of MHA and the inoculum was allowed to dry for 5 minutes. Sterilized filter paper discs (Whatman No.1 6mm in diameter) were placed on the surface of the MHA and soaked with 20µl of a solution of each sample. The inoculated plates were incubated at 37°C for 24 h in the inverted position. The diameters (mm) of the inhibition zones were measured [8]

RESULTS and DISCUSSION

FT-IR Spectra of the ligand and its metal complexes

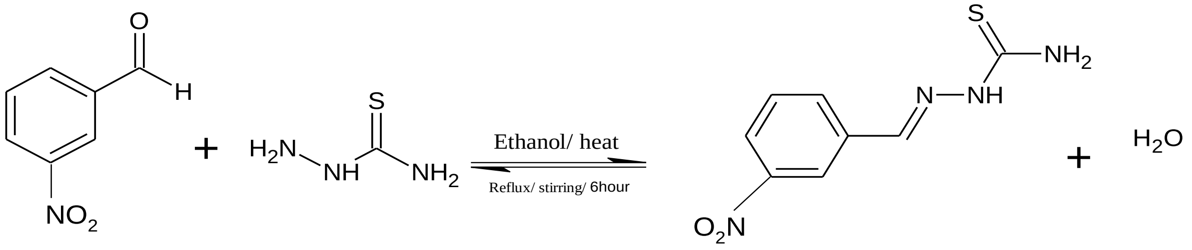
The infrared absorption bands become very useful for determining the mode of coordination of the ligands to metal. The IR of the ligand and it's complexes confirm the formation of Imines bond (-C=N-H) and the absences of carbonyl bond (C=O). The actual band of the ligand at (1527)cm-1 is assigned to stretching vibration of the imines group at (-C=N-H) these bands were observed to lower or higher frequency at 1510-1550cm-1, thus indicates the coordination of azomethine nitrogen to metal atom[8], which confirmed by the lower frequency at (520-550)cm-1 assigned to complexion M-N with metal, the band 894cm-1 in ligand assigned to C=S[9], which appear at a lower frequency (416 - 462)cm-1 with the metal complex indicating coordination of thiol sulfur atom M-S and also appearance of a new band at (802 - 840) cm-1 which assigned to v(C-S) group[10]. and band at (3487-3340) cm-1 is assigned to aromatic (C-H), The vibrational frequencies of –NH2 group slightly changed for both the ligands and the complexes (indicated to the effect of metal from Ni(II), Cu(II) and Co(II)), This evidence indicates the non-coordination of –NH2 group to metal ion[11]. All the IR spectra of the ligand and metal complexes under study are shown in table (2) and figure: (2-5). When a drop of silver nitrate solution was added to the Ni(II), Cu(II), Co(II) complexes a precipitate was formed and this confirmed that the chloride ion was out of coordination sphere, and the ligand was in bidentate form.

Electronic spectral data of the ligand and its metal complexes

Electronic spectra of the ligand and it's metal complexes have a band at (228-247 nm) are assigned to n-π* transition and absorption bands at(316-318nm) are assigned to π-π* transition**[**12**]**.

Antimicrobial activity of the ligand and its metal complexes

The antimicrobial activity of the ligand and its metal complexes are tested using four types of bacteria (E.c, Ps.a, S.a, and B.s) and one fungi (C.a) by used (disc diffusion method). The results showed that the ligand and Cu(II) complex are inactive against the four types of bacteria and one the fungi at a concentration (100,75)mg/ml but the Ni(II) complex gives good activity against four types of bacteria and fungi at a concentration (100)mg/ml, also Co(II) complex shows good activity against four types of bacteria and one fungus at all concentration (100,75)mg/ml. The results concluded that the ligand and Cu(II) complex was inactive against four types of bacteria and one fungus, but the (Ni(II), Co(II)) complexes exhibit good activity comparative with the standard at the same concentration (100)mg/ml. The antibacterial activity results were expressed in terms of the diameter zone of inhibition and <9mm zone was considered as inactive; 9-12mm as partially active; while 13-18mm as active and >18mm as very active**[**13**]**.



3-Nitrobenzaldehyde Thiosemicarbazide 3-Nitrobenzaldehyde Thiosemicarbazide

Scheme1. show the formation of 3-nitrobenzaldehyde thiosimecarbazon

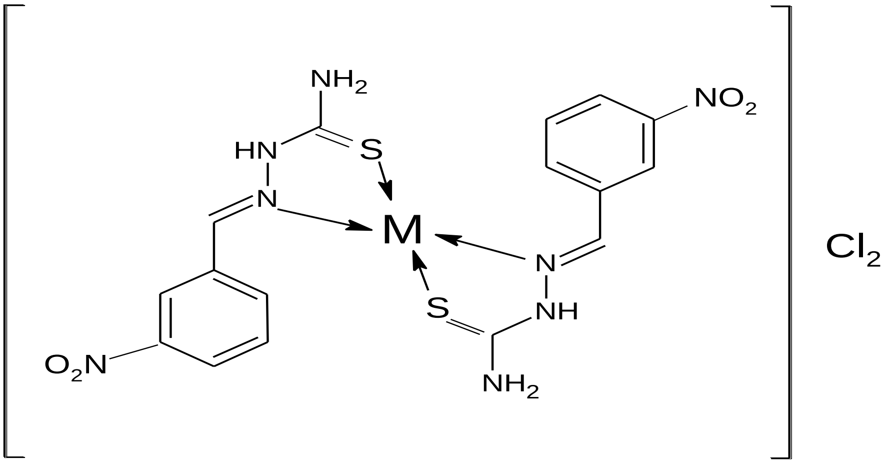


Figure1. Proposed structure of 3-nitrobenzaldehyde thiosimecarbazone complexes,
Where M = Ni(II), Cu(II) and Co(II)

Table1. Some properties of the ligand and it's metal complexes

S.No	Sample	Color	Ratio	Yield%
1	Ligand (L)	White	1:1	62.50
2	$Ni(L)_2Cl_2$	Yellow	1:2	53.10
3	$Cu(L)_2Cl_2$	Yellow	1:2	60.60
4	$Co(L)_2Cl_2$	Green	1:2	43.06

Table2. IR spectrum of the ligand and it's metal complexes

S.No	Compounds	ν**(C=N)**	ν **(C=N**	ν***(NH₂)***	ν**(C=S)**	ν **(C-S)**	ν**(M-N)**	ν**(M-S)**
1	Ligand (L)	1527	3487	3240-3155	894	___	___	__
2	$Ni(L)_2Cl_2$	1543	3441	3286-3147	___	802	524	462
3	$Cu(L)_2Cl_2$	1535	3340	3271-3163	___	810	540	424
4	$Co(L)_2Cl_2$	1550	3394	3350-3150	___	840	550	439

Table 3. U.V spectrum of ligand and it's metal complexes

S.No	**Sample**	**Absorption bands n-π* in (nm)**	**Absorption bands π-π* in (nm)**
1	Ligand (L)	318	228
2	$Ni(L)_2Cl_2$	317	232
3	$Cu(L)_2Cl_2$	316	247
4	$Co(L)_2Cl_2$	317	229

Table4. Antimicrobial activity of the ligand and it's metal complexes

S.No	**Sample**	**Conc mg/ml**	**E.c**	**Ps.a**	**S.a**	**B.s**	**C.a**
1	Ligand (L)	100	-	-	-	-	-
		75	-	-	-	-	-
2	$Ni(L)_2Cl_2$	100	15	20	16	13	16
		75	-	-	-	-	-
3	$Cu(L)_2Cl_2$	100	-	-	-	-	-
		75	-	-	-	-	-
4	$Co(L)_2Cl_2$	100	27	20	27	25	13
		75	14	10	20	26	14

6	Tetracycline	100	30	45	40	35	
		75	20	33	35	30	
7	Griseofulvin	100					15
		75					-

Tetracycline = (Anti-bacteria) Griseofulvin = (Anti-fungal)

Gram negative bacteria; E.c = *Escherichia coli*, Ps.a = *Pseudomonas aeruginosa* Gram positive bacteria; B.s = *Bacillus subtitles*, S.a = *Staphylococcus aureus*, Fungi; C.a = *Candida albcans*.

Activity: <9 inactive, 9-12 partially active, 13-18 active, >18 very active.

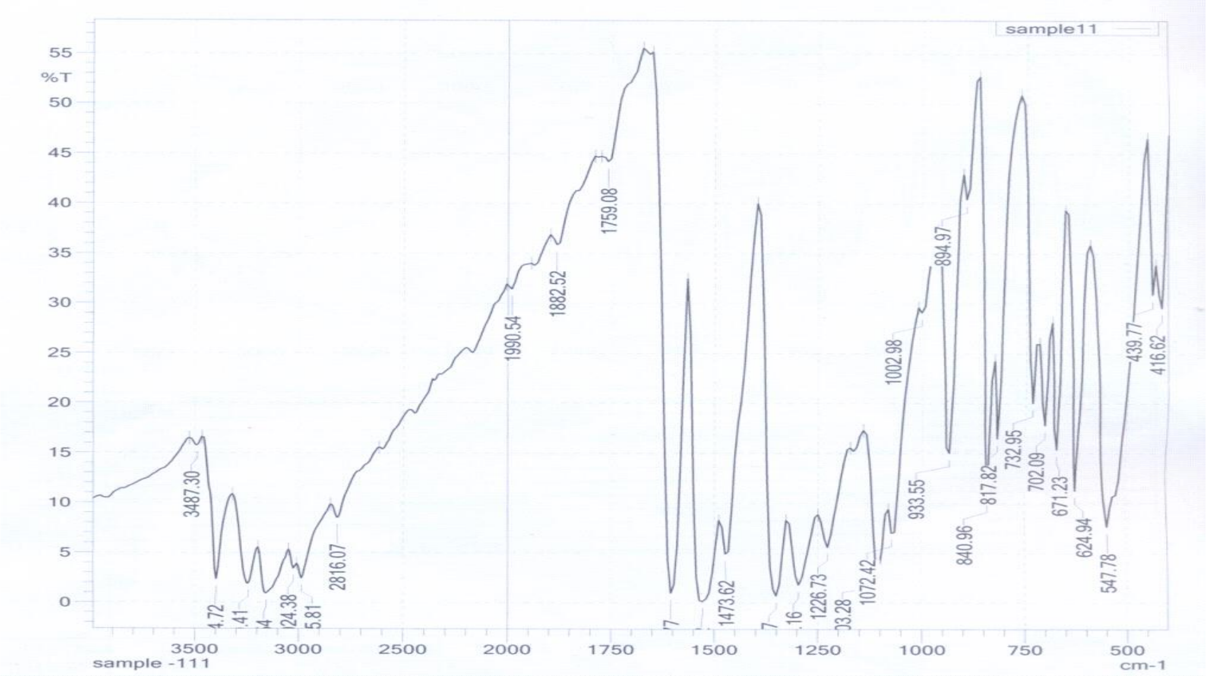


Figure2. IR-Spectra of the ligand

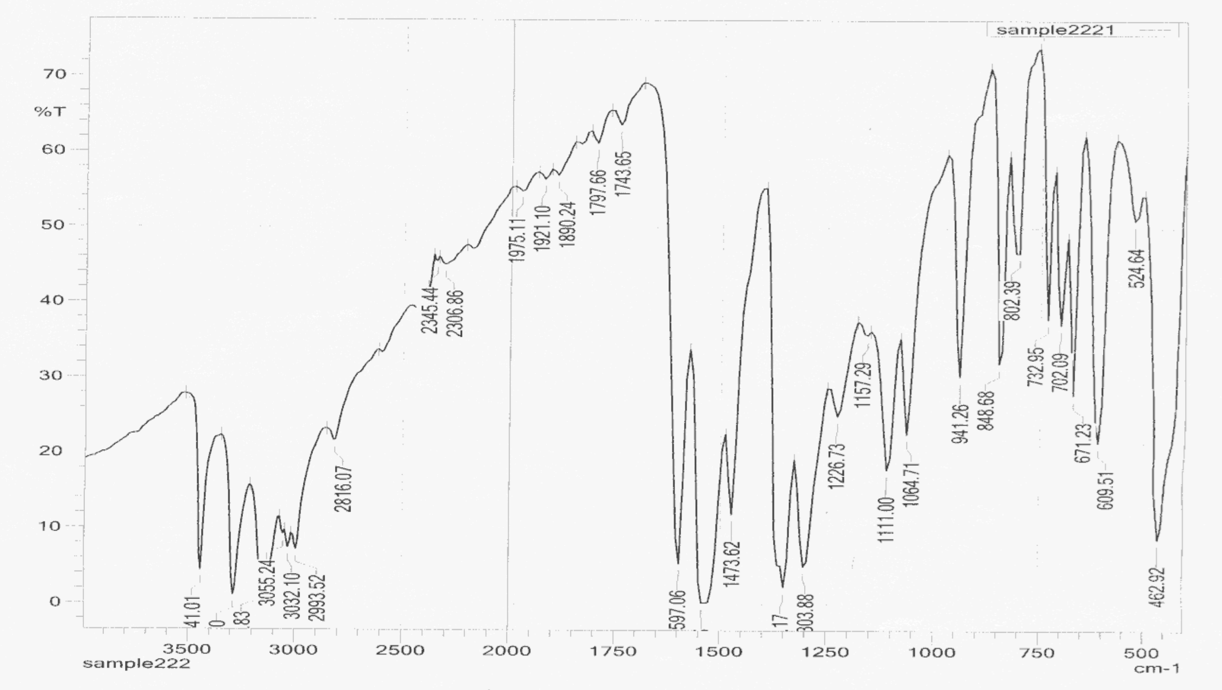


Figure3. IR-Spectra of the Ni(II) complex

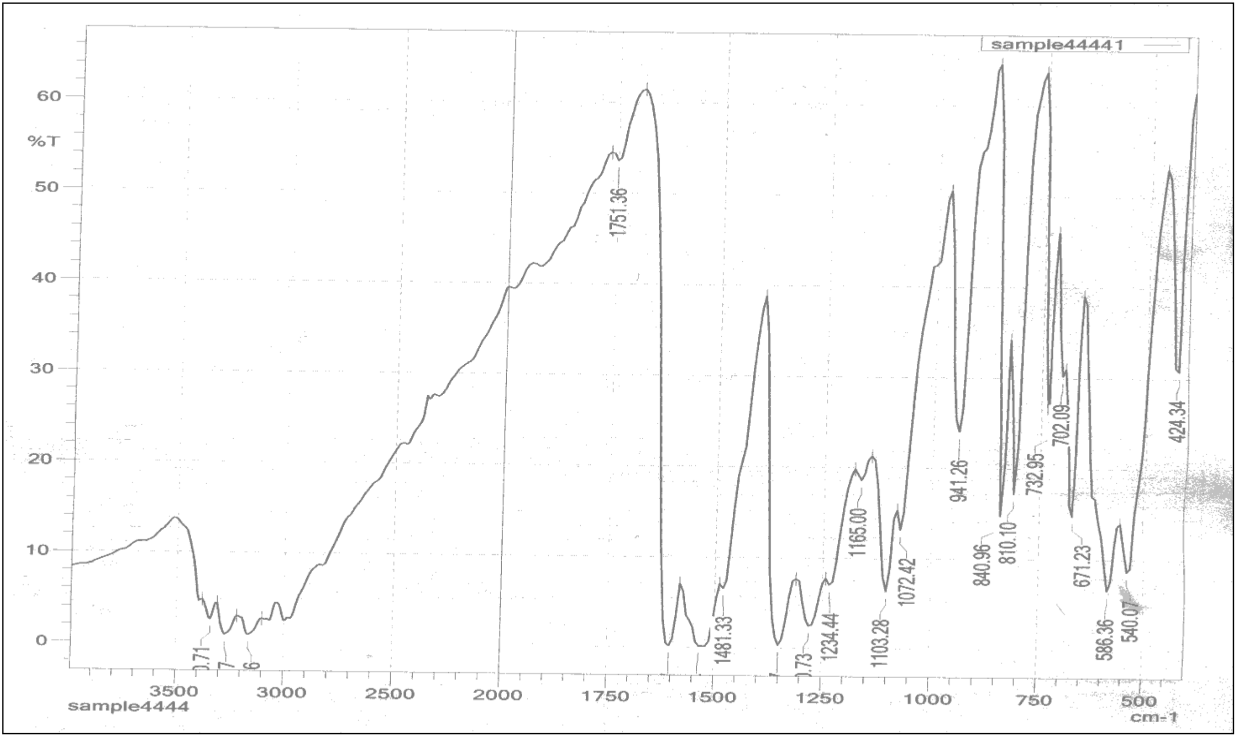


Figure4. IR-Spectra of the Cu(II) complex

Citation: Mosab Nouraldein Mohammed Hamad. “Synthesis, Characterization and Antimicrobial Study of 3-nitrobenzaldehyde Thiosemicarbazone and it's Metal Complexes” MAR Microbiology 1.4 (2020)

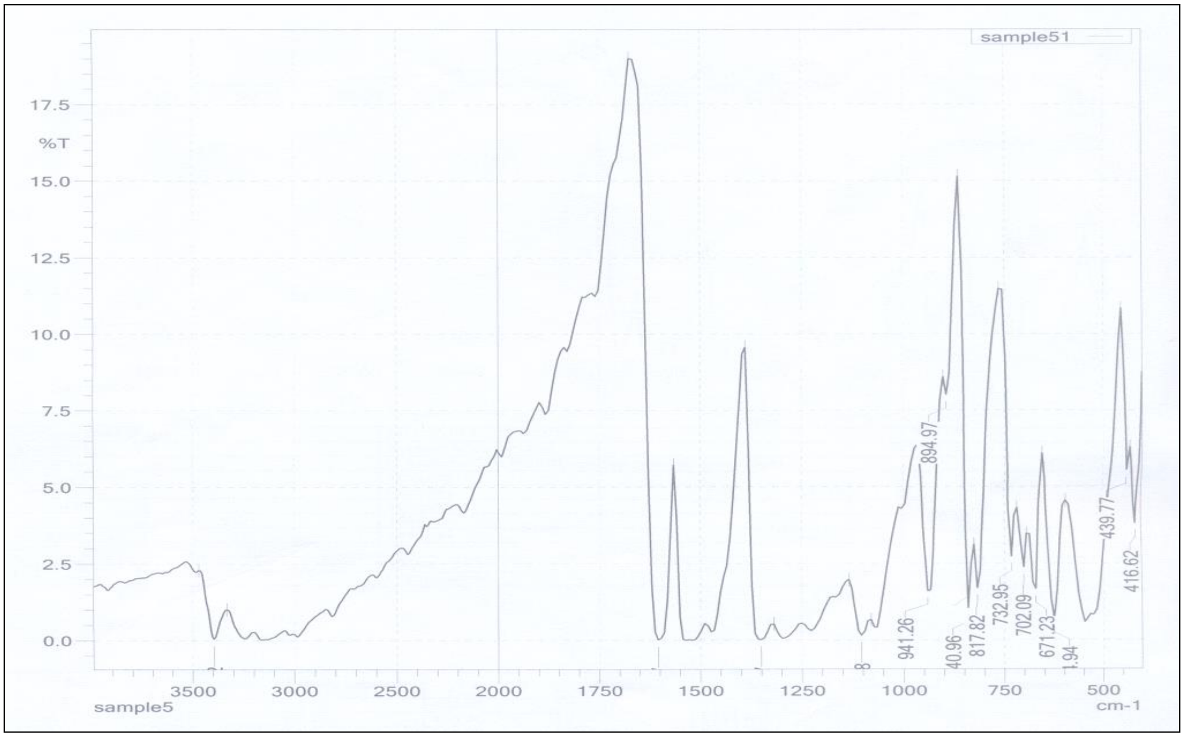


Figure5. IR-Spectra of the Co(II) complex

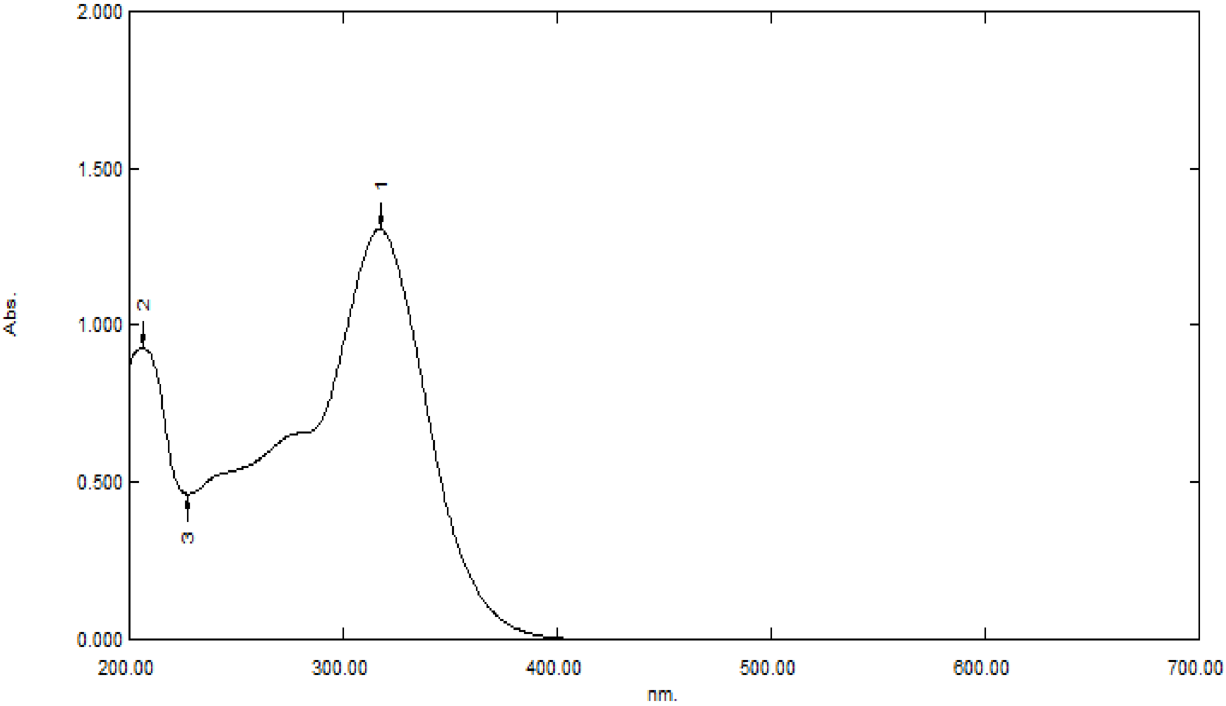


Figure6. UV-Spectra of the ligand

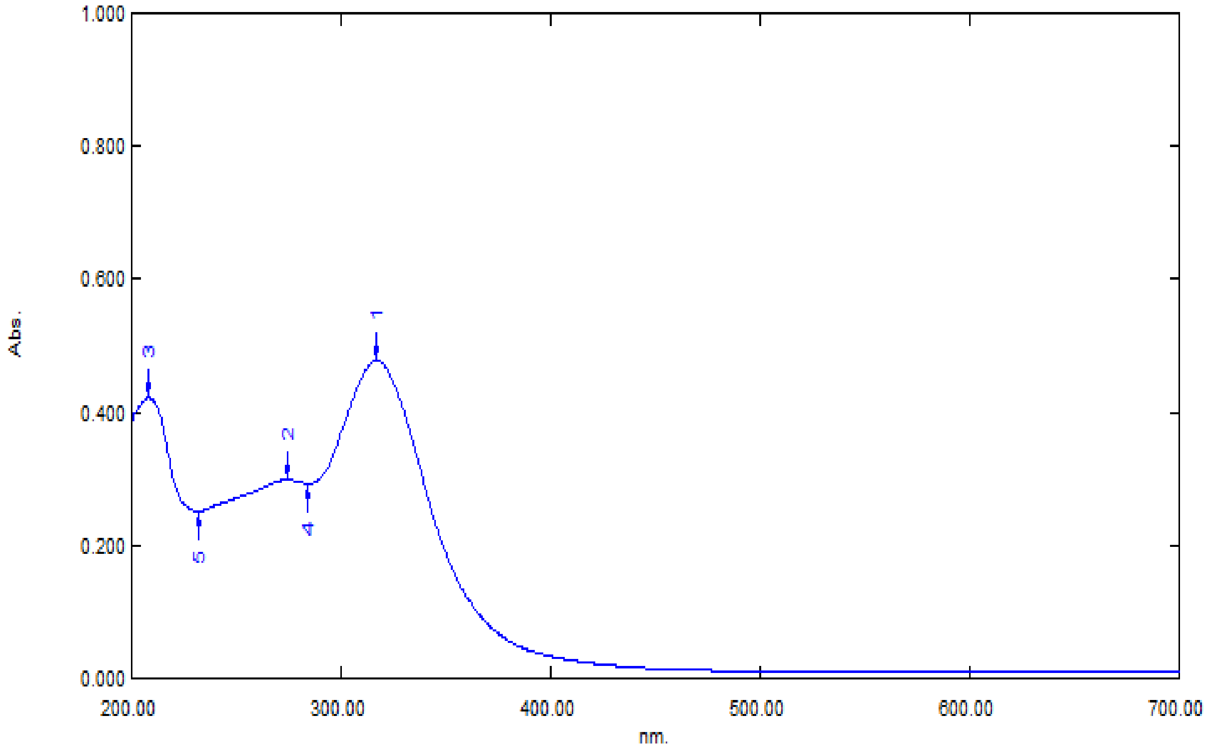


Figure7. UV-Spectra of the Ni(II) complex

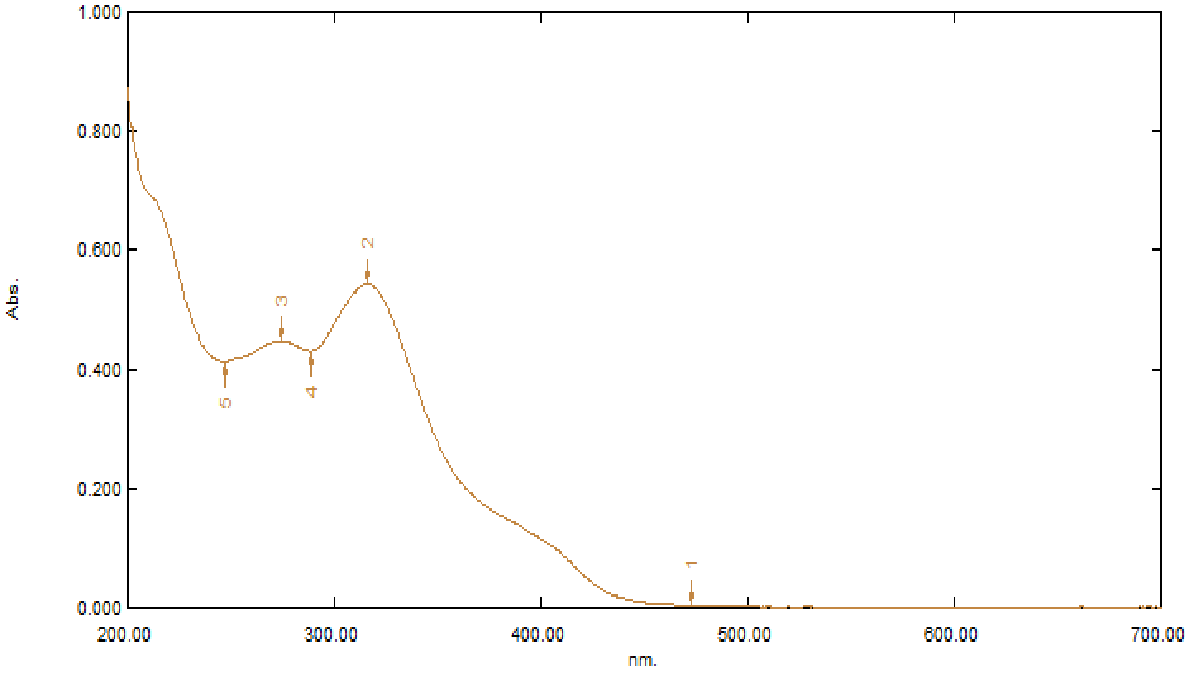


Figure8. UV-Spectra of the Cu(II) complex

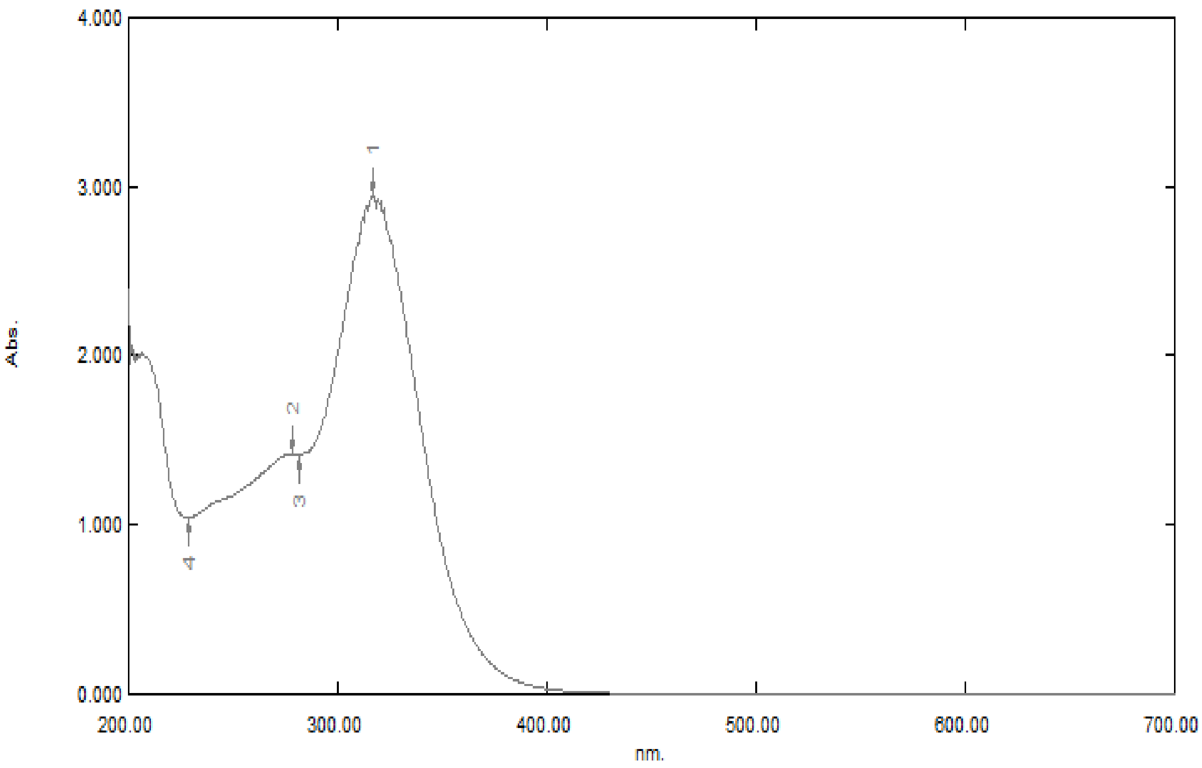


Figure9. UV-Spectra of the Co(II) complex

Conclusion:

In this study, we have synthesized biologically active thiosemicarbazone ligand and its Cu (II) and Ni (II) and Co(II) complexes. The synthesized ligands and their derivatives were characterized and identified on the basis of physical and spectral data. Antibacterial activities were found that metal complexes are more active than the ligand that is indicated the coordination increases their bioactivity.

ACKNOWLEDGEMENT

This work was impossible to be done without the help of Allah, who gave me power and strength. so I thank Allah a lot. I take this opportunity to express my profound gratitude and deep regard to the staff of the General Directorate of Forensic Evidence and the staff of the University of Medical Sciences and Technology, Great thanks extended to the staff of Sudanese Standards and Metrology Organization El-Obeid Branch and the University of Medical Sciences & Technology.

Also my thankfulness to the staff of the Department of Chemistry, Faculty of Sciences, Kordofan University for their cordial help.

CONFLICTS OF INTEREST

Authors declare that there is no conflict of interest.

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Volume 1 Issue 4 December 2020