

Synthesis and Characterization of 5-chloro 2-furaldehyde thiosemicarbazone and its Nickel, Copper and Zinc complexes

Abstract

The aim of the present study was to synthesize and characterize of divalent metal ions of Nickel, Copper and Zinc complexes of 5-chloro 2-furaldehyde thiosemicarbazone. Firstly ligand was prepared from the reaction between 5-Chloro-2-furaldehyde and thiosemicarbazide, the second step involved the synthesis of Ni(II), Cu(II) and Zn(II) complexes of 5-chloro 2-furaldehyde thiosemicarbazone. The prepared compounds (ligand or complex) was characterized using different analytical techniques such as elemental analysis, and IR, UV, Mass and ^1H NMR tests, the results obtained showed that the ligand and its Ni(II), Cu(II), Zn(II) and Co(II) complexes of 5-chloro 2-furaldehyde thiosemicarbazone were prepared successfully.

Keywords: Synthesis and characterization, thiosemicarbazone, Ni complex, Cu and zinc complex, 5-chloro 2-furaldehyde

1. Introduction

Most drugs consist of different chemical structures, but most of them contain large or small heterocyclic rings [1]. Heterocyclic thiosemicarbazone, their derivatives besides their complexes with transition metal has been one of the most class of compounds received extensive studies during the recent years, owing to the variety of whys, such as present of several donor sites, variable bonding properties, structural and medicinal aspects [2]. They show different biological activities, such as anticancer and anti-inflammatory activities [3-5]. The aromatic thiosemicarbazones is less active, than heterocyclic thiosemicarbazones [6]. By their ability to form chelates with specific metal ions thiosemicarbazone increases their antitumor activity [7]. "The anticancer activities of thiosemicarbazones were related to the presence of ketone or aldehyde group, metal chelation ability and terminal amino substitution. Among them, the parent aldehyde or ketone group was considered critical for the anticancer activity of thiosemicarbazones. The activity of these compounds is dependent on the nature of the hetroaromatic ring and the position of attachment of the ring as well as on the form of the thiosemicarbazone moiety" [8]. Thiosemicarbazones with different metal ions were extensively studied [9-12]. Despite this, there is a paucity of studies of the complexes of substituted heterocyclic were found. Therefore, the aim of this study is to keep pace with previous research in this field, so the synthesis and characterization of 2-furaldehyde

thiosemicarbazone and its nickel, copper and zinc complexes are reported here in the present paper.

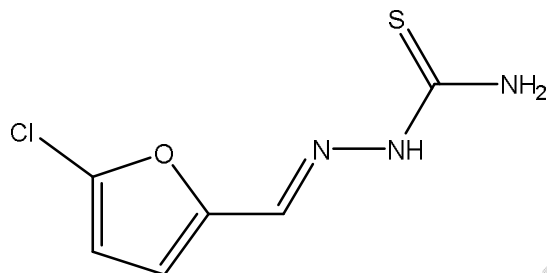


Figure (1): The 5-Chloro-2-furaldehyde thiosemicarbazone((E)-2-(5-chlorofuran-2-yl)methylene)hydrazine-1-carbothioamide) structure

2. Material and Methods

2.1. Materials

All the reagents used in this research were chemically pure. The solvents were used as received.

$\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$, NiCl_2 , ZnCl_2 , Thiosemicarbazide 98% was purchased from Sigma-Aldrich. 5-Chloro-2-furaldehyde purchased from (Merck) and was used as received.

2.2 Preparation of 5-Chloro-2-furaldehyde thiosemicarbazone (HL^2)

Thiosemicarbazide solution of (0.182 g, 0.002 mmol) in 40 mL of dry methanol was prepared with stirring and warming (about 40°C) during 1 h. 5-Chloro-2-furaldehyde (0.26 g, 0.002 mmol) in 10 mL of dry methanol was added To the warm thiosemicarbazide solution, followed by a 12 h reflux. The mixture was then cooled slowly to room temperature until the precipitate crystals were obtained.

2.3. Methods for the preparation of metal complexes (1–4)

The methods 1–4 below showed the preparation methods of the different complexes, it involved the direct reaction between the ligand and the corresponding metal salts.

2.3.1 Synthesis of $[\text{Ni}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})_2]$

Nickel chloride hexahydrated, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.0005 mmol, 0.119 g), was dissolved in 30ml distilled water. An ethanolic solution of 5-Chloro-2-furaldehyde thiosemicarbazone (0.204g, 0.001 mmol) in 10ml was added slowly to the nickel chloride solution while stirring. The mixture then was refluxed for 3 h. A pale brown precipitate was appeared, after cooling at room temperature. The precipitate was filtered, washed with small amounts of absolute ethanol and finally dried in vacuum over silica gel.

2.3.2 Synthesis of [Zn (C₆ H₆ ClN₃ SO)₂]

Zinc chloride, ZnCl₂ (0.136g, 0.001 mol) was dissolved in 20 ml warm absolute ethanol with stirring. To a solution containing 0.429g, 0.002 mol of 5-Chloro-2-furaldehyde thiosemicarbazone dissolved in 20 ml of absolute ethanol, NaOH (1M) solution was added drop wise. The mixture was refluxed for two hours. The separated dark black to brown powder was filtered washed with ethanol and dried in air.

2.3.3 Synthesis of [Cu (C₆ H₆ ClN₃ SO)₂]

A quantity of 5-Chloro-2-furaldehyde thiosemicarbazone (0.408g, 0.002 mol) was dissolved in 10 mL ethanol and was added to a solution of (0.134 g 0.001 mol) of CuCl₂.2H₂O in 10 mL ethanol. The complex appeared instantaneously and in spite of that, the reflux was carried for one hour. After recrystallization in ethanol a dark green micro crystalline product was obtained.

2.3.4 Synthesis of [Cu (C₆ H₆ ClN₃ SO)]

A quantity of 5-Chloro-2-furaldehyde thiosemicarbazone (0.204g, 0.001 mol) was dissolved in 10 mL ethanol and was added to a solution of (0.134 g 0.001 mol) of CuCl₂.2H₂O in 10 mL ethanol. Although the complex appeared instantaneously the reflux was maintained for one hour. After recrystallization in ethanol a dark green microcrystalline product was obtained.

2.4 Physical measurements

- **Elemental analysis** for (C, H, N and S) was performed using a Heraeus Carlo Erba 1108 elemental analyzer.

- **Melting points** were determined with a digital melting point apparatus using the capillary technique.

- **Mass spectra** were recorded with a Micromass LCT electrospray (Qtof Micro YA263) mass spectrometer.

- **NMR spectra** were recorded in DMSO-d₆ solution on a Bruker Advance DPX 300 NMR spectrometer.

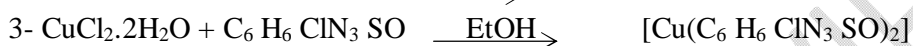
- **IR spectra** were obtained on a Perkin Elmer Spectrum Two IR spectrometer with samples prepared as KBr pellets.

3. Results and discussion

3.1. Synthesis and Physical Properties of the Complexes

Firstly, the ligands 5-Chloro-2-furaldehyde thiosemicarbazone (HL²) or (C₆ H₆ ClN₃ SO) was prepared from the reaction between 5-Chloro-2-furaldehyde and thiosemicarbazide in alcoholic medium, brown ppt was obtained, the melting point of (HL²) = 152⁰C. The elemental analytical calculation for the ligand was found C, 34.98, H, 3.46; N, 23.22 ; S, 17.6%, it's quite agreed with literature.

After that the complexes preparative reactions can be represented by the following equations:



Note that all these reaction needed areflux for certain time as mentioned in the above procedures(2.3.1-2.3.4).

All the complexes are microcrystalline or amorphous powders, stable at room temperature, and slightly soluble in common organic solvents but completely soluble in DMF and DMSO. The results of elemental analysis of the ligand 5-Chloro-2-furaldehyde thiosemicarbazone (HL²) alone and its Ni, Cu and Zn complexes were shown in table (1) below. All the analytical data are in good agreement with the empirical formula as given in Table (1).

Table (1) Elemental analysis results of the ligand 5-Chloro-2-furaldehyde thiosemicarbazone (HL²) alone and its Ni, Cu and Zn complexes

Compound	Elemental analysis found (Cal)			
	C (%)	H (%)	N (%)	S (%)
5ClFTSC	34.98(35.38)	3.46(2.94)	20.22(20.63)	15.6(15.72)
[Ni (C ₆ H ₆ ClN ₃ SO) ₂]	31.35(30.92)	2.82(2.57)	18.61(18.06)	13.54(13.76)
[Cu (C ₆ H ₆ ClN ₃ SO)]	24.11 (23.08)	1.88 (1.77)	12.25 (12.42)	9.79 (9.46)
[Cu(C ₆ H ₆ ClN ₃ SO) ₂]	27.43(26.6)	2.70(2.59)	17.13(16.80)	12.30(12.8)
[Zn(C ₆ H ₆ ClN ₃ SO) ₂]	27.24(26.5)	3.38(3.55)	16.26(16.62)	8.66(8.16)

3.2 Spectroscopic study Results of the ligand and its metal complexes:

“As might be expected for thiosemicarbazones, since it contains a thioamide -NH-C=S functional group it can exhibit thione-thiol tautomerism” [13, 14]. There is no IR band at $2500\text{--}2600\text{ cm}^{-1}$ in the spectrum of (5ClFTSC), this can be explained by the absence of S–H grouping in the free ligand. The bands in the regions of 855 and 3150 cm^{-1} , is characteristic for absorption of C=S and N–H groups, respectively, indicating that the ligand remains as a thione tautomer. This is supported by the ^1H NMR spectrum which does not show any peak at 4 ppm attributable to the S–H proton, but it shows a singular peak at 11.45 ppm relative to the NH next to C=S in ^1H NMR spectrum of (5ClFTSC), while the signal of the proton on C=N double bond appears at 7.50 ppm (see fig (2)). It is interesting to note the presence of two broad singlets for the two NH₂ protons, respectively at 7.84 and 8.22 ppm: it means that the free rotation around the C=N bond is blocked because of its partial double bond character. The bands appearing around 1345 and 785 cm^{-1} in the spectrum of the ligand are either weakened or shifted to higher wave numbers in all the complexes [14,15] and this shift can be assigned to $\nu(\text{C=S})$ vibration. On the other hand, the bands in the region $3440\text{--}3270\text{ cm}^{-1}$ attributed to symmetrical and asymmetrical stretching modes $\nu(\text{NH}_2)$ in the spectra of the ligand, undergo appreciable changes in the spectra of the complexes. This is due to the coordination of sulfur from the C=S (NH) group as reported earlier [16]. This coordination is confirmed by the presence of a new band at $405\text{--}449\text{ cm}^{-1}$ [17], which is assigned to $\nu(\text{M-S})$ for all the complexes. In ligand spectra, the strong band observed at 1600 cm^{-1} corresponds to $\nu(\text{C=N})$ vibration band [16]. This band shifts to a higher region [14,16], in the spectra of Ni–nickel complexes and this indicates the coordination of nitrogen of the azomethine group in coordination [17]. In the spectra of complexes for the ligand 5-Chloro-2-furaldehyde thiosemicarbazone the absorption band at 1465 cm^{-1} is assigned to $\nu(\text{NH}_2)$ symmetric stretching vibration, the band at 1587 cm^{-1} is assigned to $\nu(\text{C=N})$ symmetric stretching vibration, the band at 838 cm^{-1} is assigned to $\nu(\text{C=S})$ symmetric stretching vibration, and the band at 3145 cm^{-1} is assigned to $\nu(\text{NH})$ symmetric stretching vibration.

The Infra-red spectral data of the free ligand 5-Chloro-2-furaldehyde thiosemicarbazone (HL^2), shows strong absorption band at 1587 cm^{-1} due to the azomethine $\nu(\text{C=N})$ group. This band is shifted to a higher frequency in the complex $[\text{Ni}(\text{C}_6\text{H}_6\text{N}_3\text{SO})_2]$ assigned at 1625 cm^{-1} . This indicates coordination of the azomethine nitrogen with the metal ion. The $\nu(\text{C=S})$ band that appeared at 838 cm^{-1} in the free ligand is shifted to 835 cm^{-1} indicating coordination of the ligand with Ni(II) ion through the sulphur atom. In the complex of copper(II) with the ligand HL₂, $[\text{Cu}(\text{C}_6\text{H}_6\text{N}_3\text{SO})_2\text{Cl}_2]$, the band at 1587 cm^{-1} assigned to $\nu(\text{C=N})$ is shifted to

1612 cm^{-1} , indicating coordination of the ligand through the azomethine nitrogen. The band assigned to $\nu(\text{C}=\text{S})$ is shifted from 838 cm^{-1} to 933 cm^{-1} indicating the involvement of sulphur atom in complexation.

The spectral results obtained in the present paper and discussion was agreed well with many studies [18,19] carried out in the synthesis and characterization of heteroaromatic ring thiosemicarbazone metal complexes.

The IR spectral data for the complex $[\text{Cu}(\text{C}_6\text{H}_6\text{N}_3\text{SO})\text{Cl}_2]$ and $[\text{Zn}(\text{C}_6\text{H}_6\text{N}_3\text{SO})_2\text{Cl}_2]$ and all the other prepared complexes were showed in table 2

Table (2) Main IR spectral vibrations(cm^{-1})

Compound	$\nu(\text{NH}_2)$	$\nu(\text{C}=\text{S})$	$\nu(\text{C}=\text{N})$	$\nu(\text{N}-\text{N})$	Ring breath	$\nu(\text{C}-\text{O}-\text{C})$	$\nu(\text{M}-\text{N})$	$\nu(\text{M}-\text{S})$
5ClFTSC	3145	725	1587	925	1020	1271	499	443
$[\text{Ni}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})_2]$	3352	784	1673	927	1022	1271	491	435
$[\text{Cu}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})]$	3379	779	1612	935	1014	1282	503	433
$[\text{Zn}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})]$	3473	786	1610	937	1016	1201	432	405
$[\text{Cu}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})_2]$		783	1539	933	1014	1276	501	449

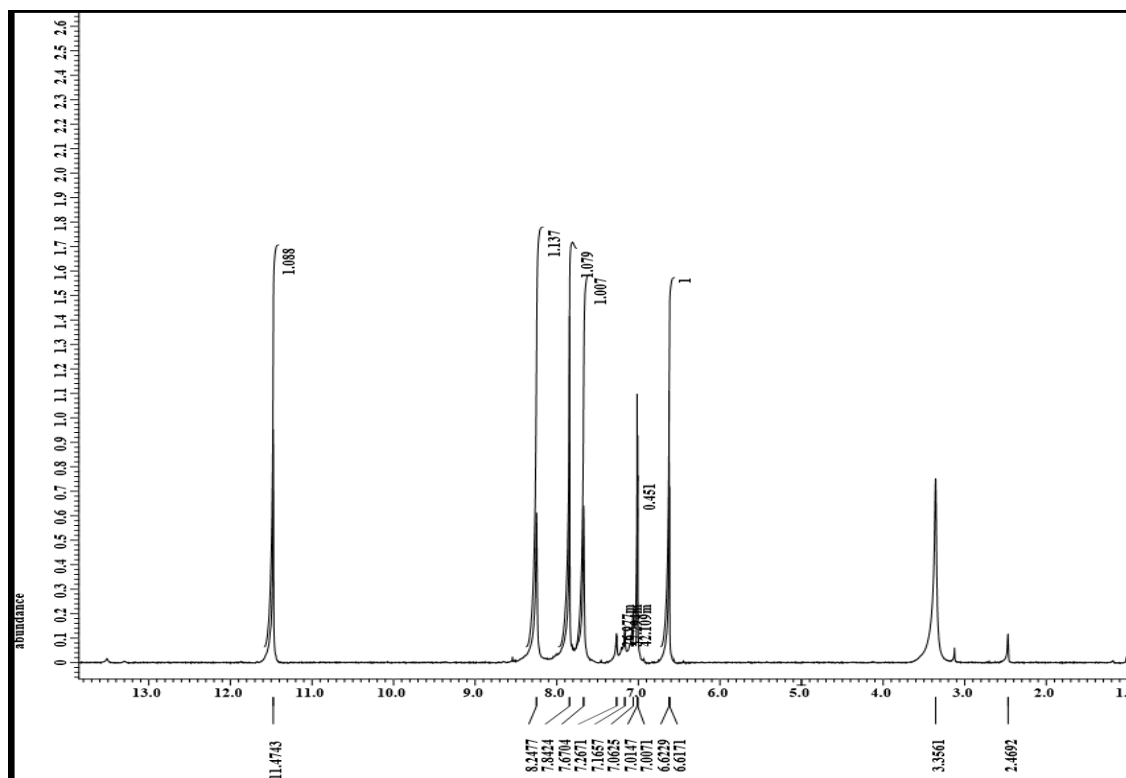
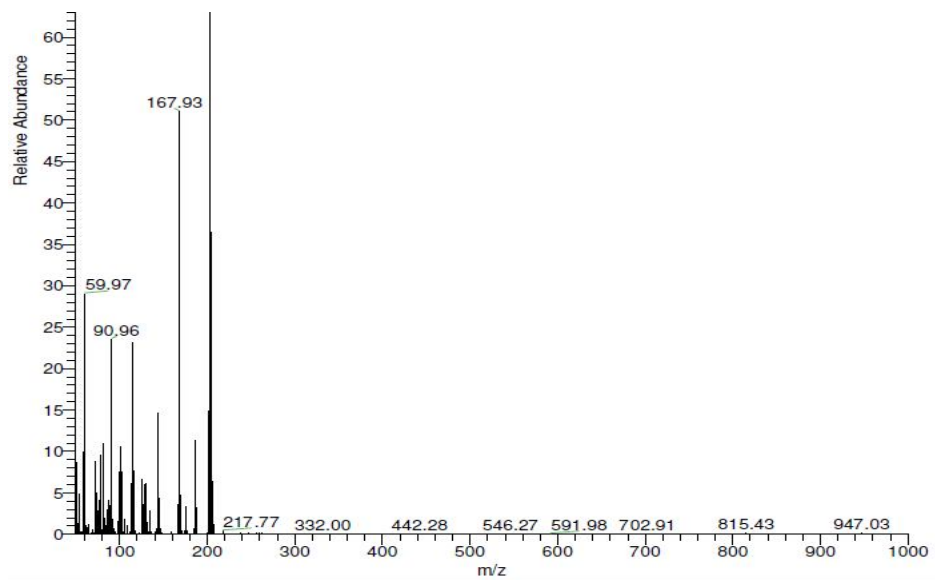


Figure (2) the proton nuclear magnetic resonance spectrum of (5CIFTSC)

Figures (3) to (7) showed mass spectrum of the ligand and its metal (Ni,Zn and Cu) complexes, all the expected fragmentations and the molecular ion peak and m/z peaks appeared successfully, from figure(3) the M.wt of the ligand appeared approximately at m/z =203.5 which is in good agreement with calculated expected value and it's also the base peak. Note that in all these mass spectrums the base peak with the highest relative abundance appear around 203 m/z or less greater than this value



Figure(3) Mass spectrum of 5CIFTSC

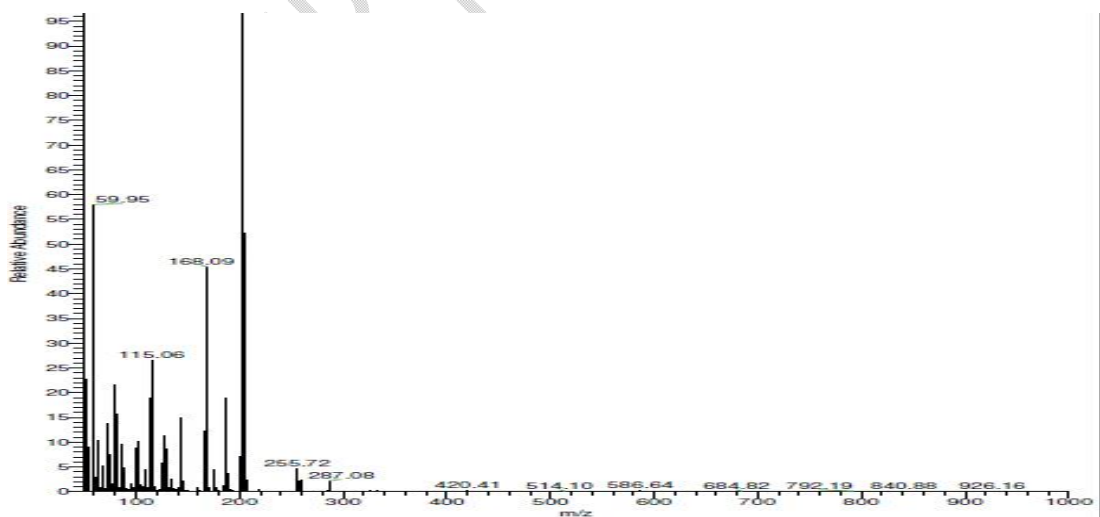
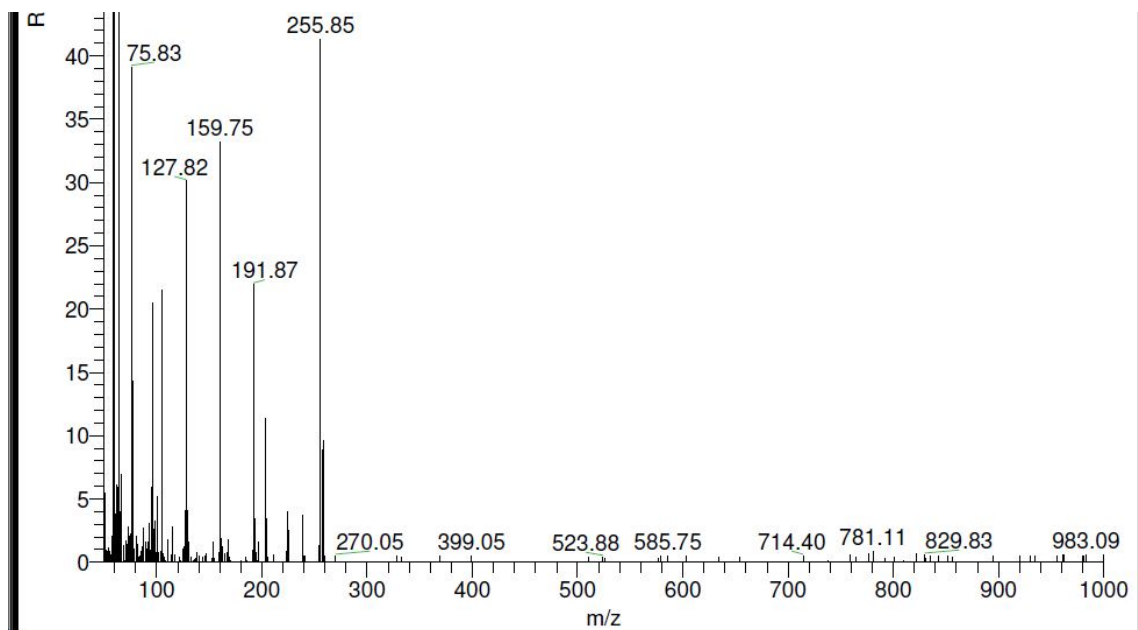


Figure (4) Mass spectrum of $\text{Ni}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})_2$



Figure(5) Mass spectrum of $\text{Zn}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})_2$

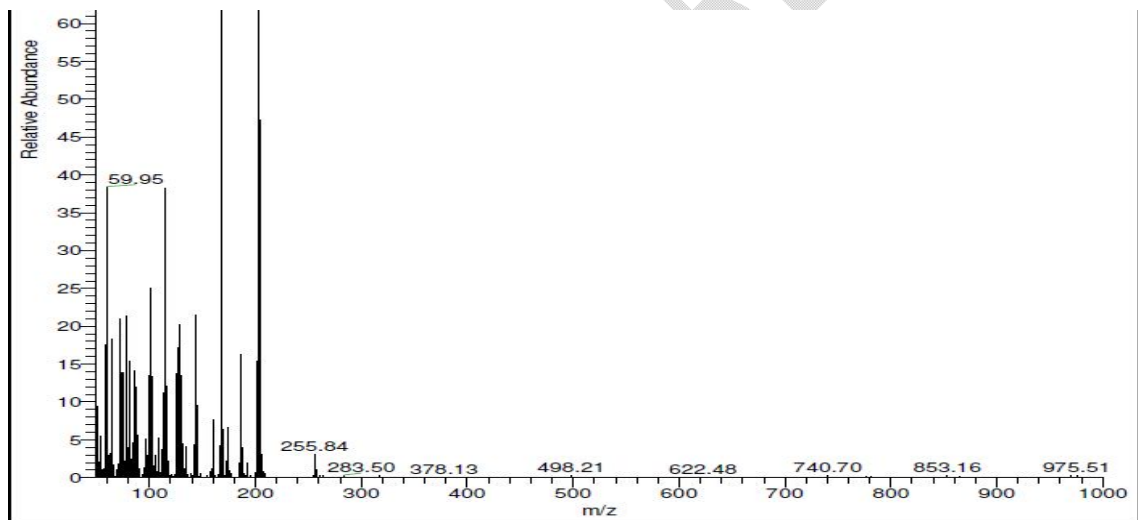
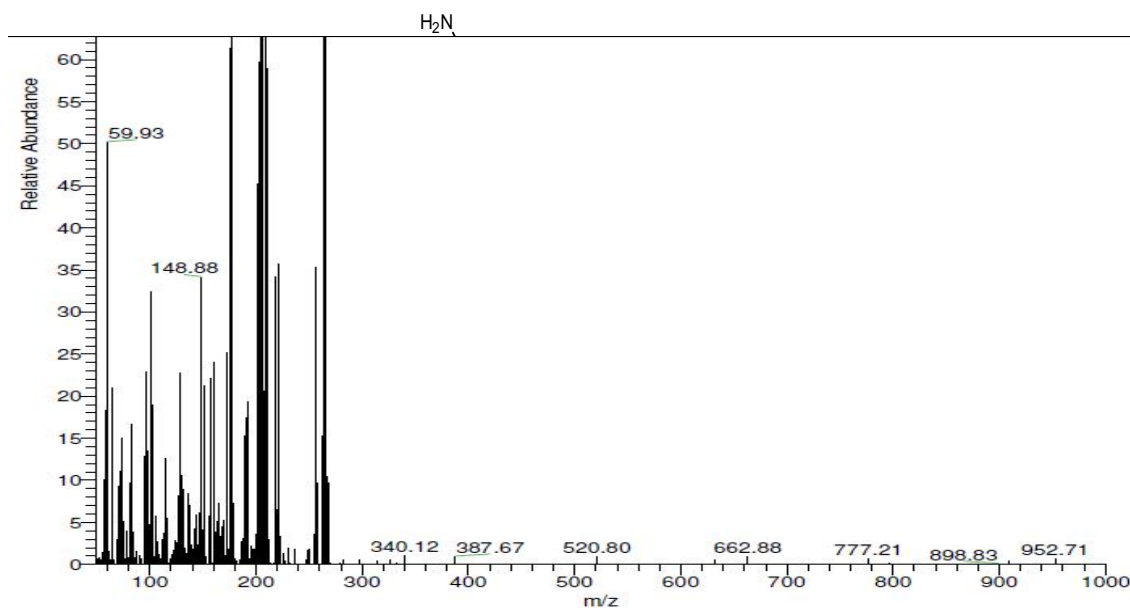


Figure (6) Mass spectrum of $\text{Cu}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})_2$



From the spectral results the proposed structure for the different metals 5-Chloro-2-furaldehyde thiosemicarbazone complexes were suggested as follow:

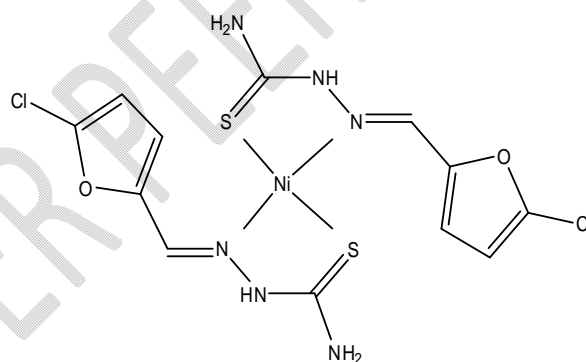


Figure (8) Structure of $[\text{Ni}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})_2]$

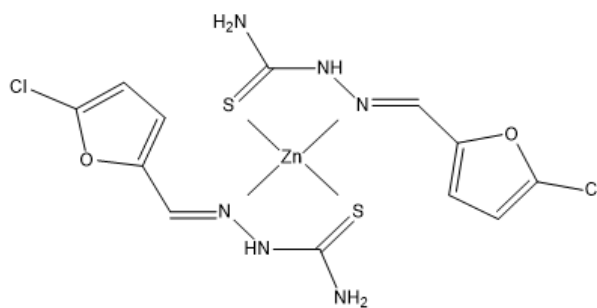


Figure (9) Structure of $[\text{Zn}(\text{C}_6\text{H}_6\text{ClN}_3\text{SO})_2]$

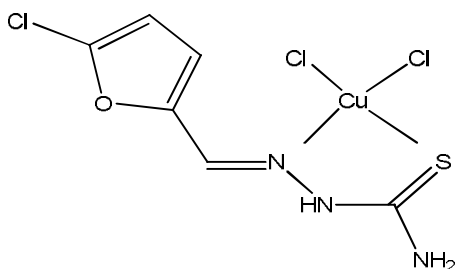


Figure (10) Structure of $[\text{Cu}(\text{C}_6\text{H}_6\text{Cl}_3\text{N}_3\text{SO})]$

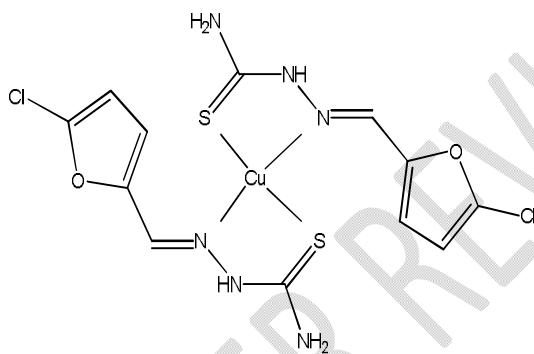


Figure (11) Structure of $[\text{Cu}(\text{C}_6\text{H}_6\text{Cl}_2\text{N}_3\text{SO})_2]$

5. Conclusions

In the present work Synthesis and Characterization of 5-chloro 2-furaldehyde thiosemicarbazone and its Nickel, Copper and Zinc complexes were carried out; the obtained spectral data confirmed the prepared ligand and its different metal complexes. The ligand acts as bidentate ligand.

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