



Synthesis, Characterization and Biological Investigation of Some New Metal Complexes of Cu^{2+} , Mn^{2+} , Co^{2+} , Zn^{2+} and Ni^{2+} ions with the Ligand of 2-[(8-hydroxy-1-quinolin-5-yl)-methyl]-1H-1,2-benzothiazole-3-(2H)-one-1,1-dioxide

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ABSTRACT

The synthesis, characterization and biological activity of new complexes of Cu^{2+} , Mn^{2+} , Co^{2+} , Zn^{2+} and Ni^{2+} ions with derivatives ligand from N-hydroxy methyl saccharin and 8-hydroxy quinoline were described and studied.

The new prepared complexes (ligands) were characterized by elemental analysis, molar conductance, IR, ^1H -NMR and ^{13}C -NMR spectroscopy studies. Coordination of the ligand atom to the metal ions was deduced by IR. All the complexes have been screened for antibacterial and antifungal.

Keywords: Saccharin, saccharin complex, hydroxyl methyl saccharin, 8-hydroxy quinoline and 1,2- benzothiazole.

تحضير، تشخيص ودراسة بايولوجية لبعض معقدات جديدة من ايونات Cu^{2+} ،
 Ni^{2+} و Zn^{2+} ، Co^{2+} ، Mn^{2+} مع الليكاند 2-[8-هاييدروكسي-1- كوينولين-5-
(يل) - مثليل] H1- 1، 2 - بنزو ثايازول-3- (H2) - أون - 1، 1- داي أوكسايد

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المخلص

حضرت معقدات جديدة من أيونات Cu^{2+} ، Mn^{2+} ، Co^{2+} ، Zn^{2+} و Ni^{2+} ذات الفعالية البايولوجية المهمة باستعمال
ليكاند مشتق من تفاعل N- هاييدروكسي مثليل سكارين مع 8- هاييدروكسي كوينولين. المعقدات المحضرة (ليكاندات) قد
شخصت بواسطة التحليل الدقيق للعناصر، التوصيلية المولارية، طيف الاشعة تحت الحمراء، طيف الرنين النووي
المغناطيسي. شخصت ذرة الليكاند المتناسق في المعقد مع ايون الفلز من قيم طيف الاشعة تحت الحمراء. جميع المعقدات
اعطت تاثيرا ملحوظا كمضاد للبكتريا و مضاد للفطر.

الكلمات الدالة: سكارين، معقدات السكارين، هاييدروكسي مثليل سكارين، 8- هاييدروكسي كوينولين، 1، 2- بنزو ثايازول.

1. INTRODUCTION

Saccharin (Hsac.) (o-sulfobenzimide; 1,2- benzothiazole- 3(2H)-one-1,1-dioxide; Hsac:
Figure (1) is one of the best known and most widely important heterocyclic compounds used
artificial sweetening agents, the amino hydrogen is acidic and, thus, the molecule can be easily
converted into the corresponding derivatives, it has been shown that the coordination chemistry
of this amine is very interesting and versatile, taking into account that it offers deferent
coordination sites to metallic centers, i.e., one N, one O (carboxylic) and two O (sulfonic) atoms,

using these donor atoms the anion can generate either N- or O-monodentate or bidentate (N,O) coordination, and also complex polymeric species with the participation of all possible donor atoms[1].

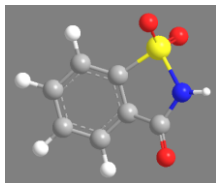
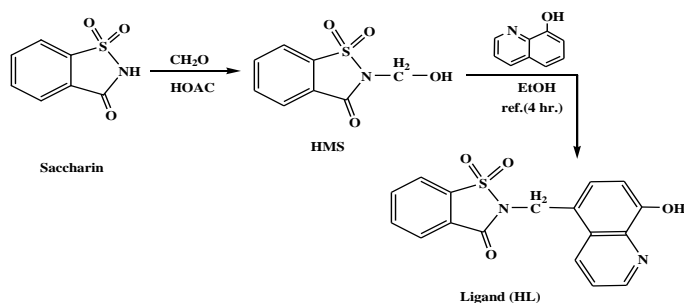


Figure (1): Schematic structure of saccharin (Hsac.)

During the last 20 years different research groups have performed systematic studies on these types of systems, obtaining a great number of new and often fascinating saccharinato-metal complexes. Saccharin itself has been frequently used as a key structural elements of industrially developed biologically active compounds[2], and has long been established as a cheap and versatile starting material for the synthesis of related heterocyclic derivatives. By their side substituted 1, 2-benzisothiazole-1,1-dioxide (pseudosaccharin) have also been shown to be important intermediates in organic synthesis[3]. Survey of literature reveals that, the importance of N-aryl hydroxy methyl saccharin derivatives as biologically, pharmacologically, hypoglycemic active and industrially important molecules[4].

Receiving impetus from the above observation and in continuation of our research programmed on complexes of the prepared ligand. In this paper, we report the synthesis of 2-[(8-hydroxy-1-quinolin-5-yl)-methyl]-1H-1,2-benzothiazole-3-(2H)-one-1,1-dioxide and its complexes with Cu^{2+} , Mn^{2+} , Co^{2+} , Zn^{2+} and Ni^{2+} and also biological activities of these complexes, hydroxyl methyl saccharin (HMS) is a potential donor ligand with four coordination sites[4], scheme (1).



Scheme (1)

2. EXPERIMENTAL

Saccharin used for synthesis of novel saccharin derivatives were obtained from local market. The metal salts and other chemicals used were laboratory grade; solvents were dried and distilled before used. The following metal salts were used to prepare complexes, copper acetate $[\text{Cu}(\text{OCOCH}_3)_2]$, manganese acetate $[\text{Mn}(\text{OCOCH}_3)_2]$, cobalt acetate $[\text{Co}(\text{OCOCH}_3)_2]$, zinc acetate $[\text{Zn}(\text{OCOCH}_3)_2]$ and nickel acetate $[\text{Ni}(\text{OCOCH}_3)_2]$ for the preparation of ligand.

2.1 Synthesis of Hydroxy methyl Sacchrine (HMS).

(0.01 mole, 2.6 g) of saccharin and (0.06 mole, 2.5 ml) of formaldehyde in (15) ml of absolute ethanol are refluxed for about (2) hours; the white precipitate washed several times in cold distilled water and recrystallized in acetone, yield (95 %) ,m.p. (138 °C)[5].

2.2 Synthesis of Ligand (HL).

To a solution of (0.04 mole, 5.8 g) of 8-hydroxy quinoline in absolute ethanol and solution of (0.04 mole, 13 g) of (HMS) in (50) ml of ethanol, (5) drops of concentrated HCl was added and mixed with vigorous stirring at room temperature. The resultant mixture was refluxed for (4) hours and cooled. The precipitate was separated, dried and crystallized with acetone; yield (80 %) m.p. (215 ° C) (uncorrected).

2.3 Synthesis of Metal Ion Complexes[6, 7, 8] .

To a solution of metal acetate (0.007) mole, (1.20-1.28) gm in water (25) ml and solution of ligand (0,014 mole, 4.84 gm) in formic acid, water mixture (50:50) (v/v) (100 ml) was added gradually with vigorous stirring at room temperature. The resultant mixture was refluxed (4) hours, the solid complexes were separated by concentrated the resultant solution and adding ethanol: water mixture (70:30) ratio. The precipitates were filtered and washed several times with ethanol: water mixture (70:30) ratio. The precipitates were dried at (60 ° C). The details of the elemental analysis, molar conductance of complexes are given in [Table \(1\)](#). Ligand and its synthesized complexes were insoluble in water, slightly soluble in methanol, ether, chloroform, benzene and other organic solvents. All the samples were measured by elemental analyzer Thermo Finigan 1101 Flash EA. The physical and analytical data for the prepared ligand and its complexes are shown in [Table \(1\)](#).

2.4 Conductance Measurement [8].

The molar conductance of the complexes was measured using Philips pw-9526 digital conductivity meter using DMSO and chloroform (0.001) M at room temperature as a solvent. The conductivity data shown in Table (1).

Table (1): Physical and analytical data of the ligand (HL) and their metal complexes.

Metal Complexes	Yeild %	M. Wt g/mole	Conductivity $\Omega^{-1} \cdot M^2$	Color	(C.H.N) (cal/found)/ %				
					C	H	N	S	Metal
HL	82	346.0	-	-	58.95	3.46	9.82	9.24	-
					58.88	3.41	9.97	9.15	-
[Cu(HL) ₂ (H ₂ O) ₂]	73	777.5	8.6	Bluish green	52.47	3.34	7.20	8.23	8.17
					52.31	3.21	7.11	8.20	7.96
[Mn(HL) ₂ (H ₂ O) ₂]	68	769.0	10.5	Yellow	53.05	3.38	7.28	8.32	7.15
					52.90	3.24	7.16	8.29	7.10
[Co(HL) ₂ (H ₂ O) ₂]	78	773.0	9.8	Purple	52.78	3.36	7.24	8.27	7.63
					52.63	3.26	7.18	8.25	7.41
[Zn(HL) ₂ (H ₂ O) ₂]	80	779.3	7.6	White	52.34	3.33	7.18	8.21	8.38
					52.21	3.12	7.11	8.18	8.25
[Ni(HL) ₂ (H ₂ O) ₂]	71	772.7	10.1	Light green	52.80	3.36	7.24	8.28	7.59
					52.61	3.18	7.12	8.22	7.29

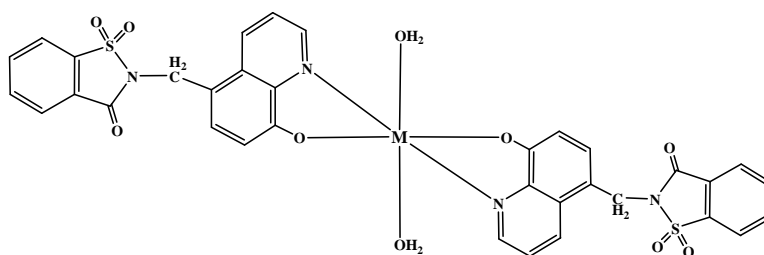
2.5 Antimicrobial Studies[9, 10, 11].

The antimicrobial activities of the synthesized metal complexes were carried out by cup-plate method. In vitro antimicrobial activity was carried out against (24) hour old cultures of four bacteria, namely *E.coli*, *Ps aeruginosa*, *Staphylococcus*, *Becillus megaterium* and (48) hour old culture of three fungi namely *Penicillium, expansum, NigrasPora sp.* and *Trichothesium sp.*

3. RESULTS AND DISCUSSION

3.1 Characterization of the Lignd and its Complexes.

The ligand (HL) and the isolated complexes of Cu(II), Mn(II), Co(II), Zn(II) and Ni(II) ions were subjected to elemental analysis (C, H, N, S and M) and presented in table (1). The complexes are colored and stable in air. They are insoluble in water and in most organic solvents but soluble in DMF. The physic-chemical and spectral data of the metal complexes are proposed to have octahedral structure **Figure (2)**.



M = Cu(II), Mn(II), Co(II), Zn(II) and Ni(II)

Figure (2): Structure of the metal complex of the new complexes

3.2 Conductivity measurement.

The conductivity measurement are widely used in coordination chemistry to determine the ionic structure of the compounds in solution [12] and in a solid, the number of the ions that complex gives in solution large, the conductivity of the solution will increase.[13]

3.3 Antimicrobial Activity.

All the prepared compounds are found to be biologically very active. It is known that chelation tends to make ligands act as more powerful and potent bacterial agents. The synthesized compounds were screened for their antimicrobial activity. The zones of inhibition measured around the discs are represented in **Table (2)** and **(3)** and comparative analysis as shown in **Figures (3)** and **(4)**.

3.3.1 Antibacterial Activity.

The antibacterial activity of the compounds was evaluated against gram positive organisms

(*Staphylococcus aureus*) and (*Becills megaterium*) and gram negative organisms (*E-coli*) and (*Ps. Aeruginosa*). The zone of inhibition was measured as the parameter of activity. Gram positive organism (*Staphylococcus aureus*) a zone of inhibition of (19 mm) for Cu. complex and for organism (*Becills megaterium*) a zone of (19 mm) for Co. complex. For the gram negative organism the higher activity is (18 mm) for (*E-coli*) organism for Cu. complex. All the data are shown in Table (2).

Table (2): Antibacterial activity of the ligand (HL) and their metal complexes

Metal Complexes	Zone of inhibition in (mm)			
	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Becillus megatrium	E - coli	Ps. aeruginosa
HL	15	13	17	16
[Cu(HL) ₂ (H ₂ O) ₂]	19	14	18	13
[Mn(HL) ₂ (H ₂ O) ₂]	15	18	11	12
[Co(HL) ₂ (H ₂ O) ₂]	17	19	13	16
[Zn(HL) ₂ (H ₂ O) ₂]	16	17	15	14
[Ni(HL) ₂ (H ₂ O) ₂]	12	18	12	15

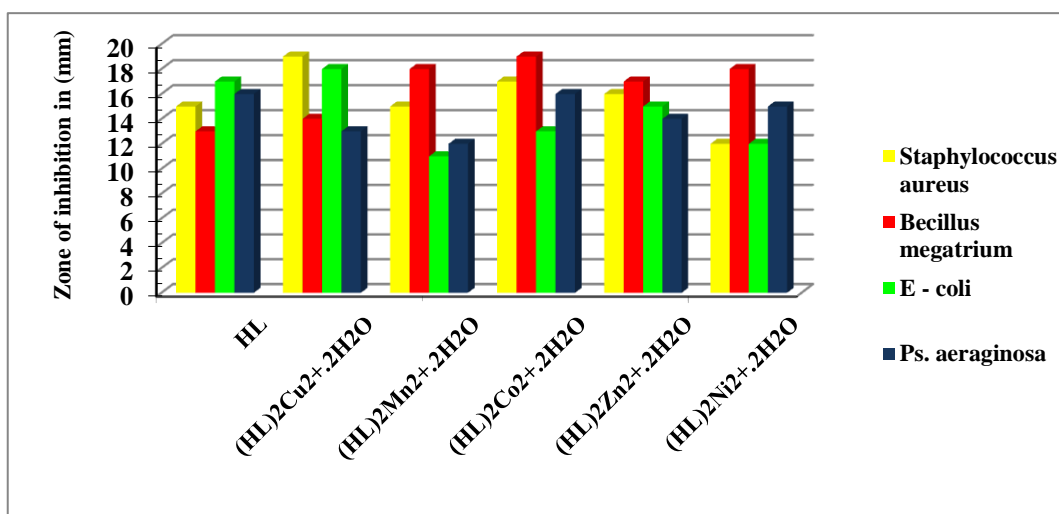


Figure (3): Comparism of antibacterial activities of HL and their metal complexes

3.3.2 Antifungal Activity.

The examination of antifungal activity of HL ligand and its complexes reveal that the ligand is moderately toxic against fungi, while all the complexes are more toxic than the ligand Table (3). Among all the complexes , Cu²⁺ complex was found to be more toxic against fungi. The antifungal activity of the metal complexes was found to be in order: Cu(II) > Zn(II) >Co(II) > Ni(II) > Mn(II). Hence such of complexes may find as agricultural and garden fungicides.

Table (3): Antifungal activity of the ligand (HL) and their metal complexes

Metal Complexes	Zone of inhibition at 1000 ppm (%)		
	Penicilium expnsum	Nigras Pora sp.	Trichothesium sp.
HL	63	66	65
[Cu(HL) ₂ (H ₂ O) ₂]	80	83	82
[Mn(HL) ₂ (H ₂ O) ₂]	68	68	67
[Co(HL) ₂ (H ₂ O) ₂]	72	75	78
[Zn(HL) ₂ (H ₂ O) ₂]	73	76	82
[Ni(HL) ₂ (H ₂ O) ₂]	69	69	76

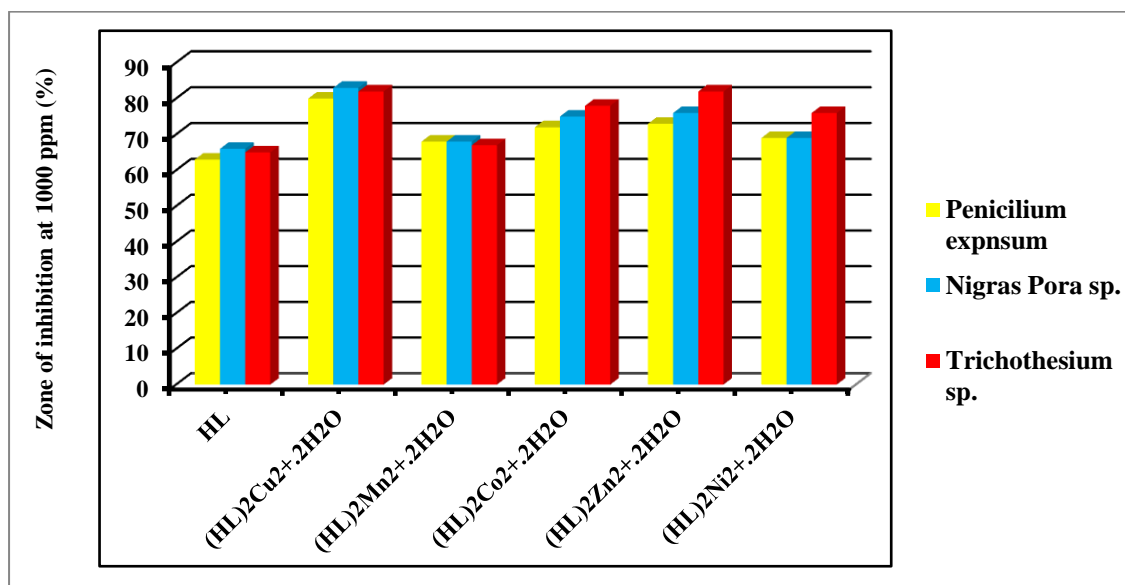


Figure (4): Comparism of antifungal activities of HL and their metal complexes

3.4 IR Spectra.

The important infrared spectral bands for the synthesized HMS, ligand and its complexes were recorded as KBr disks.

The characteristic IR absorption bands of the free ligand and its complexes are very useful to get valuable information about the coordination sites. IR spectrum of the ligand shows a broad absorption band at (3400-3350) cm^{-1} which is due to phenolic (-OH) group of 8-hydroxy quinolone moiety[14]. The vibration observed at (3050-2900) cm^{-1} are due to aromatic and aliphatic (C-H) groups. Several bands at (1300) and (1100) cm^{-1} are due to (SO_2) symmetric and asymmetric group. The spectrum of the ligand and its complexes also showed (C=O) amide at the range (1750-1730) cm^{-1} . The absorption bands in the range (445-420) cm^{-1} and (556-510) cm^{-1} are assigned to ν (M-N) and ν (M-O) bands respectively, these bands are almost identical and suggest the information of the chelate complexes [15] and [16]. All the spectral bands are shown in Table (4).

Table (4): The characteristic infrared bands for the ligand (HL) and its complexes in (cm^{-1})

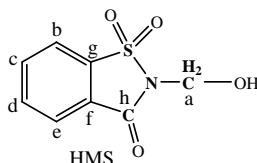
Metal Complexes	ν (O-H)	ν (C=O)	ν (C-H) ar.	ν (C-H) ali.	ν (SO_2) sym. asym.	ν (M-N)	ν (M-O)
HL	3353	1743	3065	2981	1336 1176	-	-
[Cu(HL) ₂ (H ₂ O) ₂]	3394	1740	3096	2960	1400 1170	430	520
[Mn(HL) ₂ (H ₂ O) ₂]	3400	1745	3094	2958	1390 1145	422	518
[Co(HL) ₂ (H ₂ O) ₂]	3359	1738	3074	2970	1366 1168	436	544
[Zn(HL) ₂ (H ₂ O) ₂]	3382	1735	3053	2936	1382 1175	428	530
[Ni(HL) ₂ (H ₂ O) ₂]	3351	1744	3069	2948	1369 1180	441	556

sym.: symmetric; asym.: asymmetric

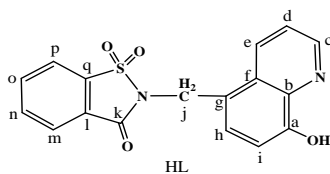
3.5 NMR Spectra.

The H^1 -NMR spectra of the compound HMS shows singlet signal at ($\delta = 2.50$ ppm) for (-OH) protons, singlet at ($\delta = 5.18$ ppm) for (CH_2) protons and multiplet at ($\delta = 6.69$ -8.50 ppm) for the aromatic ring protons. For the ligand (HL) the H^1 -NMR spectra give good evidence for the structure that there is a singlet at ($\delta = 2.50$ ppm) for one proton of (-OH), singlet for two protons of (CH_2) at ($\delta = 5.18$ ppm) and multiplet at ($\delta = 6.96$ -8.50 ppm) for four protons of aromatic ring [15] and [16]. The above spectra shown in **Figure (5)**. For almost all organic molecules complete C^{13} spectra appear between low field carbonyl carbons and high methyl carbons in the range (0–200) ppm (δ) value. TMS is the common internal reference which is used for C^{13} - NMR (CMR). One of the important advantages of using (CMR) in organic chemistry is that many of the functional groups contain carbon atom are not contains hydrogen atom to study it in H^1 -NMR and it directly observed in (CMR). Another major advantages of C^{13} over H^1 magnetic resonance spectroscopy is the increased separation of chemically shifted signals about tenfold. The ensuing improvement in resolution is a powerful aid to structural analysis [15]. The state of hybridization is the dominating factors determining the chemical shift of carbon atom SP^3 hybrid carbon atom absorb up field. While SP^2 carbon atoms absorb at lower field. In aromatic compounds, the electro donating substitution ($-NH_2$, $-Cl$) delocalize their lone electron pairs into the (π) system. Thus increasing the charge density at the orto and para carbons. Substitutions with lone pairs, thus, shield ortho and para carbons with the electro attracting groups have a deshielding influence [15]. The C^{13} -NMR spectra shown in **Table (5)** and in **Figure (6)**.

Table (5): C^{13} - NMR data of HMS and HL



Carbon atoms symbol / ppm							
a	b	c	d	e	f	g	h
63.26	121.53	135.74	135.09	126.55	125.22	136.52	161.38
65.61	121.90	135.86	135.64	128.10	125.69	136.63	
	122.03				125.84	137.67	
						139.91	



Carbon atoms symbol / ppm								
a	b	c	d	e, o, n	g, h	i	j	f, l, m, p
149.22	130.75	146.51	118.65	130.14	122.73	116.53	31.17-40.83	129.39

4.CONCLUSION

The complexes were obtained as colored powdered materials and were characterized using physical, spectral (IR, H¹-NMR and C¹³-NMR) and conductance measurements. The compounds are insoluble in water, ethanol, acetone, ether, chloroform and dichloromethane but soluble in DMF. The ligand molecules act as hexadentate ligand in all the studied metals, bonding among (N) and (O).

The structure of the complexes is octahedral for all metals. From the antimicrobial activity data, it is observed that the complexes exhibit higher activity than the free ligand. The increase in antimicrobial activity of the complexes may be due to the metal chelation.

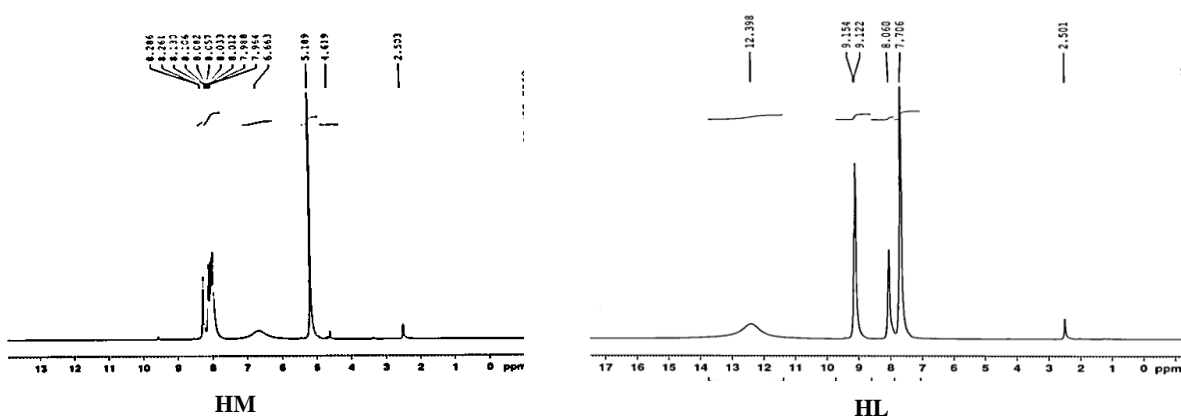


Figure (5): H^1 - NMR spectra of HMS and HL

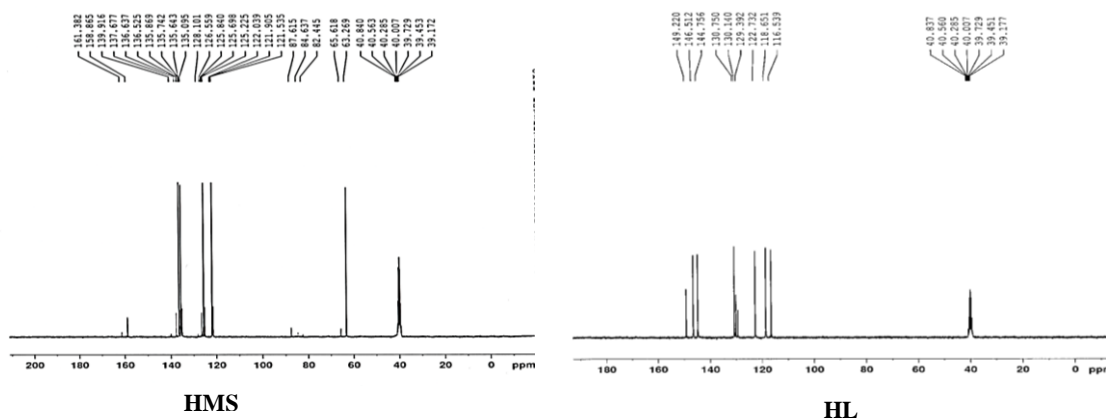


Figure (6): C^{13} - NMR spectra of HMS and HL

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