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Preparation, Characterization Of A New Polymer Of Naproxen Drug And Study Its Analytical Applications Of Elements (Pb(II), Cu(II), Ni(II), Co(II))

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ABSTRACT

New naproxen polymers prepared, by synthesis of methyl 2-(6-methoxy naphthalene-2-yl) propanoate(1) from a reaction2-(6-methoxy naphthalene-2-yl)propanoic acid with (MeOH) and 0.5ml of concentrated H2SO4, then prepared naproxen hydroxide (2), by reaction methyl 2-(6-methoxy naphthalene-2-yl) propanoate (1), with Hydrazine hydrate. then added 2-hydroxybenzaldehyde to compound (2) to given N'-(2-hydroxy benzylidene)-2-(6-methoxy naphthalene-2-yl)propane hydrazide (3), added a bisphenol to last product (3) to give new polymer resins. The resulted foams were examined as chelating resins toward some of the metal ions such as (Pb2+,Cu2+,Ni2+,Co2+) by using the batch process. as were from this compounds were confirmed by, Physical properties,1H- NMR, and FTIR.

Keywords: naproxen, bisphenol A, chelating resins,tetra hydro furan, paraformaldehyde.

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INTRODUCTION

Polymers are used widely for medical devices and implants. Early medical devices were based on high purity grades of commonly used industrial polymers. In recent years new polymers have been specially synthesized for medical uses. The term polymer is composed of two terms: 'poly' meaning many and 'mer' meaning unit(1), hence a polymer is molecule made up of many units. Polymers may also be classified as being. addition polymers and condensation polymers. Addition polymers are produced by free radical addition reactions from unsaturated monomers containing carbon-carbon double bonds. Examples of addition polymers are polyethylene and poly(methyl methacrylate). Condensation polymers are formed by reacting two monomers together in a reaction in which a small molecule is eliminated(2,3,4), which is often water.

Examples of condensation polymers are polyamides and polyesters. Some condensation polymers may be hydrolyzed in the body and undergo degradation(5,6,7). crystalline polymers differ significantly from other materials in that they cannot be obtained 100% crystalline(8). They do not exhibit a sharp melting point (Tm). past few decades have been a tremendous advancement in the area of drug delivery using polymeric particulate carrier systems for small and large molecules(9,10). Where Naproxen was used in the preparation of a new polymer in this work, Naproxen [(+)-(S)-2-(6-methoxynaphthalen-2-yl) propanoic acid] figure 1, is a potent non-steroidal anti-inflammatory drug (NSAID) that is often used for the treatment of acute and chronic inflammation conditions, musculoskeletal disorders, primary dysmenorrhoea, fever and also in the management of mild pain. However, the systemic use of Naproxen shows various adverse effects such as epigastric distress, gastric ulceration, hemorrhage and iron-deficiency anemia (11). These side effects are explained by two mechanisms, the first one is due to the direct contact and local irritation produced by the carboxylic acid group of the molecular structure of the Naproxen, so the utilization of prodrug can temporarily mask the carboxylic acid group of the Naproxen and decrease the gastric side effects. The second mechanism is referred to the inhibition of the prostaglandin synthesis (12).

MATERIAL AND METHODS

Infrared Spectrophotometer model Shimadzu 8400, Scale [400-4000 cm^{-1}],Melting Point Electro thermal 9300 melting point Apparatus, and ^{1}H- NMR spectrometer for proton (^{1} H-NMR) Bruker400MHz, has measurements using DMSO-d_6 as a solvent was to measure in Ahl– Albate University in Jordan. by a device Ultra shield 400 MHz. Bruker 2003.Chemical Materials Of the following companies: (Fluka, BDH, Aldrich, Merck) and materials used directly without recrystallization.

General method to preparation for methyl 2-(6-methoxynaphthalen-2-yl) propanoate(1)

2-(6-methoxynaphthalen-2-yl)propanoic acid (1g, 0.004 moles) was placed in (250) ml round bottom flask; 20 ml. The obtained solution was kept under reflux while mixing using a magnetic stirrer for one night. After the solution was cooled at room temperature, it was neutralized using sodium bicarbonate. The product was extracted in a separatory funnel using ethyl acetate. The organic phase was dried using anhydrous Magnesium (13).

synthesis of 2-(6-methoxynaphthalen-2-yl) propanehydrazide (2)

methyl 2-(6-methoxynaphthalen-2-yl) propanoate (1) (0.004 mole.) was mixed with (0.004 mole.) Hydrazine hydrate dissolved in (10) ml of ethanol mixed well and reflux condenser for five hours then cooled and filtered the product to give crystals, recrystallized from ethanol (14).

synthesis of N'-(2-hydroxybenzylidene)-2-(6-methoxynaphthalen-2-yl)propanehydrazide (3)

add (0.01 mole) of 2-(6-methoxynaphthalen-2-yl)propanehydrazide dissolved in (10 ml) of ethanol absolute to 2-hydroxybenzaldehyde (0.01 mole) dissolved in the same solvent and add to mixture (5) drops of glacial acetic acid. the mixture was refluxed for (eight hr). After cooling overnight, The solid thus obtained was recrystallized twice from absolute methanol(15).

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Synthesis of polymeric Chelatingresin (4)

in placed in three-necked round bottom flask equipped with a condenser, thermometer, and a magnetic stirrer, a mixture of N'-(2-hydroxybenzylidene)-2-(6-methoxynaphthalen-2-yl)propanehydrazide (0.02 mole.) in 40 mL DMF with (0.02 mole.) bisphenol and (0.02 mole.) paraformaldehyde in the round bottom flask, then add to reaction mixture (20ml) of formaldehyde and (15ml) of tetrahydrofuran, then 2–3 drops of NaOH (5%) were added to this solution with stirring magnetically for 7 h, After ending the reaction, was formed a sticky gel material (soft jelly) ,The product color was a light yellow, and equation the mix to (PH=7 - 7.5) after cooling and using cold (H3PO4 5%), evaporate the solvent then dried at (120 ° C) for two hours until the solidifying process was completed, The resulting polymer is then ground, then washed thoroughly with distilled water to dispose of the residue of the Non-interactive material and then dried Scheme(1)illustrates the proposed formula for the resin(16).Physical properties and solvents used in preparation methods are shown in Table (2).

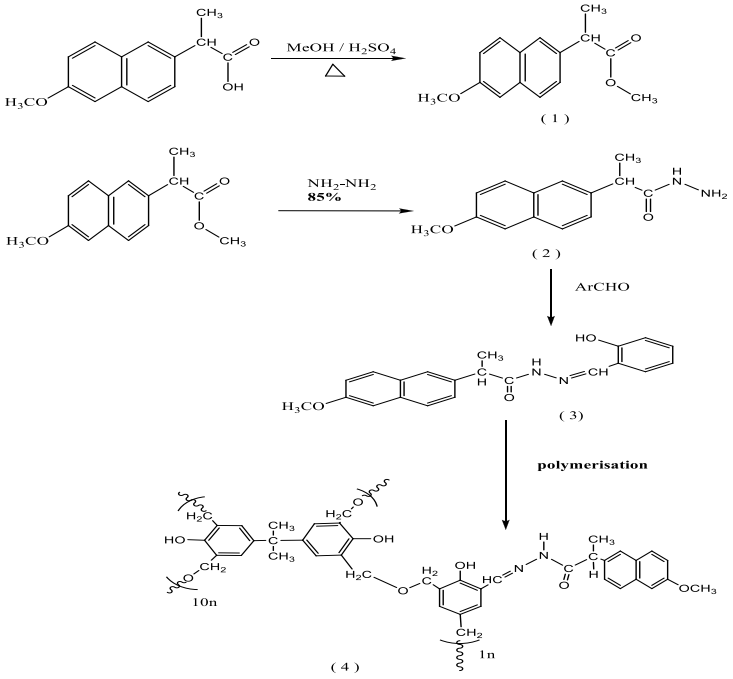
Preparation the standard solutions for element ion

standard solutions were prepared by dissolving an of nitrate in a little amount of water and (2 mL) of HNO_3 then complete the required volume by adding demineralized water up to (500 mL).(17).

Table (1): The weights of metallic salts, used for the preparation of standard solutions (1000 ppm) of the metal ion.

No.	Metal salt	Weight (gm.) in (500mL)
1	$Pb(NO_3)_2$	0.7992
2	$Ni(NO_3)_2.6H_2O$	2.4770
3	$Cu(NO_3)_2.6H_2O$	2.3260
4	$Co(NO_3)_2.6H_2O$	2.4693

Scheme 1: Path ways for synthesized compounds



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RESULTS AND DISCUSSION

Spectra

methyl 2-(6-methoxynaphthalen-2-yl) propanoate(1) was prepared from the reaction of naproxen drug with (MeOH), presence in (H_2SO_4), yield was 85%, The melting point is183-185 0C, and the data infrared = Ar- CH =(3102 cm^{-1}), Ar- C=C = (1510-1600 cm^{-1}), C=O=(1672),O-CH_3=(1157),CH-Aliphtic=(2800cm^{-1}), ^{1}H-NMR , showed, at δ=(3.80)ppm (C – H Aliph),at δ =(3.35)ppm (OCH3), δ=(1.62)ppm (CH_3),at δ =(6.82-7.79) ppm (C=C) of aromatic ring. As table (1) and Fig. (1,5).

2-(6-methoxynaphthalen-2-yl) propane hydrazide (2) was prepared by reaction of methyl 2-(6-methoxynaphthalen-2-yl) propanoate (1) with hydrazine hydrate, the infrared was band at (NH2) = (3740 cm^{-1}) , (N-H) = (3103 cm-1), (C=O)= (1665 cm-1), (Ar=CH)= (3045cm-1),(ArC=C)= (1514-1600 cm^{-1}),and (1157 cm^{-1}) for (O-CH_3) group.

^{1}H-NMR , showed, at δ=(3.04)ppm (C – H Aliph),at δ =(3.45)ppm (OCH3),at δ =(7.13-7.96) ppm , δ=(1.06)ppm (CH_3), at δ =(6.23-7.80) ppm(C=C) of aromatic ring , at δ=(11.35)ppm(NH_2), and δ(8.29)ppm (NH)., As table (1) and Fig. (2,6).

N'-(2-hydroxybenzylidene)-2-(6-methoxynaphthalen-2-yl)propanehydrazide (3) was prepared by reaction of 2-hydroxy benzaldehyde with 2-(6-methoxynaphthalen-2-yl)propanehydrazide in ethanol. IR spectrum of the compound 2-[2-(4-chlorobenzylidene) hydrazine ebenzoxazole (3), showed clear absorption bands at (3344cm^{-1}) (N-H), (2921-2985 cm^{-1}) (=C-H) ,(3080cm^{-1}) (Ar=CH) , (1612cm^{-1}) (C=N), (1450-1500 cm^{-1})(C=C) ,(1672 cm^{-1}) duo to (C=O) and (OH) at (3400), (1101 cm^{-1}) for (O-CH_3)

^{1}H-NMR , showed, at δ=(3.89)ppm (C – H Aliph),at δ =(3.51)ppm (OCH3), δ=(1.39)ppm (CH_3),at δ =(6.74-7.78) ppm (C=C) of aromatic ring , at δ=(8.23)ppm(CH=N), and δ(9.90)ppm (NH), δ(10.61)ppm (OH). As table (1) and Fig. (3,7).

Prepared resin (4) of reaction N'-(2-hydroxybenzylidene)-2-(6-methoxynaphthalen-2-yl)propanehydrazide (3) with bisphenol, in presence paraformaldehyde, showed clear absorption bands at (2852-2921 cm^{-1}) duo to (=C-H) and (OH) = (3220-3272 cm^{-1}) , As Table (1) and Fig. (4).(18).

Table (2): The physical properties for Compounds (1, 2)

Comp. No.	Molecular formula	Color	M.P(^{0}C)	Yield (%)	Recryst. Solvent
1	C15H16O3	White	84-86	85	MeOH
2	$C_{14}H_{16}N_2O_2$	Dark Yellow	122-124	55	EeOH
3	$C_{12}H_{20}N_2O_3$	Yellowish Brown	91-94	60	MeOH
4	/	Brown	/	86	/

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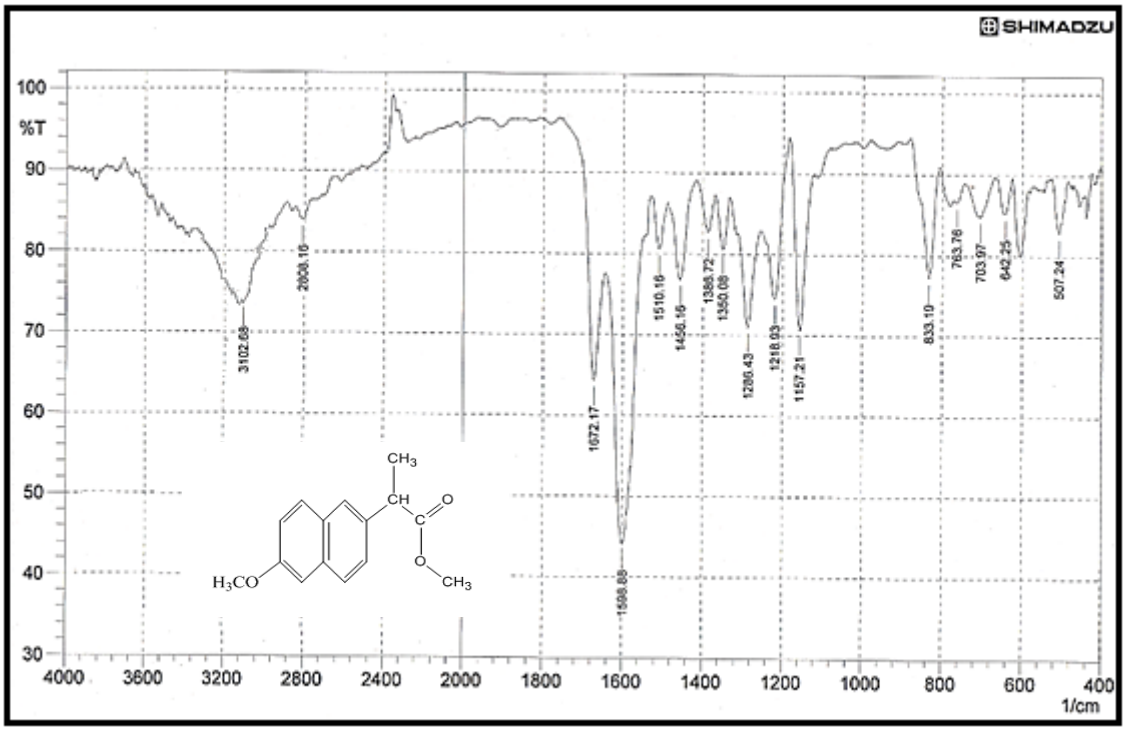

Figure 1: FT-IR spectrum for compound(1).

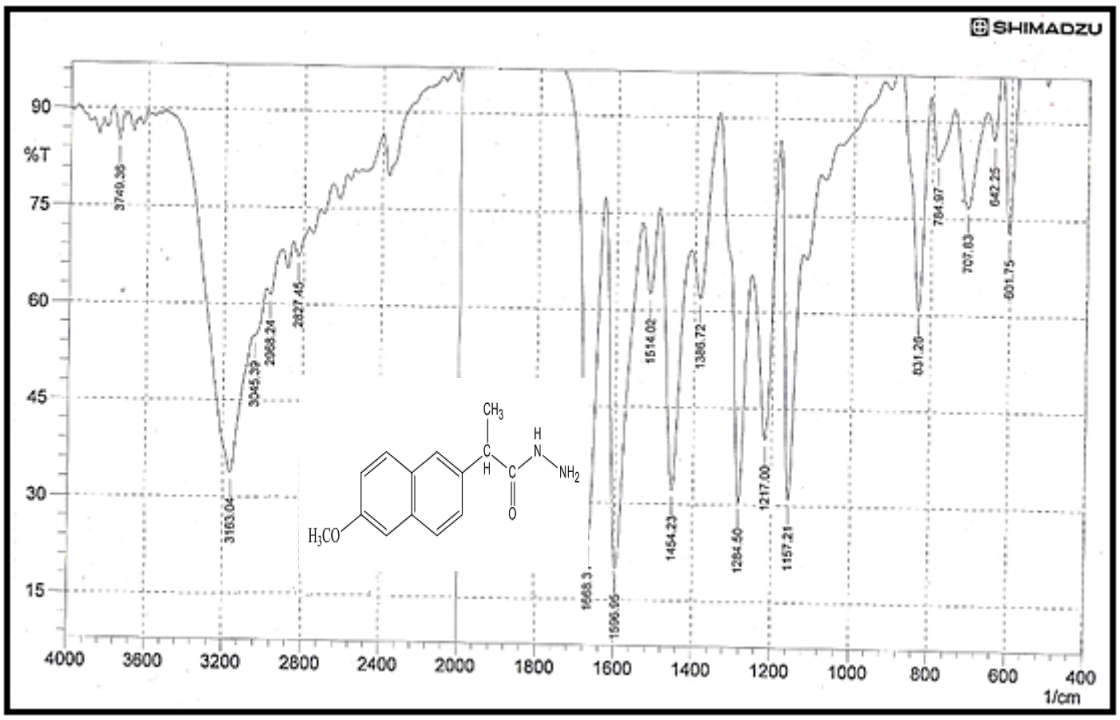

Figure 2: FT-IR spectrum for compound(2).

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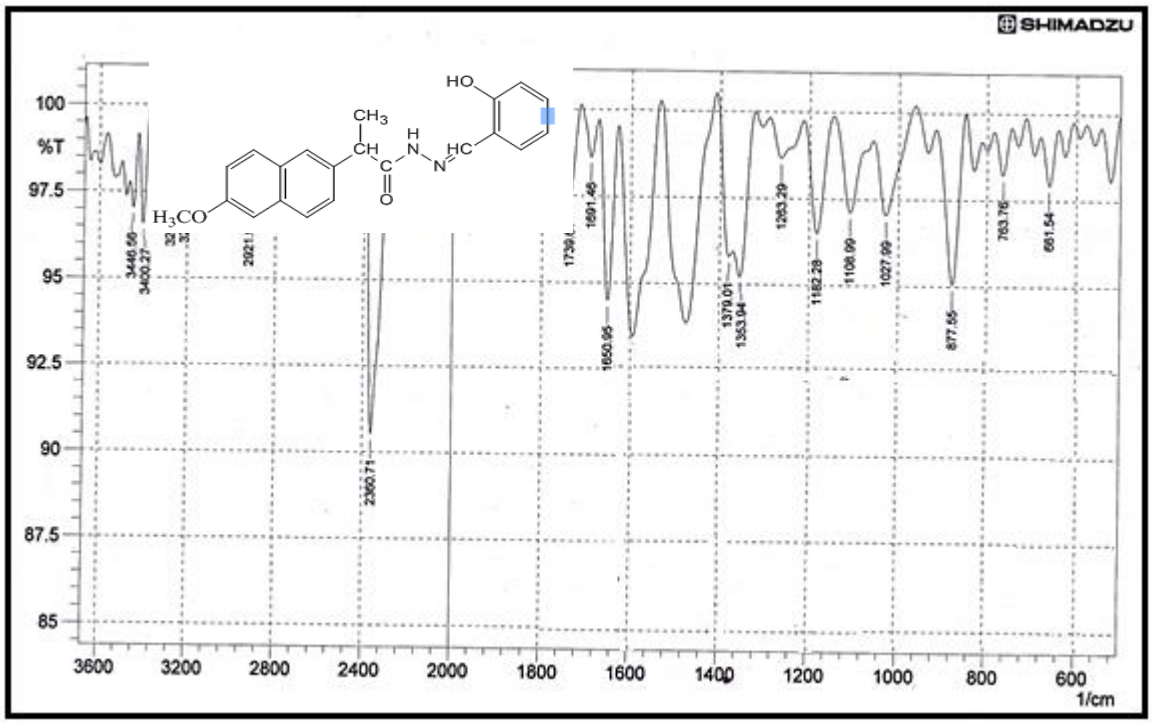

Figure 3: FT-IR spectrum for compound(3).

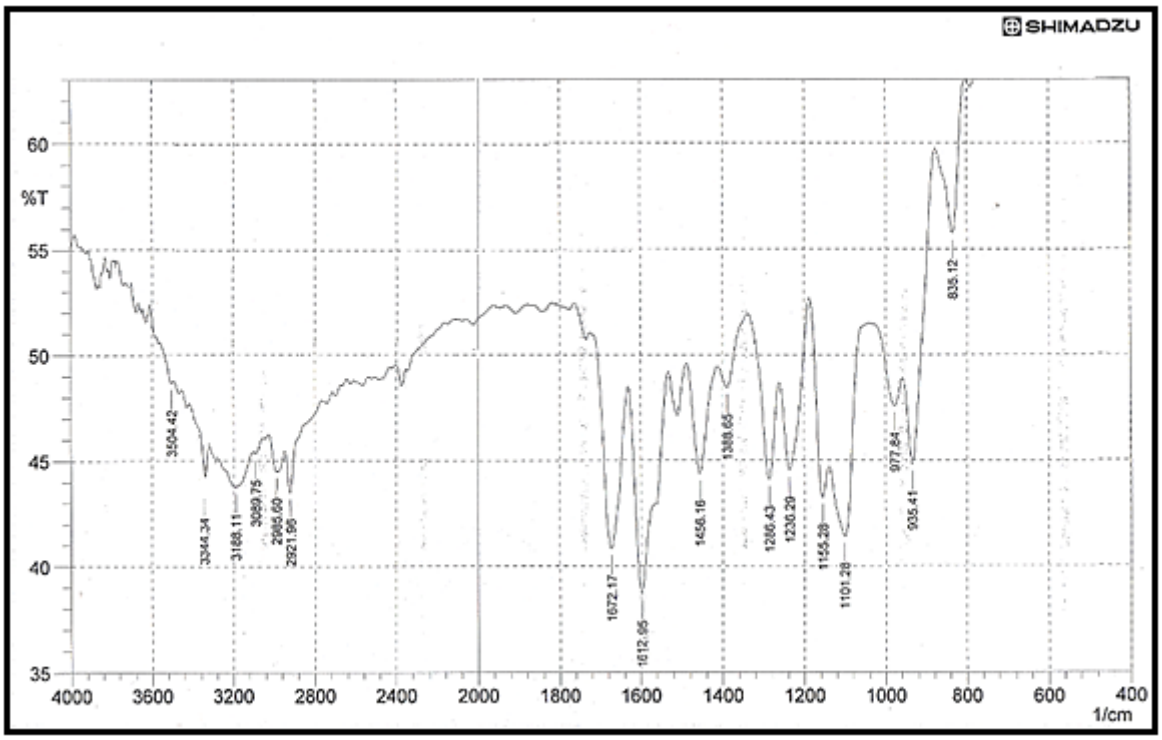

Figure 4: FT-IR spectrum for compound(4).

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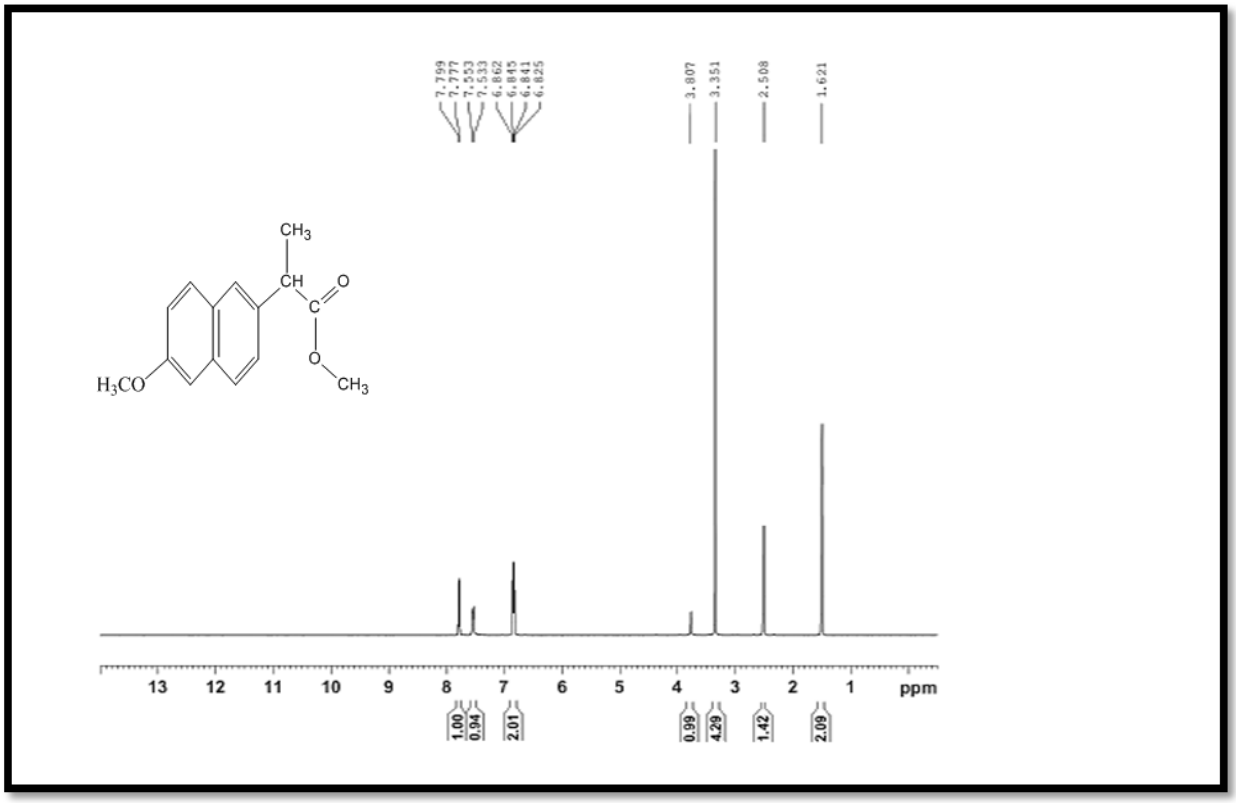

Figure 5: [1] H-NMR spectrum for compound(1).

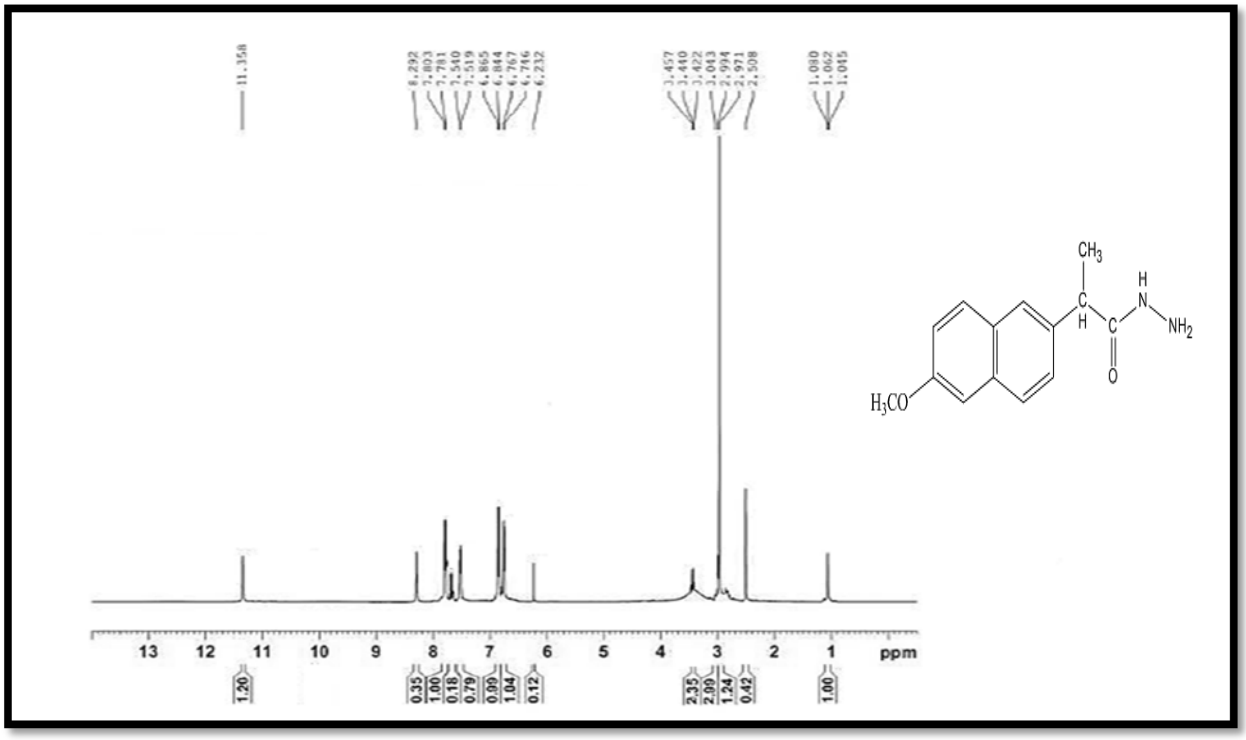

Figure 6: [1] H-NMR spectrum for compound(2).

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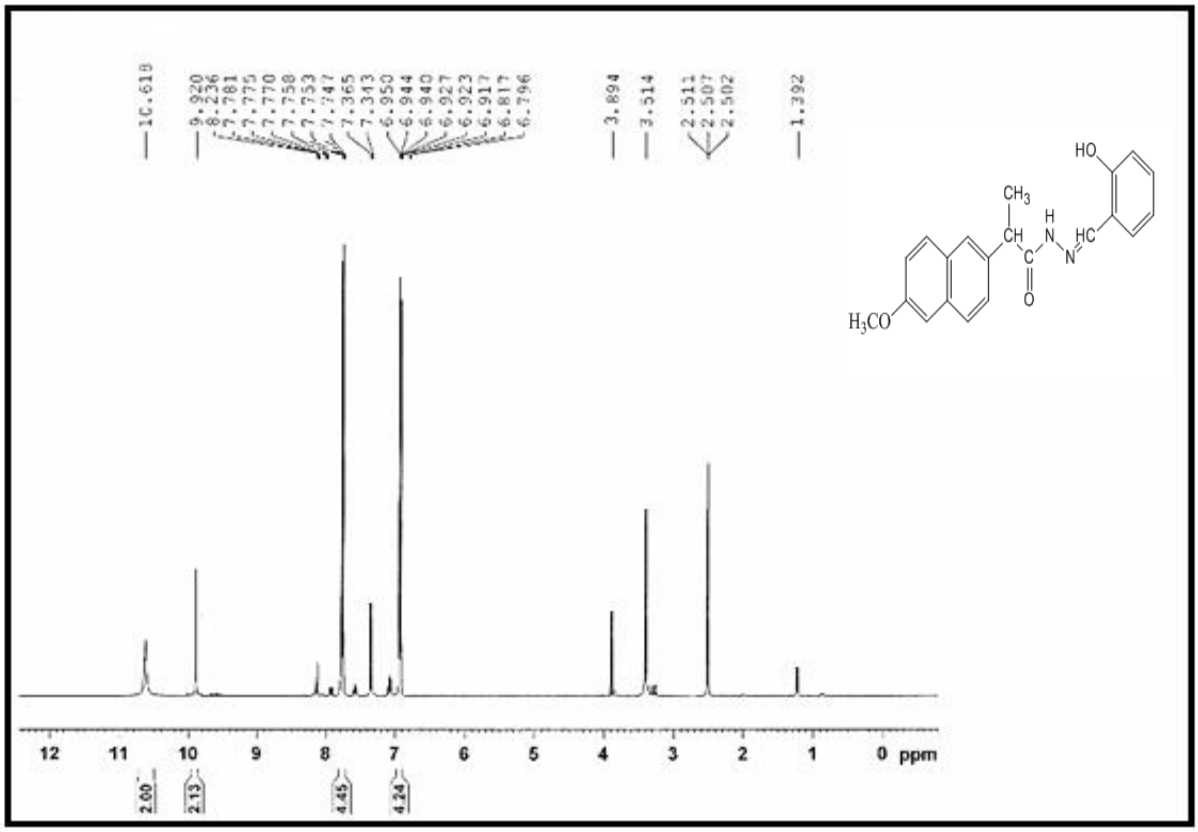

Figure 7: [1] H-NMR spectrum for compound(3).

The Analytical Measurements Used to Study the Efficiency of the Prepared Chelating Resins.
The Effect of Contact Time on the Maximum Loading Capacity of (4)

In this study, we observed that by increasing the contact time for the solutions of the ions under study, the resin loading capacity became higher. The ions (Ni2+, Pb2 +, Cu2+, Co2+) reached to the equilibrium after about nine hours from their existing in solution together with the chelate resin. The increase in the loading capacity then went down gradually until reaching the higher contact time (24 hours). Table (3) and (Fig. 8,9,10,11) indicates the effect of contact time on the loading capacity of polymer (4) with metallic ions (Ni^{2+}, Pb^{2+}, Cu^{2+}, Co^{2+}) at a specific pH values recovered by (0.1g) of resin polymer (4) as a function of time and at different PH values.

Number of milligrams of ions (Ni^{2+}, Pb^{2+}, Cu^{2+}, Co^{2+})Table(3):
Drawn by 0.1g of resin (4) as a function of time in different acidic functions

Ions	pH	Capacity mg/g resin				
		Time(hr.)				
		0.5	1	3	9	24
Ni^{2+}	2	0.6	1.2	2.5	6.0	6.2
	4	2	2.8	3.4	6.2	6.9
	6	3.5	3.7	4.2	7.0	7.5
	8	4.5	4.8	5.1	7.2	7.9
Pb^{2+}	2	6.3	7.1	7.9	10.0	12.1
	4	7.0	7.6	8.1	11.1	13.0
	6	8.6	9.1	10.2	13.5	15.3

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Cu^{2+}	2	1.5	1.8	2.2	5.3	6.0
	4	2.3	2.7	3.6	6.0	7.5
	6	4.2	4.6	5.1	8.1	9.3
Co^{2+}	2	1.3	1.4	2.0	4.8	5.1
	4	1.9	2.5	3.8	5.7	6.5
	6	2.0	2.6	3.8	5.8	6.7

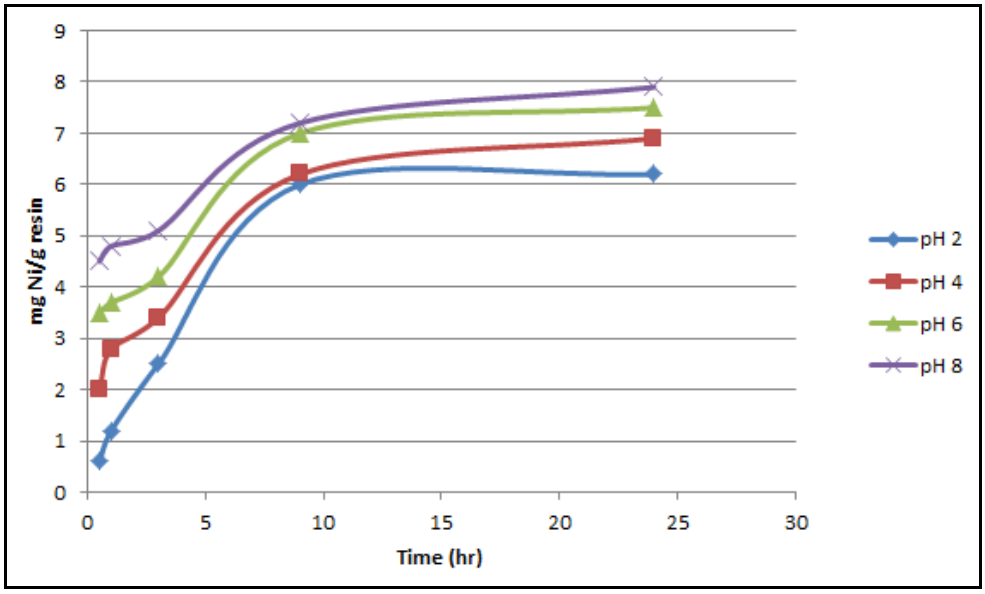

Figure 8: Number of Ni^{2+} Mg withdrawn by (0.1g) of resin (4) as a function of time in different acidic functions.

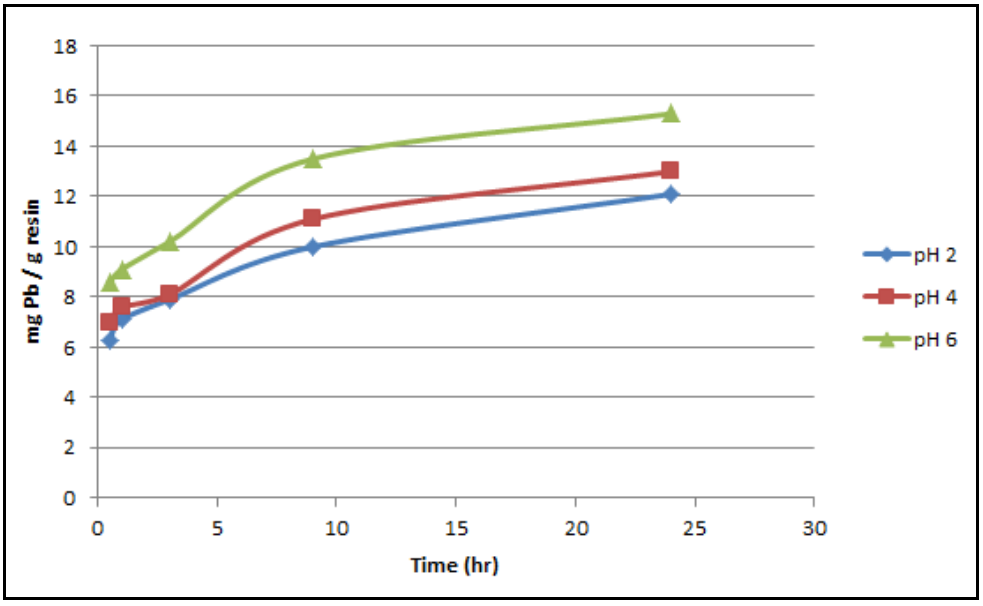

Figure 9: The number of pb^{2+} mg withdrawn by (0.1g) of resin (4) as a function of time in different acidic functions.

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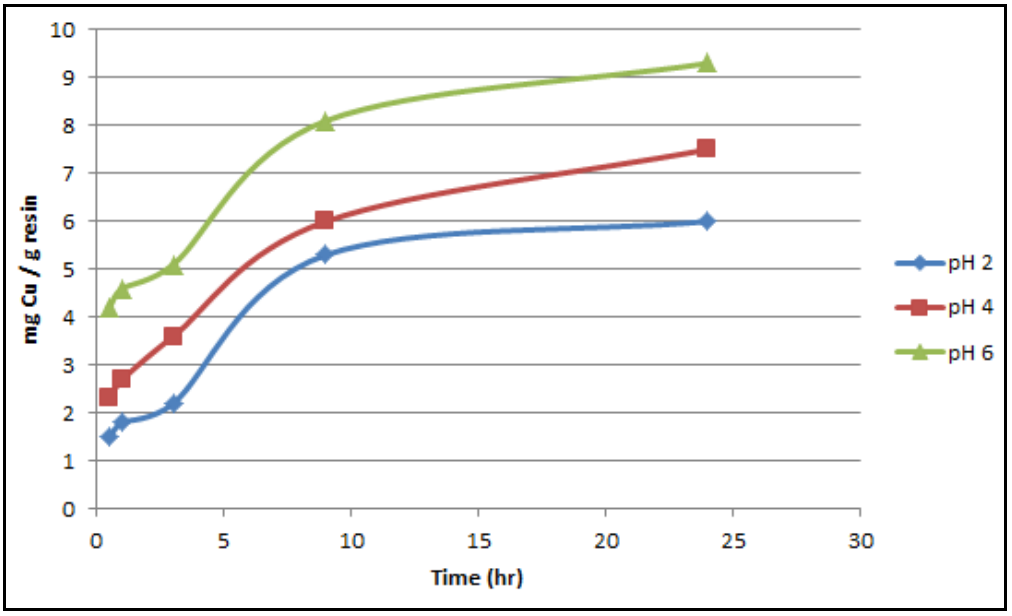

Figure 10: The number of Cu^{2+} pliers withdrawn by (0.1g) of resin (4) as a function of time in different acidic functions.

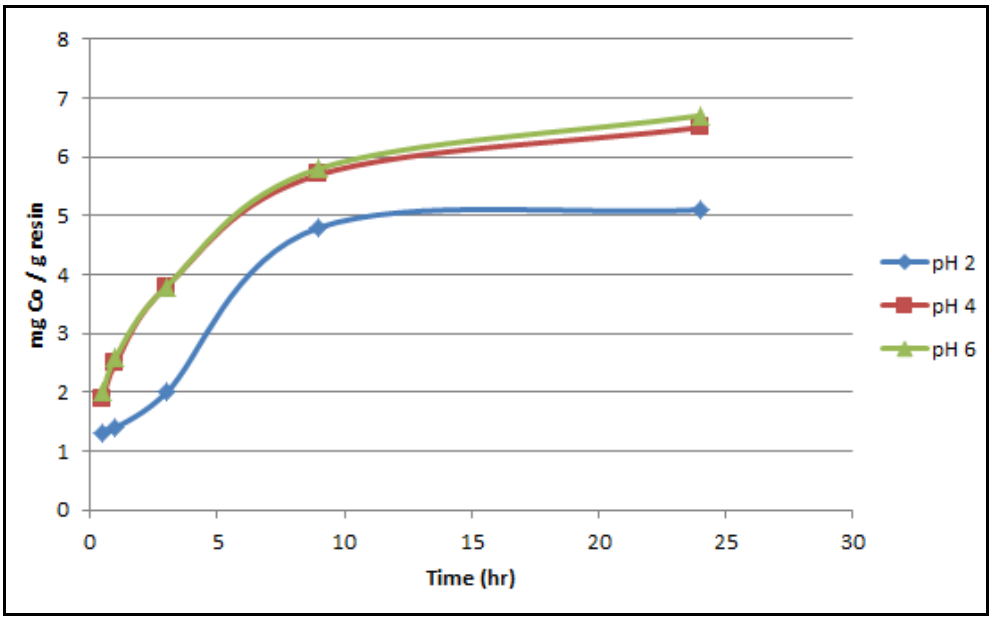

Figure 11: The number of Co^{2+} mg / s withdrawn by (0.1g) of resin (4) as a function of time in different acidic functions.

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