Polycondensation of Allopurinol with EDTA and CDTA as Chelation Polymers for Transition Metals

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Abstract

Chelation polymers for transition metals were prepared by copolymerization of Allopurinol, a known drug for the treatment of gout and hyperuricaemia, with ethylendiaminetetraacetic acid (EDTA) or cyclohexyldiaminetetraacetic acid (CDTA). The prepared condensed polymers were characterized by using the following spectrometric techniques: UV-visible, ^{1}H-NMR and FT-IR. Their thermal behavior were studied by using thermogravimetric analysis, The intrinsic viscosities in DMF were calculated, and their % swelling in water was measured at 30°C.Their softening point were measured, Also the carboxylic acid functional groups content were measured by acid-base titration.

When they were polymerized with as a diamine drug compound; these new drug polymers were modified with metal ions as good ligand, which could be complexes with many poison metal ions.

الخلاصة

في هذا البحث ادخل الاثلين ثنائي امين رباعي حامض الخليك او هكسيل حلقي ثنائي رباعي حامض الخليك ضمن السلسلة الرئيسية للبوليمرات المتكاثفة ، عند بلمرته مع الالوبيورينول كمركب ثنائي امين دوائي . حورت البوليمرات الجديدة المحضرة مع ايونات العناصر كمركب مخلبي , والذي بامكانه ان يتفاعل ويكون معقدات مع عدد من ايونات العناصر السامة.

شخصت البولمرات التكاثفية المحضرة بواسطة طيف الاشعة فوق البنفسجية والاشعة تحت الحمراء وطيف الرنين النووي المغناطيسي ودرست التحاليل الحرارية الوزنية وقيست المجاميع الكاربوكسيلية بواسطة التسحيح . شخصت المعقدات البولمرية المحضرة بالتقنية الطيفية ، وقيست اللزوجة باستخدام ثنائي مثيل فورماميد كمذيب بدرجة 30م°،وقيست نسبة الانتفاخ المئوية في الماء بنفس الدرجة الحرارية.

Introduction

The use of condensation reactions is a common procedure to prepare chelating polymers such as polyester and polyamide. Such procedure enables the preparation of a series of polyamides by inserting EDTA anhydride with various diamines [1]. Unfortunately, the presence of hydrolytically unstable group in the polymer chain has limited commercial application [2]. Aminocarboxylic acid molecules such as ethylenediaminetetraacetic acid (EDTA), diethylenetriaminepentaacetic acid (DTPA), and their derivatives, are widely described in the literature [3].Complexing abilities are found vast application in medicine, and analytical chemistry [4]. Many polymers bearing such groups have form stable complexes with heavy metal ions [5]. EDTA as a suitable and common complexing compound was inserted into the polymer back bone with polyaddition reactions separately between hexamethylenediamine HMDA or poly (ethylene glycol) and ethylenediaminetetraacetic acid dianhydride (A-EDTA) [6]. EDTA can be used as a decalcifying agent making it possible to cut sections using an icroatome once the tissue sample is demineralized [7]. EDTA is in such wide spread use that it has emerged as persistent organic pollutant [8].

The synthesis and characterization of a kegging-type mono-rhenium (V). Substituted polyoxotungestats are described [9]. Efficiency and selectivity of metalligation can also be affected by polymeric structure including functional group density, rigidity, and bulkiness of pendent groups [10].

The growing interest in nanotechnology as well as biomaterials and biomimetic system appears to be shaping the future of polymeric environmental remediation [11].Commonly used water soluble poly-aminocarboxylic acid chealaters, require intravenous or subcutaneous administration due to their poor bioavailability [12]; this may have some advantages for decoporation of certain metals and radionuclides [13].

Experimental

(a)Materials and Instruments: EDTA, Dioxane and DMF were purchased from BDH and used without further purification; Allopurinol was obtained from Baghdad Pharmacy College. FT-IR spectra were recorded with Fourier transform Shimadzu 7R-46E spectrometer by using KBr disc in the range of 400-4000cm^{-1}. UV-visible Spectra were recorded with Shimadzu UV.256f.w spectrophotometer .intrinsic viscosities were measured by Ostwald Viscometer at 30°C.Thermogravimitric analyses were carried out on dupond 950 US, softening points were measured using Kalen-Camp apparatus.

(b)Preparation of condensed polymers P_1&P_2 : EDTA (1g. 0.01 mole) was dissolved in 5ml of DMF, and a solution of allopurinol (0.7g, 0.01 mole) were introduced in a single-neck round-bottom flask which was equipped with a

condenser, the mixture was refluxed and stirred for 1hour, the solvent was evaporated to leave a clear polymer (**P_1**), which was washed with diethyl ether. The product was dried under vacuum until a constant weight was obtained, the yield was 90% and softening point was listed in table (1). Similar procedure was followed for the condensation of cyclohexyldiamine tetraacetic acid with Allopurinol as P_2 polymer.

(c) Swelling percentage : Swelling percentage for prepared polymers was studied in water as shown in Fig. (5), swelling % calculated according to the formula [$S\% = (m_1-m_0)/m_0 x\ 100$], where m_0 is the weight of dry polymer. And where m_1 is the weight of swelled polymer in water.

(d) Preparation of metal complex polymers : A mixture of 0.02 moles of one of the metal ions aqueous solution, and 0.01 mole of the prepared condensed EDTA polymer P_1. The metal complex polymers were prepared by using different pH values and the physical properties of each were listed in table (2)**.**

Results and Discussion

Allopurinol, which is a known drug for the treatment of gout and hyperuricaemia, contain two amine functional groups within its penta-membered ring. It is possible to condense with carboxylic groups of EDTA or CDTA, to produce polyamides, the reaction pathway presented in schemes (1) and (2).

The EDTA-Allopurinol polymer can behave as ligand for different metal ions which could incorporate through polymer chain, the presence of pendant carboxyl group and diamine with heterocyclic Allopurinol act as a high effective polymeric complex forming site to bind with metal ions in aqueous solutions.

The FT-IR absorption spectrum of condensed polymer figure (1) shows the ν C=0 amide band at 1650cm^{-1} and ν C=0 of allopurinol was observed at 1730 due to extended with more conjugation system. The ν OH carboxylic acid was appeared a broad band at 3450cm^{-1} with disappearing –NH group of allopurinol ring at 3200cm^{-1}, the ν C-N band was observed at 1360cm^{-1} as shown in fig. (2) for the complex polymer with iron, at the same time the absorption band of ν-OH was disappeared. The absorption band of ν -C=O appeared at 1629cm^{-1} with observed small shift.

The UV.vis, Spectra of condensed polymer–Ni^{+2} complex, and the absorptions were observed at 220, 400 and 750nm, which indicate the complexation of polymer with metal ion.

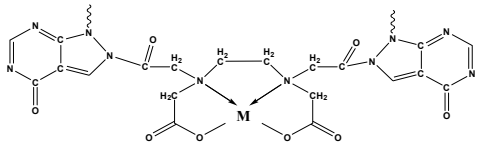
The change in IR and visible absorption bands confirm the creation of metal binding on polymer.

Fig. (3) Showed TGA and DSC of prepared polymers P_1 (Allopurinol with EDTA) which indicate the high thermal resistance, and showed two steps of weight loss-temperature, the first is ranged at 229.7C° with 39,127 % weight loss % , and the second at

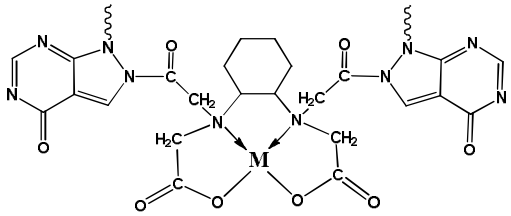
620.38 C° with 61.734% weight loss % . This high thermal resistance is indicating the high molecular weight of the polymer containing aromatic rings through back bone of its structure.

Fig. (4) Shows the ^{1}HNMR. spectrum of the prepared polymer P_2 which indicate the formation of of P_2 and shows the following signals: 2CH=N δ (9.7ppm), 2CH=C δ (8ppm), 4CH_2C=O δ (3.4ppm), -CH_2-CH_2- δ (d.1.2ppm), CH_2cyclo δ (t. 2.9ppm) and 2COOH δ (12ppm).

The following structures were suggested for chelate polymer with divalent metal ion:

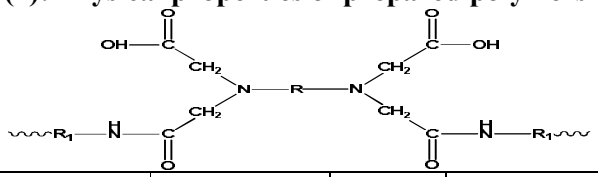


P1-M



P2-M

Table (1): Physical properties of prepared polymers P_1&P_2



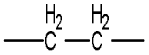
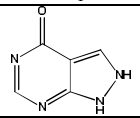
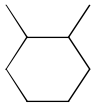
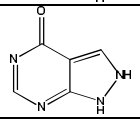
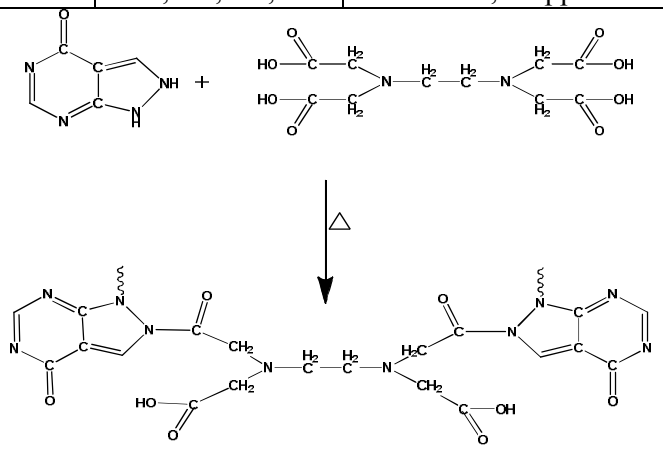
NO.	-R-	-R_1-	S.P. °C	yield%	μ_{ln}dl/g
P_1			600-620	90	0.85
P_2			500-530	95	0.9

Table (2): **Physical properties of prepared EDTA-Allopurinol condensed polymers complexes**

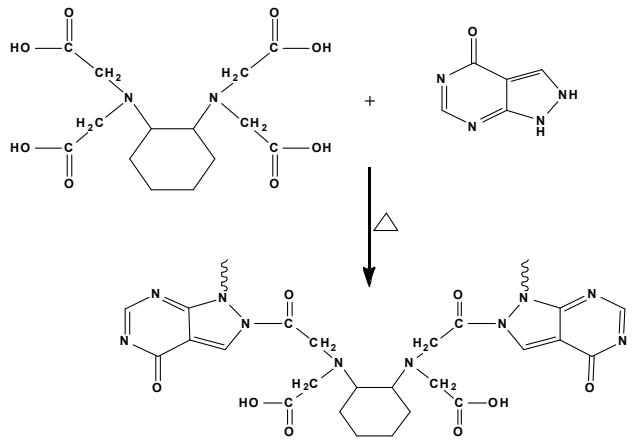
No.	**Polymers metal**	**Color**	**Yield%**	μlndl/g	**S.P./ °C**
1.	P_1- Ni	Turquoise	70	0.41	>300
2.	P_1- Cr	Green	60	0.45	>300
3.	P_1- Pb	White	56	0.43	>300
4.	P_1-Co	Faint violet	75	0.46	>300
5.	P_1-Fe	Dark green	80	0.45	>300

Table (3): Spectroscopy results of prepared polymersFor P_1 complexes

No.	Polymers metal	UV-Vis λ_{max}	FTIR (cm^{-1})
1.	P_1- Ni	200,400,750	νCO 1626 , ν-OH at3400
2.	P_1- Cr	200,250,500	disappear -NH at 3200 of allopurinol
3.	P_1- Pb	190,250,550	νC=N1650,disappearance of OH carboxylic
4.	P_1-Co	200,530,600	νC=N1650,disappearance of OH carboxylic
5.	P_1-Fe	190,250,350,600	νC=N1650,disappearance of OH carboxylic



Scheme 1



Scheme 2

The EDTA, Allopurinol condensed polymer P_1 could formed a stable chelate with any metal ion, also its pharmacologic effects of the condensed polymer can be used for clinical application and it could be used for removing the toxic metal ions of sea water, to remove the toxic environmental pollution, also the P_2 polymer was obtained containing allopurinol units which enhanced the

bioactivity for this a new biopolymer, P_2.

Conclusion

The results showed that polyamide can be conveniently prepared in DMF solvent, and the linear polyamide have pendant carboxyl groups and able to bind with metal ion in aqueous solution. The metal complex polymers were prepared after adjustment of pH values, and the colored solid polymers were isolated.

Chelate-forming polymer is much easier to complex and the factors that encourage ion selectivity include ionic solvation variation and swelling changes. In different pH values, which is enhance the chelate-forming polymer with different metals ions.

The main applications could be suggested for chelating polymers are based on the high selectivity of materials for particular ions, which could be used for treated with many mining pollution or with toxic ions mixtures.

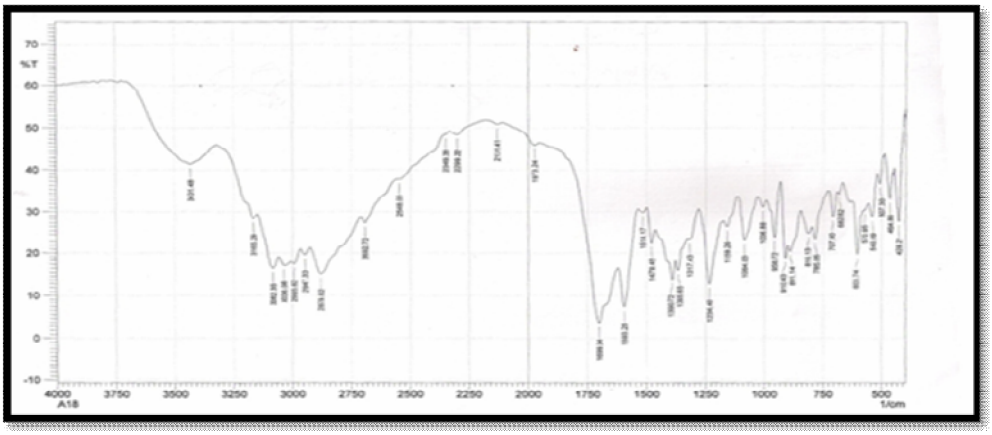


Fig.(1) FTIRspectra of EDTA- Allopupinol Condensed polymer

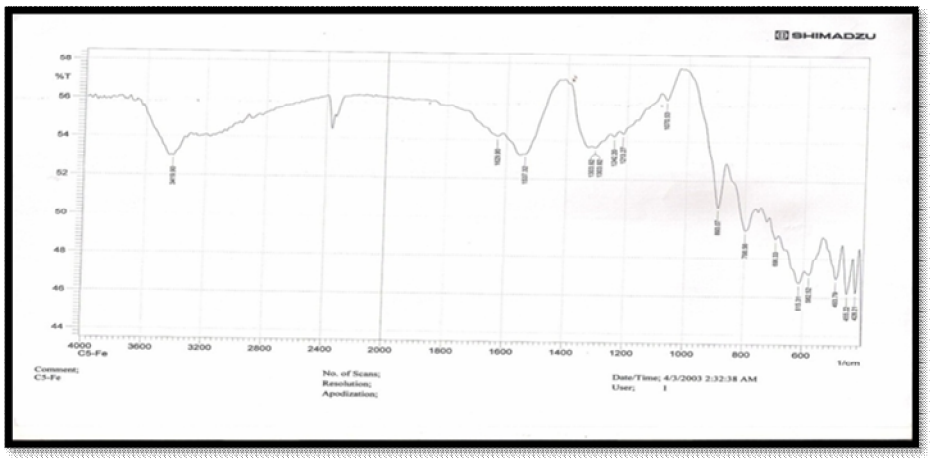


Fig.(2) FTIR spectra of complexed polymer with Fe

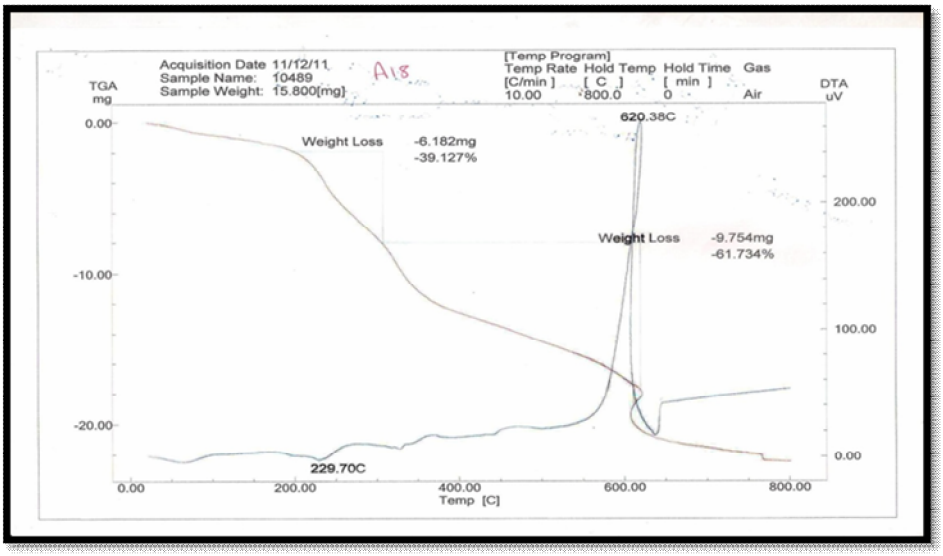


Fig.(3)TGA and DSC of prepared polymers P_1

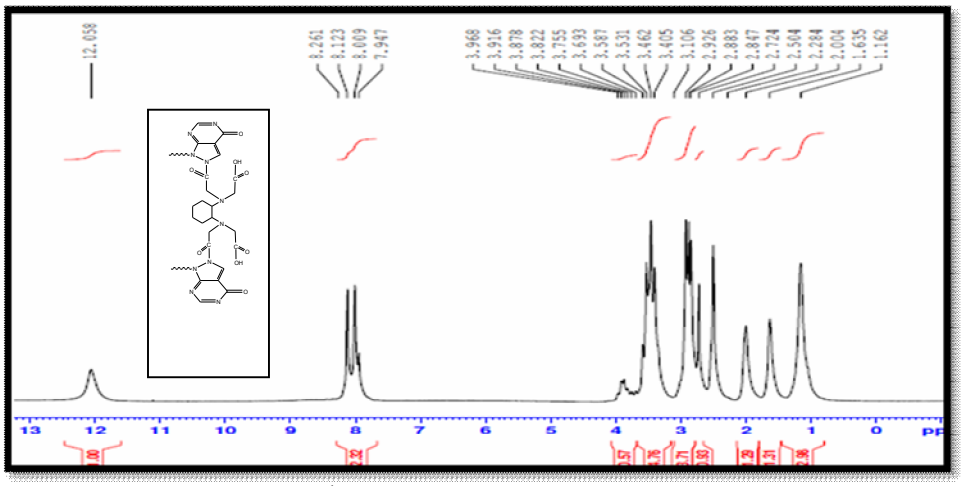


Fig.(4) ^{1}H-NMR for prepared polymer P_1

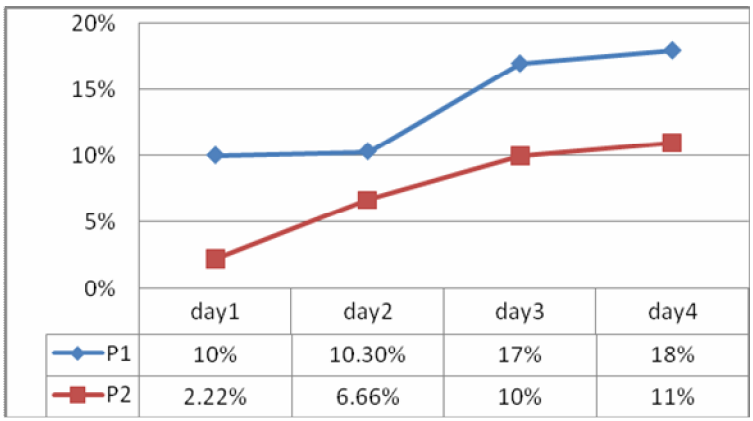


Fig. (5) Swelling % of prepared polymers in water at 30 C°

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