Preparation of Poly (N- Imidazolyl maleamic acid)

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Abstract

In this research preparation of poly (maleamic acide) which substituted with imidazole as a bioactive material is performed. It was prepared from reaction of maleic anhydride with imidazole and Ring opening of maleic anhydride by imidazole, then the substituted maleamic acid was polymerized by freeradical polymerization by using dibenzoylperoxide as initiator. The structure of synthesized polymer was confirmed by FTIR, UV. and ^{1}H-NMR spectroscopes, The controlled release of imidazol units was studied in different pH values at 37 ^{0}C. All physical properties of prepared polymer were measured.

Keywords: Preparation, N-Imidazolyl, maleamic acid.

Introduction

Imidazole is an organic compound with the formula $C_3H_4N_2$. This aromatic heterocyclic is a diazole and is classified as an alkaloid [1].

Imidazole is a 5-membered planar ring, which is soluble in water and other polar solvents. It exists in two equivalent tautomeric forms, 1*H*-imidazole and 3*H*-imidazole, because the hydrogen atom can be located on either of the two nitrogen atoms. Imidazole is a highly polar compound, as evidenced by a calculated dipole of 3.61D, and is entirely soluble in water. The compound is classified as aromatic due to the presence of a sextet of π-electrons, consisting of a pair of electrons from the protonated nitrogen atom and one from each of the remaining four atoms of the ring [2,3].

Imidazole incorporated into many important biological molecules. The most pervasive is the amino acid histidine [4], which has an imidazole side-chain, Histidine is present in many proteins and enzymes and plays a vital part in the structure and binding functions of hemoglobin [5,6].

Histidine can be decarboxylated to histamine, which is also a common biological compound. It is a component of the toxin that causes urticaria , which is another name for allergic hives [7]. One of the applications of imidazole is in the purification of histagged proteins in immobilized metal affinity[8].

Imidazole has became an important part of many pharmaceuticals. Synthetic imidazoles are present in many fungicides and antifungal antiprotozoal and antihypertensive medications. It found in tea leaves and coffee beans, that stimulates the central nervous system. It is present on the anticancer medication mereaptopurine, with combats leukemia by interfering with DNA activities [9].

Imidazol has been used extensively as a corrosion inhibitor on certain transition metals, such as copper. Preventing copper corrosion is important, especially in aqueous system, where the conductivity of the copper decreases due to corrosion. The thermostable polybenzimid azd contains imidazole fused to benzene ring and linked to a benzene and acts a fire retardant, it can also be found in various compounds that are used for photography and electronics [10]. Both the imidazole and amidine functionalities were introduced to construct an active site for catalytic ester hydrolyze.[11]. The imprinted polymers, having both the amidine and imidazole as functional groups [14], were expected to have improved hydrolytic activity compared with other imprinted polymers having the corresponding single functional group [12].

Synthesis and biological screening of some newly synthesized imidazole is divided into different categories [13]. Derivatives of imidazole were reported for anti inflammatory,

analgesic, tuberculostatic, anticancer and antidepressant and microbial and antifungal activities.[13,14].

Experimental

Materials

Maleic anhydride and imidazole were purchased from BDH, dibenzoylperoxide was obtained from Fluka, DMF and dioxane were commercially available and of analytical grade.

Characterization

Fourier transform infrared (FTIR) spectra were recorded on a Perkin-Elmer spectrophotometer, 4000-400cm^{-1} **,** ^{1}H NMR spectra were obtained at 25^{0}C on a Bruker AV 400NMR spectrometer samples for ^{1}H-NMR spectroscopy were prepared by dissolving about 10 mg of products in an appropriate amount of deutrerated DMSO.

Quantitative analysis corresponding to the amount of pendant carboxyl groups incorporated onto prepared polyamic acid, by titration method as follows: 0.1g. of prepared polymaleamic acid was put in 20ml of dioxane, then the solution was directly titrated to phenolphthalein end-point using sodium hydroxide (0.02M) in methanol. Result were expressed as the content of carboxyl groups which is defined as the mole percentage of the polymaleamic acid.

Thermal analysis was performed using TGA instruments and differential scanning calorimeter equipped with a RCS accessory under nitrogen atmosphere, the standard procedure is as follows :- the samples (about 5mg.) were heated and the effect of heat treatment on the crystalline structure of the polymers, a rate of 20 ^{0}C min $^{-1}$

Preparation of N- imidazoyl maleamic acid

In a beaker, 0.5g. (5mmole) of maleic anhydride was dissolved in 5ml of dioxane at ambient temperature with rapidly stirring for 1h, 0.5mmol of dissolved imidazole was added to the mixture. The reaction was continued to the corresponding time at 25 ^{0}C, the white product was formed, filtered and subsequently dried under vacuum.

Polymerization of imidazoyl maleamic acid

0.3g. of prepared monomer was dissolved in 5ml of dioxane, and 0.05% weight of dibenzoyl peroxide was added, under nitrogen atmosphere, the polymerization tube was covered, heated by water bath at 90^{0}C about 25 mins. The colorless polymer was obtained with 85% yield with m.p about 275-285^{0}C

Swelling studies

Dynamic swelling studies of polymer made as follows:-

Polymer was swollen in solution with pH 7 at 37 ^{o}C to determine the parameters of swelling and diffusion. Swollen gels removed from the water bath at regular intervals were dried superficially with filter paper. Weighted and placed in the same bath.

To investigate the time –dependent swelling behavior of polymer in solutions with pH7, we performed dynamic swelling studies. The swelling S% is calculated from the following relation:-

$S\% = (M_1 - M_0)/M_0 \times 100$

Where:- M_0 is the mass of dry polymer at time 0.

M_1 is the mass of swollen polymer at time t.

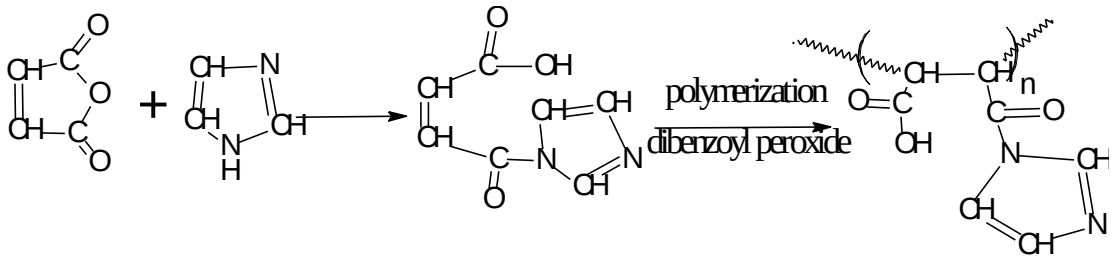
Swelling curves of polymer in water with pH 7 at 37 ^{o}C shown in Fig. (3).

Studying of controlled release of polymer

A mixture of 50:50ml of polymer and solution in (pH4, pH 10) was kept in a cylinder 100 mg of polymer was added, kept at 37C^{0} without stirring, release sample was periodically drown with an analysis by UV spectra at 330 nm to determine the amount of release imidazole. A calibration curve was constructed with soft ware built in the computerized UV photometer and the controlled release polymer were carried out in different pH value (pH4, pH 10) at 37 ^{0}C .

Results and Discussion

In this study the polymer was prepared containing imidazole units as pendant groups the poly (maleamic acid) which acted as drug or antimicrobial agents. The following reaction was explained as below:-



To acid in the structural elucidation of poly(imidazoyl maleamic acid) which functionalization chemistry, with carboxyl groups and imidazole groups along the backbone was analyzed using FTIR spectroscopy, and assignments for the characteristic groups were developed FTIR spectra of prepared polymer is given in Fig. (2) a new band appeared at 1710 cm^{-1} which confirmed the presence of carboxyl groups and the absorption of OH carboxylic was appeared at 3450-2962 cm^{-1} with comparing with Fig. (1) of imidazole alone.

Supporting evidence for the structural elucidation was revealed by ^{1}H NMR analysis, Fig. (5) indicated the content of protons at 2.6 ppm are assigned to –CH-CH- of succinamic and the CH of imidazole was appeared at 7-8 ppm in addition, the undetectable resonance of protons in the COOH may be due to the formation of hydrogen bonding between inter-or intra-molecules and the proton of carboxylic acid was appear at 9.3 ppm.

Thermal Analysis

In this new prepared polymer which containing imidazole groups, in attempt to understand the link between the incorporation of functional groups and the crystallization of poly maleamic acid was investigated by DSC.

The sample subjected at 300 ^{0}C and kept at this temperature for 5 min then cooling to 50 ^{0}C, and finally reheating from 50 ^{0}C to 300 ^{0}C, both heating and cooling rates are 20 ^{0}C min^{-1}, the crystallization endothermic of polymer occurs at the highest crystallization temperature (T_c) and has the sharpest crystallization exothermic.

Table (1) lists the weight loss % of polymer through different temperature and T_m of polymer sample is about 280 ^{0}C, this indicated the presence of imidazole group which may explained the effect of substituted groups.

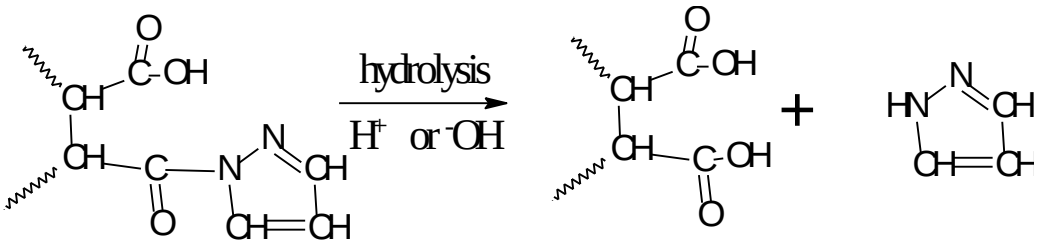
Table (1)
Weight loss % of prepared polymer.

Weight loss %	*Temp. ^{0}C*
15	120
50	260
75	280

The glass transition temperature (T_g) also helps in understanding the effects of functional groups on the movement of the polymer chains due to the interactions between the acid group as hydrogen bonding.

Controlled bioactive release

Controlled bioactive release was illustrated in Fig.(4) at pH4,10 indicated the more hydrolysis in basic medium, this hydrolysis in acidic or basic medium acts as a smart bioactive polymer, that release of imidazole as antimicrobial agent at suitable condition at 37 ^{0}C, the amide is hydrolyzed gradually and this cleavage produces an amine and carboxylic acid polymer. As shown in scheme below:



We concluded from this research that the new prepared bioactive polymer and the main goal in this work is investigation of efficient imidazol as a carrier and the effect of pH values on the imidazole release.

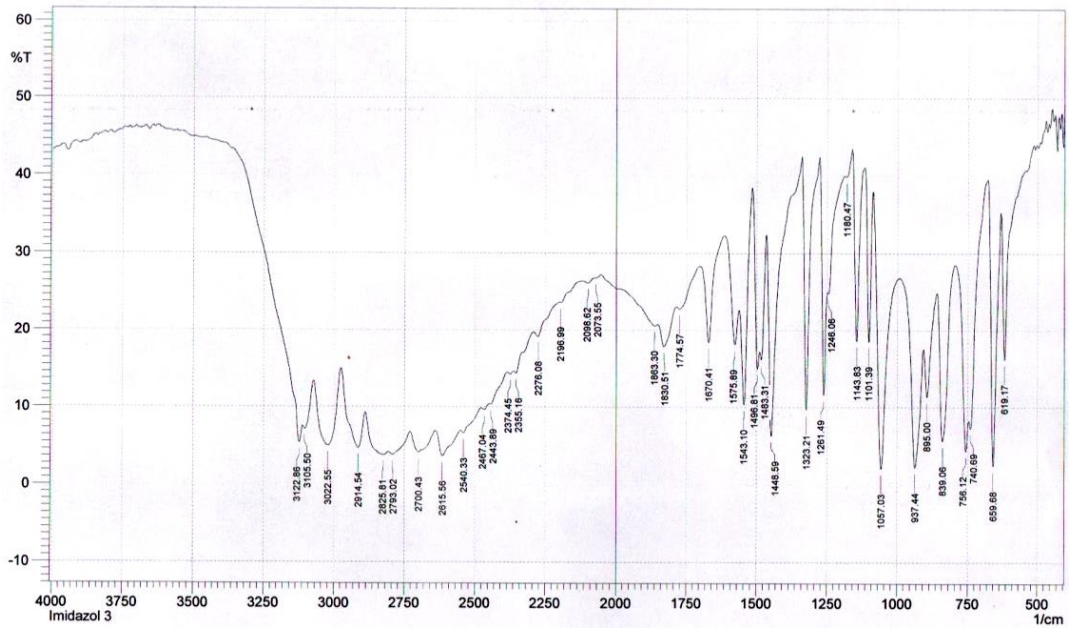


Fig. (1) FTIR spectra of Imidazole.

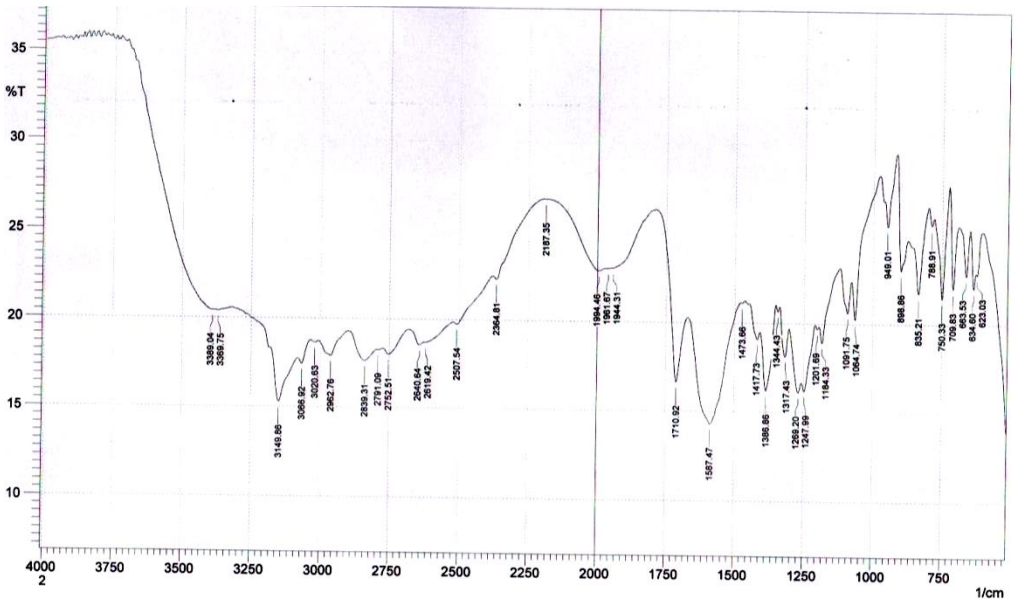


Fig. (2) FTIR spectra of Poly(N- Imidazol maleamic acid).

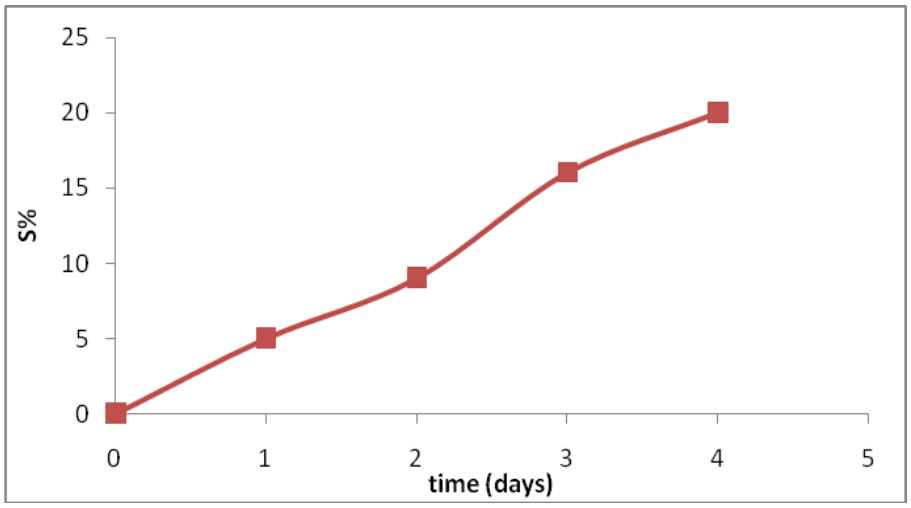


Fig. (3) Swelling curves of polymer in water with pH 7 at 37 °C .

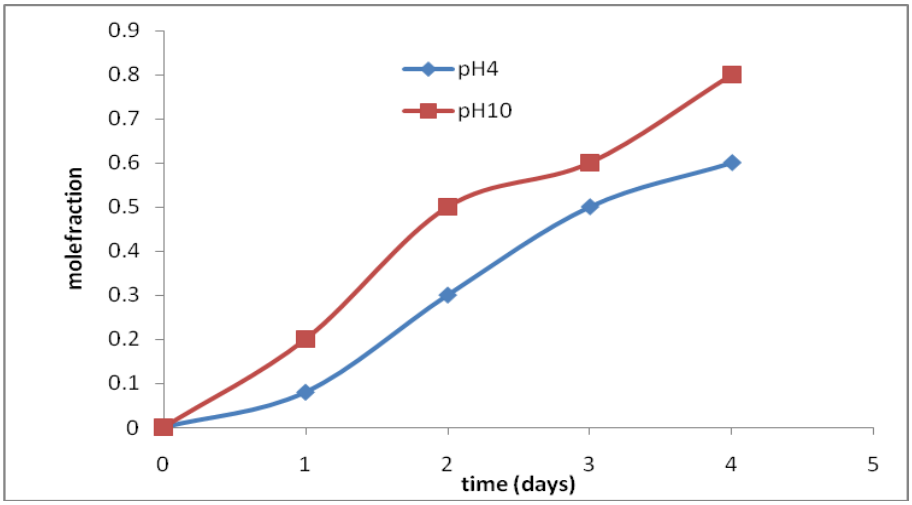


Fig. (4) Controlled release of polymer in different pH value (pH4, pH 10) at 37 ^{0}C .

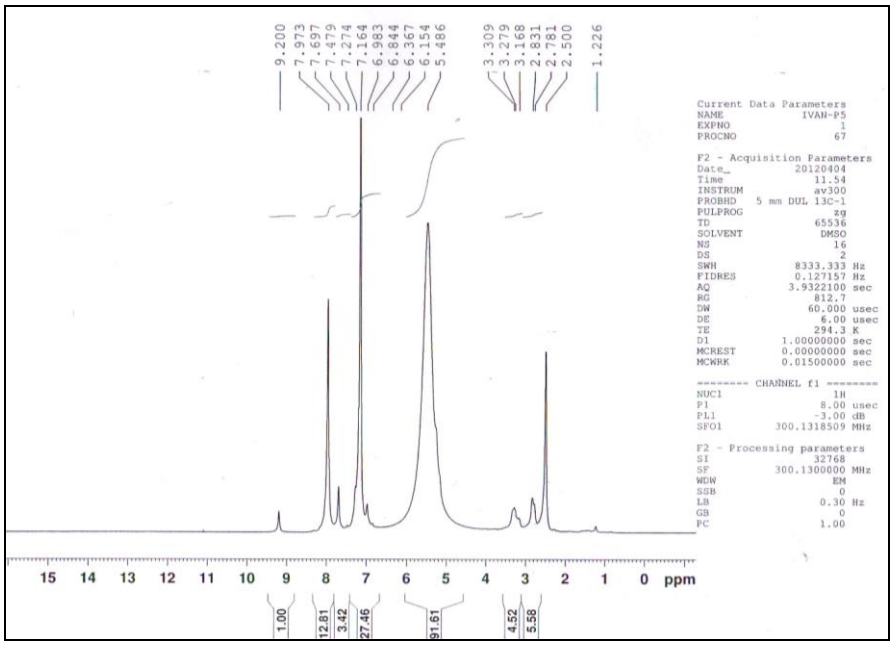


Fig. (5) ^{1}H NMR spectrum of Poly(N- Imidazol maleamic acid).

الخلاصة

حضر في هذا البحث بولي حامض المالي اميك الذي عوض بالايميدازول كمادة فعالة بايولوجيا، وقد حضر من تفاعل حامض الماليئك اللامائي مع الايميدازول وبفتح حلقة الماليئك اللامائي بواسطة الايميدازول، ثم بلمر حامض المالي اميك المعوض بطريقة الجذور الحرة باستعمال الداي بنزويل بيروكسيد. شخص البوليمر المحضر بواسطة طيف الرنين النووي المغناطيسي ومطياف الاشعة تحت الحمراء والاشعة فوق البنفسجية. درست سرع التحرر المحكم لوحدات الايميدازول بدوال حامضية مختلفه وبدرجة ٣٧م، درست جميع الصفات الفيزياوية للبوليمر المحضر.

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