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Gelatin Grafted Procaine Polyacrylamide Polymer Synthesis, Characterization and Study Controlled Release

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Abstract

A new was prepared by reacted of gelatin with acrylic acid in presence of ammonium per-sulfate and the acyl chloride derivative product was modified at 60℃. acyl chloride derivative was reacted with Procaine to give the target molecule. Gelatin was used in current study as a natural nontoxic agent.

All prepared monomers, polymers characterized by FT-IR and ^{1}HNMR techniques, and the controlled release of drug performed at different pH values at certain temperature equal to 37℃. The synthesized method of polymer showed good characterized polymers comparing with other known methods. The synthesized polymer was water soluble and has pharmaceutical application which was considered as a novel biomaterial polymer that can be used as sustained drug delivery agent with increasing the selectivity and specificity of drug.

Keywords: Gelatin, Acrylic acid, Procaine, drug delivery, and pro-drug polymer

1. INTRODUCTION

Gelatin is a biomaterial has different properties such as swelling and soluble in cold water and hot water. Gelatin used in different applications like biodegradable material as a carrier for drugs, hydrogels, and swelling. The researcher interested on using gelatin with different biological activities [1-3].

Manufacturing drug depends on the selection of type of polymer backbone to utilize in the delivery of drugs. Type of selecting polymer concerning with drug compatibility, toxicity, and degradation. Natural polymers is a good substitute for the synthetic polymers due to their side effects can be controlled by natural polymers [4].

Hydrolysis of the drug from polymer backbone slowly reflected the limited efficiency of prodrug polymers. The hydrolysis or enzymatic degradation of the bonds depending on 'the type of the bridging groups. In addition, the activity of these polymers can affected by the class of substitutions and the degree along the polymer [5].

Modification of polymers is the best way to prepare wide range of polymeric drug delivery systems [6]. The purpose of prodrug system is to remove the unfavorable drug properties, like lowest target selectivity, low water soluble, undesirable taste, instable chemically, irritation, and toxicity [7-9]. The improvement of drug therapy determined form the increasing of therapeutic activity and reducing the number of using of the drug, drug release achieved by distribution and temporal control [10, 11].

2. EXPERIMENTAL

Gelatin and dimethylformamide purchased from Merck; acrylic acid purchased from Aldrich, and thionyl chloride obtained from Fluka.^{1}HNMR Shimadzu spectrophotometer in (DMSO-d_6), FT-IR (4000-400cm^{-1}) Shimadzu spectrophotometer, Cintra5-UV.Visble spectrophotometer and Gallenkamp MF B-600 apparatuses were used in the characterization.

2.1 Preparation of graft co-polymerization (F_1).

The solution of Gelatin 2g in10 mL distilled water heated in water bath 60 ºC and a solution of ammonium persulfate 2g in 5ml H_2O added gradually to gelatin solution and stirred for 15 min. After that, acrylic acid 1.5 g was added to solution while the mixture stirred for 10 min. The mixture cooled to room temperature, filtered, washed by ethanol, and dried at 50℃ for 60 min. afforded yellow polymer (F_1) in 69% and the softening point of (F_1) is (105-115) ℃.

2.2 preparation of acrylic co-gelatin Procaine polymer (F_2).

Polymer (F_1) 1.5g was dissolved in dioxane and the mixture (DMF 10 ml + 1ml of thionyl chloride) was added gradually to the solution of F_1 which heated to 50℃ and 1ml of triethylamine with acyl chloride derivative added to solution of Procaine 2g. The mixture stirred under reflux for 2 hrs., then evaporated , washed by ether and dried. The brown polymer (F_2) afforded in 75% and the softening point is (F_2) was (202-212) ℃.

2.3 Drug Release Controlled [12-14]

Pro-drug polymer (F_2) 0.1g was poured in 100 ml of buffer solution like acidic (solution pH 1.1) and (phosphate buffer pH 7.4). Kept the buffer stirring at 37℃ then 4 ml of solution determined by spectrophotometer each time to compare with the computerized calibration curve under similar medium. Fig. (4).

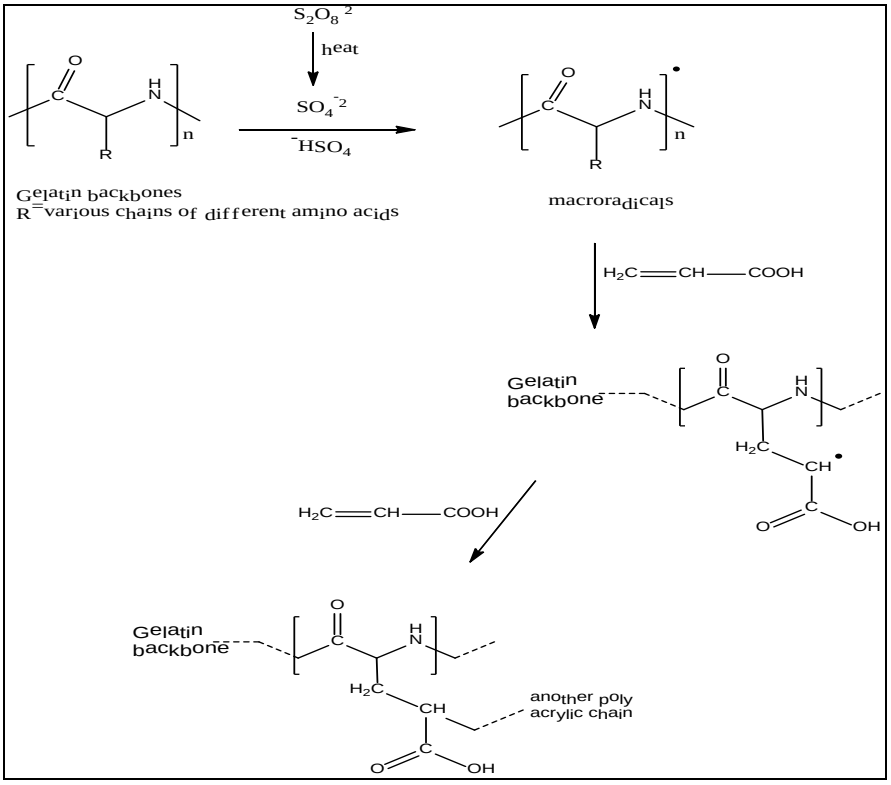
3. RESULTS AND DISCUSSION

Ammonium per-sulfate used as a radical initiator grafted Acrylic acid onto gelatin backbone in a homogeneous medium (scheme 1). Thermally dissociating initiator includes decomposed of ammonium-per sulfate to give anion-radical of sulfate under heating conditions which take hydrogen from the functional group in substrate to form radical that grafted gelatin to form a graft copolymer [15, 16]. Gelatin-g-poly acrylic acid (F_1) was substitution with procaine to convert into gelatin poly acryloyl chloride which reacted with amino derivative to get gelatin procaine amide polymer Scheme (2) [17].

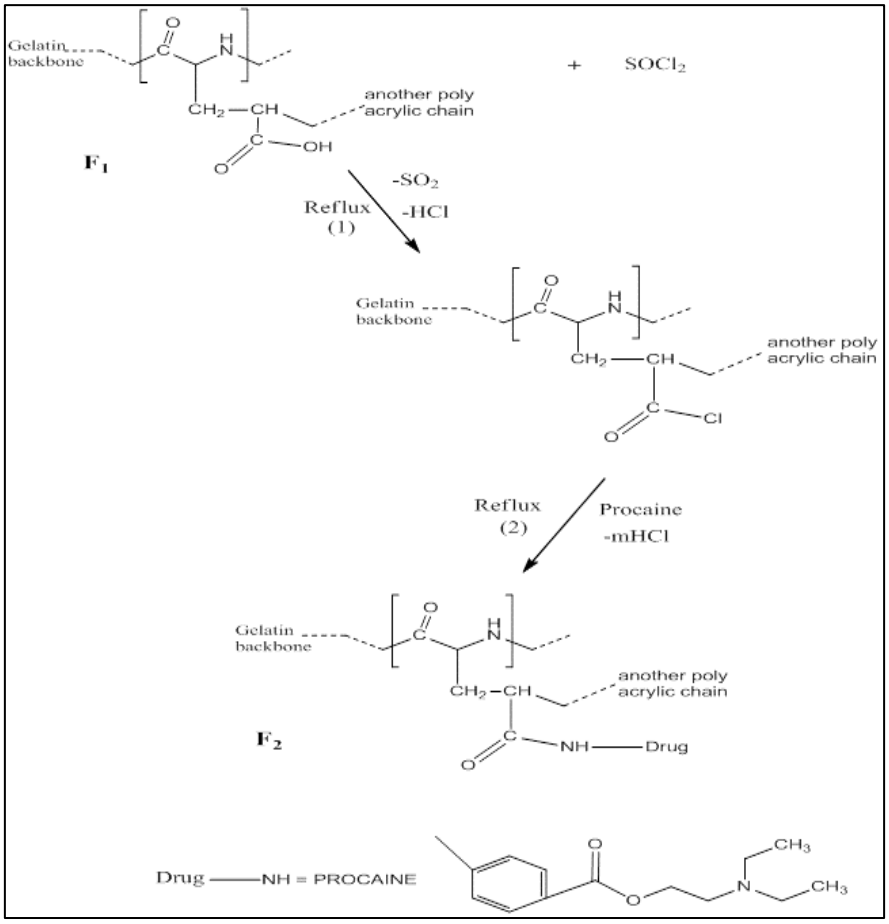
The modified polymers (F_1) and (F_2) FT-IR shows absorption at around 2500-3400 cm^{-1} OH (COOH) of poly acrylic acid. 3220-3400 cm^{-1} due to the amine of Gelatin and 2850-2900 cm^{-1} were of C-H aliphatic. 1728 , 1651cm^{-1} and the bands at 1450 cm^{-1} and 1550 cm^{-1} to C=O ester and amide stretching and abroad bond at 1200 cm^{-1} to C-N group, Fig(1). Figure 2 showed the FTIR spectrum of F_2, appearance of absorption at 3362cm^{-1} of –OH stretching carboxylic group and broad bond at 3240-3540 cm^{-1} amine of gelatin. C-H aliphatic at 2781-2958 cm^{-1}, 3047 cm^{-1} of CH aromatic, 1641 cm^{-1} for C=O amid. The bands were appeared at 1480 cm^{-1} and 1560 cm^{-1} to C=O in carboxyl amide of Gelatin. A broad bond at 1250 cm^{-1} of C-N bond, peak appeared at 1649 cm^{-1} for C=O amide. [18]

^{1}HNMR spectrum of polymer F_2 as shows the signal δ: 1.6 ppm ($2CH_2$−CH, 2H, d.) δ: 2.3 ppm (CHCOOH, 1H), δ: 2.3 ppm (CH−CO,1H), 2.8 ppm (C−NH,1H, d.) δ: 2.9 ppm (CH−NH, 1H) of Gelatin, δ: 6.95 ppm (NH_2, 2H), δ: 7.4 ppm (NH, 1H, d.), δ: 7.7- δ:7.8 ppm (3H). of aromatic ring, δ: 8.5 -9. ppm of (4H), δ: 11.4 ppm (COOH, 1H, S.). Fig (3), [19]

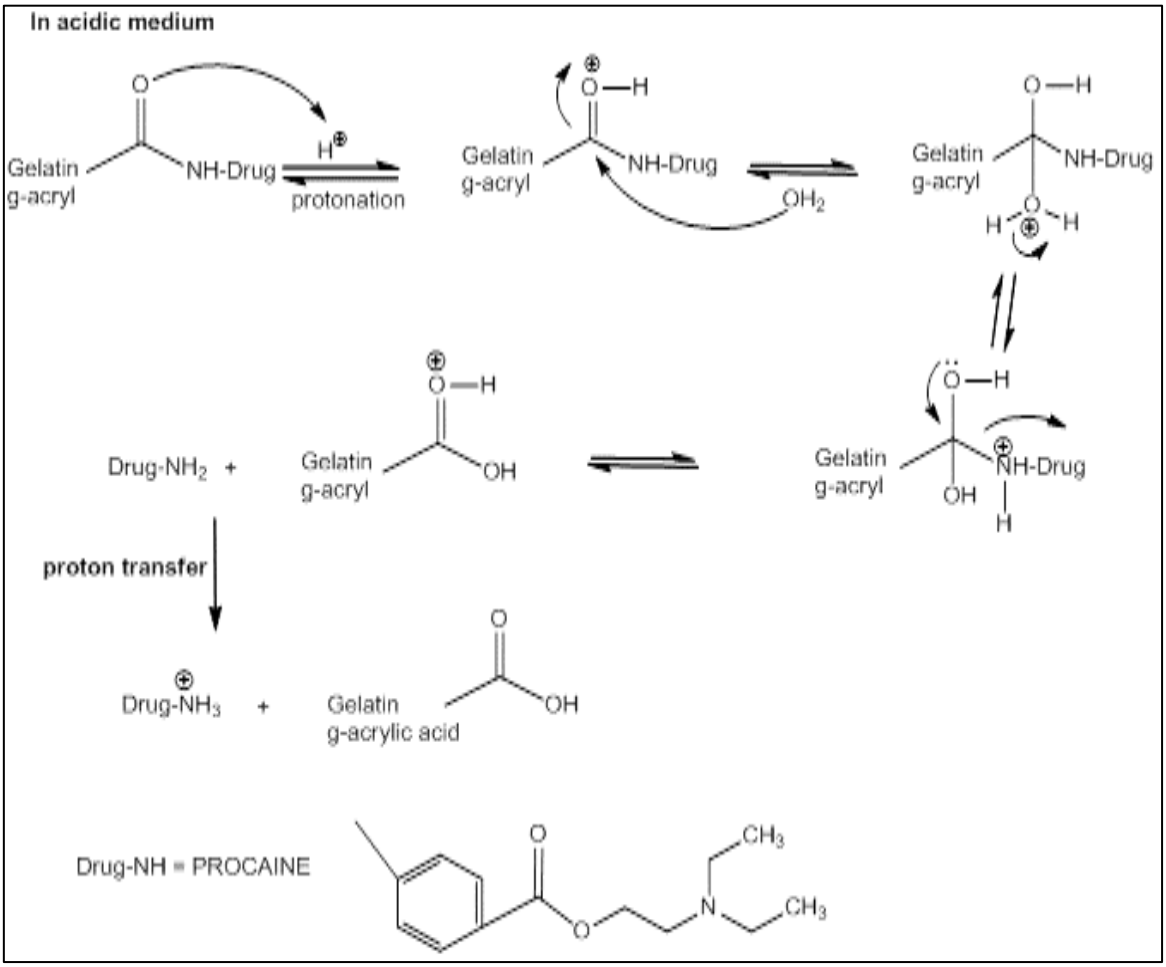
The UV. Spectrum of (F_2) show absorbance at 220 and 355 nm due to. (n-π*) and (π-π*) prove that electron transition for drug conjugation structures. Hydrolyzed the prodrug in acidic or basic solution due to ester bonds evaluated by study the controlled release rates (Schemes 3 and 4) [20,21]:-



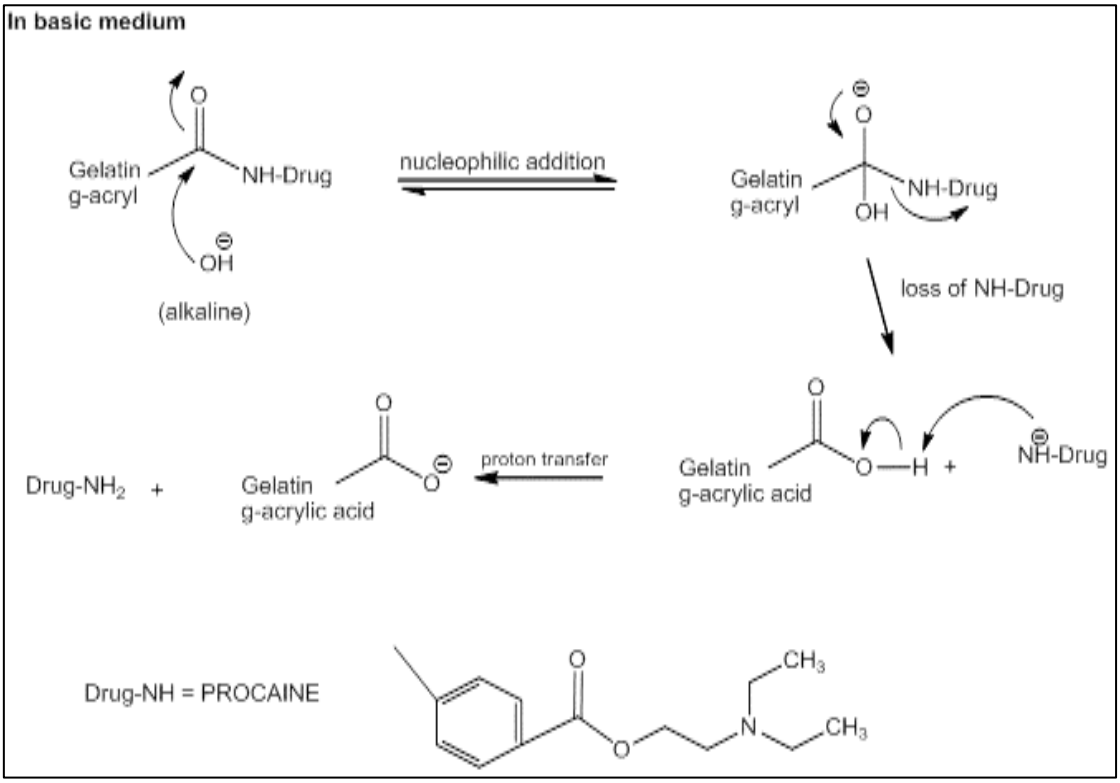
Scheme 1: Synthesis of polymer F1



Scheme 2: Synthesis of polymer F2



Scheme 3: Hydrolysis F_2 in acidic solution



Scheme (4) Hydrolysis in basic medium for (F_2)

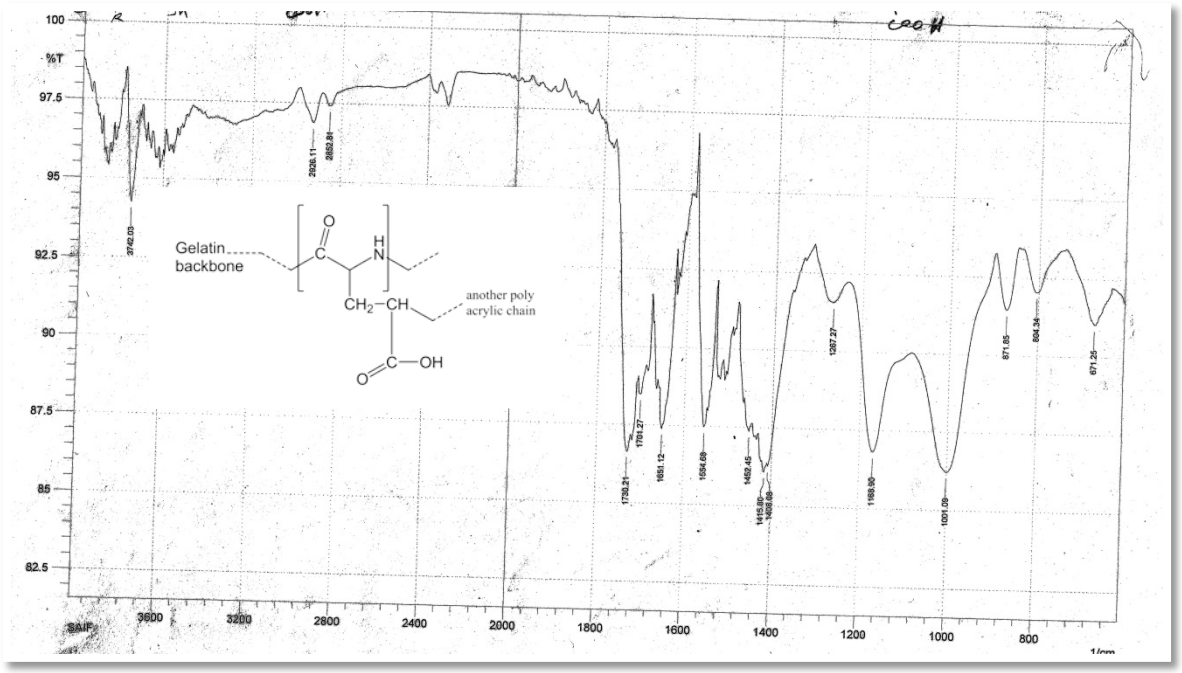


Fig. 1: FT-IR spectrum of (F_1)

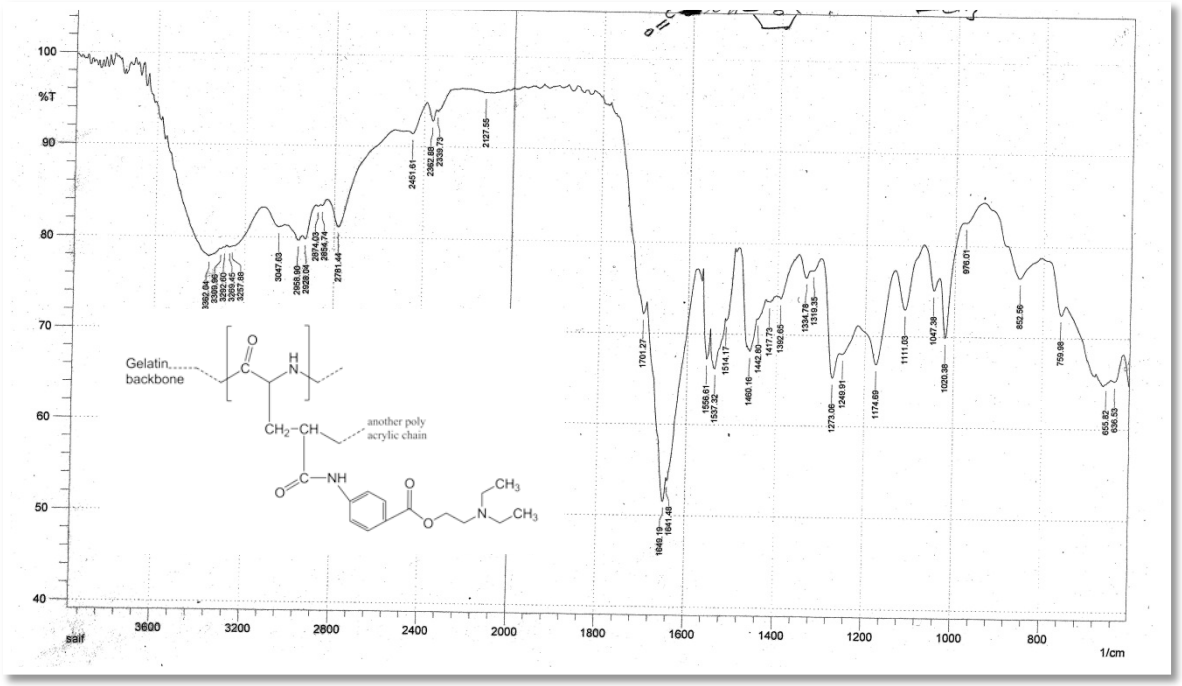


Fig. 2: FT-IR spectrum of (F_2)

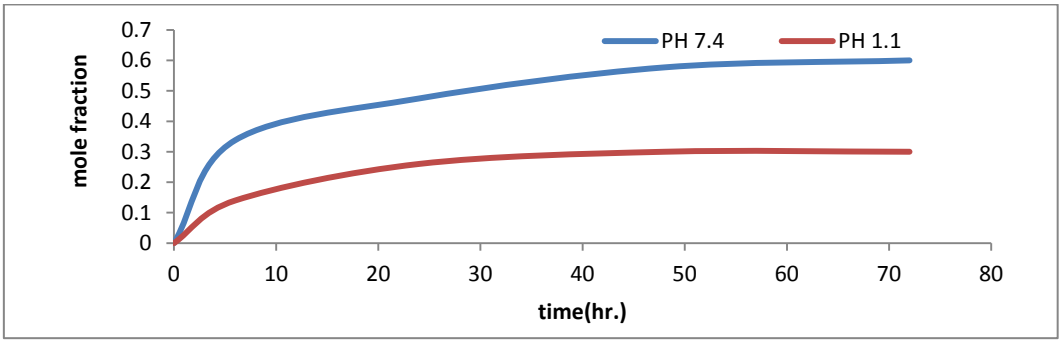


Fig (4): Release of drug from F_2 in pH 1.1 and 7.4 at 37°C

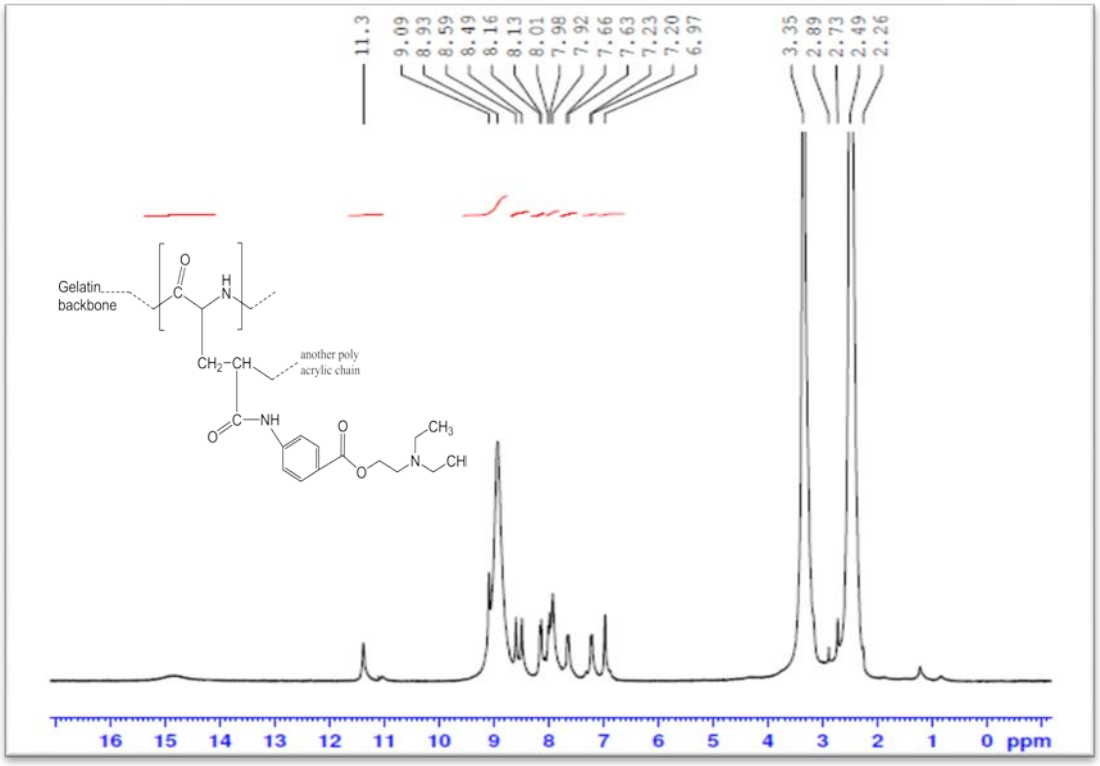


Fig.(3): H-NMR spectrum of polymer (F2)

4. Conclusion

A new Gelatin-grafted N- Procaine polyacrylamide was synthesized where grafted gelatin reacted with acrylic acid in presence of ammonium pesulfate. The product was modified to the acyl chloride derivative and substitution of amino group of procaine. The synthesized polymer was investigated by FTIR and ^{1}H-NMR techniques the synthesized method of polymer showed good characterized polymers comparing with other known methods. The controlled drug release as drug polymers was studied in basic and acidic medium in different pH values which hydrolyzed due to ester bonds at certain temperature equal to 37℃.

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