

Gum Acacia and Methacrylic Acid Hydrogels: Preparation and Swelling Characteristics

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Abstract— pH sensitive hydrogels of gum acacia (GA) and poly(methacrylic acid)(PMA) were synthesized by ceric ion initiated graft copolymerization in aqueous medium in the presence of varying amount of N, N-methylene bisacrylamide as a crosslinking agent. The copolymers were characterized by FTIR spectroscopy and swelling measurement. These hydrogels were used for the in vitro drug release studies using paracetamol as the model drug. The drug release was studied as a function of pH. The release was much slower in first 3 hrs at pH 1.2 for all the hydrogels which may attribute to the matrix compaction and stabilization through hydrogen bonding at lower pH. At pH 7.4 the amount of drug release was 60 – 70% in 12 hr. The kinetic study shows that the release of the drug from hydrogels was probably controlled by the swelling and relaxation of the polymers indication a super case II transport. These results indicate that the hydrogels may be useful to overcome the harsh environment of the stomach and can be used as excipient in colon targeting matrices.

Keywords: PMA, GA, IPN

I. INTRODUCTION

Hydrogels are water swollen polymer matrices, with a huge tendency to absorb water. Their capacity to swell, under physiological conditions, makes them a perfect material for biomedical applications [1]. The hydrophilicity of the network is due to the presence of chemical residues such as hydroxylic, carboxylic, amidic, and primary amidic and others that can be present within the polymer backbone or as chains. It is possible to produce hydrogels containing a hydrophobic chain by blending or copolymerizing hydrophilic and hydrophobic polymers, or by producing interpenetrating networks (IPN) or semi-interpenetrating polymer networks (s-IPN) of hydrophobic and hydrophilic polymers. Hydrogels can be prepared from natural polymers such as collagen, alginate, cellulose, starch, chitosan. Polysaccharides graft copolymerized with acrylic acid or acrylamide form super absorbent hydrogels, with water absorption as high as 420 times its weight[2]. Several hydrogels have been prepared by crosslinking of water soluble natural or synthetic polymers. Chemical crosslinking involves use of a difunctional reagent. Physical crosslinking has been achieved through several ways [3] such as ionic interactions [4-7], crystallization [8], hydrogen bonds [9-10], protein interaction [11] and hydrophobic interaction [12]. Hydrogel network structure depends on several factors such as the nature of the monomer and the crosslinking agent, the degree of crosslinking, method of preparation, and use of solvent. Depending on the substituent groups on the monomer, the hydrogels may be neutral, anionic, cationic or ampholytic.

Hydrogels have been widely applied as intelligent carriers in controlled drug delivery systems, Temperature-sensitive hydrogels [13], pH sensitive hydrogels, Glucose-sensitive hydrogels [14], Other stimuli sensitive hydrogels [15].

In the present investigation we have used a natural polysaccharide material i.e. Gum Acacia also known as Gum Arabic. Gum arabic is a branched, neutral or slightly acidic, complex polysaccharide obtained as a mixed calcium, magnesium, and potassium salt. The backbone consists of 1,3-linked β -D-galactopyranosyl units and the side chains are composed of two to five 1,3-linked β -D-galactopyranosyl units, joined to the main chain by 1,6-linkages. Both the main and the side chains contain units of α -L-arabinofuranosyl, α -L-rhamnopyranosyl, β -D-glucuronopyranosyl, and 4-O-methyl- β -D-glucuronopyranosyl, the latter two mostly as end-units [16]. Gum Arabic has excellent emulsifying properties, artificial sweeteners, in chewing gum as a coating agent and as a pigment stabilizer. In aerated confectionery products, such as marshmallows, nougats, and meringues, Gum Arabic acts as a whipping and stabilizing agent. It is still used as a suspending agent, emulsifier, adhesive, and binder in tableting and in demulcent syrups. Gum Arabic functions as a stabilizer in lotions and protective creams, where it increases viscosity, imparts spreading properties, and provides a protective coating and a smooth feel. It is used as an adhesive agent in blusher and as a foam stabilizer in liquid soaps. Gum Arabic is also used in the preparation of etching and plating solutions in the lithography industry. It is used as a dispersant in paints and insecticidal/ acaricidal emulsions [17]. In this investigation, we have grafted methacrylic acid onto Gum Acacia using ceric ammonium nitrate (CAN) as an initiator in aqueous medium and with varying the amount of crosslinker N,N methylene bis acrylamide. These hydrogels were used as matrix for the study of release rate of paracetamol as a model drug, at two different pH, 1.2 and 7.4.

II. EXPERIMENTAL

A. Material

Gum acacia (s.d. Fine chemicals, India) was used. Methacrylic acid (Thomas Baker, India), was freshly distilled under reduced pressure before use. Ceric ammonium nitrate (Qualigens, Germany) was dried at 110C for 1 h. N,N'-methylene bis acrylamide (Thomas Baker, India), Paracetamol (Gift sample from Vamsi Labs, India) and other chemicals were used as such.

B. Preparation of Hydrogels

Gum Acacia (2g) was dissolved in distilled water with constant stirring for 1h at 70°C under nitrogen atmosphere. It was allowed to cool and ceric ammonium nitrate (0.005M in 1M HNO₃) was added over a period of 15 minutes, followed

by addition of required amounts of distilled methacrylic acid and crosslinker N, N–methylene bisacrylamide. The reaction was proceeded under N₂ atmosphere for 3h at 37°C. After completion of the reaction the hydrogel was washed 2-3 times with distilled water to remove homopolymers, if any, and filtered through sintered crucible. The final product was dried under vacuum until constant weight [18]. A series of hydrogels were prepared by varying the amount of crosslinker (0.5, 2.0 and 5.0 mole %).

C. IR Spectral Analysis

IR spectra of gum acacia (GA), poly (methacrylic acid) (PAA) and the graft copolymer were taken on Perkin Elmer FTIR spectrum BS spectrophotometer using KBr pellet technique.

D. Swelling Studies

The equilibrium swelling was measured according to a conventional “tea bag” method. The completely dried preweighed hydrogel sample was placed in 200 mL of distilled water and buffer solution of desired pH at 37°C, respectively. The swollen gel was taken out at regular time intervals, wiped superficially with filter paper to remove surface water, weighed, and then placed in the same bath. The mass measurements were continued until the attainment of the equilibrium. The percentage of mass swelling (Se) was determined using the following expression¹⁷.

$$\%Se = \frac{Mt - Mo}{Mo} \times 100$$

where Mo and Mt are the initial mass and mass at different time intervals, respectively. All the experiments were carried out with three samples and the average values have been reported in the data.

E. Tablet Preparation

Two hundred milligrams of hydrogel and paracetamol (200 mg) were mixed until homogenous mixture was obtained and directly compressed in hydraulic press using a 12-mm flat faced punch of a force of 90 kg/cm² to obtain tablets.

F. In Vitro Drug Release Studies

To study the release of the drug from the tablets, the tablets were placed in 50 mL of phosphate buffer solution of pH 7.4 (USP XXIII) at 37°C under unstirred condition as well as in simulated gastric fluid pH 1.2 (2 g NaCl + 7 mL conc. HCl, diluted to 1 L by distilled water, USP XXIII). After predetermined time interval, the aliquot was removed and its absorbance was measured on Shimadzu UV–vis spectrophotometer at $\lambda_{max}=299$ nm.

G. Statistical Analysis

All the data are the means of results from three experiments \pm SD. Statistical data analysis was performed using the one-way variance with P<0.05 as the minimum level of significance.

III. RESULT AND DISCUSSIONS

Gum acacia-based copolymer hydrogels were synthesized by free radical copolymerization of methacrylic acid onto the gum using methylene bis acrylamide as crosslinker.

A. Spectral Analysis

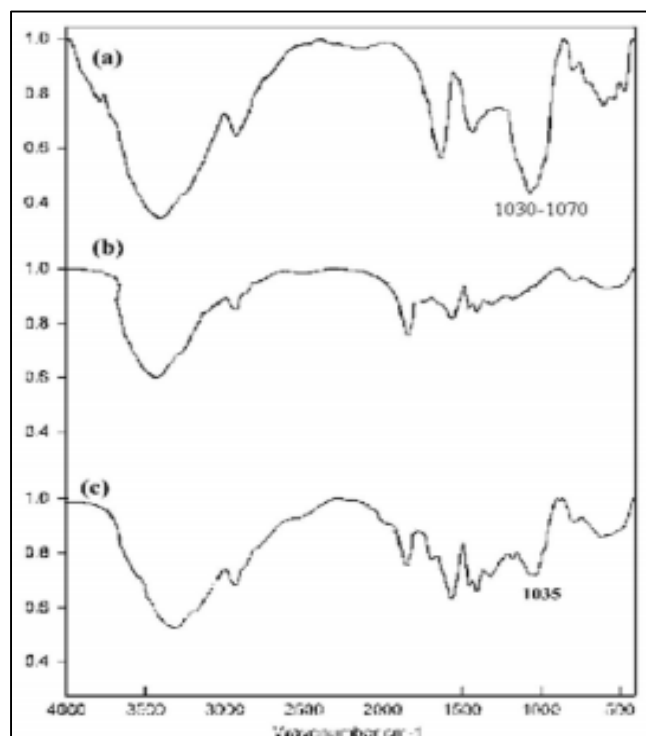


Fig. 1: FTIR spectra of the gum acacia (GA) (a), poly (methacrylic acid)(PMA) (b), and GA-methacrylic copolymer (c).

Fig. 1 shows the FTIR spectra of the gum acacia (GA) (a), poly (methacrylic acid)(PMA) (b), and GA-methacrylic copolymer (c). As indicated in Figure 1(c), characteristic bands of both the gum and of the poly(methacrylic acid), are present in the spectrum of hydrogel. The strong, broad peak at 3427 cm⁻¹ is related to the OH stretching of the carboxylic and hydroxyl groups of methacrylic and polysaccharide parts. The medium peaks at 1030–1070 cm⁻¹, due to stretching vibration of C–O–C and C–O–H bonds, confirm the polysaccharide structure of the hydrogel. The very sharp peak at 1717 cm⁻¹ is attributed to the carboxyl groups (>C=O stretching) of PMA and the IR spectra also shows a shoulder at 2179 cm⁻¹, which is due to the presence of the –C–N–group of the crosslinking agent (N,N–methylene bisacrylamide). Since the copolymers had already been extracted to remove the soluble contents, its FTIR analysis proved that it is not a physical mixture but chemical linkages have been formed during the free radical polymerization reaction.

B. Swelling Kinetics

The swelling behavior of hydrogel is influenced, besides its chemical composition, by several factors such as pH, temperature of swelling media and the amount of crosslinker used. To ascertain the effect of pH, swelling measurements were conducted in media of pH 1.2 and 7.4 at 37°C. Table 1 shows that at pH 1.2, the percent swelling decreases with increasing the amount of the crosslinker. Thus the extent of swelling in pH 1.2 at 37°C for GA-PMA 1, GA-PMA 2 and GA-PMA 3 was 174%, 143% and 108%; at pH 7.4 was 665%, 599%, and 396% respectively figure 2 and 3.

Sr. No	Crosslinker (N,N-methylene bisacrylamide) (mole%)	Equilibrium swelling Se in	
		pH 1.2	pH 7.4
1	0.5	174	665
2	2	143	599
3	5	108	396

Table 1: Gum acacia-methacrylic acid graft copolymer hydrogels

The data indicate that as the mole percent of the crosslinking agent increases, the equilibrium swelling (Table 1) as well as time the amount of water absorbed at different time interval (Figure 2 and 3) decreases. This may be attributed to the fact that as the mole percent of crosslinking agent increases, the number of crosslinks per unit volume increases and the chain length between the crosslinks decreases resulting in decrease in the free space available between the crosslinks and thus providing less space for accommodation of water molecules in the networks¹⁷. The pH of the swelling medium plays an important role in influencing swelling behavior of hydrogels. If the hydrogel contains some ionizable groups, which can dissociate or get protonated at some suitable pH of the swelling media, then the degree of swelling of hydrogels undergoes appreciable change with external pH. Figure 3 and 4 depict the dynamic uptake of water by the hydrogels in the buffer media of pH 1.2 and 7.4, respectively, at 37°C. The hydrogel exhibits low swelling in the medium of pH 1.2, and high swelling at pH 7.4. The degree of swelling increases with time until reaches the equilibrium value. The pH dependant swelling can be attributed to the fact that when the hydrogel is allowed to swell in the media of pH 1.2, the -COOH groups present within the network remain almost nonionized, thus imparting almost nonpolyelectrolyte type behavior to the hydrogel. Moreover, there exist strong H-bonding interactions between -COOH groups of acrylic acid and hydroxyl groups of gum acacia, resulting in a compact structure that does not permit much movement of polymeric segments within the hydrogel, thereby, restricting the water uptake. However, in the medium of pH 7.4, the almost complete ionization of -COOH groups results in extensive chain relaxation due to repulsion among similarly charged -COO⁻ groups present along the macromolecular chains. Moreover, the ionization also causes an increase in ion osmotic pressure. These two factors are thus responsible for a higher degree of swelling in the medium of pH 7.4.

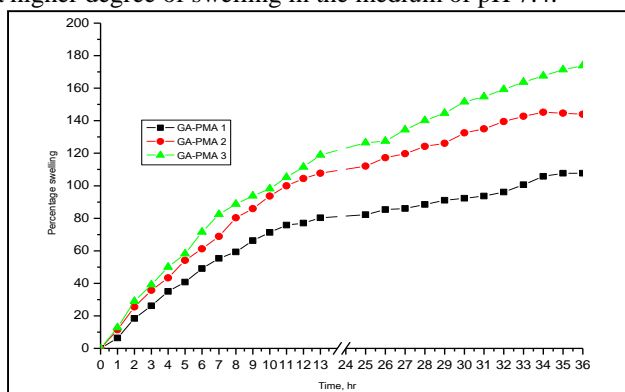


Fig. 2: Dynamic uptake of water as a function of time for GA – PMA graft copolymer hydrogels with different degrees of crosslinking at pH 1.2

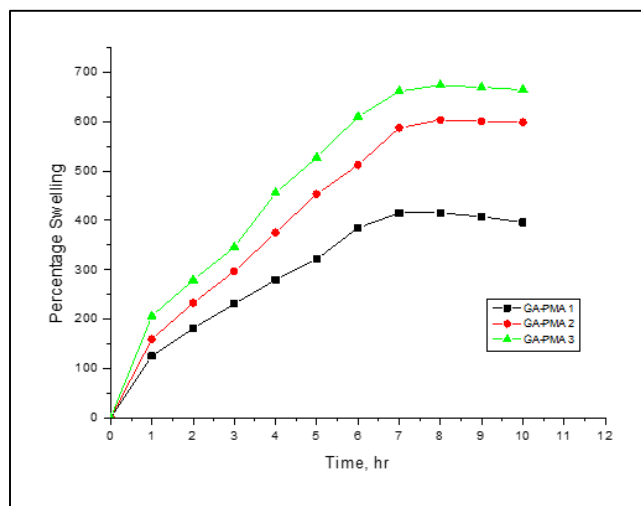


Fig. 3: Dynamic uptake of water as a function of time for GA – PMA graft copolymer hydrogels with different degrees of crosslinking at pH 7.4

IV. CONCLUSION

From the results obtained in above study, it can be concluded that the graft copolymer hydrogels prepared from gum acacia and methacrylic acid undergo a sharp volume phase transition with the change in pH of the swelling medium from an acid to an alkaline one, thus suggesting that diffusion of the entrapped drug will be greatly enhanced with a change in pH of the medium. The amount of crosslinker also influences the water uptake of hydrogels. Finally, the hydrogels seems to have potential to be used for colon targeted drug delivery through oral administration.

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