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# Collagen-based highly porous hydrogel without any porogen: Synthesis and characteristics

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**Abstract**

In this contribution we have developed a collagen-based highly porous hydrogel by neutralizing the grafted poly(acrylamide-co-acrylic acid) after gel formation. Preparation of the hydrogels involved free radical polymerization of a combination of hydrolyzed collagen, acrylic acid (AA), acrylamide (AAm) and distilled water, in appropriate amounts and contained a crosslinking agent called $N,N'$-methylene bisacrylamide (MBA). The chemical structure of the hydrogels was characterized by means of FTIR spectroscopy, DSC and TGA thermal methods. Morphology of the samples was examined by scanning electron microscopy (SEM). Systematically, the certain variables of the graft copolymerization were optimized to achieve maximum swelling capacity. The absorbency under load (AUL) and centrifuge retention capacity (CRC) were measured. The swelling ratio in various salt solutions was also determined and additionally, the swelling of hydrogels was measured in solutions with pH ranged 1–13. The synthesized hydrogel exhibited a pH-responsiveness character so that a swelling-collapsing pulsatile behavior was recorded at pH 2 and 8.


*Keywords:* Protein; Hydrogel; Porous; Hydrolyzed collagen; Swelling behavior

## 1. Introduction

Hydrogels are chemically or physically cross-linked hydrophilic networks that do not dissolve in water at a physiological temperature or pH, but swell considerably in an aqueous medium [1,2]. Since their response to changing environmental conditions such as temperature [3], pH [4] and solvent composition [5], these materials have been attracting much attention in medical and mechanical engineering fields. However, the technological success of these applications is today limited by their low efficiency and slow rate of response. The efficiency and the response rate of the gel to external stimuli can be adapted by controlling the degree of porosity.

The porosity plays the multiple role of enhancing the total water sorption capability and the rate of response by reducing the transport resistance [6,7]. Therefore, creation of porosity in hydrogels has been considered as an important process in many ways. The phase-separation technique [8], the water-soluble porogens [9] and the foaming technique [10,11] are three different methods for preparing porous hydrogel structures.

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Natural-based hydrogels have attracted in medical and pharmaceutical interests since their non-toxicity, biocompatibility and biodegradability. Because of a few studies have been reported in the case of protein-based hydrogels [12–14], this paper deals to describe the preparation and characterization of a hydrolyzed collagen-*g*-poly(acrylamide-*co*-sodium acrylate) porous hydrogel as a new natural-based polymer. As a consequence of the collagen sensitivity to alkaline hydrolysis, it was not practicable to prepare poly(acrylamide-co-sodium acrylate) copolymer directly from partially hydrolysis of polyacrylamide. The effect of reaction variables affecting the water absorbency of the hydrogel and swelling behavior in various salt and pH solutions was investigated. Morphology studies were shown that the pores were induced into the gel by water evaporation resulting from neutralization heat.

## 2. Experimental

### 2.1. Materials

Hydrolyzed collagen (Parvar Novin-E Tehran Co.) was industrial grade which is available in market and has nearly 25% insoluble phosphate salt. *N*,*N*′-methylene bisacrylamide and potassium persulfate (Fluka), acrylic acid and acryl amide (Merk) were used without further purification. All other chemicals were also analytical grade. Double distilled water was used for the hydrogel preparation and swelling measurements.

### 2.2. Preparation of hydrogel

Hydrolyzed collagen (1.33 g) was dissolved in 50 ml distilled water and filtered to remove its insoluble phosphate salt. Then the solution was added to a three-neck reactor equipped with a mechanical stirrer (Heidolph RZR 2021, three blade propeller type, 300 rpm). The reactor was immersed in a thermostated water bath preset at a desired temperature (80 °C). Then the initiator solution (0.02–0.14 g KPS in 5 ml $H_2O$) were added to the mixture. After stirring for 5 min, certain weight ratio of AAm/AA (0.19–8.75 g in 10 ml $H_2O$) and MBA (0.02–0.14 g in 5 ml $H_2O$) were simultaneously added to the reaction mixture. After 60 min, the certain amount of 1 N NaOH solution, depend on AA content, was added to the produced hydrogel. The mixture was immediately stirred vigorously using a spatula for 2 min and then poured to excess non solvent ethanol (200 ml) and remained for 3 h to dewater. After ethanol was decanted, the product scissored to small pieces (diameter ~ 5 mm). Again, 100 ml fresh ethanol was added and the hydrogel was remained for 24 h. Finally, the filtered hydrogel is dried in oven at 60 °C for 10 h. After grinding, the resulted powder was stored away from moisture, heat and light.

### 2.3. Swelling measurements using tea bag method

The tea bag (i.e. a 100 mesh nylon screen) containing an accurately weighed powdered sample ($0.1 \pm 0.001$ g) was immersed entirely in 200 ml distilled water and allowed to soak for 2 h at room temperature. The sample particle sizes were 40–60 meshes (250–400 μm). The tea bag was hung up for 15 min in order to remove the excess solution. The equilibrium swelling (ES) was calculated according to following equation:

$$\mathrm{ES}\ (\mathrm{g/g}) = W_s - W_d/W_d \tag{1}$$

where $W_s$ and $W_d$ are the weights of the swollen superabsorbent and the dry sample, respectively.

### 2.4. Swelling in various salt solutions

Hydrogel absorbency was evaluated in 0.15 M solutions of LiCl, NaCl, KCl, CsCl, $MgCl_2$, $CaCl_2$, $SrCl_2$, and $BaCl_2$ according to the above method described for swelling measurement in distilled water. In addition, swelling capacity of the hydrogel was measured in different concentration of NaCl, $CaCl_2$, and $AlCl_3$ salt solutions.

### 2.5. Absorbency at various pH values

Individual solutions with acidic and basic pH values were prepared by dilution of NaOH (pH 13.0) and HCl (pH 1.0) solutions to achieve pH $\geqslant$ 6.0 and pH < 6.0, respectively. The pH values were precisely checked by a pH-meter (Metrohm/620, accuracy ±0.1). Then, 0.5 (±0.001) g of the dried hydrogel was used for the swelling measurements according to Eq. (1).

### 2.6. pH-sensitivity

pH-sensitivity of the hydrogel was investigated in terms of swelling and deswelling of the final product at two basic (pH 8.0) and acidic (pH 2.0) solutions, respectively. Swelling capacity of the hydrogels at