Interpenetrating hydrogel networks: 3. Properties of the gelatin–sodium carboxymethylcellulose system*

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The aqueous solubility of gelatin and the sodium salt of carboxymethylcellulose (CMC) together with the sol$\rightleftharpoons$gel transition of gelatin and its crosslinking reaction with glutaraldehyde is exploited to synthesize interpenetrating complexes of these two macromolecules. This material exhibits swelling properties, typical of ionic hydrogels, which vary as a function of CMC content. Several compositions were cast into films. The protein component contributed more towards the mechanical properties of these films. The gels responded to an electric stimulus by a change in dimensions. The striking compositional resemblance of this system to cartilage tissues is discussed.

(Keywords: hydrogels; protein; polysaccharide; cartilage)

INTRODUCTION

Biological hydrogels are usually protein–polysaccharide systems as, for example, in cartilage tissues, where collagen fibres are laid out in the mucopolysaccharide matrix[1]. However, the synthetic hydrogels developed exclusively for biomedical applications have a totally alien chemistry and structure. They are generally crosslinked polymer networks of hydrophilic acrylates or methacrylates. It is indeed surprising that very little effort has been focused on developing hydrogel systems closer in chemistry and composition to their biological counterparts. Since it is impossible to mimick the architecture of a biological hydrogel composite simpler alternatives were explored. Gelatin, the water soluble degradation fragment of collagen, was chosen as the protein component because of its ability to undergo a sol$\rightleftharpoons$gel transition in concentrated aqueous solutions[2]. The gelation of gelatin involves the formation of collagen-like folds through a number of favourably placed hydrogen bonds. This transition can be induced in the presence of a polysaccharide. This should lead to the formation of a protein network with entrapped polysaccharide. The entire topology could subsequently be reinforced with glutaraldehyde crosslinking[3–7]. This should yield a hydrogel composite with compositional and at least limited structural and functional resemblance to a biological hydrogel. The sodium salt of carboxymethylcellulose (CMC) was used as the polysaccharide, because of its water solubility, mucous-like consistency and its ability to interact with gelatin leading to complexation[8]. This paper reports the interesting features of this interpenetrating hydrogel network system.

EXPERIMENTAL

Gelatin, the sodium salt of CMC, glutaraldehyde (25% aqueous solution) and other chemicals were supplied by Loba Chemicals, Bombay.

Blocks of the interpenetrating networks (IPNs) were prepared by pouring aqueous solutions of CMC and gelatin onto rectangular moulds and allowing to set overnight. The firm gels were carefully dislodged and immersed in aqueous solutions of 1% glutaraldehyde for 6 h.

The blocks were allowed to dry at room temperature for several days to constant weight. The swelling studies were carried out by immersing the blocks in double distilled water or aqueous saline solutions as described elsewhere[9]. The time-dependent swelling was followed gravimetrically. The swelling capacity was taken as the ratio of the equilibrium swelling capacity weight (w_s) to the initial dry weight (w_d).

The electric responses of the gel were monitored in a perspex cell ($8 \times 2 \times 2\,\text{cm}^3$) fitted with thin platinum wire electrodes. Distilled water was used as the suspending medium for the gel.

Films of the IPNs were made by casting the respective solutions onto silicon-coated perspex sheets and allowing them to dry at room temperature. The thickness of the films was measured using a hand-held micrometer. The mechanical tests were carried out using an Instron universal (model 1026) instrument. The specimens (200 μm thick and 2.5 cm wide) used were 5 cm long.

RESULTS AND DISCUSSION

The swelling behaviour of ionic networks in electrolyte solutions is a function of the ionic strength of the

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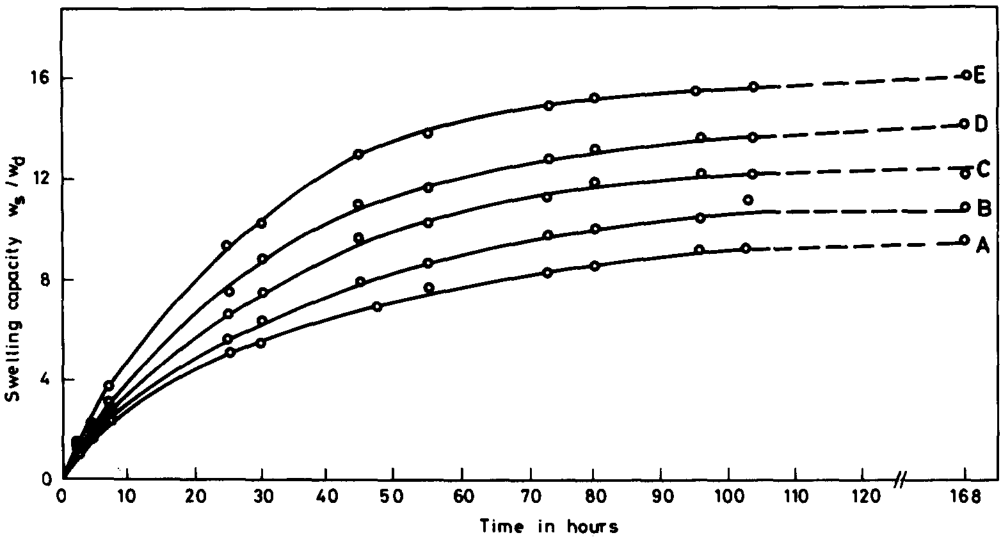

Figure 1 Swelling pattern of crosslinked gelatin–CMC semi IPNs in distilled water. The gelatin–CMC (w/w) ratios are: (A) 1:0.05; (B) 1:0.10; (C) 1:0.15; (D) 1:0.20; (E) 1:0.25

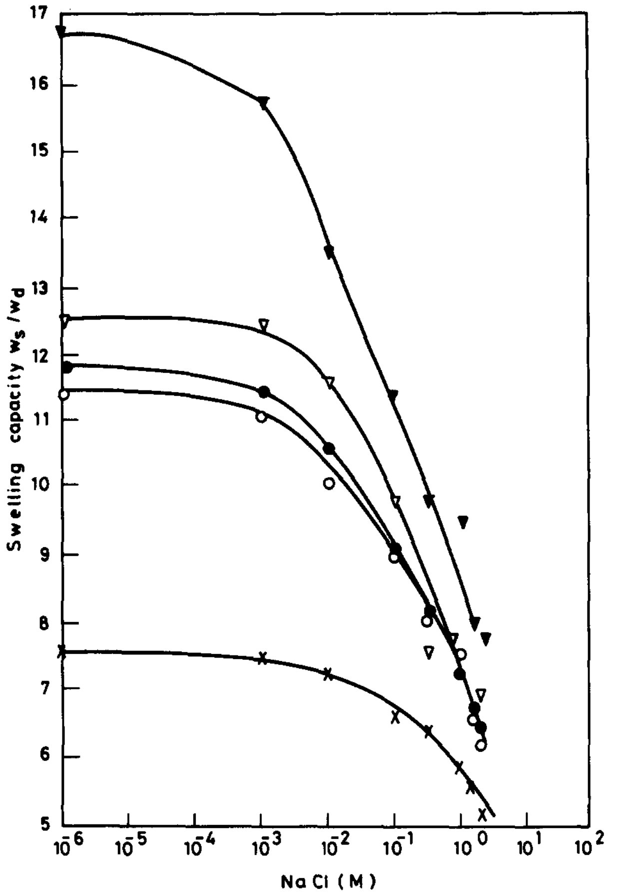

Figure 2 Swelling behaviour of crosslinked gelatin–CMC semi IPNs as a function of sodium chloride concentration. The gelatin–CMC (w/w) ratios are: (×) 2:0.1; (○) 2:0.2; (●) 2:0.3; (▽) 2:0.4; (▼) 2:0.5

medium[9–13]. The thermodynamic interpretations of the swelling phenomena of polyelectrolyte gels involve three processes: the polymer–solvent mixing, the accompanying changes in the topology of the chain segments and the interaction between the fixed charges of the network and the mobile counter ions of the swelling medium. Conceptually one can equate the combination of these forces to the swelling pressure. At the swelling equilibrium, the effective swelling pressure experienced by the gel is zero.

Several schools[9–13] have attempted to construct theoretical models for the swelling of neutral and ionic networks to analyse the experimental values obtained. It has been pointed out that insufficient data on the gel structure prevents closer correspondence between theoretical predictions and experimental observations. For this reason, we had reservations in applying general swelling laws to the gelatin–CMC networks. Our attempts were limited to correlating composition with the equilibrium swelling. Although there is a definite interaction leading to complexation between gelatin and CMC, the nature of the interaction is unclear[8]. This prevents us from accepting the crosslinked gelatin–CMC system as a simple IPN and complicates the computation of values of the elastic contribution term.

Earlier, we reported[4,6] the preparation and properties of gelatin–polyacrylamide IPNs, where the weight ratios could be varied from 1:1 to 1:5. Here with the gelatin–CMC system the CMC had to be kept proportionately low to facilitate gelling. Systems with higher CMC contents remained as viscous fluids.

The general swelling behaviour of crosslinked gelatin–CMC is shown in *Figures 1–4*. The rate of swelling decreased with time and reaches a plateau. Since CMC is ionic the swelling is greatly influenced by the ionic strength of the medium. The suppression of swelling with increasing salt concentration is evident from *Figures 2* and *3*. The swelling profiles in *Figure 4*, plotted as a function of CMC, clearly illustrate the dependence of swelling capacity on CMC concentration and its decrease with increase in NaCl concentration.

Several compositions were cast as films on the perspex sheets. The percentage elongation at break and load (in kg) for these films are shown in *Figures 5* and *6*. These data suggest that the CMC contribution towards elongation is negligible. With gelatin, there is an initial rise which falls off at higher concentrations. One plausible reason for this could be that at higher gelatin concentrations, an increase in the inter- and intrachain entanglements could lead to a reduction in the number of elastically efficient segments.

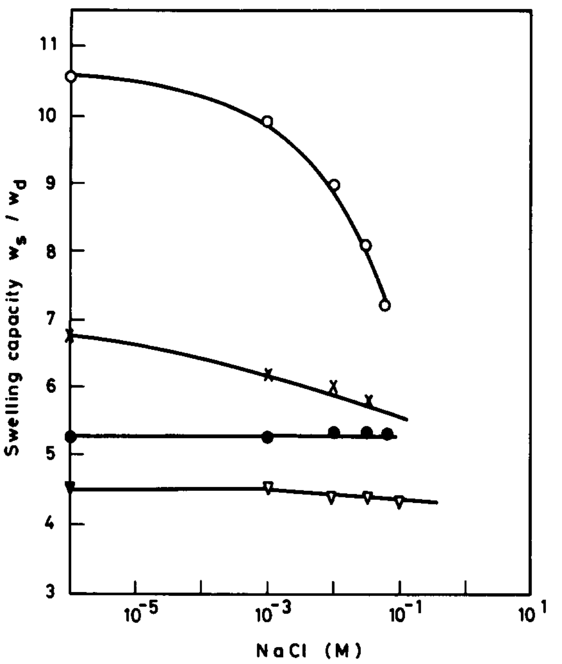

Figure 3 Swelling behaviour of crosslinked gelatin–CMC semi IPNs as a function of sodium chloride concentration. The gelatin–CMC (w/w) ratios are: (○) 2:0.2; (×) 3:0.2; (●) 4:0.2; (▽) 5:0.2

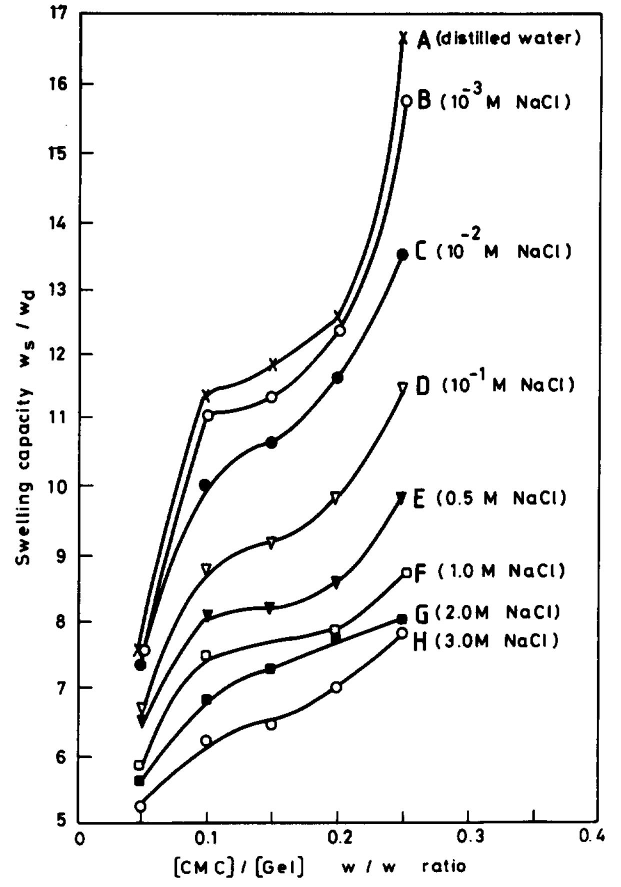

Figure 4 Swelling pattern of crosslinked gelatin–CMC semi IPNs in distilled water and aqueous sodium chloride

Compostionally the gelatin–CMC system bears a striking resemblance to collagen-rich tissues (*Table 1*). For example, cartilage tissues are ~70–75% water, 15–20% collagen and 2–10% proteoglycan with small quantities of glycoproteins[1]. In the most simplified model it is a hydrogel stabilized by oriented collagen fibres. An analysis of its mechanical performance reveals its load bearing and distributing patterns. The orientation of collagen fibres suggests anisotropy, while the hydrogel matrix indicates time-dependent mechanical responses. The individual roles of the matrix and the fibre in determining the mechanical responses have been thoroughly investigated. It has been established that while there is positive correlation between collagen content and tensile properties, the matrix contributes more towards the

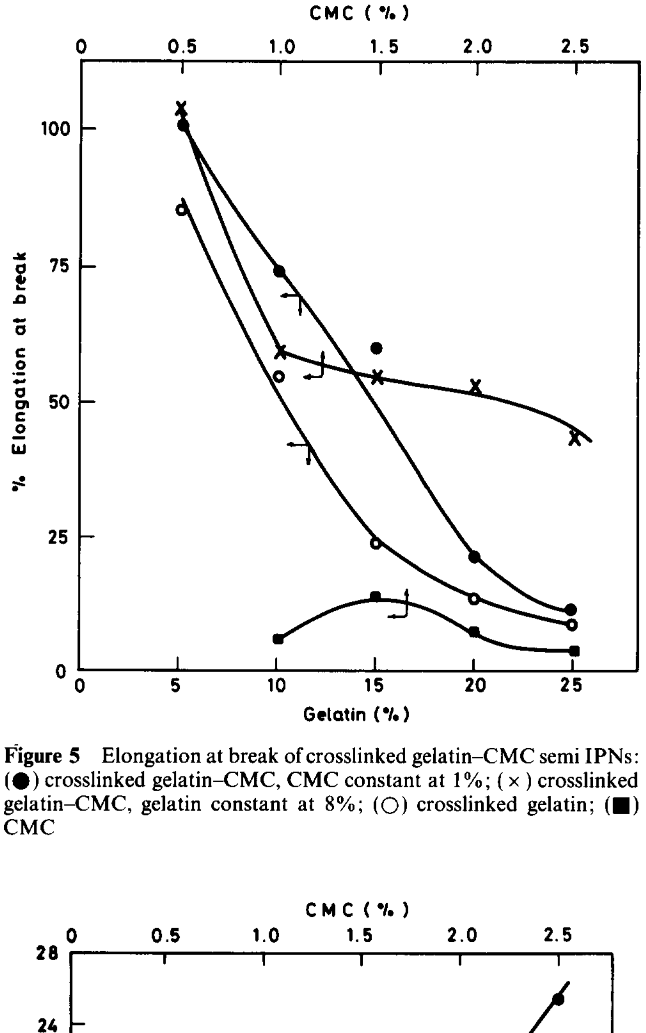

Figure 5 Elongation at break of crosslinked gelatin–CMC semi IPNs: (●) crosslinked gelatin–CMC, CMC constant at 1%; (×) crosslinked gelatin–CMC, gelatin constant at 8%; (○) crosslinked gelatin; (■) CMC

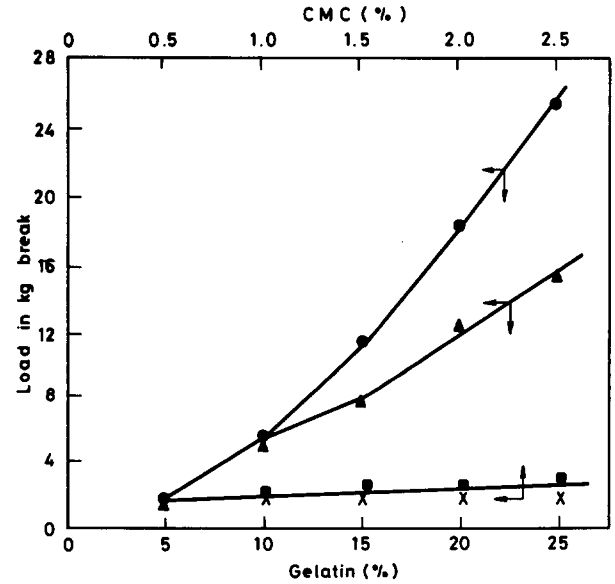

Figure 6 Load (in kg) at break for crosslinked gelatin–CMC semi IPNs: (●) crosslinked gelatin; (▲) crosslinked gelatin–CMC, CMC constant at 1%; (■) crosslinked gelatin–CMC, gelatin constant at 5%; (×) CMC

Table 1 Composition of cartilage and gelatin–CMC IPNs

System	Protein (%)	Polysaccharide (%)	Water (%)
Cartilage[a]	15–20 (collagen)	2–10 (proteoglycan)	70–75
Gelatin–CMC IPNs[b]			
I	4–17	1.5–2	60–80
II	9–20	2–4	77–85

[a] From reference 1
[b] Equilibrated in water for 24 h

stiffness of the material. This was precisely the observation here with the crosslinked gelatin–CMC IPNs.

The ionic nature of CMC is responsible for the response of the IPN to an electric stimulus. Though no attempt was made to accurately measure the shrinkage in length as a function of the voltage applied, it was observed that the shrinkage in length (along with the axis of current flow) was countered by a thickening in the perpendicular direction, the dimensional changes being within 5–10% depending upon the gel composition. This observation is at variance with those made by Tanaka *et al.*[14] on partially hydrolysed polyacrylamide gels, which suffered isotropic volume shrinkage by a factor of several hundreds.

We interpret our results as follows. The crosslinked gelatin–CMC IPN system is qualitatively different from partially hydrolysed crosslinked polyacrylamide gels. There is a two-component system where the protein (gelatin) forms a network of permanent covalent bonds and labile hydrogen bonds entrapping the ionic polysaccharide. Presumably the shrinkage suffered by the ionic polysaccharide could facilitate the effective transportation of the hydrogen bonds from one plane to another similar to muscle bulging associated with muscle contraction[15,16].

CONCLUSIONS

Protein–polysaccharide IPNs are novel hydrogel systems with close chemical and compositional resemblance to cartilage tissues. These synthetic hydrogels can be elegant model systems for extensive studies on the structure–function relationships of biological hydrogels.

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