

HYDROGELS WITH HYDROPHOBIC NANODOMAINS

PEKAŘ Miloslav, JARÁBKOVÁ Sabína, SMILEK Jiří, MRAVEC Filip

*Brno University of Technology, Faculty of Chemistry, Materials Research Centre, Brno,
Czech Republic, EU*

Abstract

Ionic interactions between oppositely charged polyelectrolytes and surfactants can - under proper conditions - lead to formation of physical gels. The surfactants form micellar structures enabling to solubilize hydrophobic substances in the otherwise aqueous environment of the gel. Resulting materials can find use in the formulation of delivery systems, e.g. for hydrophobic drugs especially in topical applications. We report on the techniques of preparation of such materials from positively charged polysaccharides (chitosan, cationized dextran) and negatively charged surfactant and on their rheological properties in dependence of their composition.

Keywords: Hydrogels, polyelectrolytes, micelles, nanodomains, surfactants

1. INTRODUCTION

It is well-known that polyelectrolytes can interact with oppositely charged surfactant by electrostatic forces and form various types of colloids, nanocolloids or even bulk materials, see, e.g., the monograph by Holmberg et al. [1]. Under a proper control and at sufficiently high surfactant concentration, the surfactant micelles can act as crosslinking points and gelled material is formed. These hydrogels contain hydrophobic domains formed by the surfactant micellar structures. Dimensions of these domains are thus within the area of nanomaterials. The domains should be capable of solubilization of hydrophobic substances within the otherwise hydrophilic gel matrix. They can be then favorably employed in variety of applications, especially in the fields of (bio)medicine, biomaterials, drug delivery, cosmetics, but even in agriculture or environment protection. From the point of view of polarity of their constituents such gels can be viewed as hybrid - hydrophilic-hydrophobic - materials. This hybrid character is the base of the specific material, structural, and colloidal properties of such materials [2]. This work is focused on the preparation of such gels from positively charged polysaccharide polyelectrolytes and negatively charged surfactant and on the study of their rheological properties.

2. EXPERIMENTAL PART

Chitosan (medium molecular weight) and dextran hydrochloride (powder prepared from dextran of average molecular weight 500,000) were purchased from Sigma Aldrich and used as cationic polysaccharides without further treatment. Sodium dodecylsulphate (≥ 99.0 %, Sigma Aldrich), anionic surfactant, was also used as received. Gels were prepared by mixing polyelectrolyte and surfactant solutions prepared in deionized water (Purelab Flex, ELGA) or in 0.15 M NaCl. Dextrane stock solutions were prepared at concentrations of 1 and 4 % (weight), chitosan stock solution of 2 % (weight) was prepared in the presence of acetic acid at concentration of 5 % (weight). Surfactant stock solutions were prepared at concentrations of 100 and 400 mM. Gels were prepared in vials by mixing equal volumes of stock solutions of polysaccharide and surfactant to achieve four different final concentrations as given in **Table 1**. The vials were left on a shaker overnight to complete gelation and separation of the gel phase.

Table 1 Final concentrations in gelling systems

sample	polyelectrolyte	surfactant
	weight %	mM
1	2	200
2	0.5	50
3	2	50
4	0.5	200

Oil red O (Sigma Aldrich) was used as a hydrophobic dye to test solubilization capabilities of the gels visually. A small amount of the dye powder was added to the vial with freshly prepared gel and left solubilize overnight on shaker.

Prodan was used as a universal fluorescence probe to further test solubilization properties of the gels. Stock solution of prodan in acetone (0.2 mM) was first added to the vial in such amount as to achieve its final concentration of 2 μ M, acetone was left to evaporate and then the gel preparation followed as described above. Fluorescence spectra were measured at laboratory temperature using Fluorolog (Horiba Scientific) and the excitation wavelength of 361 nm.

3. RESULTS AND DISCUSSION

3.1. Chitosan gels

The type of the aqueous environment had no visible influence on the gel formation. The amount of the formed gel was dependent on the polymer concentration - the higher the polymer concentration the higher the gel amount. Solubilization tests confirmed the presence of hydrophobic domains in samples 1, 2, and 4 (see the red color of the gels in **Figure 1**); the red color of the supernatant (especially in the case of sample 4) indicates that not all micelles were incorporated into gels. The gel sample 3 was not colored by the hydrophobic dye (cf. **Figure 1**) which means that either the hydrophobic domains were not formed or were inaccessible for the hydrophobic dye due to some structural reasons.

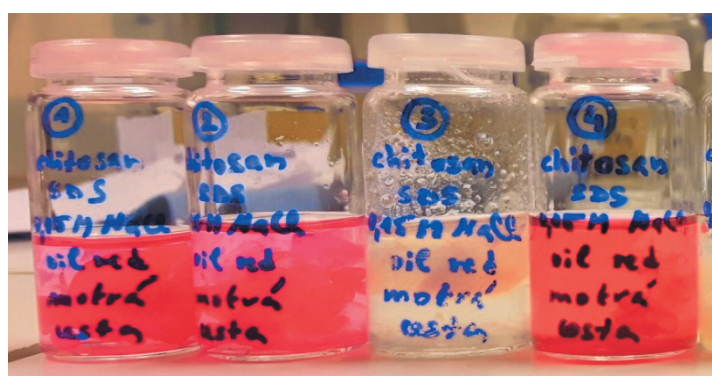


Figure 1 Results of solubilization tests of chitosan gels prepared in 0.15 mM NaCl

Rheological experiments did not reveal substantial effect of the type of aqueous environment on the viscoelastic properties of the formed gel materials. **Figure 2** shows the dependence of both rheological moduli on the deformation frequency. It is clear that mechanical properties (toughness) of the gels can be controlled in a broad range by the composition of the gelling system. The elastic (storage) module was well above the viscous (loss) module over the whole tested frequency range for all samples. This clearly demonstrates dominating elastic response, i.e., the gel character, of prepared materials. Further, the moduli are almost independent of the deformation frequency. This is typical for densely crosslinked polymers or rigid gels or

dispersions [3]. Composition has significant effect on the rheological properties of the gels; their toughness as measured by the moduli values decreased in the order of the sample numbers: $1 > 4 \approx 2 > 3$. Thus, the high concentration of both polyelectrolyte and surfactant is necessary for high toughness, on the other hand, the surfactant concentration seems to be more significant for the preparation of weaker gels which sound logically as the surfactant nanodomains are supposed to serve as the gel crosslinking nodes.

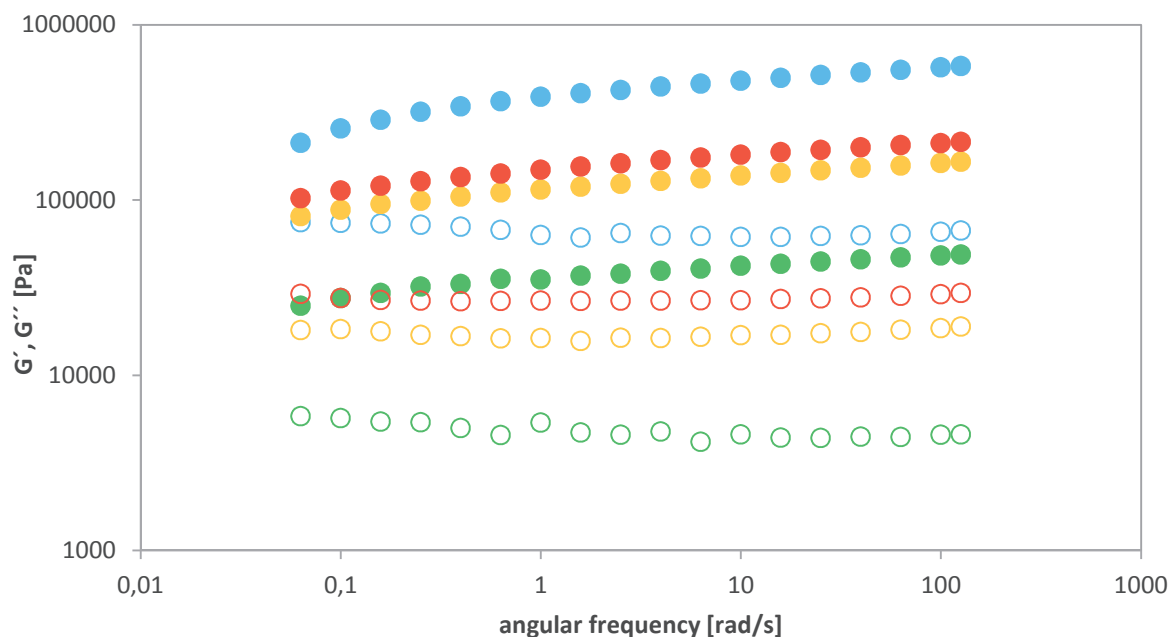


Figure 2 Storage (filled symbols) and loss (empty symbols) moduli of chitosan gels prepared in 0.15 M NaCl; sample 1 (blue), 2 (orange), 3 (green), and 4 (red)

3.2. Dextran gels

In this case the gel formation was clearly dependent on the aqueous environment. When deionized water was used gel was formed only with the sample composition 3 (otherwise only clear solutions resulted probably due to the disruption of micelles which then could not serve as crosslinking points) whereas in the environment of 0.15 mM NaCl gels were formed for all compositions. Interestingly, in the latter case the solubilization test of samples 1, 2 and 4 gave similar results as shown in **Figure 1** whereas in the case of sample 3 only the gel was colored and sank in colorless supernatant. This means that all micellar structures were incorporated into the gel which is in strict contrast to sample 3 prepared with chitosan. This is probably consequence of the lower charge density on dextran hydrochloride in comparison with chitosan - the content of nitrogen, which bears the positive charge, in dextran is declared by the producer to be around 3.2% whereas that of chitosan (at the average declared degree of deacetylation of 80%) should be around 7.2%. The high charge density at high polyelectrolyte and low micelle concentrations (sample 3) probably leads to disruption of micelles and bounding either surfactant monomers or some submicellar structures to chitosan chain.

Rheological properties of these gels are completely different from those of chitosan gels, cf. **Figure 3**. First, both moduli have significantly lower values pointing to mechanically weaker materials. Further, the loss modulus for dextran samples 1 and 3 is higher than the storage modulus for (almost) all frequencies, indicating that these samples are more viscoelastic liquids than true soft solid materials. Both moduli of sample 2 have very similar values whereas sample 4 shows untypical behavior - the storage moduli is higher (and almost frequency-independent) at low frequencies and then, at medium and high frequencies, practically equal to the loss modulus. Generally, the values of all moduli of all samples increase with the frequency and do not reach

the high frequency plateau. This means sparsely crosslinked material with lower crosslinking density than was in the case of **Figure 2**. Again, this should be consequence of the dextran lower charge density.

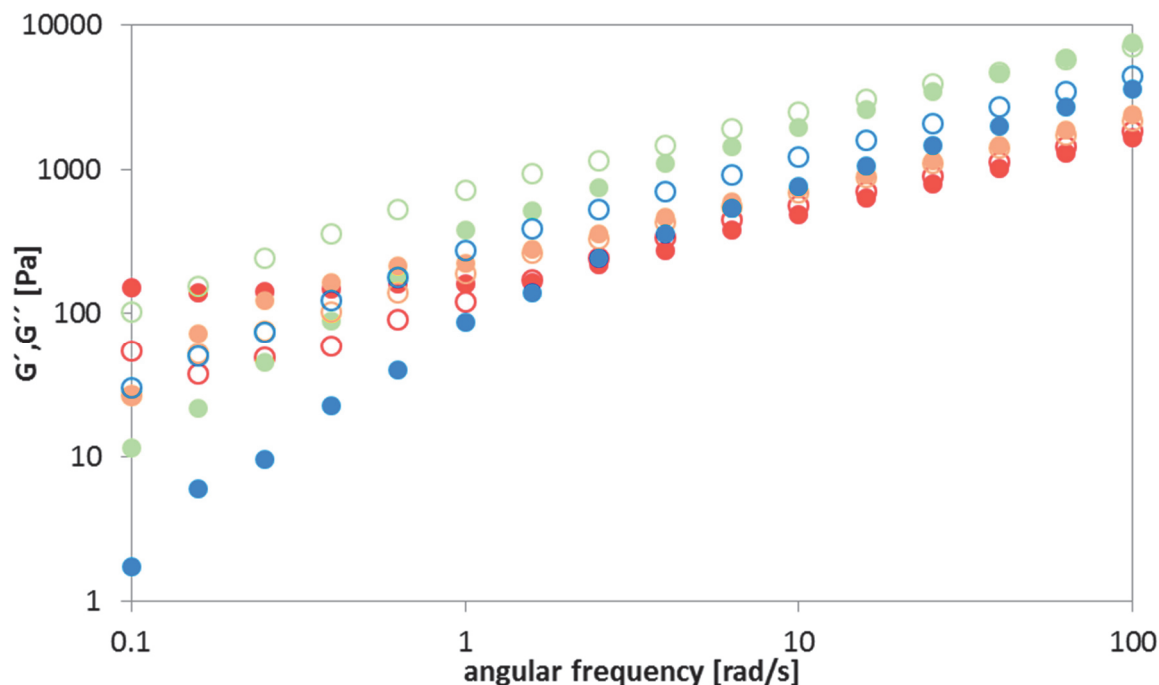


Figure 3 Storage (filled symbols) and loss (empty symbols) moduli of dextran gels prepared in 0.15 M NaCl; sample 1 (blue), 2 (orange), 3 (green), and 4 (red)

3.3. Fluorescence probe

Prodan was solubilized in selected gel samples as a fluorescence probe sensitive to its environment and capable of solubilization in both hydrophobic and hydrophobic domains. Increasing the polarity causes the bathochromic shift of the prodan emission spectra - the maximum is located around 401 nm in cyclohexane, 496 nm in ethanol, and 531 nm in water.

The spectra were rather broad indicating distribution of prodan in regions of different polarity, nevertheless, the maximum was clearly seen and its location was dependent on the polyelectrolyte type but not dependent on the sample composition. For the chitosan-based hydrogels the maximum was located around 490 nm whereas in the case of dextran hydrogels around 477 nm. Thus, in the dextran hydrogels the prodan molecules are located in domains of lower polarity than in the case of chitosan gels. This points to some structural differences between these two gel types, their different hydration characteristics as well as to the potential disturbance of original micellar structures as mentioned in section 3.2. Further research and more structure-specific methods are needed to explain these differences.

4. CONCLUSION

Cationic polyelectrolytes and anionic surfactants can form physically crosslinked hydrogels upon simple mixing at proper concentrations in proper aqueous medium. The hydrogels incorporate micellar hydrophobic nanodomains capable of solubilization of hydrophobic molecules. Of course, hydrophilic substances can be also entrapped within the hydrogel matrix. Structure and rheological properties of the resulting materials can be controlled by the polyelectrolyte type as well as by the concentration of the solutions from which the gels are prepared. These materials can find applications as drug delivery systems, particularly in topical (skin or mucous membrane) treatments.

ACKNOWLEDGEMENTS

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