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CHEMICAL CROSSLINKIG OF "SMART" CHITOSAN HYDROGELS: EFFECT ON THE THERMAL AND pH SENSITIVITY

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Chitin cold aqueous NaOH solutions (1.6% w/w in NaOH 16% w/w) undergo phase separation and gelation under controlled conditions [1,2]. Using this strategy, cylindrical hydrogels were set from alkali chitin. After thoroughly washed to neutrality the chitin in the gels had converted into chitosan (i.e. degree of acetylation ~30-40%; soluble in dilute acidic solution). Freeze dried cylindrical chitosan hydrogels show Fickian solvent diffusion kinetics and negative thermal response in their swelling degree in the range 2 to 25 °C (*i.e.* decreasing swelling levels with increasing temperature). Such changes are more pronounced at pH in the vicinity of 7.6 [2]. This behavior is consistent with a "U"-shaped lower critical solution temperature (LCST) phase diagram observed in alkali chitin [1]. In order to confer them mechanical stability at pH ~7.0, chitosan hydrogels were chemically cross-linked with glutaraldehyde at two extremely low stoichiometric ratios (equivalents of glutaraldehyde to chitosan), R(=2[-CH=O]/[-NH_3]), of 1.8 and 3.6×10^{-4}. In Figure 1 are shown the results for the changes in swelling of the gels as a result of stepwise changes in temperature between 40 and 2 °C at the three investigated pH values, namely 7.0, 7.6 and 8.0. Inspection of Figure 1a, summarizing the results for the gels of $R=1.8 \times 10^{-4}$, allows to realize that the system responds in markedly distinctive manner to stepwise thermal change in dependence of the pH. At pH 7.0, cooling from 40 to 2 °C results in contraction of the gel network structure. While rising the temperature from 2 to 40°C leads to a rapid swelling response (*i.e.* ca. 2-fold increase in the amount of solvent uptake). Subsequent cooling to 2°C is accompanied by a new contraction cycle.

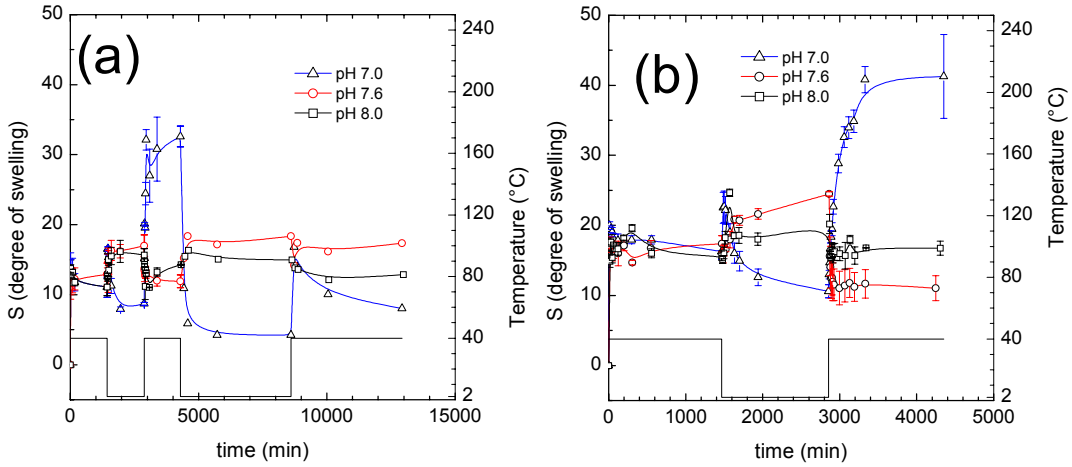

Figure 1. Swelling changes in chitosan hydrogels cross-linked with glutaraldehyde at stoichiometric ratios, R (=2[-CH=O]/[-NH_3]), of (a)1.8 and (b) 3.6×10^{-4} in response to stepwise temperature changes between 40 and 2°C in citrate-phosphate buffer of pH 7.0, 7.6 and 8.0 (as shown in labels).

At pH ≥ 7.6 the swelling-contraction behavior is exactly the opposite than that observed at pH 7.0. Very similar trends were also observed for the gels with greater degree of crosslinking (Figure 1b). The swelling-shrinking behavior observed in gels of pH ≥ 7.6 is similar in kind to that previously documented for uncrosslinked chitosan hydrogels and has been interpreted in terms of lower critical solution temperature (LCST) phase transitions found in alkali chitin driven by hydrophobic association, presumably involving residual acetyl groups in chitin [1]. Alkali chitin has a LCST value at ~ 32°C, and it is likely that this value persists in chitosan. The presence of greater amounts of ionized –NH_3 groups at pH 7.0 than at 7.6 and possibly their interaction with phosphate ionic species dissociated at the various pH of the buffer solutions, could account for the drastic difference in swelling behavior for such a small change in pH. This behavior is currently being translated into the fine tuning and control over the properties of highly specialized devices for biotechnology and biomedicine.

References.

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