



Swelling Properties of Poly(*N*-isopropylacrylamide)/Calcium Alginate Interpenetrating Polymer Network Hydrogel containing Zirconia

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Received: 13 January 2015;

Accepted: 18 February 2015;

Published online: 26 May 2015;

AJC-17280

Temperature-responsive poly(*N*-isopropylacrylamide)/calcium alginate interpenetrating polymer network hydrogels containing different percentages of zirconia were prepared and evaluated for their swelling properties. The pore size of the interpenetrating polymer network hydrogels decreased with increasing content of zirconia. Incorporation of zirconia into the interpenetrating polymer network hydrogel decreased its ability to swell at temperatures below its lower critical solution temperature but resulted in larger shrinkages at temperatures above its lower critical solution temperature. The swelling-deswelling behaviour of the interpenetrating polymer network hydrogels between 25 °C and 37 °C was, however, rapid, responsive and reproducible.

Keywords: Poly(*N*-isopropylacrylamide)/Calcium alginate, Hydrogel, Zirconia, Swelling ratio, Interpenetrating polymer network.

INTRODUCTION

Intelligent hydrogels, which undergo dynamic swelling and shrinkage processes, and dimensional changes in response to external stimuli such as temperature, pH, enzymes and electric fields, have attracted much research interest because of their unique properties and potential in advanced biomedical applications¹⁻⁴. Poly(*N*-isopropylacrylamide) (PNIPAAm) hydrogel is one of the most studied biocompatible thermoresponsive hydrogels that has a lower critical solution temperature of around 34 °C, which is close to body temperature⁵. Poly(*N*-isopropylacrylamide) copolymer hydrogels with varying lower critical solution temperature have been explored for specific applications such as controlled drug and gene delivery⁵⁻⁸, regenerative medicine⁹ and enzyme immobilization¹⁰. In recent years, considerable efforts have been focused on studying the temperature and pH responsiveness of PNIPAAm hybrid hydrogels. Sodium alginate, a hydrophilic polymer, has been used to improve the deswelling rate of the PNIPAAm hydrogel¹¹. Ceramic oxides such as silica were incorporated into the PNIPAAm hydrogels to form nanocomposite hydrogels. Generally, porous PNIPAAm hydrogels can be prepared by free radical polymerization in the presence of spherical silica particles of different sizes followed by acid extraction of silica¹². It is reported that the deswelling properties of PNIPAAm hydrogels was facilitated by a decreased silica particle size and increased silica content. Haraguchi and Takehisa¹³ have also

successfully synthesized a nanocomposite hydrogel by *in situ* free radical polymerization of *N*-isopropylacrylamide (NIPAAm) in the presence of clay. The resulting gels exhibited high structural homogeneity, superior elongation with near complete recovery, good swellability and rapid de-swelling in response to temperature changes. Van den Brom *et al.*¹⁴ reported synthesis of new responsive nanocomposite material, which is very stable and has excellent thermal responsive properties, by mixing PNIPAAm hydrogel and “super-crosslinking” silica nanoparticles in solution followed by spin-coating a thin film and then photocrosslinking by a UV radiation. Zirconium oxide (zirconia), is another ideal candidate which may improve temperature responsiveness of PNIPAAm/Alginate hydrogels, because it is a biocompatible material with favourable mechanical properties and has been widely used in restorative dentistry¹⁵. In addition, zirconia is highly resistant to corrosion and stable to hydrolysis. In medicine, zirconia is being used as a material for hip prosthesis and its functionality is proven by clinical tests and examinations for years¹⁶. The aim of this study was to prepare and characterize the swelling properties of PNIPAAm/calcium alginate interpenetrating polymer network hydrogel containing zirconia.

EXPERIMENTAL

N-Isopropylacrylamide (NIPAAm; Sigma ≥ 99 %) was purified by recrystallization from *n*-hexane. *N,N'*-methylenebisacrylamide (NMBA; Sigma ~99 %), ammonium persulfate

(APS; Sigma $\geq 98\%$), *N,N,N',N'*-tetramethylethylenediamine (TEMED; Sigma 99%), sodium alginate (Acros about 100%), zirconium oxide (Zirconia; Acros 98.5%), calcium chloride (Sigma $\geq 97\%$), sodium phosphate dibasic dihydrate (Sigma $\geq 99.5\%$) and sodium phosphate monobasic monohydrate (Sigma $\geq 98\%$) were used as received. All other reagents were of analytical grade and were used without further purification.

General procedure

Preparation of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels: The PNIPAAm/calcium alginate interpenetrating polymer network hydrogels were prepared by a free radical polymerization in deionized water using 1.04 g of NIPAAm, 4 mol % NMBA, 1 mol % APS, 1 mol % TEMED, 8 wt % sodium alginate and different amount of zirconia (all molar percentages are based on the amount of NIPAAm). The mixture was immediately injected into the hollow core of a rubber O-ring sandwiched between two glass plates. Polymerization was carried out at 25 °C for 1 day. The gel was then further crosslinked in calcium chloride solution at room temperature for 2 h. The resulting gels were then immersed in an excess of deionized water for 2 days followed by drying at 40 °C for 3 day and in a vacuum oven for 1 day.

Detection methods:

Volume phase transition temperature (VPTT): The volume phase transition temperature of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels were analyzed using a differential scanning calorimeter (Mettler Toledo DSC 823e). All hydrogels were immersed in deionized water at room temperature and allowed to swell for 24 h to reach the equilibrium state. The DSC analyses were performed from 25 °C to 45 °C at a heating rate of 3 °C min⁻¹ with a nitrogen flow rate of 40 mL min⁻¹.

Scanning electron microscopy (SEM): PNIPAAm/calcium alginate interpenetrating polymer network hydrogels were immersed in deionized water at room temperature for 24 h. Samples were then subjected to freeze-drying for at least 24 h until all water had sublimed. The freeze-dried hydrogel surfaces were sputter-coated with gold and their surface morphology was observed by SEM (Hitachi TM3000).

Dynamic swelling ratio measurement¹⁷: The dried gel was weighed (W_d). It was then immersed in an excess amount of deionized water at 28, 32, 36 and 40 °C respectively. The gel was removed and weighed (W_w) at each 1 h interval for up to 8 h. The amount of water absorbed at each 1 h interval at different temperatures was recorded and the results were plotted as a function of time. The swelling ratio (SR) is calculated from:

$$SR (\%) = \frac{(W_w - W_d)}{W_d} \times 100$$

Equilibrium swelling ratio measurement¹⁷: Two pre-weighed dried gels were immersed in deionized water, respectively at 28, 32, 36 and 40 °C for one day. After equilibrium, the gels were weighed and the final weight (W_f) was recorded. Equilibrium swelling ratios for the gels are calculated from:

$$SR (\%) = \frac{(W_f - W_d)}{W_d} \times 100$$

Thermoreversibility measurement: The pre-weighed dried gels were equilibrated in 10 mL deionized water at 25 °C and weighed. The gels were then transferred into 10 mL deionized water at 37 °C and weighed again after 1 h. The gels were transferred into deionized water at 25 °C again and weighed after immersion for 1 h. The procedures were repeated for up to 8 h.

RESULTS AND DISCUSSION

Appearance and morphology of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels: Fig. 1 shows the images of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels prepared. The zirconia free PNIPAAm/calcium alginate interpenetrating polymer network hydrogel sample was transparent while zirconia loaded PNIPAAm/calcium alginate interpenetrating polymer network hydrogel was white and opaque. Zirconia is a white powder and thus the resulting hydrogel would appear to be white. Fig. 2 shows the SEM micrographs of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels. The texture of PNIPAAm/calcium alginate interpenetrating polymer network hydrogel varied with zirconia composition. The zirconia-free interpenetrating polymer network hydrogel had the largest pore size while the interpenetrating polymer network hydrogel containing 30 % of zirconia had the smallest ones. Generally, the pore size of the PNIPAAm/calcium alginate interpenetrating polymer network hydrogels decreased with increasing amount of zirconia added. This indicates that zirconia was embedded in the bulk of the hydrogel and occupied spaces, resulting in reduced pore size.

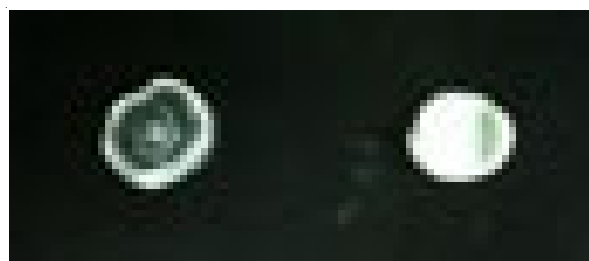


Fig. 1. Images of PNIPAAm/calcium alginate interpenetrating polymer network hydrogel without zirconia (left) and with zirconia (right)

Volume phase transition temperature (VPTT): The temperature at the onset point of the phase transition of hydrogel in DSC thermograms is referred to as volume phase transition temperature^{18,19}. The small heat capacity shift at the transition in the DSC thermogram is due to water detaching from the hydrogel. Fig. 3 shows the DSC thermograms of the PNIPAAm/calcium alginate interpenetrating polymer network hydrogel samples, all of which indicated similar volume phase transition temperature at around 34 °C. This indicated that zirconia had no effect on the volume phase transition temperature of the interpenetrating polymer network hydrogels. There was no significant difference between volume phase transition temperature of the control and zirconia loaded interpenetrating polymer network samples implying that PNIPAAm/calcium alginate interpenetrating polymer network retained its inherent property and is free from chemical interaction with zirconia.

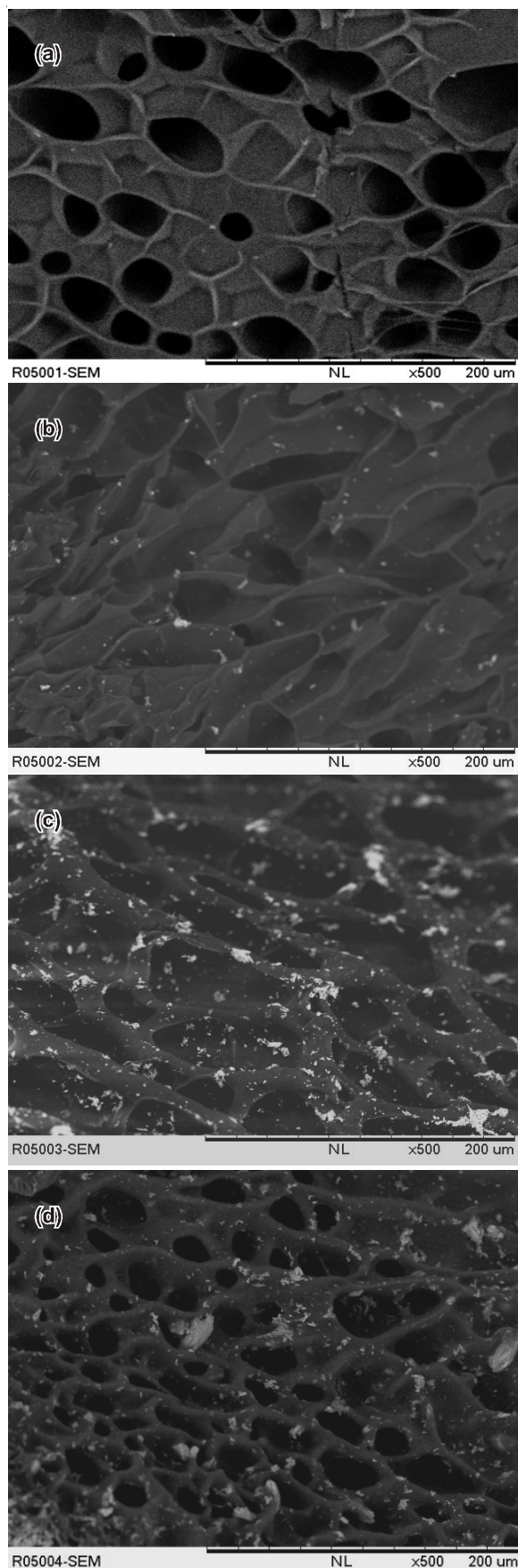


Fig. 2. Scanning electron microscope micrographs of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels containing: a) 0 % zirconia (control), b) 10 % zirconia, c) 20 % zirconia and d) 30 % zirconia

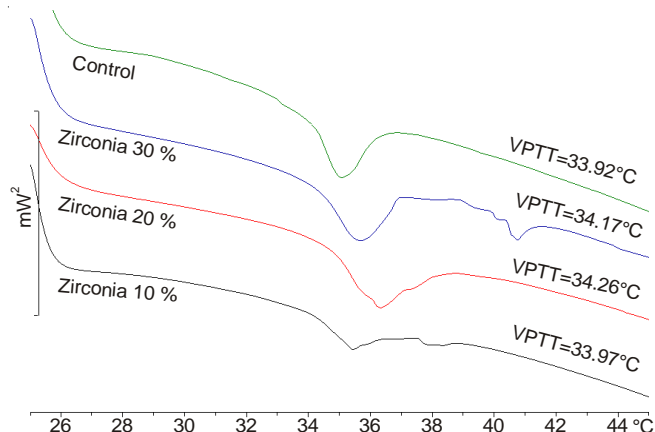


Fig. 3. DSC thermograms of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels containing 0 % (control), 10 %, 20 % and 30 % of zirconia

Dynamic swelling ratios: The dynamic swelling ratios of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels at various temperatures were investigated. PNIPAAm/calcium alginate interpenetrating polymer network hydrogels had the highest swelling ratio as compared to zirconia loaded interpenetrating polymer network hydrogels at temperatures of 28, 32, 36 and 40 °C as shown in Fig. 4a to 4d. At 28 and 32 °C, the interpenetrating polymer network hydrogel samples containing 30 % of zirconia had the lowest swelling ratio (Fig. 4a and 4b), while there was no significant difference in swelling ratio among the interpenetrating polymer network hydrogels with 10 to 30 % zirconia at 36 and 40 °C, as shown in Fig. 4c and 4d, respectively.

This observation could be attributed to the smaller pore size in PNIPAAm/calcium alginate interpenetrating polymer network hydrogel containing zirconia. As the pore size of the hydrogel becomes smaller, so would its pore volume. The amount of water that could be absorbed would be less, thus, leading to a lower overall swelling ratio. Moreover, zirconia may have enhanced gel rigidity which in turn decreases the ability of the interpenetrating polymer network hydrogel to expand. On the other hand, PNIPAAm/calcium alginate interpenetrating polymer network hydrogels containing 10-30 % of zirconia had lower swelling ratios as compared to zirconia free interpenetrating polymer network hydrogel at 36 and 40 °C as shown in Fig. 4c and 4d, respectively. At these temperatures, which are above the lower critical solution temperature of PNIPAAm/calcium alginate hydrogel, the interpenetrating polymer network hydrogels would tend to shrink and expel the bulk of water maximally.

Equilibrium swelling ratios: The measurement of equilibrium swelling ratio of the interpenetrating polymer network hydrogels was performed above and below its volume phase transition temperature to determine their temperature sensitivity and temperature dependency of the swelling and deswelling processes. Regardless of zirconia content, all the hydrogel samples shrank, expelling water from their bulk resulting in a minimum residual swelling ratio at 40 °C (Fig. 5). It was reported that below lower critical solution temperature, the hydrogen bonds between hydrophilic groups on its side chain and water molecules predominate over the hydrophobic

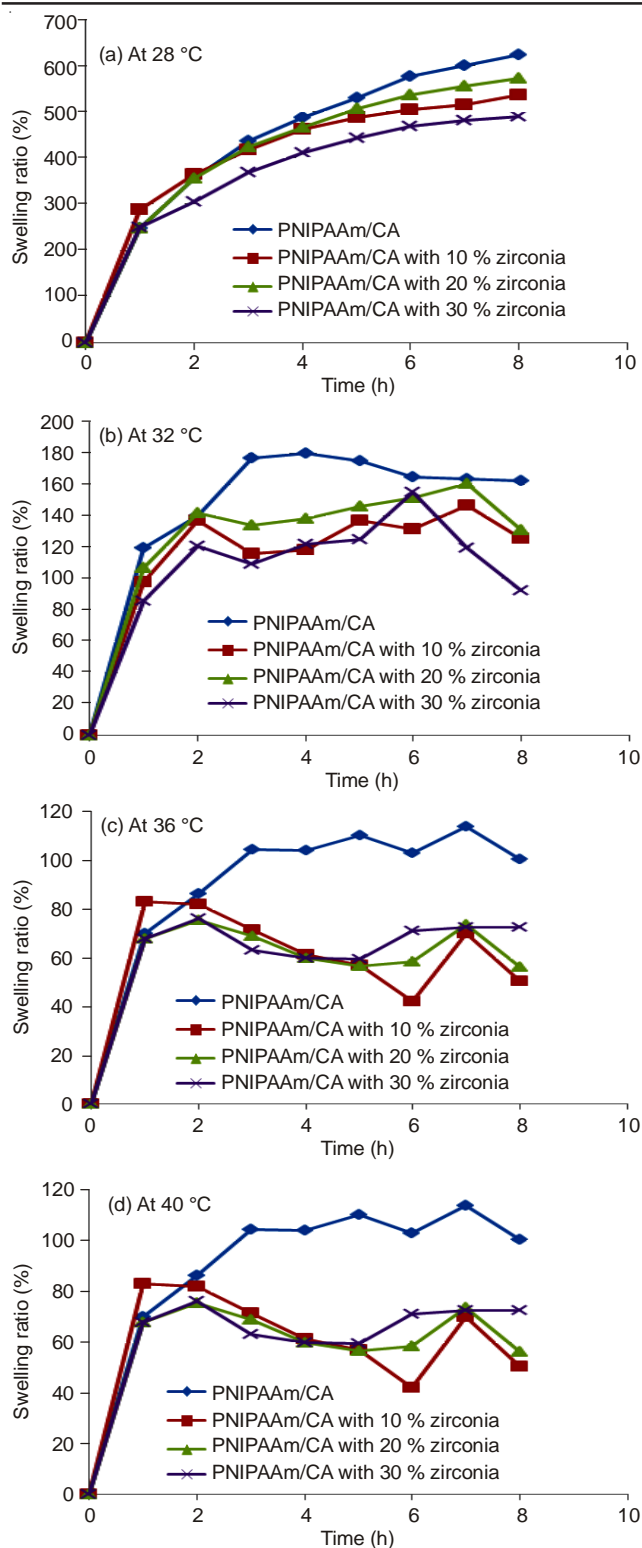


Fig. 4. Dynamic swelling ratios of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels containing 0 %, 10 %, 20 % and 30 % zirconia at different temperatures

interaction among hydrophobic groups, which resulted in migration of water molecules into the hydrogel¹¹. Above lower critical solution temperature, the differences between the equilibrium swelling ratios of hydrogels become less significant as the hydrophobic interaction become fully dominant in the hydrogel and water molecules are released to a maximum limit²⁰.

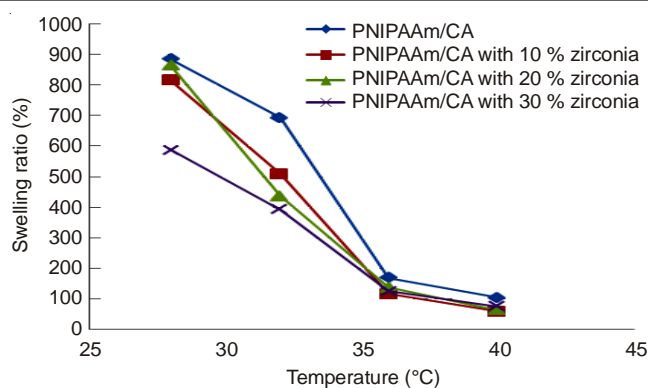


Fig. 5. Equilibrium swelling ratios of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels at various temperatures

The thermoreversibility of the hydrogels was studied. Fig. 6 shows the swelling-deswelling behaviour of the PNIPAAm/calcium alginate interpenetrating polymer network hydrogels between temperatures of 25 and 37 °C. All PNIPAAm/calcium alginate interpenetrating polymer network hydrogel samples exhibited excellent, rapid and similar thermoreversibility for 4 swelling-deswelling cycles, which indicated that the addition of zirconia did not affect the thermoreversibility of the hydrogels. The swelling-deswelling process was reproducible in accordance with changes in temperature.

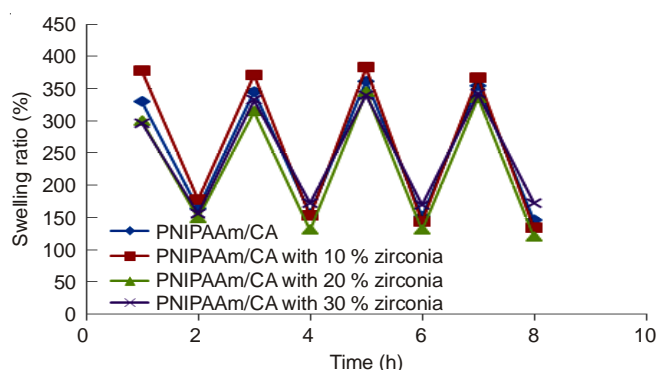


Fig. 6. Swelling-deswelling (at 25 °C and 37 °C) behaviour of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels containing 0 %, 10 %, 20 % and 30 % zirconia

Conclusion

Zirconia incorporation did not alter the volume phase transition temperature of PNIPAAm/calcium alginate interpenetrating polymer network hydrogels. The PNIPAAm/calcium alginate interpenetrating polymer network hydrogel pore size decreased with increasing amount of zirconia added, so did its swelling ratios below lower critical solution temperature. Zirconia loaded PNIPAAm/calcium alginate interpenetrating polymer network hydrogels shrank maximally above lower critical solution temperature, resulting in minimum residual swelling ratios. The interpenetrating polymer network hydrogels containing 10-30 % zirconia also showed rapid thermoreversibility behaviour, which is as good as that of zirconia free interpenetrating polymer network hydrogel.

ACKNOWLEDGEMENTS

The authors thank the International Medical University (IMU) for financial support of this work.

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