Investigation of ZnO-Release Behavior of Poly(*N*-isopropylacrylamide-*co*-maleic acid)/ZnO Composite Hydrogels by Differential Pulse Polarography

Recai İnam,[1] Tuncer Çaykara,[1] Sibel Akkoç,[1] Ömer Kantoğlu[2]

[1]*Gazi University, Faculty of Art and Science, Department of Chemistry, 06500 Beşevler, Ankara, Turkey*
[2]*Ankara Nuclear Agriculture and Animal Research Center, Turkish Atomic Energy Authority, Ist. Yolu 30 km Kazan, 06983 Ankara, Turkey*

ABSTRACT: Poly(*N*-isopropylacrylamide-*co*-maleic acid)-zinc oxide [P(NIPA/MA)/ZnO] composite hydrogels, containing a definite amount of ZnO, were prepared from *N*-isopropylacrylamide (NIPA) and maleic acid (MA) monomers with 0–31.15 mol % MA in aqueous saturated zinc oxide solutions by radiation-induced polymerization and gelation using γ rays from a ^{60}Co source. The amounts of released ZnO from these composite hydrogels were determined by differential pulse polarography (DPP) using the characteristic peaks obtained at about $-1,000$, $-1,050$, and $-1,300$ mV at pH 2.0, 5.5, and 7.05, respectively. It was found that the ZnO-release behavior of P(NIPA/MA)/ZnO composite hydrogels depended strongly on the MA content and pH of the medium. © 2004 Wiley Periodicals, Inc. J Appl Polym Sci 92: 2411–2414, 2004

Key words: hydogels; irradiation; release

INTRODUCTION

Hydrogels are hydrophilic three-dimensional polymer networks capable of absorbing a large volume of water or other biological fluid. Stimuli-sensitive hydrogels have the capability to change their swelling behavior, permeability, or mechanical strength in response to external stimuli, such as small changes in pH, ionic strength, and temperature.[1–4] Because of these useful properties, hydrogels have numerous applications, and they are particularly useful in the medical and pharmaceutical fields.[1,2,5]

All pH-responsive hydrogels contain ionizable groups on polymer chains.[6,7] These acidic pendant groups on the polymer backbone release protons in response to changes in their environmental pH. Electrostatic repulsions are originated, and the uptake of solvent in the polymeric matrix is increased, when acidic pendant groups of the hydrogel are incorporated. The swelling ratio of hydrogels with the acid pendant groups (e.g., carboxylic acid) increases when the pH of the solution exceeds the pK_a of the ionizable pendant groups. The swelling ratio depends on the amount of ionized acidic groups; consequently, swelling increases with the pH of the swelling solution.

Various polymeric and copolymeric pH-responsive hydrogels have been synthesized with monomers of acrylic acid, *N*-isopropylacrylamide, and acrylamide.[8,9]

Because of these characteristics, pH-responsive hydrogels have been studied to develop drug-delivery systems.[10] Recently, Şen et al.[11] investigated the delivery of a positively charged antifungal drug, terbinafine hydrochloride (TER-HCl), from poly(acrylamide/maleic acid) P(AAm/MA) hydrogels. They determined the effect of MA content and pH of the medium on the release properties of P(AAm/MA) hydrogels.

Poly(*N*-isopropylacrylamide) has also proved to be a biocompatible polymer used in various biotechnological applications.[12] Zinc oxide is the main active chemical in zinc oxide ointment, used as a sunscreen or for the treatment of dermotophyte filamentous.[13] For this reason, we chose *N*-isopropylacrylamide and maleic acid as monomers with doped ZnO, and attempted to prepare a P(NIPA/MA)/ZnO composite hydrogel system by γ-ray irradiation. The ZnO release kinetics of these composite hydrogel systems were investigated by using differential pulse polarography (DPP) as a function of time at various pH. First and foremost, DPP has been used for trace element analysis because of its highly sensitive and inexpensive instrumentation.[14] Other accessible techniques capable of heavy–heavy determination, such as atomic absorption spectroscopy, UV spectrophotometry, and γ spectrometry, often do not offer sufficient sensitivity

and selectivity for accurate determination at trace concentrations. These are all time-consuming procedures, and losses of these metals are also possible.

EXPERIMENTAL

Apparatus

A polarographic analyzer system (PAR 174 A), equipped with a mercury drop-timer, was used for determination of ZnO release from P(NIPA/MA)/ZnO composite hydrogels. The drop time of the mercury electrode was approximately 2–3 s (2.75 mg/s). A Kalusek electrolytic cell with reference-saturated electrode (SCE), separated by a liquid junction, was used in the three-electrode configuration: the counter electrode was platinum wire. The polarograms were recorded with a Linseis LY 1600 X-Y recorder. Pulse polarograms were recorded under the conditions of a drop life of 1 s, scan rate of 5 mV/s, pulse duration of 50 ms, and pulse amplitude of 50 mV.

Materials

The two monomers used in this study, NIPA and MA were supplied by Merck. Zinc oxide (ZnO) was obtained from Aldrich. Glacial CH_3COOH, H_3PO_4 (85%), H_3BO_3 and standardized NaOH were used to prepare Britton-Robinson (B-R) buffers. B-R buffer solution was prepared in such a way that 2.3 mL glacial acetic acid, 2.7 mL phosphoric acid, and 2.4720 g boric acid were dissolved by dilution of triple-distilled water to 1.0 L; 50 mL portions of this solution were taken and the pH was adjusted to 2.2, 5.5, and 7.05 by addition of the appropriate amount of $2.0M$ NaOH.

Preparation of P(NIPA/MA)/ZnO composite hydrogels

P(NIPA/MA)/ZnO composite hydrogels were prepared in 6.0 mL saturated ZnO aqueous solution (solubility:1.6×10^{-4} g ZnO/100 mL) from NIPA (1.50 g) and MA (0.08, 0.135, 0.180, and 0.360 g) monomers. These solutions were placed in poly(vinylcloride) straws of 4 mm diameter and irradiated to 80 kGy in air at room temperature in a ^{60}Co γ-irradiator at a fixed dose rate of 3.36kGy/h. The composite hydrogels were removed from the poly(vinylchloride) straws, cut into pieces ~5 mm in height, and then dried in a vacuum oven at 50°C until they reached a constant weight.

For the determination of hydrogel composition, the composite hydrogels were equilibrated in distilled water for 10 days. An aliquot from this solution was taken into polarographic cell and there was no peak for the electroactive species of MA,[15] which indicated 100% gelation for all composite hydrogels. Mole percentages of MA in P(NIPA/MA)-1, P(NIPA/MA)-2, P(NIPA/MA)-3, and P(NIPA/MA)-4 hydrogels were 8.08, 10.20, 18.50, and 31.15, respectively.

RESULTS AND DISCUSSION

P(NIPA/MA) hydrogels were synthesized by a radiation-induced polymerization technique. Some basic properties such as swelling ratio and structural parameters had been determined in previous work.[16] In this study, P(NIPA/MA)/ZnO composite hydrogels were also prepared by the radiation-induced polymerization technique and the amounts of released ZnO from these composite hydrogels were determined via the DPP technique. For this purpose, a certain amount of the vacuum-dried P(NIPA/MA)/ZnO composite hydrogel (~0.05 g) was put into a polarographic cell, which contained 10 mL B-R buffer solutions of pH 2.0, 5.5, or 7.05 at 20 ± 0.1°C, and then high-purity nitrogen (99.999%) was passed through the solution at a flow rate of 100 mL/min. The nitrogen provided both release of ZnO, at a constant rate, by control with a gas flow-meter, and working conditions in the deoxygenated medium. Polarograms were taken through the scanning potential from −800 to −1,500 mV at a scan rate of 5 mV/s and pulse amplitude of 50 mV (pulse duration 50 ms). The reduction peaks for released ZnO were observed at –1,000, −1,050, and –1,300 mV at pH 2.0, 5.5, and 7.05, respectively. The polarograms were recorded at predetermined time intervals. The peak currents increased continuously, depending on release time (Fig. 1). The amounts of ZnO were determined by the standard addition method.

The amount of released ZnO from the P(NIPA/MA)/ZnO composite hydrogels depends on both the pH of the solution and MA content in the composite hydrogel. The ZnO-releasing kinetics of these composite hydrogels at pH 2.0, 5.5, and 7.05 are shown in Figure 2. The ZnO-releasing values of nonionic PNIPA/ZnO composite hydrogels at different pH levels were nearly the same and negligible (0.234–0.294 mg ZnO/g dry gel) compared to the MA containing PNIPA composite hydrogels. The data show that the ZnO-releasing rate increased with an increase of MA content in the composite hydrogel, as from P(NIPA/MA)-1 to P(NIPA/MA)-4. The P(NIPA/MA)-1 composite hydrogel released about 0.403 mg ZnO/g dry gel (pH 2) or 0.636 mg ZnO/g dry gel (pH 7.05) within 120 min, whereas the P(NIPA/MA)-4 composite hydrogel released about 0.746 and 13.22 mg ZnO/g dry gel, respectively, within the same time and at the same pH. The increments in ZnO release with pH and MA content could be attributed to the ionization of pendant carboxylic acid groups on the polymer chain. Because these acidic groups release protons easily, as the pH exceeds the pK_a values of MA (pK_{a1} = 1.87 and pK_{a1} = 6.23), the repulsion between negatively

charged carboxylate groups facilitates the uptake of water in the polymeric matrix, resulting in higher ZnO release. Since the ionization of composite hydrogels with the greatest MA content was highest, their ZnO release was observed to be greater than the others.

In conclusion, the results indicated that P(NIPA/MA)/ZnO composite hydrogels, due to the presence of ionizable carboxylic groups, are pH sensitive, and their swelling ratio increases at higher pH. The release of ZnO from these composite hydrogels depends not only on the pH sensitivity of the polymeric matrices but on the MA content in the composite hydrogel, which causes a larger amount of ZnO to be released at pH 7.05 rather than pH 2.0.
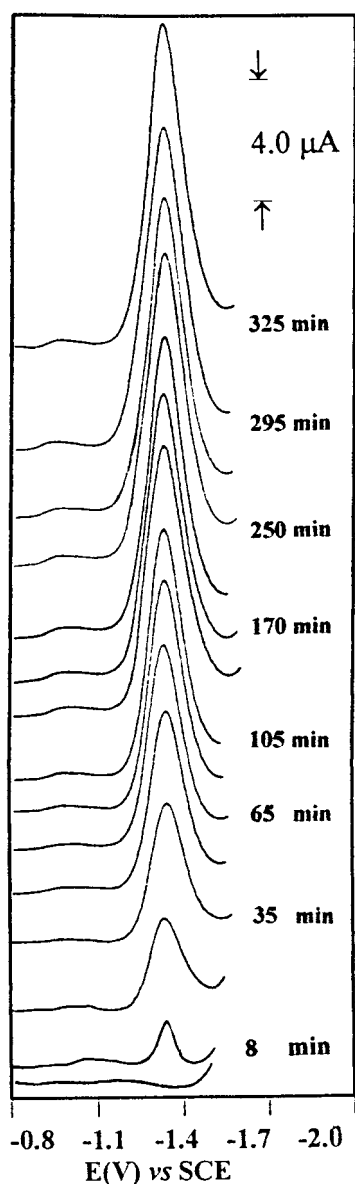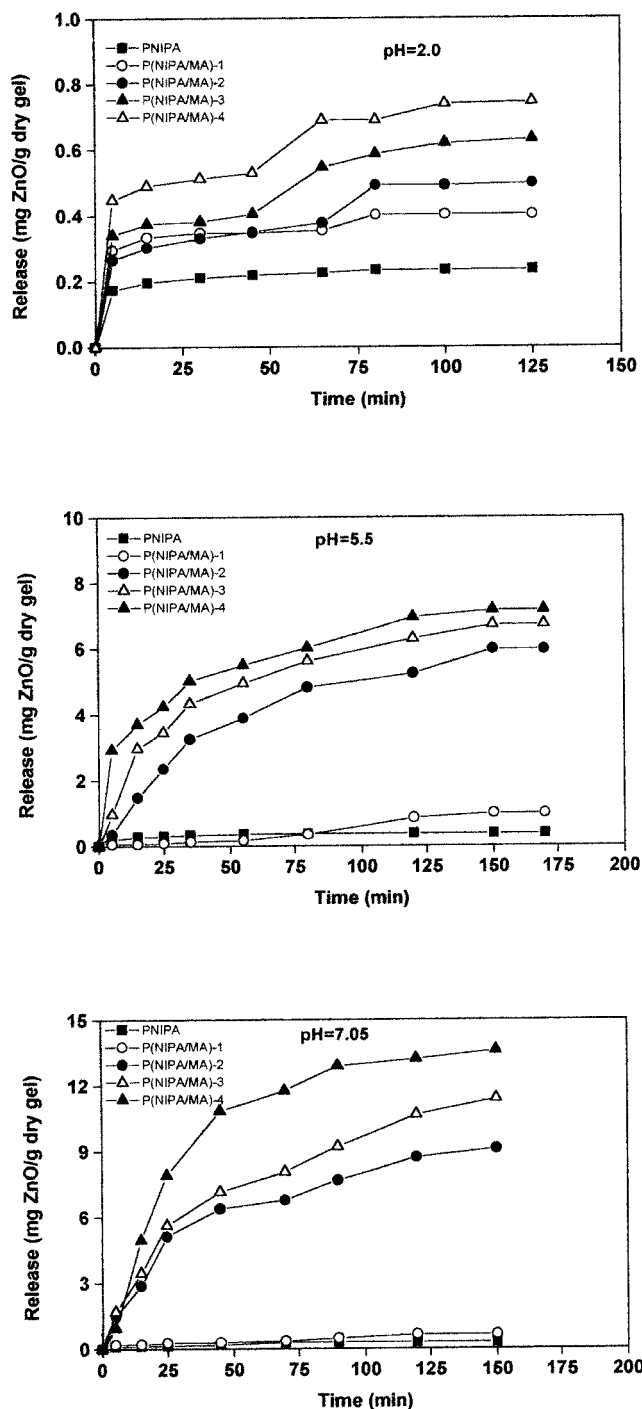

Figure 2 Release of ZnO in P(NIPA/MA)/ZnO composite hydrogels with time (release pH values are given)

References

1. Ju, H. K.; Kim, S. Y.; Lee, Y. M. Polymer 2001, 42, 6851.
2. Peppas, N. A.; Bures, P.; Leobandung, W.; Ichikawa, W. Eur J Pharm Biopharm 2000, 50, 27.
3. Hirasa, O.; Ito, S.; Yamauchi, A.; Fujishige, S.; Ichijo, H. Polymer Gels: Fundamentals and Biomedical Application. Plenum Press, New York, 1991; p. 247.
4. Ju, H. K.; Kim, S. Y.; Kim, S. J; Lee, Y. M. J Appl Polym Sci 2002, 83, 1128.

Figure 1 Differential pulse polarogram for ZnO release from P(NIPA/MA)-4/ZnO composite hydrogels (pH 7.05).

5. Miyata, T.; Asami, N.; Uragami, T. Natura 1999, 399, 746.

6. Brannon-Peppas, L.; Peppas, N. A. Chem Eng Sci 1991, 46, 715.

7. Scranton, M. B.; Rangaragan, B.; Klier, J. Adv Polym Sci 1995, 120, 1.

8. Yoo, M. K.; Sung, Y. K.; Lee, Y. M.; Cho, C. S. Polymer 2000, 41, 5713.

9. Dhara, D.; Nisha, C. K.; Chatterji, P. R. J Pure Appl Chem A 1999, 36, 197.

10. Kim, B.; Flame, K. L.; Peppas, N. A. J Appl Polym Sci 2003, 89, 1606.

11. Şen, M.; Uzun, C.; Güven, O. Int J Pharma 2000, 203, 149.

12. Hoffman, A. S.; Afrassiabi, A.; Dong, L. C. J Control Release 1986, 4, 213.

13. Baldvin, S.; Odio, M. R.; Haines, S. L.; O'Connor R. J; Englehart, J S.; Lane, A. T. J Eur Acad Dermatol 2001, 15, 5.

14. İnam, R., Somer, G. Talanta 1998, 46, 1347.

15. Çaykara, T.; İnam, R., Özyürek, C. J Polym Sci Part A Polym Chem 2001, 39, 277.

16. Çaykara, T. J Appl Polym Sci 2004, 92, 763.