Effects of Dynamic Process of Hydrogel on Solute Release

Masakatu Yonese,* Shuichi Sugie, Tsutomu Nagata, and Kousin Kiyohara
Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467

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Releases of sodium benzoate from calcium alginate (CaAlg) gel beads were studied during deformation processes resulting from the changes of osmotic pressures. The releases were found to be suppressed concomitant with the deformation in the region of high concentrations of adding substances. The suppression was discussed from an advancing boundary.

Recently, hydrogels have attracted special interests as matrices of drug delivery systems based on the development of studies of gels, such as the phase transition and the mechano-chemical reactions.[1-4] Releases of solute from gel were reported to be controlled by the squeezing and the skin effects during the shrinkage resulting from changes of circumstances, i.e., the release is accelerated by the former effect concomitant with the efflux of water and suppressed by the latter effect resulting from the formation of a dense surface layer.[5] In our laboratory, releases of solute from hydrogels have been studied during dynamic processes such as the deformations resulting from the change of osmotic pressure. This report shows the suppressing effects of the deformation of alginate gel on the releases.

Alginate (Alg) is a major structural polysaccharide found in intercellular substances of brown algae, and is a linear block copolymer composed of β-D mannuronate and its C-5 epimer, α-L-guluronate. They are gelled by the addition of divalent metal ions except for Mg^{2+} ion.[6] Purified sodium alginate NaAlg was prepared from commercial origin (Kibun Food Chemifa Co., 150 M) as described in previous papers[7,8] and the weight average molar mass was 185000 g/mol. Alginate gel CaAlg beads were prepared by dropping aqueous solutions of NaAlg (W_{NaAlg}=1.0 w/v%) from a capillary (outer diameter: 0.05 cm, inner diameter: 0.03 cm) into $CaCl_2$ (1.0 mol/dm^3) solutions in which they were immersed for 3 days at least. Their radii were almost 0.15 cm. As an inorganic gel, molecular sieve (MERCK, 0.4 nm beads of radii about 0.1 cm) was used, of which composition is sodium aluminum silicate. Sodium benzoate (NaBA) was used as a solute of release. CaAlg gel beads and molecular sieves were dipped in NaBA solution (0.01 mol/dm^3) for 1 day to attain its equilibrium partition.

The releases of NaBA from molecular sieves were measured in various concentrations of glucose solutions (C_{glu} = 0 - 1 mol/dm^3) by absorbance (λ=224 nm) at 25 °C under stirring (400 rpm) in an absorbance cell (length :1cm), in which one gel sample was put on a net. Figure 1 shows time courses of the relative amounts of release Q/Q_∞, in which Q_∞ is the limiting amount at t=∞. As increasing with C_{glu}, the rates of NaBA release were found to retard slightly without any lag time. Their slopes obtained in the initial stage from linear relations between ln Q/Q_∞ and ln t increased from 0.43 to 0.56 as increasing with C_{glu}. In the cases of C_{glu}=0, 0.05 and 0.1 mol/dm^3, the slopes were almost 0.43 which agreed with the theoretical value as expected from Fickien diffusion from a sphere.[9] In the cases of C_{glu}=0.5 and 1.0 mol/dm^3, the slopes were 0.55 and 0.56. Theses deviations from 0.43 are considered to results from the cross diffusion of the efflux of NaBA and the influx of glucose.

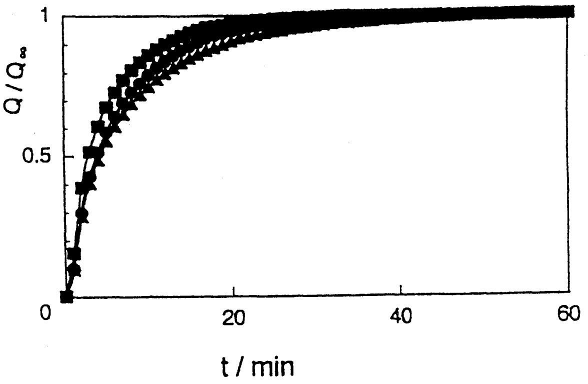

Figure 1. Effect of adding glucose on NaBA release from Molecular seive. Glucose conc./mol/dm^3: ■ ; 0, ● ; 0.5, ▲ ; 1.0.

The releases of NaBA from CaAlg gel beads were measured, in the same manner as those of molecular sieves, in glucose and $CaCl_2$ solutions whose concentrations (C_{glu} and C_{CaCl2}) were in the region of 0 - 1.0 mol/dm^3. As shown in Figures 2 and 3, the rates of releases were found to depend significantly on C_{glu} and C_{CaCl2}. In the region of C_{glu} and C_{CaCl2} = 0 - 0.1 mol/dm^3, the releases occurred without any lag time and retarded slightly with increasing their concentrations. However, as increasing with C_{glu} and C_{CaCl2} furthermore, the releases were found to be suppressed in the initial stages. Strong suppressions were followed by the slow and the rapid releases. In the step of the rapid releases, the rates of the release were apt to increase as increasing with C_{glu} and C_{CaCl2}. Furthermore, in the systems of NaBA releases into $CaCl_2$ solutions, it was found that $CaCl_2$ influxed even in the suppression processes of NaBA releases and the rapid releases of NaBA started after the concentration became constant.

To certify the effects of the adding substances on the

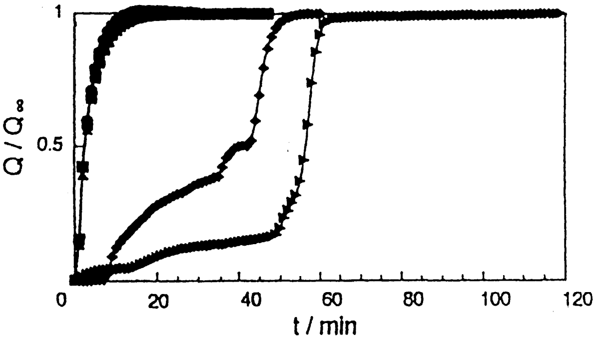

Figure 2. Effect of adding glucose on NaBA release from CaAlg gel bead. Glucose conc./mol/dm^3: ■ ; 0, ● ; 0.05, ▲ ; 0.1, ◆ ; 0.5, ▶ ; 1.0.

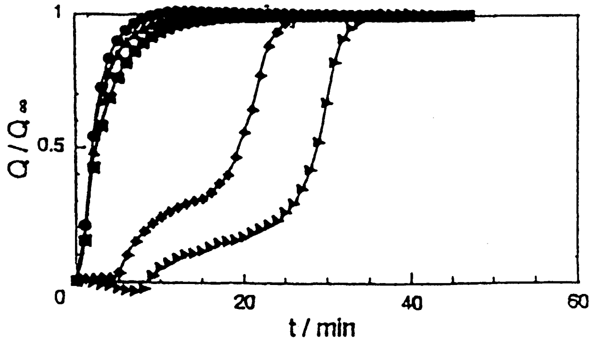

Figure 3. Effect of adding $CaCl_2$ on NaBA release from CaAlg gel bead. $CaCl_2$ conc./mol/dm^3: ■ ; 0, ● ; 0.05, ▲ ; 0.1, ◆ ; 0.5, ▶ ; 1.0.

suppression of the releases, after 2 min of the release of NaBA, glucose was added to the bulk water, i.e., an osmotic shock was added on the way of the release process. When C_{glu} were smaller than 0.1 mol/dm^3, the releases were not suppressed. However, when C_{glu} became greater than 0.5 mol/dm^3, the release was suppressed instantaneously and after lag times of about 5-10 min the release started.

Although molecular sieves did not change their radii in glucose and $CaCl_2$ solutions, CaAlg gels deformed in the solutions due to the changes of the osmotic pressure. Time courses of the relative values of radii r/r_0 of CaAlg in glucose and $CaCl_2$ solutions are shown in Figure 4. r_0 is the original radius of CaAlg gel dipped in NaBA solution and is in the state just before the releases experiments. As Ca^{2+} in CaAlg gels are partly exchanged to Na^+ ions, a part of junctions should be disintegrated. Then, the values of r/r_0 in water increased gradually. In glucose solutions, they also increasesd to almost the same level as that of water. On the other hand, in $CaCl_2$ solutions, the values of r/r_0 decreased. As increasing with C_{CaCl2}, the degree of the shrinkage and times to attain to the equilibrium increased slightly, which result from the enhancement of the crosslinkes of CaAlg gels and the decreases of the osmotic pressure.

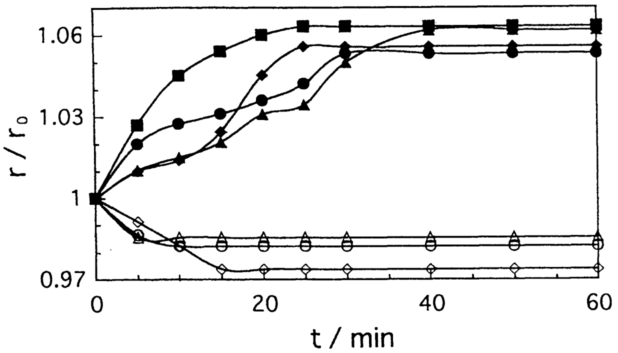

Figure 4. Time courses of radius of CaAlg gel bead in glucose and $CaCl_2$ solution. Glucose conc./mol/dm^3: ■ ; 0, ● ; 0.05, ▲ ; 0.1, ◆ ; 0.5, $CaCl_2$ conc./mol/dm^3: ○ ; 0.05, △ ; 0.1, ◇ ; 0.5.

From these results, it was found that the suppressions of the releases of NaBA from CaAlg gels occurred during both the shrinking and the swelling processes in high concentrations of adding substances and after the value of r became constant the rapid releases started. In considering the results of molecular sieves shown in Figure 1, the deformation processes of CaAlg gels are main factor contributing to the suppression of the NaBA releases. However, to suppress the releases, the concentrations of added substances in the bulk solutions need to exceed a critical one.

When gels deform due to adding substances, the network front under strain extends to the core. Then, the suppression of solute releases is considered to be a problem of diffusion through an advancing boundary.[10] When the network front under strain moves to the core, the network perturbs vigorously and the perturbation increases as increasing with the concentrations of adding substances. Especially, higher strain is exerted on the network front comparing with the outer part of network. Then, the strained network front should play an important role in the suppression of the solute release. However, the suppressions occurred in both the swelling and shrinking processes. The outer layer of the network front under strain becomes more porous in the swelling but in the shrinking it becomes denser. Then, the releases of solutes in the perturbed network layer might be suppressed more than in the equilibrium one. The precise mechanism should be studied further.

The suppressions of solute releases resulting from added substances were observed also in other gels such as gelatin and poly(vinyl methyl ether) gel. The elucidation of the mechanism of the suppression of the releases is considered to lead to the development of the studies about diffusion through gels during the dynamic processes and the applications of gels to drug delivery systems. The control of the release using the deformation of the networks has been examined furthermore.

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