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Research paper

Modulating drug release and matrix erosion of alginate matrix capsules by microenvironmental interaction with calcium ion

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Abstract

Effect of calcium gluconate (CG) content on release of dextromethorphan hydrobromide (DMP), model drug, from capsules containing low and medium viscosity grades of sodium alginate (SA) was investigated in different dissolution media. Matrix erosion of the SA matrix capsules in distilled water and pH 7.4 phosphate buffer was compared. Molecular interaction of SA with calcium ion in surface gel layer of the SA matrix capsules was examined using Fourier transform infrared spectroscopy and differential scanning calorimetry. In distilled water and pH 7.4 phosphate buffer, DMP release rate depended on the viscosity grade of SA, whereas a comparable DMP release rate was found in 0.1 N HCl. Incorporation of CG into the SA matrix capsules caused a faster drug release in acidic medium because CG acted as a channeling agent in the hydrated insoluble gel matrix of alginic acid. Interaction of calcium ions with carboxyl groups of SA could be formed in surface gel layer of hydrated matrix capsules in distilled water. This led to a more rigid matrix gel structure that caused a slower drug release and matrix erosion. In contrast, the extent of this interaction in pH 7.4 phosphate buffer was less than that in distilled water because the common ion effect and high concentration of sodium ion retarded the hydration of SA and the binding of calcium ions with carboxyl groups of SA. Thus, a small change in drug release and matrix erosion was observed. This finding suggests that microenvironmental interaction between hydrated SA and calcium ion in distilled water could be created in the formulations prepared using low compression force. Moreover, incorporation of CG could moderate drug release and matrix erosion of the SA matrix capsules.

Keywords: Sodium alginate; Molecular interaction; Matrix erosion; Drug release; Capsules

1. Introduction

Matrix drug delivery systems have been widely used for sustaining drug release in gastrointestinal tract. These systems can be divided into two types: hydrophobic and hydrophilic matrices. Hydrophobic matrices are prepared using water-insoluble materials, from which release of drug loaded is mainly controlled by diffusion. Consequently the drug release profiles of this system gave non-constant drug release rate [1,2]. On the other hand, hydrophilic matrices could swell and erode in an aqueous medium, and drug subsequently releases from hydrated matrices. This behavior provides a potential to obtain a dissolution profile with zero-order release kinetic mechanism [3]. Materials that could exhibit this phenomenon are natural and synthetic polymers. Natural polysaccharides, such as sodium alginate [4], pectin [5], xanthan gum [6,7] and chitosan [8], have been employed to prepare hydrophilic matrices for oral controlled release dosage forms.

Sodium alginate (SA) is a sodium salt of alginic acid, a naturally occurring non-toxic polysaccharide found in marine brown algae. Alginate has been widely used as food and pharmaceutical additives, such as a tablet disintegrant,

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a thickening and suspending agent [9]. It contains two uronic acids, α-L-guluronic and β-D-mannuronic acids, and is composed of homopolymeric blocks and blocks with an alternating sequence [10]. Gelation occurs by cross-linking of the uronic acids with divalent cations, such as calcium ion. The primary mechanism of this gelation involves extended chain sequences which adapt a regular twofold conformation and dimerize with specific chelation of calcium ion, the so-called 'egg-box' structure [11]. Each calcium ion takes part in nine co-ordination link with an oxygen atom, resulting in three-dimensional network of calcium alginate. This phenomenon has been applied for preparing an alginate bead [12,13] and microparticles [14] employed as a delivery system of bioactive agents.

SA has also been widely used as a drug release modifier in matrix tablets [15–19] and capsules [20–22]. The gel formation of SA matrix tablets in different dissolution media had been previously reported [16]. SA is converted to alginic acid and porous hydrated structure is consequently formed in acidic condition, whereas viscous gelatinous layer creates around the tablets in neutral phosphate buffer [16]. This led to different drug release behavior from the SA matrix. Viscosity of SA also affects drug release. Lower viscosity grade of SA provides faster drug release due to fast and complete erosion of SA matrix in distilled water [18]. Moreover, the drug release rate from matrix capsules is dependent on the viscosity grades of SA as it affects penetration of neutral phosphate buffer into the capsules [22]. The alternative method for modifying drug release from the SA matrix capsules is the formation of calcium alginate gel in the capsules by adding calcium chloride. This results in slow release of drug in neutral dissolution medium [21]. However, matrix erosion and cross-linking between SA and calcium ion in microenvironment hydration of surface gel layer capsules have not yet been examined. Recently, this method has been applied to retard drug release from pectin-based matrix tablets prepared by direct compression [23] and wet granulation/compression [24]. The researchers described that the slower drug release resulted from the cross-linking of pectin with calcium ions. The cross-linking can easily take place after hydration because particles are tightly packed under high compression force. So, it is of interest to verify the occurrence of interaction between SA and calcium salt in capsules where particles are loosely packed using low compression force.

In the present study, the effect of calcium gluconate (CG) content on release of dextromethorphan hydrobromide (DMP), model drug, from SA matrix capsules in different dissolution media was investigated. Low and medium viscosity grades of SA were used. Matrix erosion of the SA matrix capsules in distilled water and pH 7.4 phosphate buffer was investigated and compared. Molecular interaction of SA with calcium ion in surface gel layer of the hydrated SA matrix capsules was examined using Fourier transform infrared (FTIR) spectroscopy and differential scanning calorimetry (DSC).

2. Materials and methods

2.1. Materials

Low viscosity grade of sodium alginate (LVSA; viscosity of 2% dispersion at 25 °C: 250 cps) and medium viscosity grade of sodium alginate (MVSA; viscosity of 2% dispersion at 25 °C: 3500 cps) were purchased from Sigma Chemical Company (MO, USA). DMP was a gift from F. Hoffmann-La Roche (Basel, Switzerland). CG in the form of monohydrate was obtained from Fluka (Buchs, Switzerland). The substances mentioned were used after sieving through 80-mesh screen. All other reagents used in this study were of analytical grade and used as received.

2.2. Preparation of capsules

The capsules consisted of 13.6% w/w DMP, 0–20% w/w CG, and appropriate amount of SA used to adjust weight of each capsule to 220 mg. The batch size of each formulation was 30 capsules. All ingredients were mixed geometrically in a glass bottle for 15 min. The mixtures were filled into no.2 transparent hard gelatin capsule shells using manual capsule filling machine (Model PANVIV.A01, The Union Chemical and Surgical, Thailand).

2.3. In vitro drug release studies

A USP dissolution apparatus I (Hanson Research, Northridge, USA) was used to characterize the release of DMP from the LVSA and MVSA matrix capsules. The baskets were rotated at 100 rev/min at 37.0 ± 0.5 °C. The dissolution media (750 ml) used were 0.1 N HCl, distilled water, or pH 7.4 phosphate buffer. Samples (7 ml) were collected and replaced with a fresh medium at different time intervals. The amount of DMP released was analyzed spectrophotometrically at 278 nm (Shimadzu UV1201, Japan).

The DMP release kinetics from the capsules in different dissolution media were investigated by fitting the release data into Eq. (1) as follows:

$$Q = kt^n \quad (1)$$

where Q is the percentage of drug released at a given time (t), k is the release rate and n is the diffusion exponent. The n value could be defined as 0.5 and 1, which indicates square root of time and zero-order kinetics, respectively [25]. The release rate was estimated by fitting the experimental drug release data into both models and analyzed by linear regression analysis.

2.4. Matrix erosion studies

Determination of matrix erosion was carried out using CG-MVSA matrix capsules containing no drug in distilled water and pH 7.4 phosphate buffer. The method used in this study was modified from that of the previous report [26]. Weighed capsule (W_i) was placed in basket (W_b)

and subjected to the condition of the release studies described above. Each basket was taken out at predetermined time intervals, placed in a small beaker (W_c), and then put in an oven at 55 °C until the constant weight (W_f) was obtained. The % matrix erosion can be calculated using the following equation.

$$\text{Matrix erosion } (\%) = \left[\frac{(W_i - W_{cs}) - (W_f - W_b - W_c)}{(W_i - W_{cs})}\right] \times 100 \quad (2)$$

where W_{cs} is the mean weight of capsule shell which was found to be 62.5 ± 0.9 mg ($n = 6$). After erosion studies, dried surface gel layer of matrix capsules was collected, and ground to fine particles using mortar and pestle. Interaction of SA and calcium ions in the surface gel layer of the SA matrix capsules was investigated using FTIR spectroscopy and DSC.

2.5. Fourier transform infrared (FTIR) spectroscopy

FTIR spectra of MVSA, CG and the surface gel layer of the SA matrix capsules obtained from matrix erosion studies were recorded with a FTIR spectrophotometer (Spectrum One, Perkin-Elmer, Norwalk, USA) using KBr disc method. Each sample was gently triturated with KBr powder in a weight ratio of 1:100 and then pressed using a hydrostatic press at a pressure of 10 tons for 5 min. The disc was placed in the sample holder and scanned from 4000 to 450 cm^{-1} at a resolution of 4 cm^{-1}.

2.6. Differential scanning calorimetry (DSC)

DSC thermograms of MVSA, CG, CG-MVSA mixture and the surface gel layer of the SA matrix capsules obtained from matrix erosion studies were recorded using a differential scanning calorimeter (DSC822, Mettler Toledo, Switzerland). Each sample (2–2.5 mg) was accurately weighed into a 40-μl aluminum pan without an aluminum cover. The measurement was performed between 30 and 350 °C at a heating rate of 10 °C/min.

3. Results

DMP release profiles of LVSA and MVSA matrix capsules with different contents of CG are shown in Figs. 1–3. DMP release profiles of the SA matrix capsules showed nonlinear lines in 0.1 N HCl (Fig. 1), whereas nearly straight lines were obtained in distilled water and pH 7.4 phosphate buffer (Figs. 2 and 3). This suggested a different release kinetic of DMP from the SA matrix capsules. The DMP release in acidic condition followed a square root of time kinetic with R^2 higher than 0.97, indicating a matrix diffusion controlled mechanism. These results were similar to those of the previous study of Hodsdon et al. [16]. In distilled water and pH 7.4 phosphate buffer the drug release

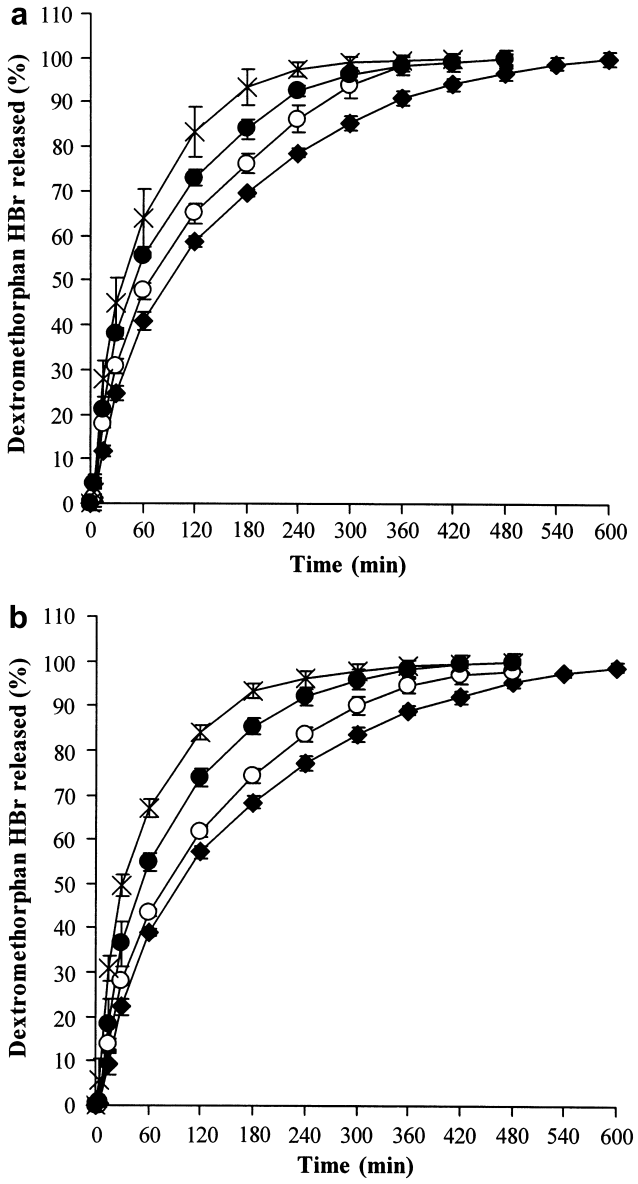

Fig. 1. Effect of CG content on the release of DMP-SA matrix capsules using (a) LVSA and (b) MVSA in 0.1 N HCl: (◆) 0; (○) 5; (●) 10; (×) 20% w/w CG. Each point is the mean ± SD, $n = 3$.

gave a good fitting with a zero-order kinetic with R^2 more than 0.98, suggesting a swelling and erosion controlled mechanism. The release rates of DMP from the SA matrix capsules in different media are presented in Fig. 4. It was indicated that LVSA and MVSA matrix capsules gave a comparable DMP release rate in 0.1 N HCl (Fig. 4a), whereas MVSA matrix capsules had a lower DMP release rate than LVSA matrix capsules in distilled water and pH 7.4 phosphate buffer. Moreover, higher DMP release rates in distilled water were found when compared with those in pH 7.4 phosphate buffer (Fig. 4b and c).

Incorporation of CG into the SA matrix capsules affected DMP release patterns (Figs. 1–3). The DMP release rate in acidic medium increased with increasing amount of CG, and comparable release rate was found in both viscosity

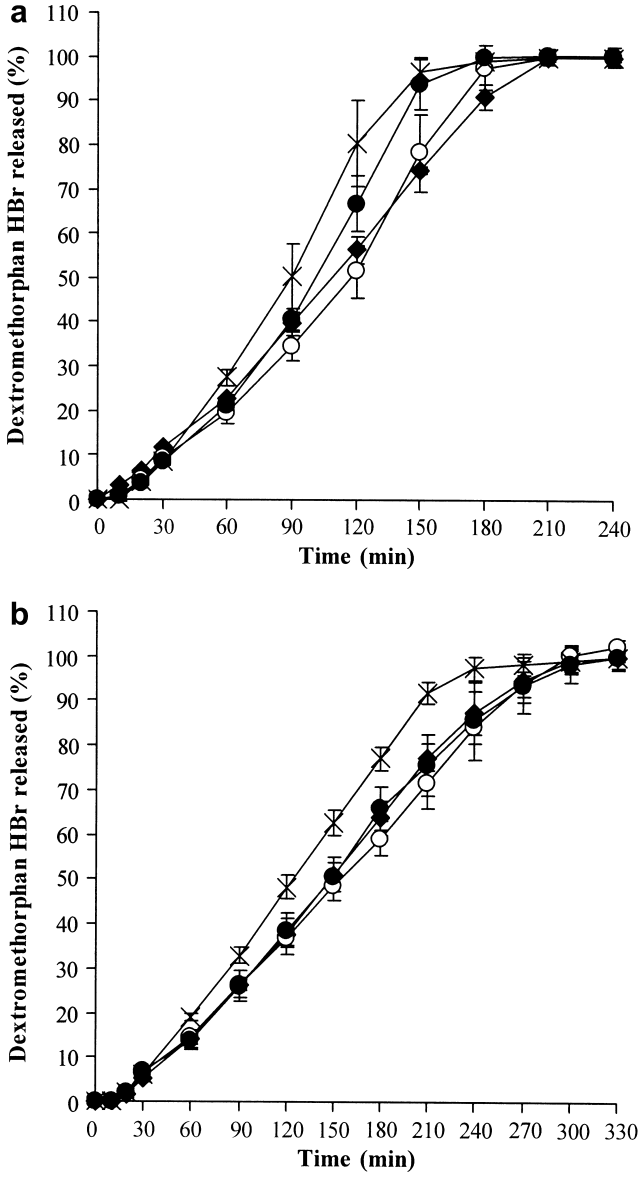

Fig. 2. Effect of CG content on the release of DMP-SA matrix capsules using (a) LVSA and (b) MVSA in pH 7.4 phosphate buffer: (◆) 0; (○) 5; (●) 10; (×) 20% w/w CG. Each point is the mean ± SD, $n = 3$.

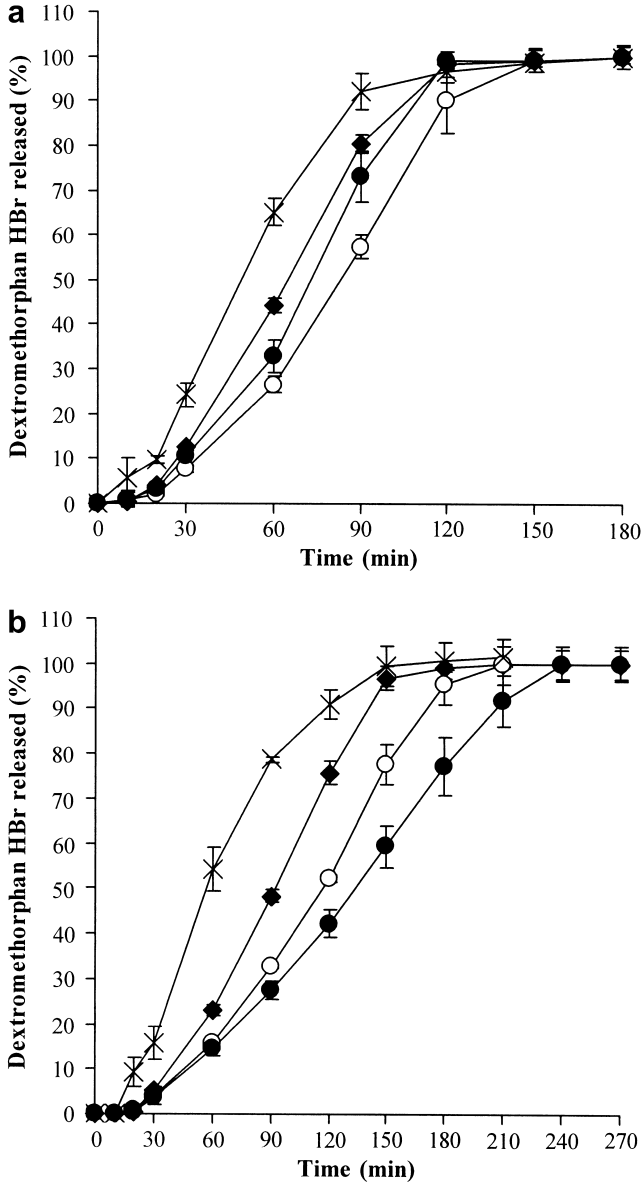

Fig. 3. Effect of CG content on the release of DMP-SA matrix capsules using (a) LVSA and (b) MVSA in distilled water: (◆) 0; (○) 5; (●) 10; (×) 20% w/w CG. Each point is the mean ± SD, $n = 3$.

grades of SA (Fig. 4a). The DMP release rate in pH 7.4 phosphate buffer tended to increase as amount of CG increased (Fig. 4c). However, the DMP release rate in distilled water decreased when lower amounts of CG were added (5% CG in LVSA matrix capsules and 5–10% CG in MVSA matrix capsules), followed by increase of drug release when CG was further added to 20% w/w (Fig. 4b).

Matrix erosion of CG-MVSA matrix capsules without DMP was performed in distilled water and pH 7.4 phosphate buffer as shown in Fig. 5. In distilled water, incorporating 5% and 10% CG into MVSA matrix capsules caused a decrease in matrix erosion at 1 and 2 h of the test. However, addition of 20% CG to MVSA matrix capsules gave slower erosion at 0.5 and 1 h, followed by complete erosion at 2 h of the test. Moreover, matrix erosion of MVSA and CG-MVSA matrix capsules in pH 7.4 phosphate buffer was lower than that in distilled water. Using pH 7.4 phosphate buffer, increasing content of CG in MVSA matrix capsules did not affect the matrix erosion, except 20% CG-MVSA matrix capsules showed higher erosion at 2 h of the test. Relationship between DMP released and matrix erosion of CG-MVSA matrix capsules is shown in Fig. 6. The increase in 5–10% CG content caused a decrease in drug release and matrix erosion in distilled water (Fig. 6a). However, 20% CG in the matrix capsule gave the slowest matrix erosion at 0.5 and 1 h, but the drug release was very rapid (Fig. 6a). On the other hand, similar relationship between both parameters in all levels of CG was observed in pH 7.4 phosphate buffer (Fig. 6b). Furthermore, the slope value of the linear correlation of all data between drug

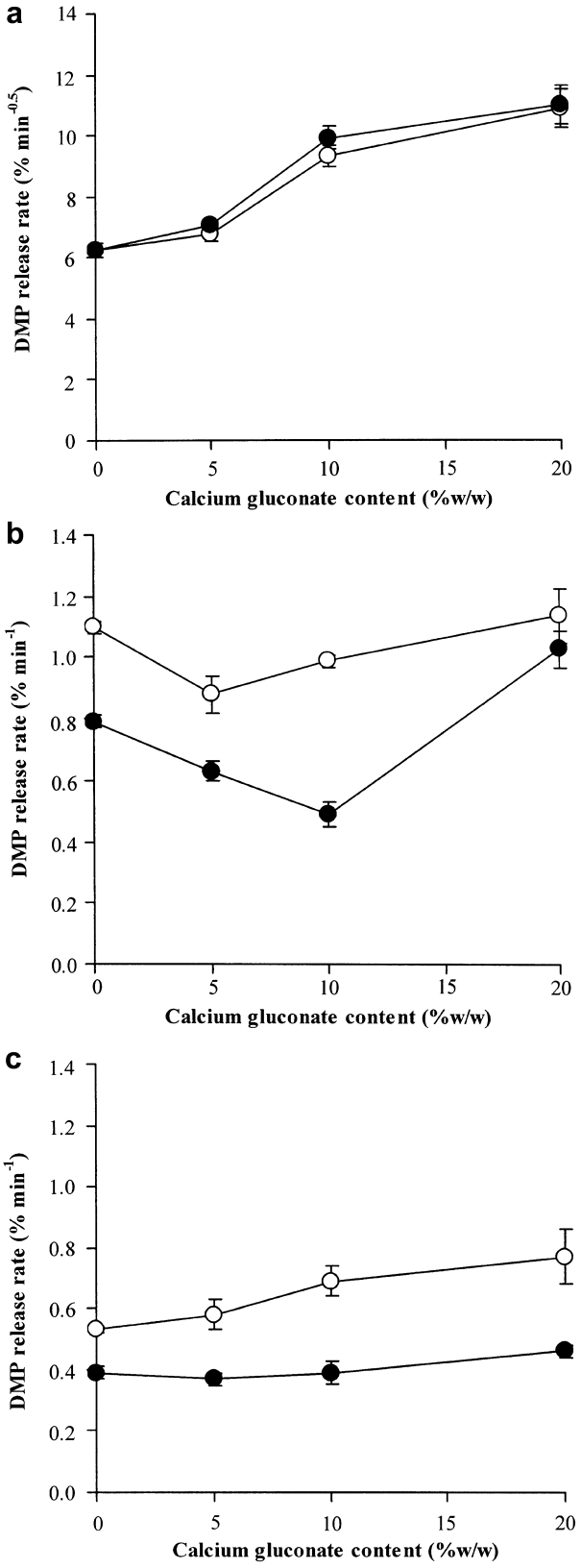

Fig. 4. Relationship between drug release rate and CG content in DMP-SA matrix capsules using (○) LVSA and (●) MVSA in (a) 0.1 N HCl, (b) distilled water, and (c) pH 7.4 phosphate buffer. Each point is the mean ± SD, $n = 3$.

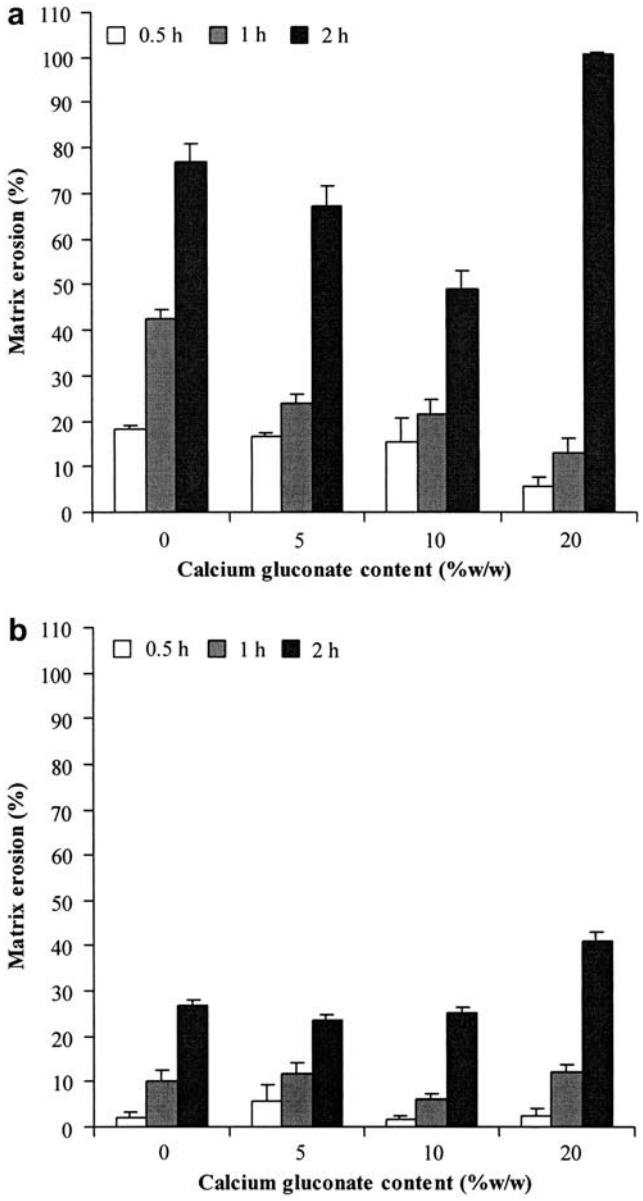

Fig. 5. Matrix erosion of MVSA matrix capsules containing different CG contents in (a) distilled water, and (b) pH 7.4 phosphate buffer. Each value is the mean ± SD, $n = 3$.

released and matrix erosion was 0.836 for distilled water and 1.212 for pH 7.4 phosphate buffer (Fig. 6). The determination coefficient of this relationship in distilled water was worse than that in pH 7.4 phosphate buffer owing to the deviation of matrix erosion of 20% CG-MVSA matrix capsules in distilled water. The slope value less than unity in distilled water suggested that the release of drug was slower than the matrix erosion. This indicated that the drug release in distilled water was controlled by matrix erosion mechanism rather than in pH 7.4 phosphate buffer.

Molecular interaction between MVSA and CG in surface gel layer of the hydrated matrix capsules was investigated using FTIR spectroscopy and DSC. FTIR spectra of MVSA powder presented the peaks at 3435, 1611,

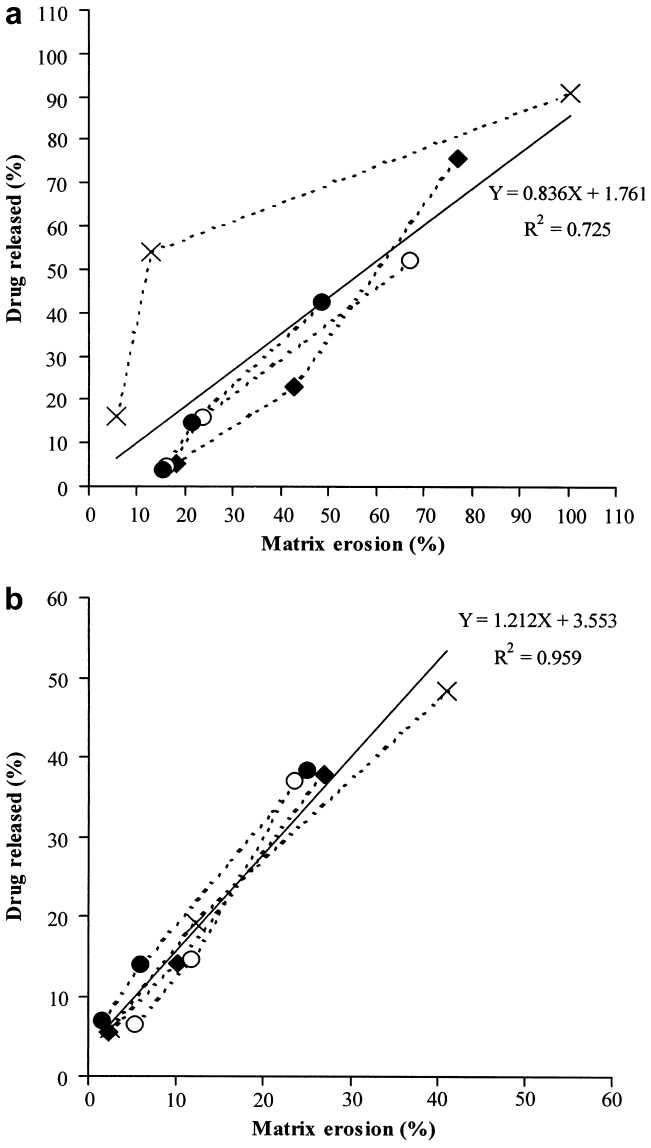

Fig. 6. Relationship between matrix erosion and drug released of MVSA matrix capsules (broken lines) with different CG contents in (a) distilled water and (b) pH 7.4 phosphate buffer: (◆) 0; (○) 5; (●) 10; (×) 20% w/w CG. The solid line is the linear regression line of all data.

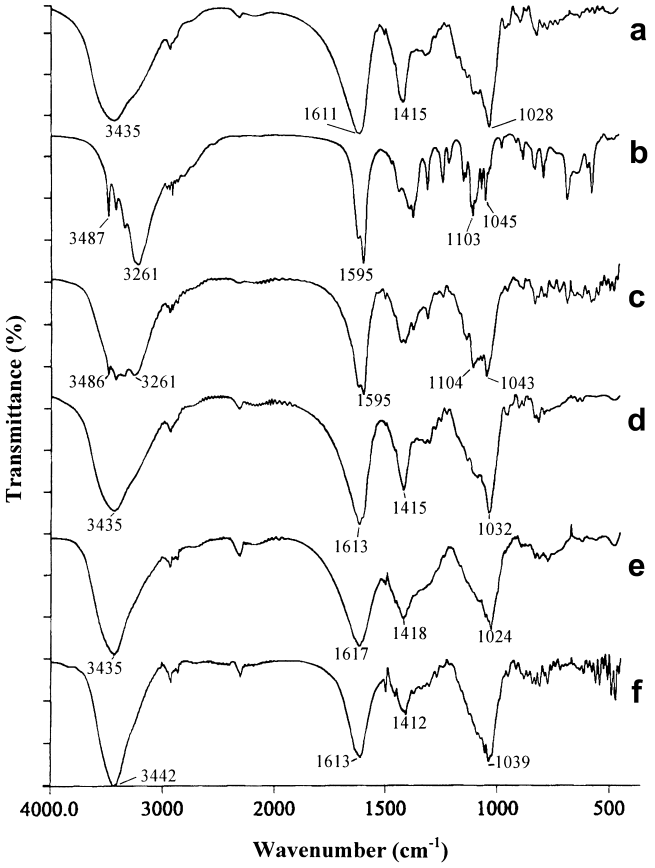

Fig. 7. FTIR spectra of (a) MVSA, (b) CG, (c) 20% CG-MVSA mixture, surface gel layer of MVSA matrix capsule with (d) 0 and (e) 20% w/w CG at 1 h of erosion test using distilled water, and surface gel layer of MVSA matrix capsule having (f) 20% w/w CG at 2 h of erosion test using pH 7.4 phosphate buffer.

1415, and 1028 cm^{-1}, which were due to the stretching of O–H, COO^- (asymmetric), COO^- (symmetric), and C–O–C, respectively (Fig. 7a). Mixture of 20% CG-MVSA showed the peaks of CG at 3486, 3261, 1595, 1104, and 1043 cm^{-1} (Fig. 7c). The peaks of the surface gel layer of MVSA matrix capsules in distilled water were similar to those of MVSA powder (Fig. 7d), and those in pH 7.4 phosphate buffer also showed similar spectra (data not shown). The shift of COO^- peaks at 1613 and 1415 cm^{-1} to higher wavenumber, as well as a decrease in intensity, was found in the surface gel layer of 20% CG-MVSA matrix capsules in distilled water (Fig. 7e), indicating ionic binding between COO^- of SA and calcium ions of CG [27,28]. On the other hand, these peaks of the surface gel layer of 20% CG-MVSA capsules in pH 7.4 phosphate buffer did not shift to higher wavenumber, but lower intensity of these peaks was also found (Fig. 7f). This suggested that the ionic binding between carboxyl groups of SA and calcium ion in distilled water occurred to a higher extent than that in pH 7.4 phosphate buffer. Moreover, the O–H peak intensity of the surface gel layer from both conditions became narrower and larger, indicating an increase in intermolecular bonding of SA [27]. Additionally, it was observed that the peaks of CG did not appear in the surface gel layer of CG-MVSA matrix capsules tested in both media, indicating that CG could be ionized to give available or free calcium ions to form complex with SA.

DSC thermogram of MVSA powder showed an exothermic decomposition peak at 253 °C (Fig. 8a). This exothermic peak also presented in 20% CG-MVSA mixture (Fig. 8c). Two endothermic peaks at around 145–180 °C of CG were observed in CG (Fig. 8b) and 20% CG-MVSA mixture (Fig. 8c). The surface gel layer of MVSA matrix capsules in distilled water showed an exothermic peak followed by endothermic peak at around 205–215 °C (Fig. 9a). A shift to lower temperature and a decrease in peak intensity of these peaks were observed as amount of CG in MVSA matrix capsules increased (Fig. 9b–d).

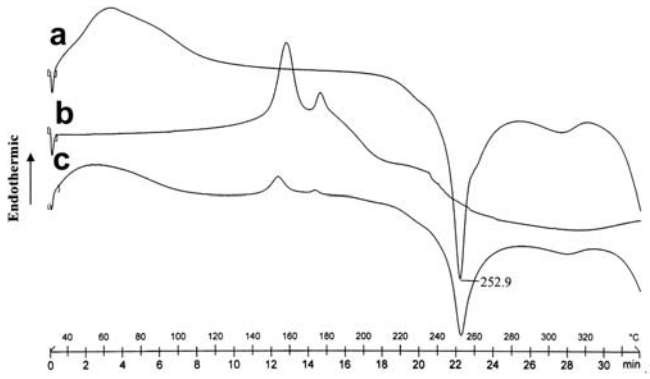

Fig. 8. DSC thermograms of (a) MVSA, (b) CG, and (c) 20% CG-MVSA mixture.

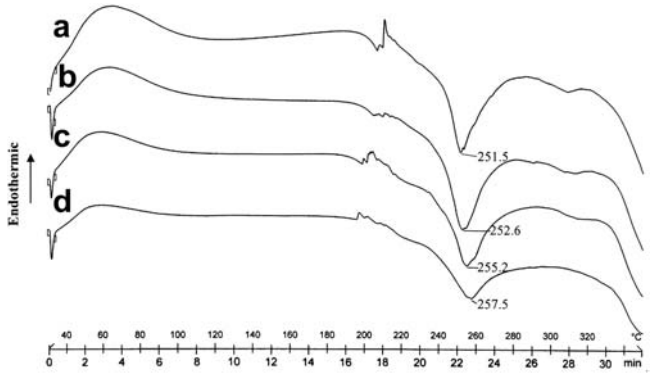

Fig. 9. DSC thermograms of surface gel layer of MVSA matrix capsules with (a) 0, (b) 5, (c) 10, and (d) 20% w/w CG at 1 h of erosion test using distilled water.

Moreover, the exothermic decomposition temperature gradually increased from 252 to 258 °C and a lower intensity of decomposition peak was observed when 20% CG was added. In contrast to the surface gel layer in pH 7.4 phosphate buffer, the peaks at around 205–215 °C showed a lower intensity and were not significantly affected by addition of CG (Fig. 10a–d). No change in the exothermic decomposition peak at 254 °C was observed, except 20% CG-MVSA matrix capsule showed a shift to higher temperature (257 °C) and a lower intensity of this peak. These phenomena suggested that molecular interaction between SA and calcium ion in distilled water caused a change in crystal structure formed and a more rigid gel formation was obtained. Furthermore, the DSC patterns of the surface gel layer of the SA matrix capsules did not present the endothermic peaks of CG, which confirmed the results of FTIR spectroscopy.

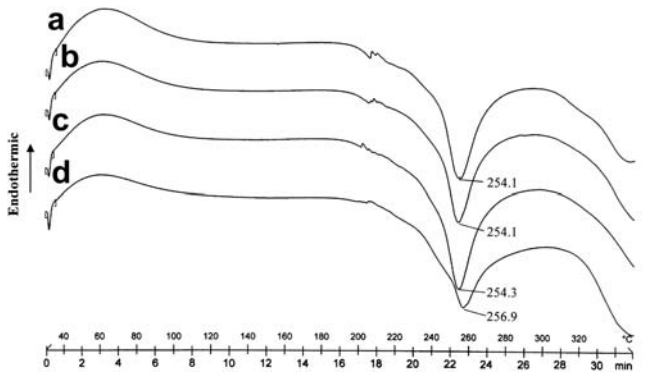

Fig. 10. DSC thermograms of surface gel layer of MVSA matrix capsules with (a) 0, (b) 5, (c) 10, and (d) 20% w/w CG at 2 h of the erosion test using pH 7.4 phosphate buffer.

4. Discussion

The release of DMP from LVSA and MVSA matrix capsules was investigated in different dissolution media. In acidic medium, SA are converted to alginic acid, and subsequently formed a hydrated insoluble gel matrix [16]. From this reason, the DMP release followed a matrix diffusion controlled mechanism. A comparable release rate of DMP from LVSA and MVSA matrix capsules was found, suggesting that the hydrated insoluble gel of alginic acid formed did not depend upon the viscosity grade of SA. This finding was in agreement with that reported by Veski et al. [22]. However, LVSA tablets gave a slower drug release than HVSA (high viscosity grade of SA) tablets in HCl, which resulted from an unexpected lamination of HVSA tablets [18]. In this study, LVSA and MVSA matrix capsules could form similar structure of insoluble matrix of alginic acid as a low compression force was applied in the capsules. The insoluble matrix did not break to a small piece of matrix during release testing that it can be visually observed. Efentakis and Buckton [18] reported that the matrix erosion of SA tablets was less than 25% after 8 h testing in acid medium. Thus the matrix erosion in this medium is not interesting. In distilled water and pH 7.4 phosphate buffer, SA could be hydrated to form hydrophilic gel matrix. This led to a swelling and erosion controlled mechanism of DMP release from the capsules. However, the DMP release rate and matrix erosion in distilled water were greater than those in pH 7.4 phosphate buffer (Figs. 4 and 5). This was due to the effect of sodium ions on dissolution medium. Generally, high ionic strength in SA solution had a profound effect on polymer chain extension and solution viscosity [10]. Moreover, intrinsic viscosity of SA solutions decreased with increasing concentration of the added salt, sodium chloride [29], suggesting that SA could not be fully hydrated in the high concentration of sodium ions. This is likely due to the common ion effect of sodium ion on SA. From these reasons, surface gel hydration of the SA matrix capsules in pH 7.4 phosphate buffer was slower when compared with that in distilled water. This led to a mainly controlled release of drug by erosion mechanism of hydrated gel in distilled water. Furthermore, LVSA matrix capsules provided a faster DMP release than MVSA matrix capsules in both media because hydrated LVSA matrix had greater erosion and thus higher DMP release rate was obtained [17,18].

The DMP release from the SA matrix capsules in pH 7.4 phosphate buffer followed a zero-order kinetic. This result was different from that of the previous study that used pseudoephedrine HCl as model drug which drug release gave a good correlation with a square root of time kinetic in pH 7.2 phosphate buffer [22]. This could be explained using the differences in molecular size and water solubility of drug [30]. A small molecule ($M_W = 201.7$) and freely soluble in water (1:1.6) of pseudophedrine HCl [31] caused a faster drug release rate than erosion rate of the hydrated SA matrix capsules. On the other hand DMP is a larger molecule ($M_W = 370.3$) and sparingly soluble in water (1:60) [31], leading to a slower drug release that the release rate of DMP was close to the matrix erosion of the hydrated SA matrix capsules. Therefore, a zero-order release kinetic of DMP was observed. Moreover, the release kinetic of DMP was similar to the release of an acidic ibuprofen [20] that was slowly dissolved in neutral phosphate buffer. This suggested that the release kinetic of sparingly soluble drug could be mainly controlled by erosion of the hydrated SA matrix capsules.

Incorporation of CG caused a faster release and a comparable release rate of DMP from LVSA and MVSA matrix capsules at all levels of CG because CG, showing high solubility in acidic medium, acted as a channeling agent in the hydrated insoluble matrix of alginic acid. Therefore, the higher the CG content, the faster the DMP released from the capsules was found (Fig. 4a). It can be expected that the change of SA to alginic acid and fast dissolution of CG resulted in less possibility of the formation of ionic bonding between SA and calcium ions in this medium. In distilled water the MVSA matrix capsules with CG showed slower matrix erosion because carboxyl groups of hydrated SA could form ionic bonding with soluble calcium ions in microenvironmental condition, which was revealed by FTIR spectroscopy. However, it can be observed that the COO^- peaks had little shift to higher wavenumber (3–4 cm^{-1}), which was remarkably different when compared with the higher wavenumber shift (10–20 cm^{-1}) of calcium alginate beads [28]. Furthermore, the exothermic peak followed by endothermic peak at around 205–215 °C was shifted to lower temperature, and the lower intensity of the exothermic decomposition peak was observed. These results were similar to the interaction of SA with clay [32]. This indicated that the interaction of the hydrated gel of SA and calcium ions did not lead to formation of egg-box structure of insoluble calcium alginate due to a low concentration of calcium ions. However, the interaction of SA with low concentration of calcium ion led to more rigid gel structure and this gel could erode slowly. From these reasons the slower drug release was observed. The matrix erosion of MVSA matrix capsules decreased with increasing content of CG below 10% (Fig. 4b). This suggested a stronger interaction of SA and calcium ions depended on concentration of calcium ions dissolved. However, using 20% CG the matrix erosion was slower at 0.5 and 1 h of the test and complete erosion was obtained at 2 h because high concentration gradient of soluble CG in the hydrated matrix gel caused the fast release of CG and the rigid gel structure could not be created. In addition the ratio of SA in the capsules was decreased with increasing content of CG. This resulted in the faster drug release in 20% CG-MVSA matrix capsules. The viscosity grade of SA also influenced the interaction with calcium ions. It can be observed that the drug release from LVSA matrix capsules was slower when adding 5% CG and gradually faster at the higher content of CG. The higher viscosity of hydrated matrix gel of SA could retard the release of soluble CG, which increased a possibility of calcium ions to interact with SA. It can be observed in MVSA matrix capsules that the matrix erosion was gradually slower when CG content was less than 10%.

In pH 7.4 phosphate buffer, the DMP release and matrix erosion of LVSA and MVSA matrix capsules were not affected by incorporating less than 10% of CG. At pH 7.4, CG has a low solubility and FTIR spectroscopy and DSC revealed a complete dissolution of CG from the hydrated matrix gel of 20% CG-MVSA matrix capsules. These suggested that SA could not interact with calcium ions in pH 7.4 phosphate buffer, although alginate had a higher selectivity on calcium ion than monovalent sodium ions [33]. It can be explained by the fact that low concentration of calcium ions could not compete with higher concentration of sodium ion to bind with carboxyl groups of SA. Moreover, common ion effect of sodium ions in SA and the formation of insoluble phosphate in the medium at pH above 5.5 [34] caused a less possibility of interaction between SA and calcium ions. However, the faster drug release and matrix erosion of 20% CG-MVSA matrix capsules were obtained. This was due to the decrease of the SA ratio in the capsules.

5. Conclusions

Incorporation of CG into the SA matrix capsules caused a faster drug release in acidic medium because CG acted as a channeling agent in the hydrated insoluble gel matrix of alginic acid. Molecular interaction between calcium ion and SA could be formed in distilled water. This led to a more rigid matrix gel structure, which provided slower drug release and matrix erosion. On the other hand, the interaction of SA with calcium ion was weaker and to a lower extent in pH 7.4 phosphate buffer because the common ion effect and high concentration of sodium ion retarded the hydration of SA and the binding of calcium ion with carboxyl groups of SA. Thus, a change of drug release and matrix erosion was not clearly found. This finding suggests that addition of CG could moderate drug release and matrix erosion of the SA matrix capsules prepared using low compression force. The discrepancy in drug release and matrix erosion was due to molecular interaction of SA with calcium ion in surface gel layer, which was dependent upon the nature of dissolution medium.

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