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Impact of salt form and molecular weight of chitosan on swelling and drug release from chitosan matrix tablets

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ABSTRACT

Magnetic resonance imaging (MRI) and gravimetric techniques were used to assess swelling and erosion behaviors of hydrophilic matrix tablets made of chitosan. The impact of salt form, molecular weight (MW) and dissolution medium on swelling behavior and drug (theophylline) release was studied. The matrix tablets made of chitosan glycolate (CGY) showed the greatest swelling in both acid and neutral media, compared to chitosan aspartate, chitosan glutamate and chitosan lactate. MRI illustrated that swelling region of CGY in both media was not different in the first 100 min but glassy region (dry core) in 0.1 N HCl was less than in pH 6.8 buffer. The tablets prepared from chitosan with high MW swelled greater than those of low MW. Moreover, CGY can delay drug release in the acid condition due to thick swollen gel and low erosion rate. Therefore, CGY may be suitably applied as sustained drug release polymer or enteric coating material.

1. Introduction

Hydrophillic polymer matrix systems are widely used in oral controlled drug delivery systems because of their flexibility to obtain a desirable drug release profile, cost effectiveness, and broad regulatory acceptance. Drug release from hydrophilic matrix tablets is known to be a complex interaction between dissolution, diffusion and erosion mechanisms (Maderuelo, Zarzuelo, & Lanao, 2011). During drug release process, various layers in a tablet are formed. As the medium penetrates into the tablet, a penetration front between glassy region (inside, dry core) and hydrated glassy region emerges. Then, swelling medium keeps penetrating into the polymer making the hydrated glassy region transforms to a rubbery state known as a gel layer. The interface between the glassy and rubbery regions is called swelling front. After that, the swollen polymer erodes, resulting in an interface between the swollen tablet and bulk medium (eroding front). Several transport phenomena take place through this gel layer: the entry of the aqueous medium and the exit of the drug to the outside of the system, and phenomena of matrix erosion. The thickness of the gel layer increases as more and more water enters the system. At the same time, the surface-most polymer chains, which become hydrated earlier than the others, gradually relax until they lose consistency, after which matrix erosion begins (Colombo, Bettinia, Santia, & Peppas, 2000). Therefore, the thickness of rubbery region (or gel layer) and erosion rate are crucial to determine drug release kinetics.

Swelling behavior of polymer has been investigated by many techniques such as gravimetric technique (weight difference between dry and wet polymer) (Sriamornsak, Thirawong, & Korkerd, 2007; Sriamornsak, Thirawong, Weerapol, Nunthanid, & Sungthongjeen, 2007), optical observation technique (fix polymer in Plexiglass®) and magnetic resonance imaging (MRI) (Huanbutta et al., 2011). Monitoring of swelling and erosion progresses by gravimetric technique has been used for many decades since the method is not complicated and inexpensive. However, this technique is not a continuous monitoring, thus a large number of samples have to be prepared for each time point of investigation and weighing error from removing excess solvent from the samples might be occurred. MRI is an alternative technique used to observe swelling behavior of hydrophilic polymers and complicated drug delivery systems by monitoring the concentration and mobility of water and polymer using nuclear magnetic resonance signal of the hydrogen nucleus (^{1}H), the most sensitive signal (Baumgartner, Lahajnar, Sepe, & Kristl, 2005; Clarke et al., 1995;

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Dvinskikh, Szutkowski, & Furó, 2009; Richardson, Bowtell, Mäder, & Melia, 2005). In MRI technique, swelling and glassy regions are *in situ* observed without interference. Consequently, this technique has been extensively used to investigate swelling properties of many pharmaceutical materials such as hydroxypropyl methylcellulose (HPMC), starch, xanthan gum and bentonite (Dvinskikh et al., 2009; Laity, Mantle, Gladden, & Cameron, 2010; Mikac, Sepe, Kristl, & Baumgartner, 2010; Tajarobi, Abrahmsen-Alami, Carlsson, & Larsson, 2009; Thérien-Aubin & Zhu, 2009; Tritt-Goc & Pislewski, 2002).

Recently, there has been a growing interest in the use of chitosan (CS) as drug release controller in several pharmaceutical dosage forms, such as compression coated tablets, film-coated tablets, matrix tablets and nano/microparticles (Maestrelli, Zerrouk, Chemtob, & Mura, 2004; Nunthanid, Puttipipatkhachorn, Yamamoto, & Peck, 2001; Nunthanid et al., 2004, 2008, 2009).

However, native CS, in base form, has been infrequently used due to its low solubility in water. Therefore, CS was prepared in several salt forms to improve its solubility. However, the drug release profiles are different for each salt form of CS due to the gel structure, thickness of gel layer as well as swelling and erosion behaviors in different dissolution media (Huanbutta et al., 2011; Maestrelli et al., 2004; Orienti et al., 2002). In previous study, Orienti et al. (2002) prepared several spray-dried CS salts and investigated the influence of different CS salts on release of diclofenac sodium in colon (specific delivery). They found that chitosan aspartate and chitosan glutamate provided the slowest drug release at acidic pH and the fastest at neutral pH. However, other CS salts have not yet been thoroughly investigated. Swelling behavior information of CS in different salt forms may be useful to understand drug release kinetics.

In the present study, we aimed to examine swelling and erosion progresses of CS base and different CS salts assessed by gravimetric and MRI techniques and their impact on *in vitro* drug release. Two molecular weight (MW) of different CS salts, *i.e.*, chitosan aspartate (CA), chitosan glycolate (CGY), chitosan glutamate (CG) and chitosan lactate (CL) (see Fig. 1), were prepared by spray-drying technique. Anhydrous theophylline (TPL) was used as a model drug. Gravimetric technique was employed to screen swelling behaviors of all CS salts, then MRI techniques was used to profoundly explore swelling progresses of CS salts having the slowest and the fastest drug release. To explore the influence of pH of dissolution medium on the swelling behaviors of CS salts, 0.1 N HCl (pH 1.2) and pH 6.8 Tris–HCl buffer solutions were used as dissolution medium to represent gastric and intestinal fluids, respectively.

2. Materials and methods

2.1. Materials

CS with degree of deacetylation of 87–89% and MW of 45 kDa and 200 kDa were purchased from Seafresh Co., Ltd., Thailand (Lot Nos. COA050507 and COA240702, respectively). TPL was a gift from BASF (Thai) Co., Ltd., Thailand (Lot No. 00099360-A). All other chemicals were of reagent grade or pharmaceutical grade and used without further purification.

2.2. Preparation of chitosan salts

CS salts were prepared by a spray-drying technique as described in previous report (Nunthanid et al., 2009). Briefly, CS flakes were dissolved in different aqueous acid solutions, including aspartic acid, glycolic acid, glutamic acid and lactic acid. The CS solutions were then spray-dried using a spray dryer (model SD-60, Labplant, UK) under the following conditions: inlet temperature of 140 °C, outlet temperature of 80–90 °C, and feeding rate of 5 mL/min. The obtained powders were collected and kept in a desiccator for further investigation.

2.3. Preparation of CS matrix tablets and drug-loaded CS matrix tablets

Two hundred milligrams of different CS salts were compressed into tablets using a hydraulic press (Specac Inc., USA) at a fix compression force of 2 tons and dwelling time of 20 s using a 9.5-mm diameter flat-faced punch set. The drug-loaded CS matrix tablets composed of CS salt and TPL at 1:1 ratio were also prepared under similar conditions to the CS matrix tablets. The compressed tablets were kept in a dessicator overnight before further investigation.

2.4. Tablet thickness and tablet strength

The thickness (H) and diameter (D) of the matrix tablets was determined using a caliper (Mitutoyo Dial Thickness Gauge, Mitutoyo, Japan). The tablet hardness was measured using texture analyzer (model TA-XT plus, Stable Micro System, UK) in compression mode. The maximum force at break (F) was recorded and the tablet strength (σ_x) was calculated from the following equation.

$$\sigma_x = \frac{2F}{\pi DH} \quad (1)$$

2.5. Swelling and erosion studies

Swelling behavior of tablets made of CS and different CS salts with MW of 45 kDa and 200 kDa were evaluated by gravimetric technique. Then, CS salts with MW of 45 kDa which provided the fastest and slowest drug release were selected for further investigation by MRI.

2.5.1. Gravimetric technique

Measurement of swelling and erosion rates of CS matrix tablets (without drug) was carried out, after immersion of tablets in test medium (Sriamornsak, Thirawong, & Korkerd, 2007; Sriamornsak, Thirawong, Weerapol, et al., 2007). The weighed tablets (W_0) were placed in the closed plastic containers with the mesh underneath the tablets. The testes were run under agitation condition using an Environment Shaker-Incubator (model ES-20, Biosan, Latvia) at 150 rpm in different test media (*i.e.*, 0.1 N HCl (pH 1.2) or pH 6.8 Tris–HCl buffer) at 37 ± 0.5 °C. After 2, 5, 10, 20, 60, and 120 min, each container was removed from the incubator, the tablet with the mesh was withdrawn from the medium and blotted to remove excess water and then weighed (W_1) on an analytical balance (model AG204, Mettler-Toledo, Switzerland). The wet samples were then dried in an oven at 80 °C for 24-h time period, allowed cooling in a desiccator and finally weighed until constant weight was achieved (final dry weight, W_2). The experiment was performed in triplicate for each time point and fresh samples were used for each individual time point.

The percentage increase in weight due to absorbed liquid or water uptake was estimated at each time point from Eq. (2):

$$\%\,\text{weight change} = \left[\frac{W_1 - W_2}{W_0}\right] \times 100 \quad (2)$$

The percentage remaining of tablets after erosion (ES) was calculated from Eq. (3):

$$\%\,\text{remaining} = 100 - ES \quad (3)$$

where ES was estimated from Eq. (4):

$$ES = \left[\frac{W_0 - W_2}{W_0}\right] \times 100 \quad (4)$$

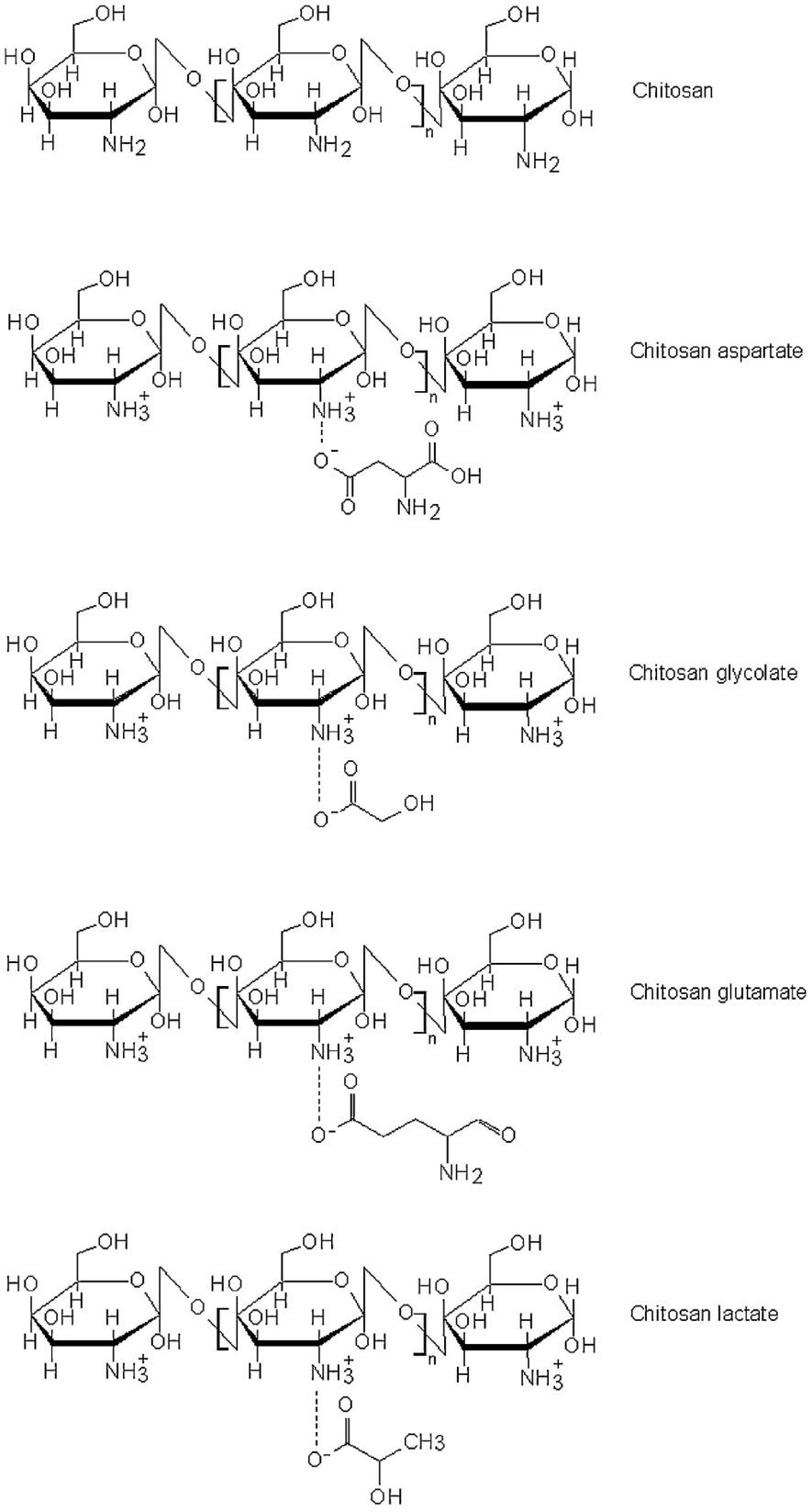

Fig. 1. Chemical structure of chitosan and its salts.

2.5.2. MRI

MRI instrument (Pharmasense™, Oxford Instruments, UK) was used to investigate real-time *in situ* swelling and erosion behaviors of drug-loaded CS matrix tablets those provided the slowest and fastest drug release. In general, MRI observes the mobile ^{1}H associated with the free water. If orthogonal magnetic field gradients are applied across the uniform static magnetic field during nuclear magnetic resonance acquisition, it is possible to spatially

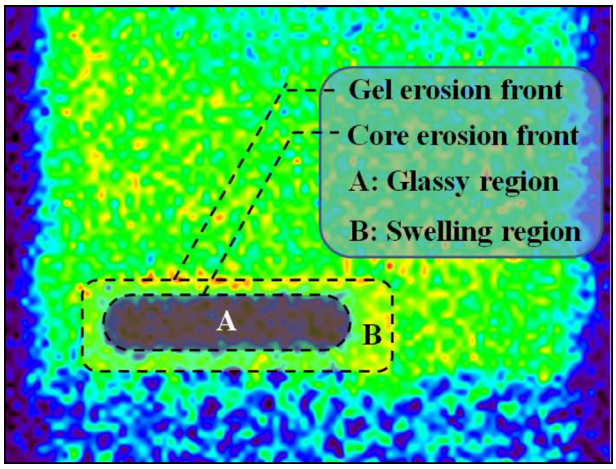

Fig. 2. Image diagram of a swollen chitosan matrix tablet from an MRI instrument.

encode the signal in three dimensions. The signal intensity of a spin-echo image is dependent on the ^{1}H density which is related to water concentration as well as the T_1 (spin–lattice relaxation) and T_2 (spin–spin relaxation) values.

In this experiment, the TPL-loaded CS matrix tablets were placed in 0.1 N HCl and pH 6.8 Tris–HCl buffer simulating to gastric pH and intestinal pH, respectively. The images were captured every 10 min, in black and white mode, until the glassy core disappeared. The flow rate and temperature of the medium were controlled at 5 mL/min and 37 ± 0.5 °C, respectively. Contour lines were used to define and analyze the non-hydrated (glassy region) and hydrated (swelling or rubbery region) areas in rainbow mode by computer program (Mac-View Version 4, Mountech, Tokyo, Japan). The percentage of swelling was subsequently calculated by the following equation:

$$\%\,\text{swelling} = \left[\frac{T_t - T_0}{T_0}\right] \times 100 \quad (5)$$

where T_0 is total cross sectional area of the original dry tablet and T_t is total cross sectional area of swollen tablet (*i.e.*, A + B in Fig. 2) measured at a time. Then, the percentages of swelling and glassy regions (mm^2) were plotted against time.

2.6. In vitro release studies

In vitro drug release of the TPL-loaded matrix tablets made of CS, CA, CL, CG, and CGY were examined by a USP dissolution apparatus I. To relate the TPL release and swelling profiles of CS, a flow-through cell dissolution connected with the MRI instrument was also utilized.

2.6.1. In vitro release studies using basket method

Drug release behaviors of TPL-loaded CS matrix tablets were investigated by USP dissolution apparatus I equipped with baskets which were operated at a speed of 100 rpm. Nine hundred milliliters of either 0.1 N HCl or pH 6.8 Tris–HCl buffer, as the dissolution medium, were placed in the glass vessel, the apparatus assembled, and the dissolution medium was equilibrated to 37 °C. The samples (5 mL) were taken at various time intervals, *i.e.*, 5, 10, 15, 30 min, 1, 2, 4, 6, 8, 12 h. Then, the amount of TPL release was measured by UV-spectrophotometer (model Lambda 2, Perkin Elmer, USA) at maximum wavelength of 276 nm. Each *in vitro* release study was performed in triplicate.

2.6.2. In vitro release studies using flow-through cell method

The drug release was real-time monitored with MRI study using a flow-through cell dissolution apparatus (model DZ1, Pharma Test, Germany). Two media were used, *i.e.*, 0.1 N HCl and pH 6.8 Tris–HCl buffer, as mentioned above. The 22.6-mm diameter flow cells were prepared by placing a 5-mm ruby bead in the apex of the cone and filling with 1-mm glass beads in order to create laminar media flow. The TPL-loaded matrix tablet was positioned, in the cell, on top of glass bead layers. To carry out the test, the medium was conveyed to the cells from the reservoir by the piston pump at a flow rate of 5 mL/min, 37 °C. The medium was collected at predetermined time intervals. The amount of drug was analyzed using UV-spectrophotometer (model U-3300, Hitachi, Japan) at maximum wavelength of 276 nm.

2.7. Statistical analysis

Analysis of variance (ANOVA) and Levene's test for homogeneity of variance were performed using SPSS version 10.0 for Windows (SPSS Inc., USA). *Post hoc* testing ($p < 0.05$) of the multiple comparisons was performed by either the Scheffé or Games-Howell test depending on whether Levene's test was insignificant or significant, respectively.

3. Results and discussion

3.1. Tablet strength

The tablet strength of the matrix tablets made of CS and its salts, with and without TPL, is demonstrated in Fig. 3. The tablet thickness of matrix tablets made of CS and its salts ranged from 2.15 to 2.63 mm while the diameter was fixed at 9.5 mm. All the tablet strength values were between 0.1 and 0.7 kg/mm^2. The CGY tablet, MW of 45 kDa, showed the highest strength, while the CG tablet, MW of 200 kDa, exhibited the lowest strength. It is obvious that, without drug, CS or CS salts with low MW provided higher strength. The results are in agreement with previous report by Sahasathian et al. (2007). This may be due to the high viscosity of solution prepared from CS with high MW, resulting in larger particles. It is a well-known fact that the particle size of raw materials increased, the hardness of resultant tablet decreased. When TPL was added (about 50% of total weight), the influence of salt form and MW seems to decrease. Comparable tablet strength was observed from the matrix tablets made of different CS salts or MWs.

3.2. Swelling and erosion studies

3.2.1. Gravimetric technique

The swelling behaviors of matrix tablets made of CS and its salt forms, accessed by gravimetric technique, in 0.1 N HCl and pH 6.8 Tris–HCl buffer are illustrated in Fig. 4a and b, respectively. CGY tablet showed the greatest swelling in both 0.1 N HCl and pH 6.8 Tris–HCl buffer, followed by CL, CA and CG, respectively. This may be due to the chemical structure of different salts. CGY and CL containing hydrophilic hydroxyl group (—OH) (see Fig. 1) may promote polymer wetting and swelling (Bao, Ma, & Sun, 2012; Park, Marsh, & Rhim, 2002). On the contrary, CA and CG containing amine ($—NH_2$) and carboxyl (—COOH) groups in their structures may cause interaction or attractive force between the polymer chains, resulting in low polymer swelling.

MW of CS plays a vital role in tablet swelling behavior. The tablets prepared from CS with high MW (200 kDa) swelled greater than those of low MW (45 kDa), as shown in Fig. 4. This may be due to water molecule be able to access through low MW chitosan structure well causing loose gel and high erosion rate. These diminish swelling region and swelling rate (Nunthanid et al., 2001; Tangsadthakun et al., 2007). In addition, the swelling progress of the CS matrix tablets in 0.1 N HCl was faster than those in pH 6.8

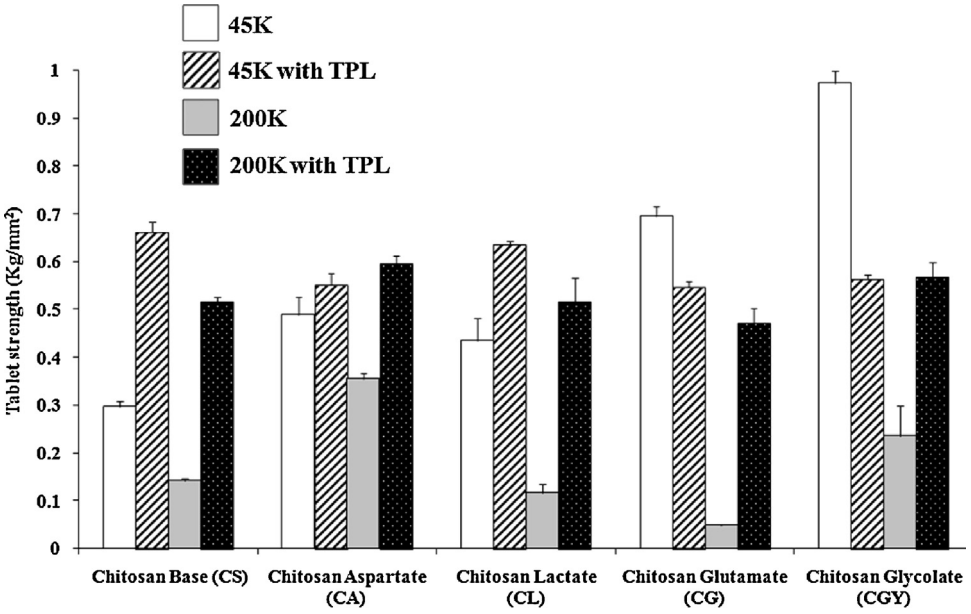

Fig. 3. Tablet strength of the chitosan matrix tablets and drug-loaded matrix tablets in different salts and MWs.

buffer. Amine group in CS molecules can be protonated in acid condition and, therefore, caused repulsive force between CS chains. This makes the tablets swell greater (Huanbutta et al., 2011). The matrix tablets made of 200-kDa CS did not swell but disintegrated; therefore, the swelling data could not be obtained.

The erosion profiles of the matrix tablets prepared from CS and its salts having different MWs, in 0.1 N HCl and pH 6.8 buffer, are depicted in Fig. 5. It was found that the tablets prepared from CS and its salts, with low MW (45 kDa), eroded faster than those with high MW (200 kDa). This is probably because CS with high MW forms viscous and thick gel layer, resulting in low erosion rate, compared to that with low MW (Tangsadthakun et al., 2007). Among various forms of CS salts, the compressed CA (45 kDa) tablets showed quick erosion in the both media (almost 100% in 0.1 N HCl and 60% in pH 6.8 buffer). On the other hand, CGY (200 kDa) exhibited the lowest erosion. Moreover, the percentage of erosion in 0.1 N HCl was

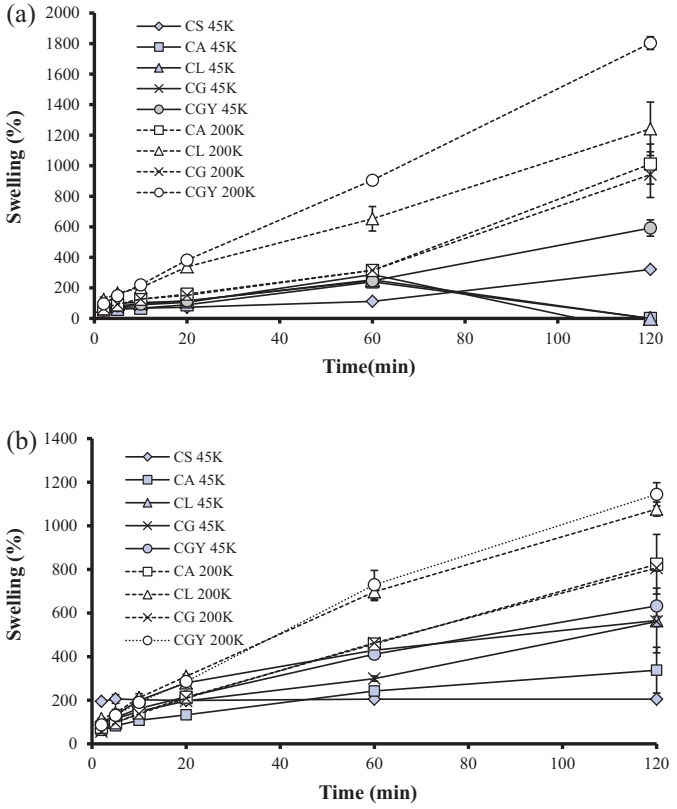

Fig. 4. Swelling (%) of the matrix tablets made of chitosan and its salt forms with different MWs in (a) 0.1 N HCl and (b) pH 6.8 Tris–HCl buffer.

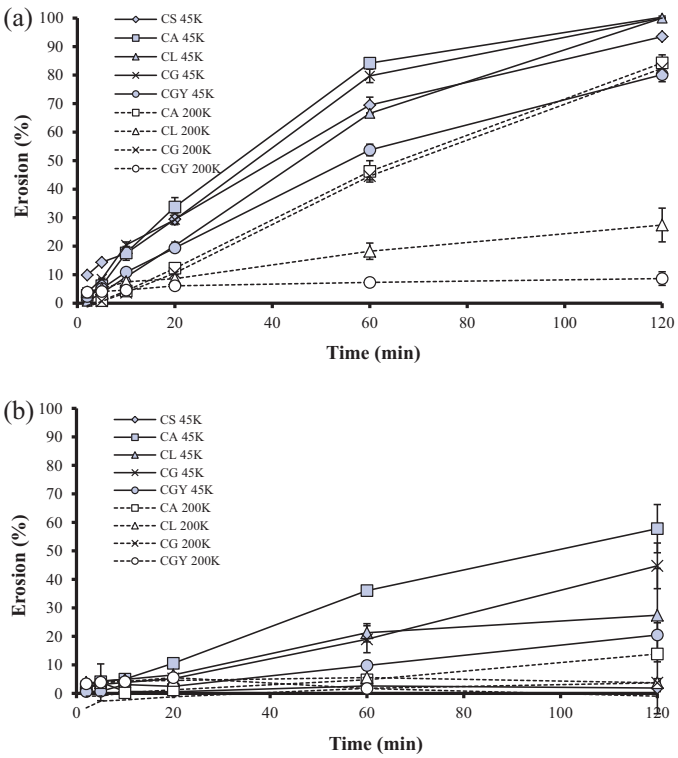

Fig. 5. Erosion (%) of the matrix tablets made of chitosan and its salt forms with different MWs in (a) acidic (0.1 N HCl) and (b) neutral pH media (pH 6.8 Tris–HCl buffer).

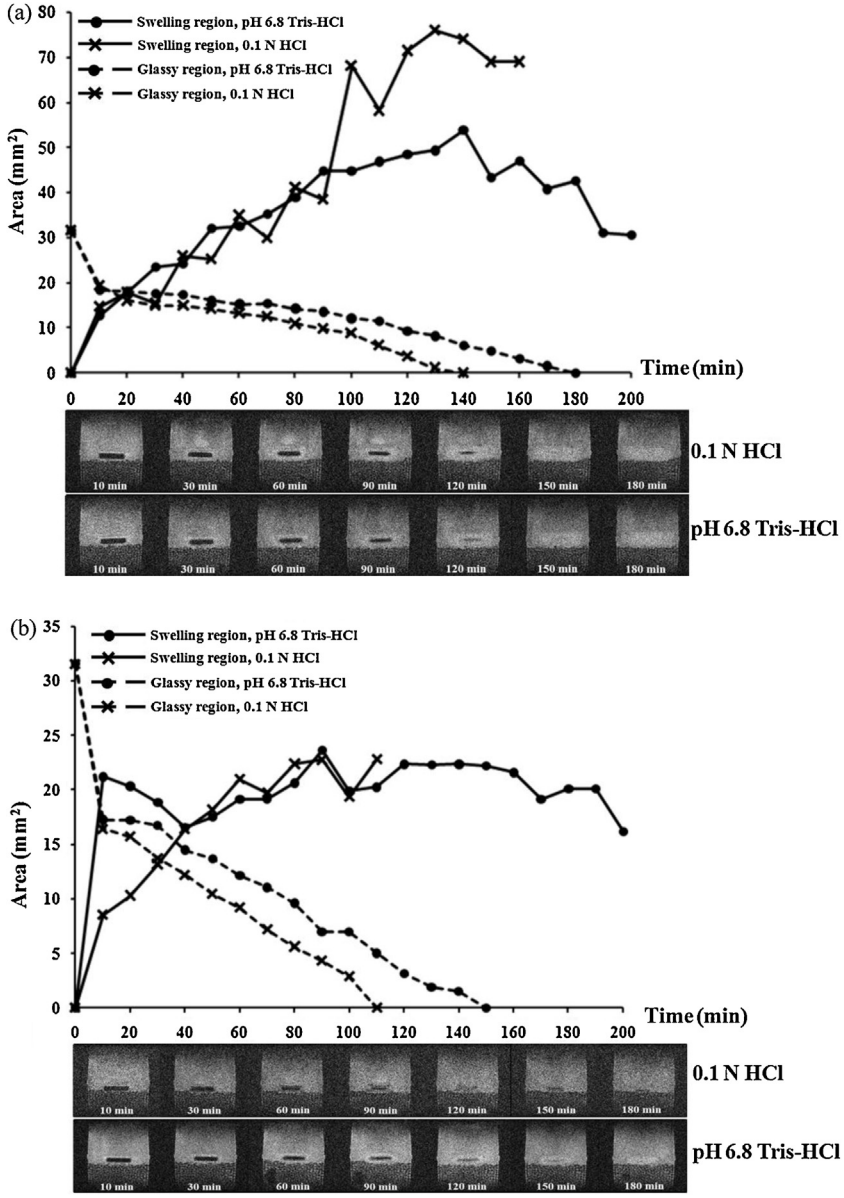

Fig. 6. Swelling/glassy regions and MRI images of swollen (a) CGY and (b) CA tablets at different time intervals in 0.1 N HCl and pH 6.8 Tris–HCl buffer.

greater than in neutral pH medium. This may be due to the higher solubility of CS in acid medium, as mentioned above.

3.2.2. Swelling and erosion studies by MRI

To intimately monitor swelling behavior of the CS salts, the matrix tablets prepared from CGY and CA (45 kDa) were chosen for further evaluation by MRI as they provided the fastest and slowest water uptake, respectively. The MRI images and swelling profiles of CGY and CA tablets in different media are shown in Fig. 6. The MRI images demonstrate high intensity of ^{1}H area (white area) associated with water ingress of the hydrated area (swelling region). The lower or zero intensity of ^{1}H region (black area) represents for the non-hydrated area (glassy region). After exposure to the medium, the penetration of water into the tablets resulted in subsequent hydration/swelling and gel formation at the interface of the tablet and the medium. The gel erosion front moved outward, resulting in the expansion of swelling region (Huanbutta et al., 2011).

The swelling profiles from MRI study were similar to those reported by gravimetric technique, *i.e.*, the swelling ability of CA in both media was lower than that of CGY. In the first 100 min, swelling rate of CGY in 0.1 N HCl and pH 6.8 buffer was not different (Fig. 5). After that, in 0.1 N HCl, CGY swelled greater until the swollen gel totally dissolved at 180 min. In pH 6.8 buffer, CGY swelled increasingly until 180 min, and then the swelling region decreased owing to erosion of CGY. It is likely that, during the first 100 min, glycolic acid played a more important role on the polymer swelling than the pH of solvent. Therefore, the swelling of CGY in both media was not significantly different in first period. When time elapsed, glycolic acid gradually dissolved. At this moment, pH of medium may directly influence the polymer swelling, thus CS in acid medium swelled greater than in neutral pH medium.

In both media, the glassy region of CGY abruptly decreased in the first 10 min, then, the declining rate was stable until the glassy core vanished. This may be due to the freely progression of medium into the matrix tablets in the beginning. Afterwards, gel layer of CGY was formed and retarded the penetration of medium. As CS can dissolve in acid condition, the CGY core disappeared more quickly in 0.1 N HCl than in pH 6.8 buffer.

As presented in Fig. 6b, the swelling region of CA in pH 6.8 buffer rapidly increased to around 20 mm^2 within 10 min then the region

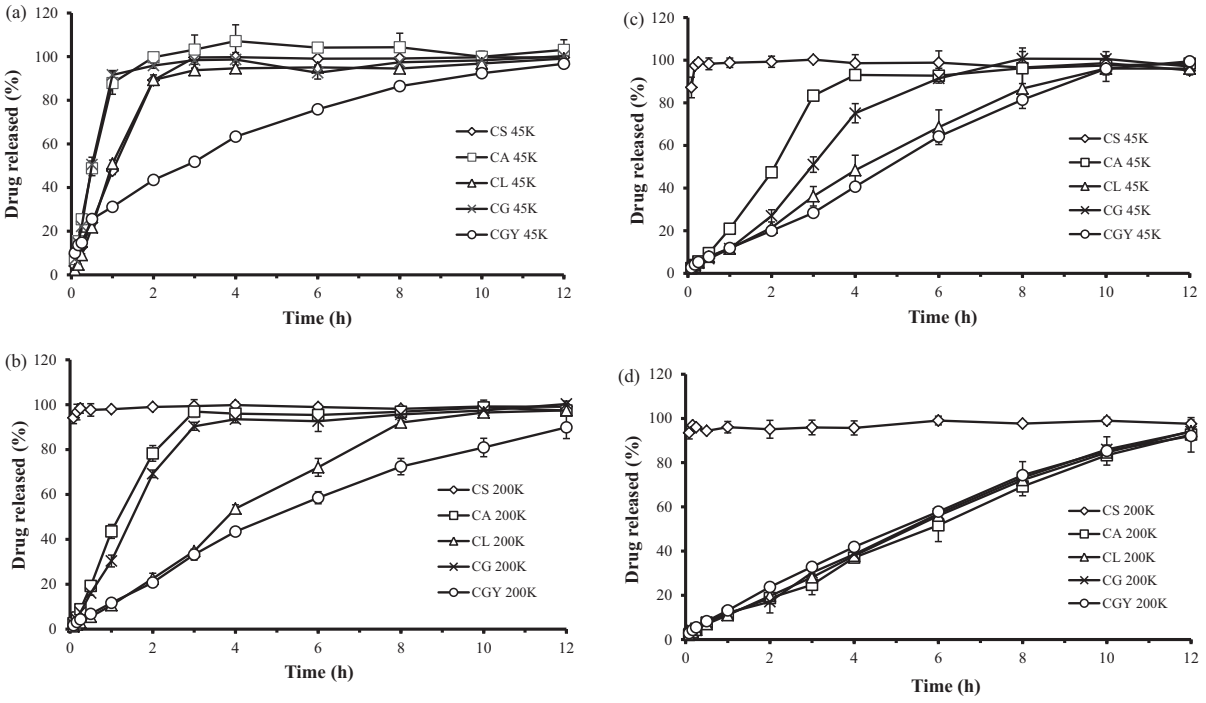

Fig. 7. *In vitro* drug (TPL) release profiles of different CS salt tablets with MW of (a) 45 kDa and (b) 200 kDa in 0.1 N HCl and MW of (c) 45 kDa and (d) 200 kDa in pH 6.8 Tris–HCl buffer.

was almost stable until 200 min. In 0.1 N HCl, CA gradually swelled until 120 min and all swollen gels were dissolved afterwards. This result is in agreement with the results obtained from gravimetric technique. The decrease in ionization of aspartic acid may be resulted from its low pK_a (*i.e.*, 1.88), thereby the swelling is lower in the acid medium.

3.3. *In vitro* release studies

3.3.1. *In vitro* release studies using paddle method

As soon as the CS matrix tablet came in contact with the dissolution media, imbibition of the dissolution medium by the matrix tablet took place, initiating the formation of a gel layer of the polymer around the tablet. The diffusion of dissolved drug through this gel layer is the determining factor in the improvement of dissolution rate. *In vitro* drug release profiles of the TPL-loaded matrix tablets of CS and its salts with two MWs (45 and 200 kDa) in 0.1 N HCl and pH 6.8 Tris–HCl buffer are demonstrated in Fig. 7. As presented in Fig. 7b–d, TPL released rapidly from the 45-kDa CS tablets (in pH 6.8 buffer) and from the 200-kDa CS tablets (in both media) due to fast tablet disintegration without polymer swelling. This result is in agreement with our previous study (Huanbutta et al., 2011), which reported a burst drug release from matrix tablets made of CS with high MW (and/or in neutral medium). However, in 0.1 N HCl, TPL did not immediately release from 45-kDa CS tablets (Fig. 7a). It is possibly due to partial swelling of CS with low MW in acid condition producing gel layer to protect the tablet structure from disintegration and, therefore, retard drug release (Caillard & Subirade, 2012).

As shown in Fig. 7a and b, CGY (both 45 and 200 kDa) and CL (200 kDa) showed retardation of TPL release in acid medium. After 2 h in 0.1 N HCl, the percentage of TPL release of matrix tablets made of high MW CGY and CL (200 kDa) was about 20%, indicating the possibility to use both salts as an enteric coating material. At neutral pH, TPL release from matrix tablets made of CGY and CL with low MW (45 kDa) was also slower than that of other salts. However, drug release from matrix tablets made of all salts, with high MW (200 kDa), were prolonged with no significant difference (Fig. 7d). It is found that the drug release results agree with the swelling studies, which demonstrated that CGY and CL could swell considerably in acid and neutral pH media. The thick swollen gel may act as a diffusion barrier for the release of drug. This swelling action of CS is, in turn, controlled by the rate of water uptake into the matrices. An inverse relationship exists between the drug release and matrix swelling (Sriamornsak, Thirawong, & Korkerd, 2007; Sriamornsak, Thirawong, Weerapol, et al., 2007). This implies that CS swelling is one of the factors affecting drug release. The swelling behavior of CS is, therefore, useful in predicting drug release.

3.3.2. *In vitro* release studies using flow-through cell method

As shown in Fig. 8, TPL release in 0.1 N HCl was faster than that in pH 6.8 buffer. This result was in agreement with the swelling results as mentioned above, *i.e.*, the swelling of chitosan in acid medium was higher than in neutral medium. It is possible that core erosion front of the CS tablet in acid medium moved inward faster than that in neutral pH medium, resulting in the dissolution of drug inside

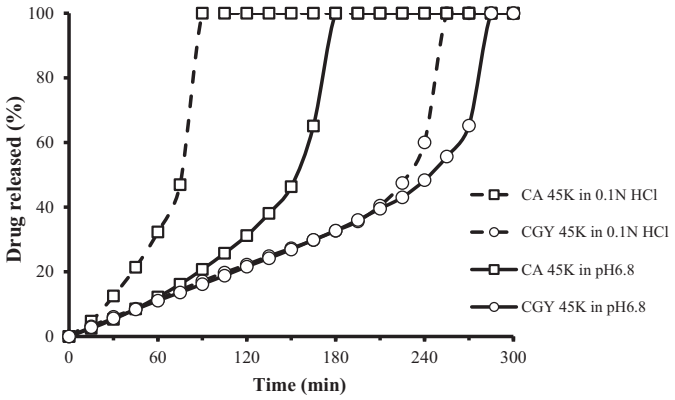

Fig. 8. Drug release profiles of TPL-loaded matrix tablets made of CGY and CA, 45 kDa, in 0.1 N HCl and pH 6.8 Tris–HCl buffer.

the matrices. Release of the drug then occurred by diffusion through the swollen gel layer (Aslani & Kennedy, 1996).

TPL release from CGY was slower than that of CA, suggesting that the gel layer became more resistant to diffusion. In the first 200 min, drug release from CGY in acid and neutral pH media was similar. After that, drug release from CGY in the acid medium was slightly faster. This is probably because, in the first 200 min, CGY swell at the same rate in the both media, thus, the diffusion path-length for drug release was not different. Afterwards, CGY began to erode in 0.1 N HCl because chitosan dissolved in acid condition, causing drug erosion and drug release. The drug release from the matrix tablets made of CGY is time- and pH-dependent when compared to other hydrophilic polymer matrix systems such as HPMC and ethylcellulose, which are only time-dependent (Nunthanid et al., 2008; Streubel, Siepmann, Dashevsky, & Bodmeier, 2000).

4. Conclusion

MRI technique was applied to reveal the penetration progress of water molecules inside the tablet, in order to understand the mechanism of drug release. The drug release does not only depend on swelling progress of polymer but also glassy region. Greater moving inward of core erosion front makes drug release faster. Different salts and MW of chitosan provided different drug release profiles due to their chemical structure and characteristics of the compressed tablets. Among several CS salts, CGY could retain drug release in acid (0.1 N HCl) and neutral pH media (pH 7.4 buffer) longer than the other salts. This may be because CGY contain hydrophilic hydroxyl group which promotes gel swelling and thus resulting in longer drug diffusion path length. CS with high MW (200 kDa) swelled greater than those of low MW and offered low erodible gels, resulting in slower drug release. From the results obtained, it can be concluded that CGY with 45 and 200 kDa demonstrates a potential biopolymer for controlling drug release and/or enteric coating.

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