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Galactomannan (from *Gleditsia sinensis* Lam.) and xanthan gum matrix tablets for controlled delivery of theophylline: In vitro drug release and swelling behavior

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ABSTRACT

Galactomannan (G) from *Gleditsia sinensis* Lam. and xanthan gum (X), as sustained release materials for controlled delivery of theophylline, were mixed in different ratios of 7:3, 5:5, and 3:7 to yield enhanced release-controlling performance. The polysaccharides content of tablets was 10% (w/w), either alone or in mixtures. From in vitro dissolution test, G10% and X10% matrices released 91.4 and 87.7% of drug within 24 h, respectively. The synergistic interactions between galactomannan and xanthan effectively retarded the drug diffusion, and the most sustained drug release (75.5% at 24 h) was found in formulation GX7:3. The drug release data fitted to the kinetic model indicated the anomalous transport mechanism ($0.5 < n < 1.0$). Additionally, the swelling behavior and morphological changes of the tablets were investigated. The results illustrated the potential of binary mixtures of *G. sinensis* galactomannan and xanthan as novel sustained release materials for controlled drug delivery.

1. Introduction

Hydrophilic polymers are popularly used as sustained release materials in controlled drug release systems. Polysaccharides are hydrophilic, biocompatible and swellable, and a majority of them are resistant to gastric and intestinal digestions but specific to be degraded by the colonic bacteria (Ashford & Fell, 1994; Chourasia & Jain, 2004). Therefore, drug delivery systems based on polysaccharides as sustained materials have been receiving considerable attention, especially for controlled drug release and colon targeting drug delivery (Hovgaard & Brøndsted, 1995; Mundargi, Shelke, Rokhade, Patil, & Aminabhavi, 2008; Peerapattana, Phuvarit, Srijesdaruk, Preechagoon, & Tattawasart, 2010; Sokker, Ghaffar, Gad, & Aly, 2009).

In the drug delivery systems, a therapeutic agent is compressed with hydrophilic polymers, and when exposed to aqueous medium, the polymer absorbs water to hydrate and swell to form three regions: gel layer, infiltrated layer and dry glassy core (Kiil & Dam-Johansen, 2003). The outer layer, constituted of highly swollen polymer gel, acts as a diffusional barrier to retard further uptake of water and the release of dissolved drug (Conti et al., 2007b). The middle layer is moderately swollen and relatively strong. The inner core is the dry glassy polymers without wetting. The drug release process from the hydrogel matrix involves three steps (Khullar, Khar, & Agarwal, 1998): (i) penetration of water in the dry matrix, (ii) hydration and swelling of the polymer, and (iii) diffusion of the drug dissolved in the matrix. The drug dissolved at the front between infiltrated and gel layers and diffused across the gel layer into the fluid.

Xanthan gum (X) is a microbial exopolysaccharide secreted from *Xanthomonas campestris*, which consists of a β-(1→4) linked glucose backbone with the substitution of trisaccharide side-chains of -[β-(1→3)-mannose-α-(1→2)-glucuronic acid-β-(1→4)-mannose] on alternate glucose residues (Jansson, Kenne, & Lindberg, 1975). Although xanthan solutions could produce high intrinsic viscosity and weak gel-like properties at low shear rates, it does not form true gels at any concentration and temperature (Millane & Wang, 1990). Nevertheless, xanthan is an effective excipient of formulations for controlled drug delivery (Talukdar & Kinget, 1995; Talukdar et al., 1998; Talukdar & Plaizier-Vercammen, 1993). In previous studies, the release-controlling ability of xanthan has been improved through interactions with various polysaccharides (Fan, Wang, Liu, & He, 2008; Patel & Patel, 2007; Phaechamud & Ritthidej, 2007; Talukdar & Kinget, 1997; Tobyn, Staniforth, Baichwal, & McCall, 1996).

Gleditsia sinensis Lam., a woody species in Leguminosae family, is widely distributed in China. Galactomannan as a storage polysaccharide exists in the endosperms of the *G. sinensis* seeds, which consists of β-(1→4) linked mannose backbone substituted by branches of single galactose unit with α-(1→6) linkage (Jian,

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Cristhian, Zhang, & Jiang, 2011; Jian, Zhu, Zhang, Qi, & Jiang, 2011; Jiang, Jian, Cristhian, Zhang, & Sun, 2011). Galactomannans are an essential hydrophilic material with a variety of properties, such as nontoxic, biodegradable, inexpensive, and readily available. The potential of galactomannans from different sources to be applied as release-controlling agents has been extensively investigated (Bhardwaj, Kanwar, Lal, & Gupta, 2000; Khullar et al., 1998; Prasad, Krishnaiah, & Satyanarayana, 1998; Varshosaz, Tavakoli, & Kheirolahi, 2006). Galactomannan was found to be degradable by the action of β-mannanase secreted by colonic flora, but resistant to the digestions of stomach and the small intestine, which formed the basis of using *G. sinensis* galactomannan for colonic drug delivery (Prasad et al., 1998). In our previous studies, galactomannan from *G. sinensis* was used as sustained release material in matrix tablets for colonic drug delivery, and the results indicated its excellent behavior as release-controlling agent in sustained drug release (Jian, Cristhian, et al., 2011; Jian, Zhu, et al., 2011). However, no investigation seems to have been carried out on the synergism in the matrix tablets based on the binary mixtures of *G. sinensis* galactomannan and xanthan gum as sustained release materials.

In this study, galactomannan derived from the seeds of *G. sinensis* was mixed with xanthan gum in varying proportions to evaluate the controlled release potential base on their synergistic interactions. The compressed matrix tablets had a hydrophilic polymer concentration of 10% (w/w), either alone (formulations G10% and X10%) or in physical mixtures (formulations GX7:3, GX5:5, and GX3:7), which is relatively lower than that of other matrices based on polysaccharides as sustained release materials (Alvarez-Manceñido, Landin, & Martínez-Pacheco, 2008; Conti et al., 2007a; Prasad et al., 1998; Ughini, Andreazza, Ganter, & Bresolin, 2004; Vendruscolo, Andreazza, Ganter, Ferrero, & Bresolin, 2005). The drug to polymers weight ratio was 1:2. The drug release from the delivery systems was investigated by in vitro dissolution test, and the data were fitted to different models to determine the release mechanisms. The contributions of diffusional and relaxational release mechanisms in drug release process were calculated from the parameters of the model. The radial swelling behavior and morphological changes during dissolution test were characterized to know about the water absorption of the matrix tablets and relate hydration to the drug release.

2. Materials and methods

2.1. Materials

Pods of *G. sinensis* were kindly supplied by Shexian Forestry Bureau from Hebei, China. The seeds were manually separated from the pods. The endosperms were separated through dehulling method of baking pretreatment (Jiang et al., 2003; Jian, Cristhian, et al., 2011; Jian, Zhu, et al., 2011), and then milled into powder through a sieve size of 0.125 mm. Xanthan gum (Keltrol) was purchased from Kelco Division Merck. The β-mannanase from *Aspergillus niger* (Novozymes), anhydrous theophylline (Britain Pharmacopoeia grade), anhydrous lactose and magnesium stearate were used in this study. All the chemicals without special illustration were of analytical grade.

2.2. Extraction and analysis of galactomannan

The gum was dispersed into water with vigorous stirring to achieve a concentration of 1.0% (w/v). The dispersion was kept in a boiling water bath for 10 min to inactivate enzymes and accelerate gum hydration, and then mechanically stirred at 30 °C for 3 h. Thereafter, the solution was centrifuged at 3000 × *g* for 20 min to remove insoluble impurity. The precipitation of *G. sinensis* galactomannan was carried out by adding 2 volumes of anhydrous alcohol. The precipitate was collected and then washed in a gradient of ethanol (70–100%) and finally dried under vacuum at 40 °C for 6 h. The *G. sinensis* galactomannan as an off-white powder was obtained. From our previous analysis (Jian, Cristhian, et al., 2011; Jian, Zhu, et al., 2011), the ratio of mannose to galactose for *G. sinensis* galactomannan is 4.5, and the weight-average molecular weight (M_w) is 3.310×10^6 Da.

2.3. Preparation of tablets

Tablets (500 mg), composed of galactomannan (excipient), xanthan (excipient), lactose (filler), magnesium stearate (lubricant) and theophylline (drug), were prepared by wet granulation. The percentage compositions of the formulations were listed in Table 1. The loading percent of theophylline was 20% (w/w) of the tablets, which was to match the dosages comparable with the commercial products. Briefly, 70% (v/v) ethanol (binder) was added to the premixed powders to prepare wet mass. The wet mass was then extruded through a 20-mesh screen and further dried at 60 °C for 6 h. The dried granules mixed with 0.5% (w/w) magnesium stearate were compressed on a single punch tabletting machine (Guoyao Longli Co. Ltd., Beijing, China) at a constant pressure of 14 kN to form 12 mm round, flat-faced tablets.

In order to determine the effective amount of theophylline loaded and the drug content uniformity in the tablets, the deviation was estimated in a spectrophotometer (model UVPC 1601, Shimadzu, Tokyo, Japan). Each tablet was dissolved in buffer (pH 6.8) with ultrasonic treatment for 2 h to ensure the drug fully dissolved. The solution was filtered through a membrane filter (0.45 μm) and then diluted to 100 ml. The absorbance was determined in a 1 cm quartz cell at λ_{max} of 272 nm using the solvent as blank control.

2.4. In vitro drug release

The dissolution test was carried out using USP apparatus II (model DT 80, Erweka, Germany) with the paddle rotating rate of 100 rpm in 900 ml dissolution medium at 37 ± 0.5 °C, to reproduce digestive physiological phases. In general, the gastric emptying time is about 2–4 h and the small intestines emptying time for 4–10 h. The pH value of the stomach varies from 1 to 3, whereas the pH value in intestines colon is in the range of 7–8 (Bayraktar, Malay, Özgarip, & Batıgün, 2005). In order to simulate the gastro intestinal tract, the tablet was subjected to 900 ml of 0.1 M hydrochloric acid for the initial 2 h. Then the tablet was transferred to 900 ml of dissolution medium of pH 6.8 phosphate buffer. After 4 h in pH 6.8 dissolution medium, β-mannanase was added to the dissolution liquor to achieve a concentration of 0.2 U/ml (Alvarez-Manceñido et al., 2008). During dissolution test, sample (1 ml) was periodically withdrawn without replacement. The cumulative amount of theophylline released from the matrix tablets was assayed spectrophotometrically at 272 nm using the validated calibration curve.

2.5. Swelling and morphological studies

The swelling behavior of the matrix tablets was studied to relate hydration to drug release. At specified time intervals in dissolution test, tablets were taken out, drained of excess medium, measured the wet weight, and returned to the fluid vessel. When contacting with the dissolution fluids, the morphological changes occurred in the structure of the matrix. In order to investigate the morphological behavior during the release process, tablets were withdrawn from the liquid at different time points (0.5, 2, 6, 12 and 24 h), and thereafter their photographs were taken by a digital microscope

Table 1
Composition and analysis of the matrix tablets (500 mg).

Formulation	Galactomannan (%)	Xanthan (%)	Theophylline (%)	Lactose (%)	Weight (mg)[a] ± SD	Density (g/cm^3)[a] ± SD	Assay (%)[b] ± SD
G10%	10	0	20	70	501.7 ± 2.7	0.997 ± 0.020	100.3 ± 1.7
GX7:3	7	3	20	70	504.3 ± 2.1	1.001 ± 0.021	100.1 ± 1.6
GX5:5	5	5	20	70	505.5 ± 2.8	1.000 ± 0.019	99.9 ± 0.9
GX3:7	3	7	20	70	505.1 ± 2.9	1.001 ± 0.022	100.4 ± 1.8
X10%	0	10	20	70	503.9 ± 2.8	0.998 ± 0.020	99.8 ± 1.4

[a] Data are the average of 10 tablets.
[b] Average of 10 tablets, determined spectrophotometrically, with 100 mg of theophylline/unity.

camera. The morphological changes of tablets, including the diameter and the thickness of the gel layer and the infiltrated layer, were studied with software of image analyzer version 1.33.

3. Results and discussion

3.1. Analysis of matrix tablets

The composition and physical control results of the prepared tablets were listed in Table 1. The obtained tablets were 12 mm in diameter and 4.5 mm in height. Each tablet was approximate 500 mg containing 100 mg theophylline anhydrous. The effective amount of the drug loaded in each tablet was within the range of 99.8–100.4% and the standard deviations (SD) were less than 6.0% as specified by United States Pharmacopeia, indicating homogenous drug content of the matrices.

3.2. In vitro drug release

The ability of different formulations based on *G. sinensis* galactomannan and xanthan as sustained release materials was evaluated by conducting studies in 0.1 M hydrochloric acid for the initial 2 h and then in pH 6.8 phosphate buffer for 4 h. After 6 h of drug release test, β-mannanase was added to the pH 6.8 phosphate buffer to obtain a concentration of 0.2 U/ml. When exposed to the dissolution fluid, the hydrophilic polymer matrix gradually hydrates from the periphery towards the core to form a gelatinous layer. The diffusion of drug from the matrix to the aqueous medium depends on the thickness of gel layer. In the initial stage, the drug release is due to the dissolution of the drug present on the tablet surface and the lag time required for polymer hydration to form viscous gel layer (Prasad et al., 1998).

The accumulative amount of drug released from tablets was plotted with time in Fig. 1. From the release profiles, the formulation of G10% showed the highest release rate of theophylline, followed by X10%. The controlled delivery systems based on the binary mixtures of *G. sinensis* galactomannan and xanthan gum displayed better release-controlling performance compared with the formulations based on single component, illustrating the synergism in the polymer interactions. The mixing ratios of galactomannan to xanthan were 7:3, 5:5 and 3:7. The drug release rate decreased with the increasing proportion of *G. sinensis* galactomannan in the formulation. After 24 h of dissolution test, the percents of cumulative theophylline released from tablets were 91.4 and 87.7% for G10% and X10%, respectively, and 75.5, 78.2 and 80.95% for the formulations GX7:3, GX5:5 and GX3:7, respectively. Therefore, the most sustained drug release (i.e. the strongest synergistic interactions) occurred when *G. sinensis* galactomannan was mixed with xanthan gum in the ratio of 7:3.

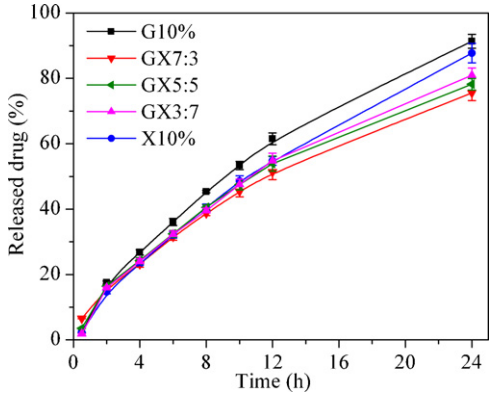

Fig. 1. The release profiles of theophylline from tablets with *G. sinensis* galactomannan and xanthan gum as sustained materials.

The differences of release profiles are probably due to the hydration behavior and the (inter- and intra-) molecular interactions of the hydrophilic polymers in the matrices. The high degree of gum hydration with simultaneous swelling resulted in the lengthening of the drug diffusion pathway and the reduction of drug release rate. The strong synergistic interactions between polymers leaded to the formation of tight network to retard the dissolved drug. Theophylline is soluble in the pH range tested, thus its release from the hydrogel matrix is dependent on the swelling and the dissolution/erosion of the matrix. During the dissolution period 2–12 h, the drug release rate for all the formulations was nearly constant, implying the synchronization between swelling and erosion of the polymer in maintaining a constant gel layer (Lee & Peppas, 1987).

3.3. Drug release kinetics mechanisms

In vitro release data of theophylline from tablets were fitted to different kinetic models for the purpose of proposing the drug release mechanism from the matrix. The Korsmeyer–Peppas (power law) equation (Korsmeyer & Peppas, 1981; Ritger & Peppas, 1987) is:

$$\frac{M_t}{M_\infty} = kt^n \quad (1)$$

where M_t/M_∞ is the fraction of drug released at time t; k is the kinetic constant correlated with the structural and geometrical properties of the dosage form; the diffusional exponent n indicating the type of drug release mechanism depends on the polymer swelling characteristics and the relaxation rate at the swelling front. Formulations with n value of 0.5 indicate Fickian diffusional release which occurs by the usual molecular diffusion of the drug due to a chemical potential gradient. For formulations, values of $0.5 < n < 1.0$ indicate anomalous transport or non-Fickian release. For $n = 1.0$, the release mechanism belongs to case-II or zero-order relaxational release associated with stresses and state-transition in hydrophilic glassy polymers which swell or erode in water or biological fluids (Peppas & Sahlin, 1989). Formulations with $n > 1.0$ indicate super case-II transport due to the combination of diffusion and polymer relaxation/dissolution.

The drug release in swellable matrices depends on two processes: (i) drug diffusion into the swollen polymer, and (ii)

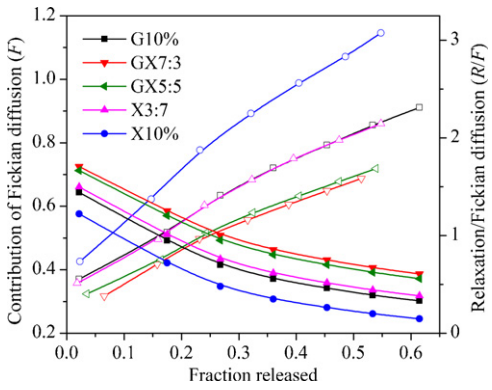

Fig. 2. The contributions of Fickian diffusion F (full symbol) and polymer relaxation/Fickian diffusion R/F (empty symbol) mechanisms over the first 60% drug release from tablets with different formulations.

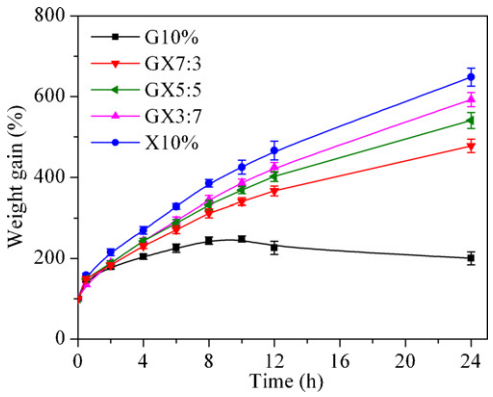

Fig. 3. Weight gain performance of matrix tablet (% of initial dry weight) in dissolution test.

matrix swelling due to the diffusion and relaxation mechanisms (Jelvehgari & Montazam, 2011). In order to estimate the diffusion and relaxation contributions during the anomalous transport process, the Peppas–Sahlin model (Peppas & Sahlin, 1989) was used:

$$\frac{M_t}{M_\infty} = k_1 t^m + k_2 t^{2m} \quad (2)$$

where k_1 and k_2 are kinetic constants related to diffusional and relaxational release, respectively. The first term on the right side of Eq. (2) represents the Fickian diffusional contribution (F), whereas the second term represents case-II relaxation contribution (R). The coefficient m is the purely Fickian release exponent for a device of any geometrical shape which exhibits controlled release. In this study, the value of m is a constant of 0.45 for the formulations with a cylinder shape.

Korsmeyer–Peppas and Peppas–Sahlin models are valid only for the early stages of drug release ($M_t/M_\infty \leq 60\%$) (Costa & Lobo, 2001). The parameters of the models in Table 2 were obtained from nonlinear regression fitting of the first 60% of drug release *vs.* time. For all the controlled release systems in this study, the fitted values of n in Korsmeyer–Peppas model (Eq. (1)) varied from 0.69 to 0.76 (Table 2), indicating the anomalous transport or non-Fickian diffusion release of theophylline from the matrix tablets. In the case of $k_1 > k_2$, the release mechanism is dominated by diffusion. For $k_2 > k_1$, the release is mainly attributed to matrix swelling. When $k_1 \approx k_2$, the release mechanism is a combination of diffusion and polymer relaxation (Kim & Fassihi, 1997). As seen from Table 2, the drug release process was dominated by Fickian diffusion mechanism for all the studied formulations except X10% in which the release mechanism of theophylline was a combination of diffusion and polymer relaxation.

The fraction of drug release owing to Fickian diffusion mechanism could be evaluated by Eq. (3):

$$F = \frac{1}{1 + k_2/k_1 t^m} \quad (3)$$

The ratio of relaxation (R) over Fickian diffusion (F) contributions (Bettini, Colombo, Massimo, Catellani, & Vitali, 1994; Peppas & Sahlin, 1989) could be calculated from Eq. (4):

$$\frac{R}{F} = \frac{k_2 t^m}{k_1} \quad (4)$$

The contribution of Fickian diffusion and the ratio of R/F were plotted with the fraction released in Fig. 2.

As illustrated in Fig. 2, Fickian diffusion mechanism dominated the drug release in the initial period, and then the contribution of polymer relaxation became the dominant mechanism. The polymer relaxation/erosion release occurred in the entire process of the dissolution test. In general, the relaxation contribution was higher for the formulation with higher n values. Therefore, the contribution of relaxational release was highest for the formulation X10% with highest n value of 0.76 (Table 2), which was in accordance with Peppas–Sahlin model ($k_2 > k_1$ in Table 2). As for the formulation GX7:3 ($n = 0.69$), Fickian diffusion mechanism played the main role in the release of theophylline from matrices.

3.4. Water uptake determination

Initially, a tablet composed of swellable polymers is in a dry glassy state. When exposed to the aqueous medium, the hydrophilic polymers in tablet will absorb water to hydrate and swell, resulting in the weight gain and the formation of three regions (i.e. gel layer, infiltrated layer and dry glassy core). The gain of weight on the basis of initial dry weight of tablet was calculated using Eq. (5):

$$\text{Weight gain}\,(\%) = \frac{W_t - W_0}{W_0} \times 100 \quad (5)$$

where W_0 is the initial dry weight of the tablet and W_t is the wet weight of the tablet at time t. The weight gain performance (% initial weight) throughout the dissolution test was shown in Fig. 3. The maximum weight gain of G10%, GX7:3, GX5:5, GX3:7 and X10% were 248, 478, 541, 593 and 648% of the initial dry weight, respectively. The formulation X10% showed excellent capacities in water absorption and retention. The maximum weight gain of G10% (248%) appeared at 10 h in the aqueous medium, whereas the wet weight decreased to 217% at 24 h, suggesting the occurrence of polymer erosion.

3.5. Radical swelling and morphological studies

In this study, the tablets hydrated as soon as contacting with the test medium, and then swelled to form hydrogel matrix. In a period of time after exposure to water, three regions will be visually distinguishable in the matrix. In the drug release process, the morphological changes of the swelled tablets, including the radial dimension and the formation of three regions, were monitored and photographed.

Three series of photos (Fig. 4) were taken for the swollen formulations of G10%, GX7:3 and X10% at 2, 6, 12 and 24 h in the dissolution test. After placed in the liquid medium, all the formulations rapidly swelled with a progressive increment in the size of the tablets. After 6 h of hydration, G10% began to lose integrity, resulting from the hydrodynamic stress induced by the dissolution apparatus (Jackson & Ofoefule, 2011). However, GX7:3 and X10% kept better integrity at the end of dissolution test (24 h). The

Table 2
In vitro drug release parameters of the formulations based on *G. sinensis* galactomannan and xanthan gum as sustained materials.

Formulation	Korsmeyer–Peppas: $M_t/M_\infty = kt^n$			Peppas–Sahlin: $M_t/M_\infty = k_1 t^{0.45} + k_2 t^{0.9}$		
	k	n	R^2	k_1	k_2	R^2
G10%	0.098	0.73	0.9981	0.061	0.046	0.9991
GX7:3	0.092	0.69	0.9978	0.065	0.034	0.9986
GX5:5	0.094	0.70	0.9974	0.066	0.036	0.9986
GX3:7	0.089	0.73	0.9967	0.056	0.040	0.9984
X10%	0.083	0.76	0.9984	0.044	0.045	0.9986

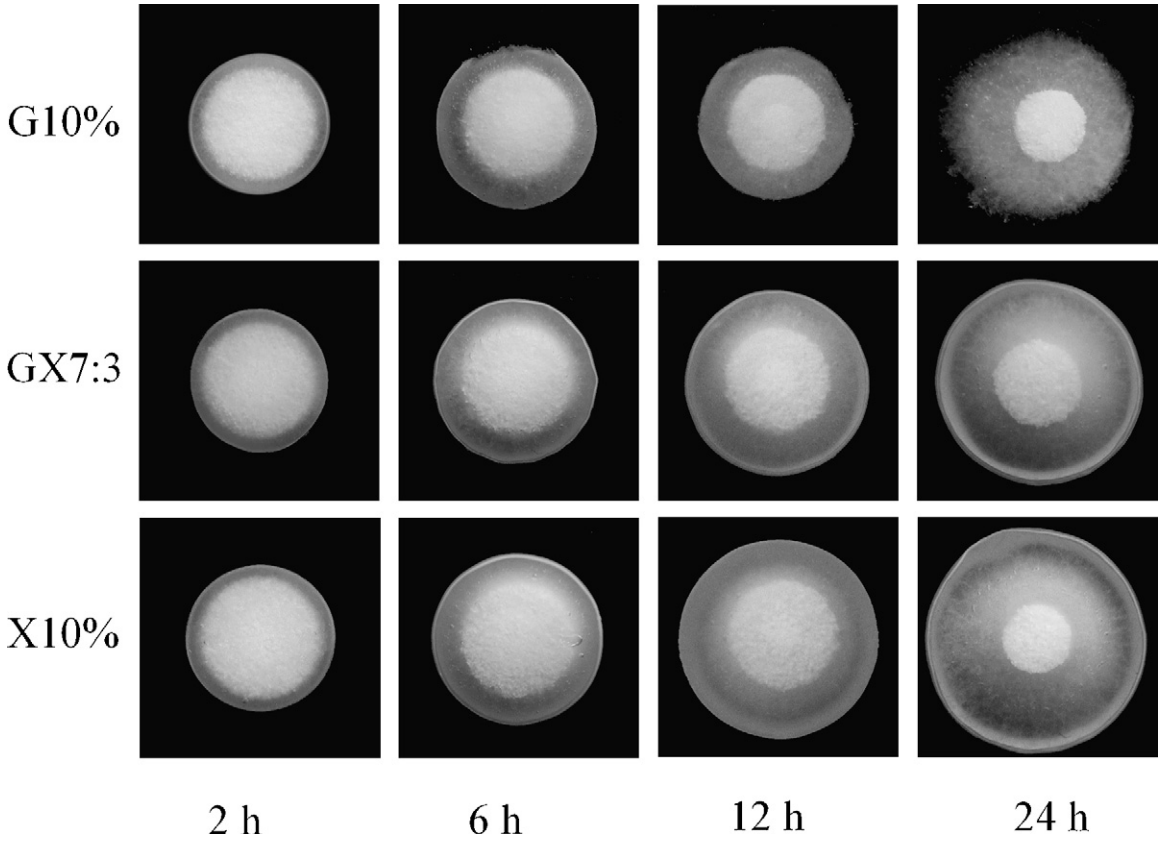

Fig. 4. Photographs taken on G10%, GX7:3 and X10% systems after swelling for 2, 6, 12 and 24 h in the dissolution test.

hydrogel has ability to maintain original shape of tablet due to isotropic swelling, and for this reason, swelling only changes the size of the matrix without deformation.

Radial swelling was expressed as a percentage of the diameter dimension to the initial and calculated according to Eq. (6):

$$\text{Radial swelling}\,(\%) = \frac{D_t - D_0}{D_0} \times 100 \tag{6}$$

where D_0 is the initial diameter of the tablet and D_t is the diameter of the tablet at time t. The radial swelling of the tablets are illustrated in Fig. 5. The overall dimensions of the matrices are affected by the rate of swelling and dissolution/erosion. No lag time could be detected in the swelling, which suggests that the gum quickly hydrated and immediately formed a sufficient gel–sol boundary. As shown in Fig. 5, a constant tablet diameter was reached for G10% at 12 h, which was resulted from the synchronization of swelling with dissolution/erosion processes of the matrix. X10% exhibited a fast increment in dimension, indicating its ability of rapid hydration and swelling. From 6 to 12 h, G10% showed decline in dimension due to the dissolution/erosion in the periphery of the matrix tablet, which was observable in Fig. 4. In the erosion dominated release, a fresh surface containing drug molecules is successively exposed to the liquid, leading to a fast release.

The system evolution during wetting was investigated by means of layer thickness to gain information of the mechanism of drug dissolution. Water diffusion into the matrix differentiates the whole

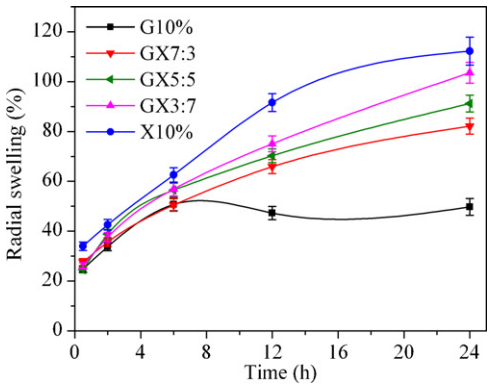

Fig. 5. Radial swelling of the matrix tablets with different formulations in dissolution test.

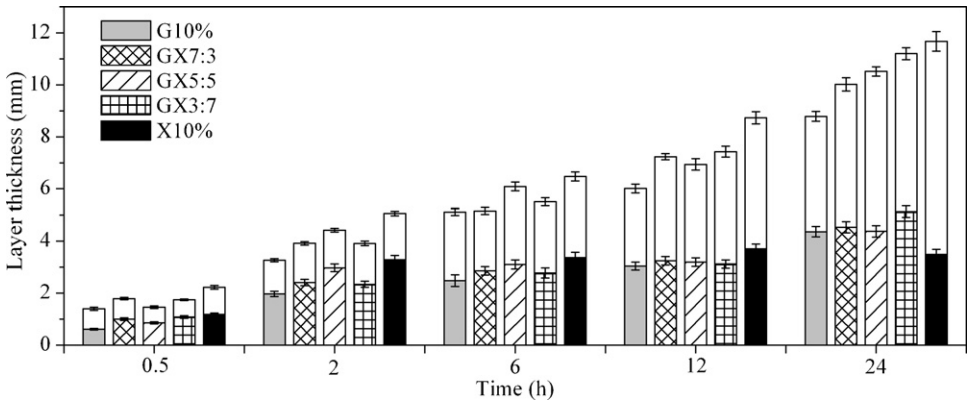

Fig. 6. Thickness of gel layer (superior bar) and of infiltrated layer (inferior bar) after swelling for 0.5, 2, 6, 12 and 24 h in the dissolution test.

matrix into three distinct regions: gel layer (soft rubber with high water content), infiltrated layer (tough rubber with middle swollen) and glass core (dry glassy with no or low water content). The water content of the matrix increases from the core to the periphery, which is the basic mechanism affecting the drug release. The normalized changes in the thickness of the region *vs.* time were presented in Fig. 6. The slow hydration rate of the polymeric matrix to achieve total swelling would result in the domination of solvent uptake over polymer dissolution/erosion. Results of our study were in agreement with the time evolution model of particular regions (Ju, Nixon, Patel, & Tong, 1995). Initially, the infiltrated layer and gel layer thicknesses almost linearly increased. Approximately after 2 h, the expansion rate of both gel layer and infiltrated layer decreased. Thereafter, the thickness of infiltrated layer reached its maximum value, when the dry glassy core disappeared. After this, the model (Ju et al., 1995) predicted that the thickness of the infiltrated layer would decrease until it finally disappeared, and meanwhile, the gel layer thickness increased at the expense of the infiltrated layer. As illustrated in Fig. 6, the infiltrated layer thickness of formulation X10% showed decline from 12 to 24 h. At a particular time point during 12–24 h of dissolution, formulation X10% may achieve totally wetted and meanwhile its infiltrated layer reached maximum thickness. After that, the infiltrated layer continued swelling to form a gel network, resulting in the decreasing of infiltrated layer thickness and the increasing of gel layer thickness.

4. Conclusions

In this study, the binary mixtures of *G. sinensis* galactomannan (G) and xanthan gum (X) were applied as sustained release materials in matrix tablets, to estimate the synergistic interactions between G and X in release-controlling performance. The in vitro evaluation of drug delivery systems showed that the GX matrices exhibited more sustained drug release than the matrix tablets with single polysaccharide component (either G or X), indicating the potential of controlled release based on the synergistic interactions between G and X. The results revealed that there was a strong synergism when G and X mixed in the ratio of 7:3. For all the formulations, the drug release mechanism was anomalous transport or non-Fickian diffusion, with Fickian diffusion playing a dominant role except X10% in which the drug release process was a combination of diffusion and polymer relaxation. In addition, the radial swelling behavior and morphological changes of the tablets were characterized to relate hydration to the drug release. The results of this study provide the possibility of *G. sinensis* galactomannan mixed with xanthan gum potential as the novel materials to sustain and control the release of drugs for colon-targeting delivery.

Acknowledgements

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