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Pregelatinized glutinous rice starch as a sustained release agent for tablet preparations

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ABSTRACT

The aim of this study was to modify the glutinous rice starch (GS) as a sustained release agent for tablet preparations. The GS slurry was physically modified by heat and then dried by spray drying. The pregelatinized GS (PGS) appeared in odorless fine white powder. Its flowability is extremely poor. The tablet containing PGS and propranolol HCl were prepared by wet granulation method. Less than 80% of propranolol HCl was released in the period of 10 h at the drug to PGS ratio of 1:2 and longer than 14 h at the ratios of 1:3 and 1:4. The higher the composition ratio of PGS, the slower the release of the drug. The mechanisms of drug release from the matrices were anomalous (non-Fickian) diffusion in both hydrochloric buffer (pH 1.2) and phosphate buffer media (pH 6.8). The compaction pressure in the range of 6.9–27.5 MPa does not affect the release of the drug from the matrices.

1. Introduction

Hydrophilic matrix (HM) system is a monolithic system prepared by compression of a powdered mixture of a hydrophilic polymer and a drug. When this device is exposed to an aqueous medium, it does not disintegrate, but immediately after hydration it develops a highly viscous gelatinous surface barrier which controls the drug release and the liquid penetration into the centre of the HM system. The overall release rate of a drug from this system is controlled by one or more of the following processes: transport of the solvent into the device, swelling of the associated matrix, diffusion of the solute through the swollen matrix, erosion of the swollen matrix, etc. (Rao & Devi, 1988).

Starch is a natural high molecular weight polysaccharide composed of glucose units. Most starches contain two types of glucose polymers: amylose and amylopectin. These two fractions occur in different amounts in starches from various botanical sources. Amylose is a linear polymer containing up to 6000 glucose units connected by α-1,4 linkage (Horton, Moran, Ochs, Rawn, & Scrimgeour, 2002). It is insoluble in cold water but absorbs a large amount of water and swells. Amylopectin has a highly branched structure consisting of short linear chains with a degree of polymerization ranging from 10 to 60 glucose units. They are connected to each other by α-1,6 linkage (Desrosier, 1977; Dyke, 1960; Imeson, 1999; Kleiner & Orlen, 1962). Amylose most likely accounts for the disintegrant properties of starch. On the other hand, amylopectin is a good binder. It also retards tablet disintegration and dissolution of active ingredient (Ingram & Lowenthal, 1966; Schwartz & Zelinski, 1978). Physical and enzymatic modifications have been used to improve the ability of swelling property in cold water of some native starches. Potato starch, corn starch, rice starch and wheat starch have been thermally modified by hot stage extrusion (Henrist & Remon, 1999). Potato starch has been thermally and enzymatically modified (Te Wierik, Eissens, Bergsma, Arends-Scholte, & Bolhuis, 1997). Chinese yam (*Dioseorea oppositifolia*) starch, Bitter yam (*Dioseorea dumetorum*) starch (Odeku, Schmid, & Picker-Freyer, 2008), waxy corn starch (100% amylopectin) (Visavarungroj, Herman, & Remon, 1990) and wheat starch (Sanchez, Torrado, & Lasters, 1995) have been thermally modified. All of them could retard the disintegration and drug release from the tablets.

Glutinous rice, waxy rice or sticky rice (*Oryza sativa* L.) is a kind of rice commonly cultivated in Thailand. Glutinous starch (GS) is widely used in food industries but not many applications in pharmaceutical industries have been reported. It is high in amylopectin (99.70%) (Kadan, Champagne, Ziegler, & Richard, 1997) which does not swell in cold water. Modified glutinous starch that can swell in cold water might be an interesting candidate for controlling release of a drug from a dosage form. In our previous study the glutinous starch from glutinous rice grains were physically modified using

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extruder, dried at ambient temperature and milled by pin mill (Peerapattana, Tattawasart, & Srijesdaruk, 2004). The matrices made from modified starch can retard the release of a drug up to a certain level. It had wide range in particle size (87.5–512.5 μm). In this study the commercial glutinous starch was used in order to control the protein and fat content which was claimed for starch quality. The pregelatinized starch paste was dried by spray drying in order to get narrow range of particle size and high production capacity. The physical characteristic of the hydrophilic matrix made from modified glutinous starch, the mechanism of drug release, the effect of compaction pressure on drug release are studied compared with HPMC matrices.

2. Materials and methods

2.1. Materials

GS was a gift from Cho Heng rice vermicelli factory (Thailand). Hydroxypropyl methylcellulose (HPMC E4M) was purchased from Colorcon (UK). Propranolol HCl was obtained from China National Chemical (People Republic of China, Batch No. 970604). All other chemicals used were of analytical grade.

2.2. Methods

2.2.1. Modification of GS

The slurry of 3% GS was heated on the water bath at the temperature of 70 °C for 5 min. The mucilage was feed via the nozzle (with the diameter of 1.5 mm) into the spray-drier chamber (Niro Mobile Minor 2000, Denmark) using the feed pump (Watson Marlow, England) at the rate of 1.5 l/h. The inlet air temperature was 180 °C and the outlet air temperature was maintained at the range of 92–95 °C. The air pressure to the nozzle was 1 bar at 35% flow meter. The products were collected via the cyclone collecting bottle. This product was named pregelatinized glutinous rice starch (PGS).

2.2.2. Physical properties of PGS

2.2.2.1. Particle size and size distribution. The size and size distribution of PGS were measured by Mastersizer 2000 (Malvern instruments, UK) using dry cell.

2.2.2.2. Scanning electron microscopy (SEM) study. The morphology of the PGS was observed using SEM. The sample was coated under argon atmosphere with gold/palladium and examined under the scanning electron microscope (Hitachi S-3200N, Japan).

2.2.2.3. Moisture content. The moisture content of the sample was measured using Sartorius Thermo Control Infrared Dryer (YTC 01L, Germany). The weights of PGS before and after being heated were recorded and the moisture content of PGS was calculated.

2.2.2.4. Flow property. The flowability of PGS was studied using Flowmeter (Pharmatest® PTG, GmbH, Germany). The PGS was allowed to flow down through the funnel onto the pan which was placed on top of the balance. The duration of PGS flow was timed and the flow rate was calculated (g/s).

2.2.2.5. Hausner ratio and Carr's indices. The bulk and tap density of PGS were determined as the volume before and after 100 taps, respectively. The Hausner ratio (Well & Aulton, 1988) was determined as the ratio of the bulk density to the tap density (Eq. (1)). Carr's index (Well & Aulton, 1988) was determined as the percentage ratio at which the PGS is packed down to the tap density (Eq. (2)). The Hausner ratio and the Carr's index are frequently used as indication of the flowability of a powder.

$$H = \frac{\rho_T}{\rho_B} \quad (1)$$

where H is the Hausner ratio, ρ_T is the tapped density of the powder and ρ_B is the bulk density of the powder.

$$C = 100 \times \left(1 - \frac{\rho_B}{\rho_T}\right) \quad (2)$$

where C is the Carr's index.

2.2.2.6. Granule swelling power.

2.2.2.6.1. Water retention capacity. Fifteen millilitres (15 ml) of 5% w/w freshly prepared PGS mucilages in purified water were centrifuged at 4500 rpm at room temperature (25 °C) for 30 min (Heraeus Sepatech, Labofuge 200, Germany). The supernatant was decanted. The sediment paste was weighed, then dried at 70 °C until constant weight obtained. The water retention capacity was calculated as the ratio of wet weight to dry weight of sediment pastes (Ring, 1985).

2.2.2.6.2. Swelling capacity. Twenty grams (20 g) of PGS was weighed in a 100 ml graduated cylinder. The tap volume was noted after 100 taps. The PGS was shaken with 80 ml of purified water until all particles were well dispersed. The mucilage was adjusted to 100 ml volume and the sedimented volume of swollen starch was observed after 24 h. The swelling capacity is the ratio of the swollen volume to the tap volume.

2.2.2.7. Solubility of PGS. The supernatants from the water retention capacity experiment were dried at 110 °C until constant weight was obtained. The dry weight was defined as the amount of soluble PGS at 25 °C and is expressed as the percentage of the initial weight of PGS sample (Kimihiko, Tooichiro, & Fumihiko, 1981).

2.2.2.8. Influence of ionic strength and pH of the medium on the viscosity of PGS mucilages. The influence of ionic strength was studied using distilled water, 0.9% NaCl (0.154 M), 2% NaCl (0.342 M) and 3% NaCl (0.513 M) solutions. The influence of pH of the medium was studied using hydrochloric acid buffer (pH 1.2), acid phthalate buffer (pH 3.0), neutralized phthalate buffer (pH 4.0 and 5.0), phosphate buffer (pH 6.0, 7.0 and 8.0) and alkaline borate buffer (pH 9.0). The ionic strength of all these buffers was equalized at $\mu = 0.136$ M by the addition of NaCl. Ten percent (10%) PGS mucilages in various media as mentioned above were prepared. The mucilages were left to fully hydrate for 2 h. The viscosity of these mucilages were measured using Brookfield rheometer (model DV-III, MC, USA) at 25 (±0.5)°C.

2.2.3. Preparation of tablets

The compositions of the formulations are given in Table 1. All materials were passed through a sieve with an aperture of 250 μm before use. Matrix tablets were prepared by wet granulation method. Propranolol HCl and matrix forming agents (PGS or HPMC) were thoroughly mixed. Ten percent (10%) PVP K30 in 95% alcohol was used as a binder. The ratios of propranolol HCl to matrix forming agent (PGS or HPMC) are 1:1, 1:2, 1:3 and 1:4 in formulation 1, 2, 3 and 4 respectively (Table 1). The alphabets P and H in front of the number indicate PGS and HPMC, respectively. The damp mass was passed through a number 12 mesh sieve (pore size = 1.41 mm). The wet granules were dried at the temperature of 60 °C for 2 h. The dry granules were passed through a number 14 mesh sieve (pore size = 1.19 mm) and further blended with 0.5% magnesium stearate for 5 min. The mixtures were compressed into flat-faced tablet of diameter 10 mm at the compaction pressure of 13.7 MPa using a KBr disc hydraulic press (Shimadzu IR accessory, Japan) with a dwell time of 5 s. Each tablet contains 80 mg of propranolol HCl. The crushing strength for 10 tablets was measured using a VanKel hardness

Table 1
Composition (%) of the matrices containing propranolol HCl and matrix forming agents (PGS or HPMC).

Composition (% w/w)	Formulation							
	P1	P2	P3	P4	H1	H2	H3	H4
Propranolol HCl	47.25	31.50	23.62	18.90	47.25	31.50	23.62	18.90
PGS	47.25	63.00	70.88	75.60	–	–	–	–
HPMC	–	–	–	–	47.25	63.00	70.88	75.60
PVP K30	5	5	5	5	5	5	5	5
Mg stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Weight/tab (mg)	170	255	340	425	170	255	340	425

tester (VK200, Germany). The mean crushing strength and standard deviation were calculated.

2.2.4. Compaction studies

They have been reported that compaction pressure has negligible influence on the drug release rate from compressed hydrophilic matrix (Ford, Rubinstein, & Hogan, 1985; Hogan, 1989; Huber & Christenson, 1968; Lapidus & Lordi, 1968; Talukdar & Plaizier-Vercammen, 1993). So the effect of compaction pressure was studied only in formulation P3 and H3 (Table 1). The tablets were compressed using a KBr disc hydraulic press (Shimadzu IR accessory, Japan) in the range of 6.9–27.5 MPa. The crushing strength for 10 tablets was measured using a VanKel hardness tester (VK200, Germany). The mean crushing strength and standard deviation were calculated and plotted against compaction pressures.

2.2.5. Dissolution studies

The USP XXVIII basket method (USP, 2005) was used with a constant temperature water bath at 37 ± 0.5 °C. The speed of basket rotation was 100 ± 1 rpm. The pH change dissolution method was used in order to simulate the environment of the gastro-intestinal tract. The dissolution media used were 0.05 M hydrochloric acid buffer (pH 1.2) for the first 90 min and 0.05 M phosphate buffer (pH 6.8) for further 22.5 h. At defined time intervals, the dissolution medium was removed for determining a drug concentration and fresh medium was replaced. The amount of drug released in the dissolution medium was measured using a UV spectrophotometer (Shimadzu UV-1201, Japan) at the wavelength of 289 nm. The studies were carried out in six vessels. The cumulative percentage of propranolol HCl released was calculated and plotted against time.

2.3. Data analysis

Korsmeyer, Gurny, Doelker, Buri, and Peppas (1983) derived a simple relationship which described drug release from a polymeric system (Eq. (3))

$$\frac{M_t}{M_\alpha} = kt^n \tag{3}$$

where M_t/M_α is the fraction of drug released, t is the release time, k is a kinetic constant (with units of t^{-n}) incorporating structural and geometric characteristics of the release device and n is the release exponent indicative of the mechanism of release. This equation can be used to analyze the first 60% of a release curve where the release is linearly related to t^n, regardless of geometric shape.

Although the constant k in Eq. (3) is one of the constants of the drug release rate, it should not be used for comparison because there are different kinetics in different test conditions. Therefore, for calculation of the release rate of the drug, the data in this study were subjected to the Higuchi equation (Eq. (4), Higuchi, 1961):

$$Q = (2ADC_s t)^{1/2} \tag{4}$$

where Q is the percentage of drug release at time t, A is the total concentration of drug in the tablet, D is the diffusion coefficient of the drug in the matrix and C_s is the solubility of drug in the matrix. This equation may be reduced to a simple equation as:

$$Q = at^{1/2} + c \tag{5}$$

Eq. (5), for release data dependent on the square root of time, would give a straight line release profile, where a is a square root time dissolution rate constant and c is a constant. The lag period, prior to the commencement of release, is defined as $(-c/a)^2$.

2.4. Statistical analysis

The effect of compaction pressure on drug release were statistically analysed by one way analysis of variance (ANOVA) using the SPSS® program version 17.0. Post-ANOVA analysis was carried out according to Bonferroni's multiple comparison test or, where appropriate, Games–Howell multiple comparison test (equal variance not assumed). The release rate of propranolol HCl from PGS and HPMC matrices were statistically analysed by unpaired t-test (Microsoft® Excel 2003).

3. Results and discussions

3.1. Organoleptic properties of PGS

The product yield from spray drying was approximately 55%. The PGS occurs as a fine, white-coloured, odourless and poor flowing powder.

3.2. Physical properties of PGS

The particle size of PGS is 5.06 μm and close to the size of the native starch (5.60 μm) (Table 2). The Carr's index of 27.44% (Table 2) shows that PGS would have flow problem. Hausner ratio is another parameter providing an indication of powder flowability, showing poor flow in accordance with Carr's index. The moisture content is 5.79%. The water retention capacity and swelling capac-

Table 2
Physical properties of pregelatinized glutinous rice starch (PGS).

Physical properties	PGS
Particle size(mean + SD) (μm)	5.06 ± 2.59
Moisture content (%)	5.79 ± 0.12
Bulk density (g/ml)	0.31 ± 0.01
Tapped density (g/ml)	0.42 ± 0.02
Flow properties	Extremely poor flow
Carr's index (%)	27.44 ± 3.15
Hausner ratio	1.38 ± 0.06
Water retention capacity (%)	2.24 ± 0.07
Swelling capacity	1.66 ± 0.10
Amount of soluble substance (%) at 25 °C	11.00 ± 2.28

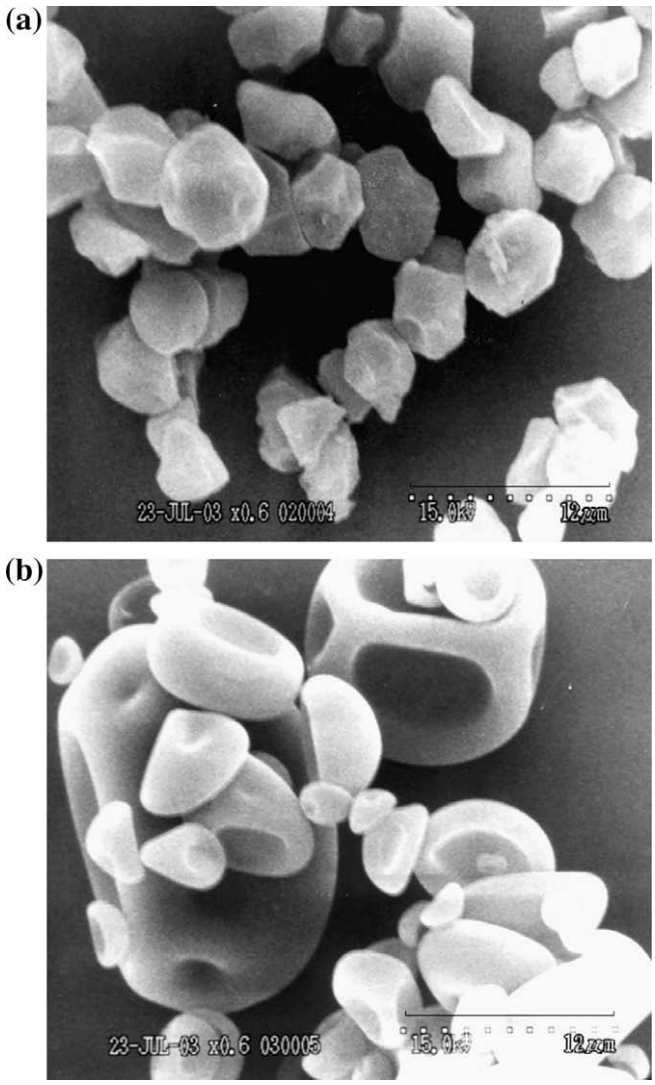

Fig. 1. SEM photos of (a) GS and (b) PGS (magnification ×2000).

ity are 2.24 and 1.66, respectively. The amount of soluble substances is 11.00%. The morphology of the glutinous rice starch had changed from angular to round shape after drying (Fig. 1a and b).

3.2.1. Influence of ionic strength and pH of the medium on the viscosity of PGS mucilages

The influence of ionic strength and pH of the medium on the viscosity of 10%w/w PGS mucilages are shown in Fig. 2. The viscosity of PGS mucilages in all saline solutions were slightly higher than in distilled water and the degree of ionic strength hardly affect the viscosity of the PGS mucilage. The viscosity of 10% PGS mucilages slightly increased when the ionic strength of the medium increased from 0.154 to 0.513. This may imply that the characteristic of the PGS will not be affected by the electrolyte in the GI tract. The PGS matrices should perform similar manner in both fasted and fed state from the stomach through the small intestine.

The pH of the medium in the range of 1–8 hardly affected the viscosity of 10% PGS mucilage. When the pH of the medium was, however, higher than 8, the viscosity was greatly increased. This can be explained by the eclipsing of the glycopyranoside units in aqueous alkaline solutions, resulting in a reorientation of the hydrogen groups from the axial to the equatorial position (Reeves & Blouin, 1957). This optical rotation tends to expand the random coil (Colson, Jennings, & Smith, 1974). These phenomena result finally in an increase in the viscosity of the starch dispersion.

3.3. Preparation of matrix tablets

The propranolol hydrochloride tablets were prepared by wet granulation method due to PGS's poor flowability. The weight variation and content uniformity of all formulations met the USP requirement (data not shown).

3.4. Dissolution studies

The dissolution profiles of propranolol HCl from PGS and HPMC matrices (formulations P1, P2, P3, P4, H1, H2, H3 and H4, Table 1) are shown in Fig. 3. Both PGS and HPMC matrices can retard the release of propranolol HCl. The higher ratio of the matrix forming

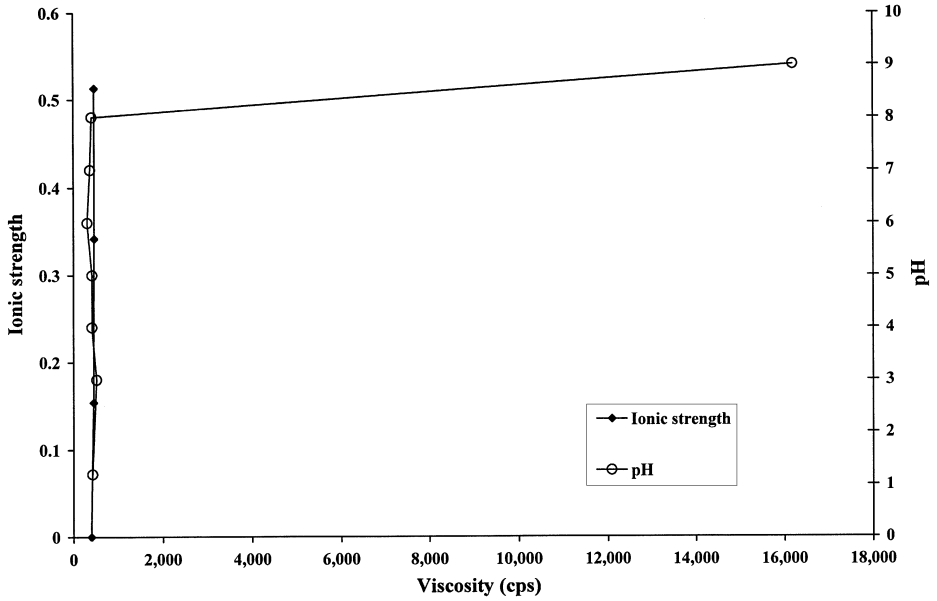

Fig. 2. Effect of ionic strength and pH of the medium on the viscosity of PGS mucilages (at 25 °C).

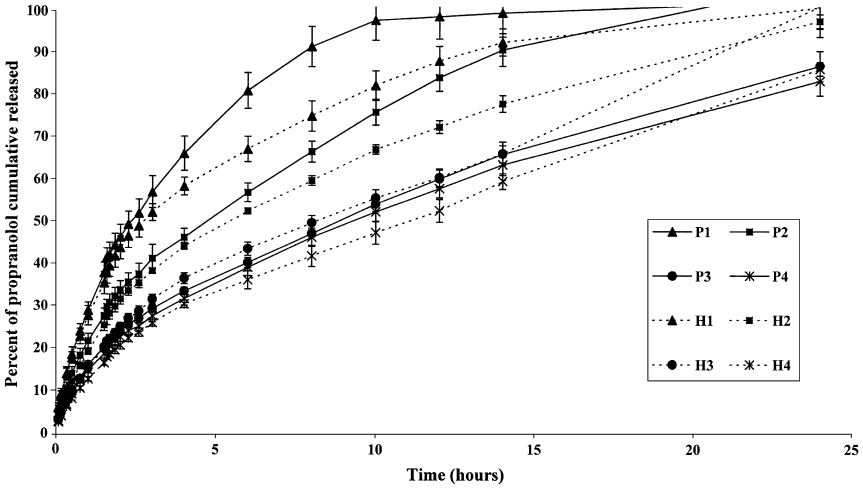

Fig. 3. The release profile of propranolol HCl from the PGS and HPMC matrices containing drug and PGS or HPMC at the ratios of 1:1, 1:2, 1:3 and 1:4 (compaction pressure 13.7 MPa).

Table 3
The release rate of PGS and HPMC matrices at various drug:polymer ratios (at compaction pressure of 13.7 MPa) in 0.05 M hydrochloric acid buffer pH 1.2 and in 0.05 M phosphate buffer pH 6.8 (mean value ± SD, $n = 6$).

Polymer	PGS		HPMC	
Ratio of drug:polymer	Release rate ($\%min^{1/2}$)	Correlation coefficient (r)	Release rate ($\%min^{1/2}$)	Correlation coefficient (r)
pH 1.2				
1:1	4.55 ± 0.13	0.9987	4.08 ± 0.33	0.9973
1:2	3.35 ± 0.15	0.9991	2.87 ± 0.12	0.9967
1:3	2.40 ± 0.03	0.9952	2.39 ± 0.06	0.9971
1:4	2.37 ± 0.09	0.9989	2.11 ± 0.13	0.9984
pH 6.8				
1:1	4.35 ± 0.20	0.9997	2.81 ± 0.07	0.9971
1:2	3.15 ± 0.08	0.9977	2.61 ± 0.18	0.9984
1:3	2.32 ± 0.08	0.9975	2.30 ± 0.07	0.9976
1:4	2.14 ± 0.10	0.9994	2.24 ± 0.11	0.9955

agent, the slower the release of the drug. However, when the content of PGS is higher than 70% (drug:PGS = 1:3), the drug release doesn't seem to be further slower. The drug release rates from PGS matrices of formulations P3 and P4 are not significantly different ($p > .05$, Table 3). At the drug to matrix forming agent ratio of 1:1, 1:2 and 1:4, HPMC matrices can retard the drug release more than from PGS matrices (compare at the same ratio) ($p < .05$). But at the drug to matrix forming agent ratio of 1:3, both PGS and HPMC matrices can retard the drug release at nearly the same degree. The release rates of P3 and H3 matrices are not significantly different ($p > .05$). The PGS content affects the drug release from HM until the concentration reaches 70 percent. Beyond this concentration drug release is very slightly affected. The optimal concentration of PGS should be carefully considered in the formulation. Beyond the optimal concentration, the ability of PGS in sustaining the release of the drug from HM is slightly lower than HMPC. This probably is due to the swelling property of the PGS itself.

The values for release exponent (n) and kinetic constant (k) with the correlation coefficient (r) for PGS and HPMC matrices are given in Table 4. A value of $n = 0.43$ indicates Case I or Fickian diffusion, $n = 0.86$ indicates Case II transport, $0.43 < n < 0.86$ indicates anomalous (non-Fickian) diffusion and $n > 0.86$ for Super Case II transport (Ritger & Peppas, 1987). The release of a drug from a hydrogel matrix is a complex mechanism which involves two release mechanisms, a Fickian diffusional release and Case-II relaxational release. Fickian diffusional release occurs by the usual molecular diffusion of a drug due to a chemical potential gradient. Case-II relaxational release is the drug transport mechanism associated with stresses and state-transition in hydrophilic glassy polymers which swell in water or biological fluids. This term also includes polymer entanglement and erosion.

The release behavior of all formulations in 0.05 M hydrochloric acid buffer (pH 1.2) were anomalous (non-Fickian) diffusion with values of n in the range of 0.616–0.710 (Table 4). The n values of PGS matrices were slightly higher than HPMC matrices. The release

Table 4
The drug release parameters from PGS and HPMC matrices at various drug:polymer ratios (at compaction pressure of 13.7 MPa) in 0.05 M hydrochloric acid buffer pH 1.2 and in 0.05 M phosphate buffer pH 6.8 (mean value ± SD, $n = 6$).

Polymer	PGS			HPMC		
Ratio of drug:polymer	Release exponent (n)	Kinetic constant (k) (min^{-n})	Correlation coefficient (r)	Release exponent (n)	Kinetic constant (k) (min^{-n})	Correlation coefficient (r)
pH 1.2						
1:1	0.650 ± 0.020	20.18 ± 3.16	0.9995	0.616 ± 0.019	21.83 ± 1.92	0.9969
1:2	0.690 ± 0.064	13.70 ± 4.25	0.9984	0.637 ± 0.020	14.36 ± 1.32	0.9974
1:3	0.681 ± 0.029	10.02 ± 1.30	0.9989	0.661 ± 0.010	10.20 ± 0.71	0.9980
1:4	0.710 ± 0.027	8.19 ± 1.01	0.9995	0.644 ± 0.011	9.05 ± 0.41	0.9987
pH 6.8						
1:1	0.514 ± 0.004	39.32 ± 2.46	0.9984	0.544 ± 0.014	32.33 ± 3.18	0.9963
1:2	0.537 ± 0.019	24.80 ± 2.89	0.9969	0.532 ± 0.013	24.56 ± 2.15	0.9952
1:3	0.561 ± 0.024	15.26 ± 2.56	0.9967	0.549 ± 0.021	17.98 ± 2.32	0.9964
1:4	0.543 ± 0.020	16.36 ± 2.19	0.9983	0.563 ± 0.014	13.31 ± 1.54	0.9975

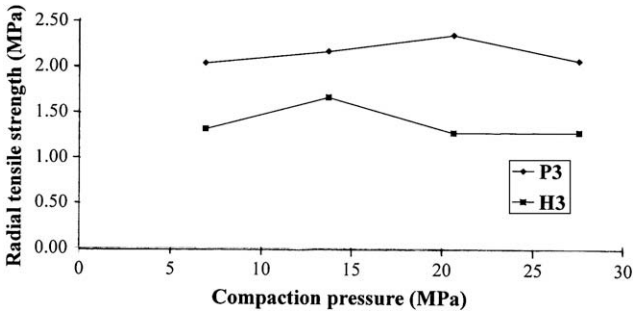

Fig. 4. Effect of compaction pressure (MPa) on the radial tensile strength (kp) of PGS and HPMC matrices (formulations P3 and H3).

behavior of all formulations in 0.05 M phosphate buffer (pH 6.8) were also anomalous (non-Fickian) diffusion with values of n in the range of 0.514–0.563 (Table 4). The n values of both PGS and HPMC matrices were very similar. The obtained n values in this experiment mean propranolol HCl released from PGS matrices via two competing release mechanisms, i.e., drug diffusion and polymer relaxation (or erosion). The drug diffusion mechanism contributed largely in phosphate buffer medium (n value was lower than in acid buffer medium), while the matrix erosion contributed more in acid buffer medium. In the acid buffer medium, the matrix was possibly not fully hydrated, so that it was eroded easily, comparing with hydrated matrix in phosphate buffer medium. In phosphate buffer medium, the matrix was thoroughly hydrated and swelled due to a longer contact time with the medium. The gel layer around the matrices was created and behaved as a barrier for a drug to diffuse out to the medium so the n value is lower.

3.5. Compaction studies

The effect of compaction pressure on tensile strength of PGS and HPMC matrices (Formulation P3 and H3) was shown in Fig. 4. The tensile strength was slightly changed when the compaction pressure was changed from 6.9 to 27.5 MPa. These results are in concordant with the drug release profiles from these matrices (Fig. 5).

The release rates of propranolol HCl from PGS and HPMC matrices in both 0.05 M hydrochloric acid buffer (pH 1.2) and 0.05 M phosphate buffer (pH 6.8) at all compaction pressures were very similar (Table 5). The release rates were in the range of 2.2–2.4 $\%min^{1/2}$ and not significantly different ($p > .05$). This result shows that the compaction pressure in the range of 6.9–27.5 MPa does

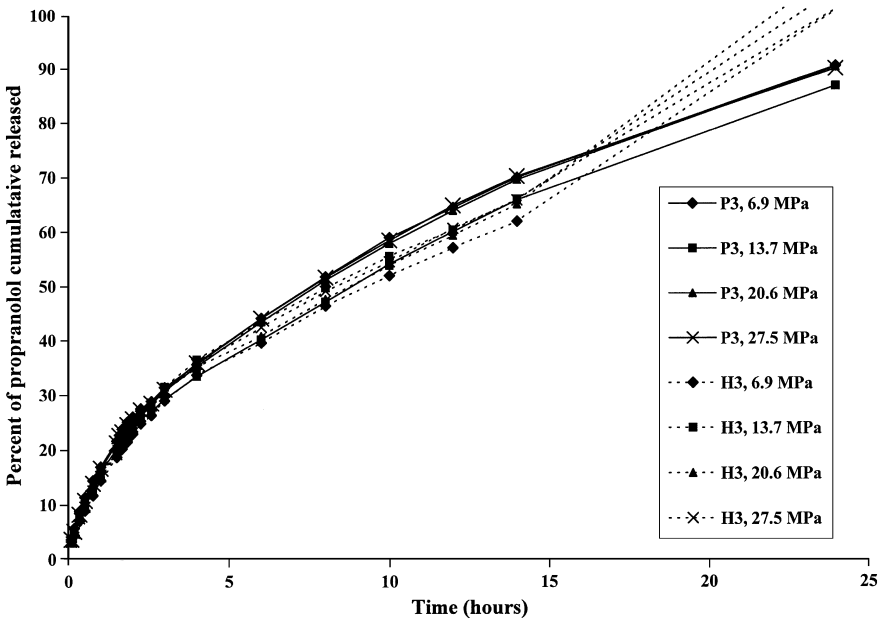

Fig. 5. The release profile of propranolol HCl from PGS and HPMC matrices (formulations P3 and H3) at different compaction pressures.

Table 5
The release rate of the PGS and HPMC matrices (drug:polymer ratio 1:3) at various compaction pressures in 0.05 M hydrochloric acid buffer pH 1.2 and in 0.05 M phosphate buffer pH 6.8 (mean value ± SD, $n = 6$).

Polymer	PGS		HPMC	
Compaction pressure (MPa)	Release rate ($\%min^{1/2}$)	Correlation coefficient (r)	Release rate ($\%min^{1/2}$)	Correlation coefficient (r)
pH 1.2				
6.9	2.42 ± 0.15	0.9993	2.27 ± 0.12	0.9952
13.7	2.40 ± 0.03	0.9952	2.39 ± 0.06	0.9971
20.6	2.46 ± 0.04	0.9988	2.34 ± 0.13	0.9950
27.5	2.39 ± 0.07	0.9959	2.36 ± 0.17	0.9972
pH 6.8				
6.9	2.34 ± 0.04	0.9991	2.28 ± 0.12	0.9992
13.7	2.32 ± 0.08	0.9975	2.30 ± 0.07	0.9976
20.6	2.33 ± 0.04	0.9990	2.32 ± 0.21	0.9963
27.5	2.36 ± 0.04	0.9994	2.26 ± 0.13	0.9969

Table 6
The drug release parameters from PGS and HPMC matrices (drug:polymer ratio 1:3) at various compaction pressures in 0.05 M hydrochloric acid buffer pH 1.2 and in 0.05 M phosphate buffer pH 6.8 (mean value ± SD, $n = 6$).

Polymer	PGS			HPMC		
Compaction pressure (MPa)	Release exponent (n)	Kinetic constant (k) (min^{-n})	Correlation coefficient (r)	Release exponent (n)	Kinetic constant (k) (min^{-n})	Correlation coefficient (r)
pH 1.2						
6.9	0.629 ± 0.013	13.29 ± 0.92	0.9992	0.660 ± 0.011	9.51 ± 0.043	0.9970
13.7	0.681 ± 0.029	10.02 ± 1.30	0.9989	0.661 ± 0.010	10.20 ± 0.071	0.9979
20.6	0.638 ± 0.014	12.53 ± 1.41	0.9991	0.645 ± 0.015	10.72 ± 0.89	0.9983
27.5	0.648 ± 0.014	11.78 ± 0.73	0.9988	0.653 ± 0.017	10.41 ± 0.76	0.9977
pH 6.8						
6.9	0.507 ± 0.013	22.77 ± 2.85	0.9988	0.557 ± 0.015	16.04 ± 1.39	0.9964
13.7	0.561 ± 0.024	15.26 ± 2.56	0.9967	0.549 ± 0.021	17.98 ± 2.32	0.9975
20.6	0.524 ± 0.008	20.04 ± 0.90	0.9990	0.582 ± 0.031	14.29 ± 3.55	0.9976
27.5	0.546 ± 0.017	17.75 ± 2.09	0.9991	0.541 ± 0.023	18.38 ± 2.45	0.9970

not affect the release rate of the drug. This may be due to the fact that PGS and HMPC can be hydrated and swelled fast enough to compensate for the difference in porosity and tortuosity under varied compaction pressures.

The drug release behavior of PGS and HPMC matrices in hydrochloric acid buffer (pH 1.2) was anomalous (non-Fickian) diffusion with n values in the range of 0.629–0.681 and 0.645–0.661, respectively (Table 6). The release behavior of these matrices in phosphate buffer (pH 6.8) was also anomalous (non-Fickian) diffusion with n values in the range of 0.507–0.561 and 0.541–0.582, respectively (Table 6).

4. Conclusions

The PGS is a potential candidate for sustained release agent. It is a natural, non toxic material and requires low production cost. The mechanisms of propranolol HCl release from PGS and HPMC matrices were similar by anomalous (non-Fickian) diffusion in both acid buffer (pH 1.2) and phosphate buffer (pH 6.8). The composition ratio of PGS affects the drug release rate from PGS matrices, the higher the PGS ratio the slower the drug release rate up to the composition ratio of 70%. The ratio beyond this affects the release very slightly. The compaction pressure does not affect the release rate from both PGS and HPMC matrices but PGS gives tablets higher radial tensile strength than HPMC. Both the composition ratio of PGS and the compaction pressure do not alter the mechanism of drug release from the matrices. All these results imply that PGS can be used as a hydrophilic matrix for alternative of synthetic polymer like HPMC.

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