Evaluation of *Plantago major* L. seed mucilage as a rate controlling matrix for sustained release of propranolol hydrochloride

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Accepted October 12, 2012

Polysaccharide mucilage derived from the seeds of *Plantago major* L. (family *Plantaginaceae*) was investigated for use in matrix formulations containing propranolol hydrochloride. HPMC K4M and tragacanth were used as standards for comparison. The hardness, tensile strength, and friability of tablets increased as the concentration of mucilage increased, indicating good compactibility of mucilage powders. The rate of release of propranolol hydrochloride from *P. major* mucilage matrices was mainly controlled by the drug/mucilage ratio. Formulations containing *P. major* mucilage were found to exhibit a release rate comparable to HPMC containing matrices at a lower drug/polymer ratio (drug/HPMC 2:1). These results demonstrated that *P. major* mucilage is a better release retardant compared to tragacanth at an equivalent content. The results of kinetic analysis showed that in F3 (containing 1:2 drug/mucilage) the highest correlation coefficient was achieved with the zero order model. The swelling and erosion studies revealed that as the proportion of mucilage in tablets was increased, there was a corresponding increase in percent swelling and a decrease in percent erosion of tablets. The DSC and FT-IR studies showed that no formation of complex between the drug and mucilage or changes in crystallinity of the drug had occurred.

Keywords: *Plantago major*, mucilage, release, HPMC, tragacanth, FTIR, DSC

Use of naturally occurring biocompatible polymeric materials has been the focus of recent research activity in the design of these dosage forms (1, 2). Polymeric hydrogels are studied for controlled release applications because of their producing drug release

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close to zero-order kinetics (3). Mucilages and gums have been well known since ancient times for their medicinal use (4). In recent times, increasing attention has been given to the application of gums of various sources as pharmaceutical excipients. Plant gums and exudates are getting screened for their use as pharmaceutical adjuvants. Mucilages are generally carbohydrate polymers obtained from woody and non-woody plant parts such as bark, seeds, sap, roots, rhizomes, fruits, and leaves. Mucilages are used for their binding, thickening, stabilizing, humidifying, disintegrating and release controlling properties in medicines (5–7). Mucilages from natural sources hydrate and swell on contact with water and have been used for the preparation of single unit dosage forms (8).

Plantago major L. is a perennial plant that belongs to the *Plantaginaceae* family. The plant produces a large amount of seeds. Leaves of *P. major* are used in traditional medicine for wound healing. Either whole or crushed leaves are used directly on burns, wasp stings and wounds of all kinds to stop bleeding, keep the wound clean and to enhance the healing process. Investigations have shown that the leaves contain a pectin type polysaccharide (PMII) and an arabinogalactan that possesses anti-complementary activity (9).

Seeds are located in capsules (8–16 per capsule) and become sticky in humid water due to the swelling of the polysaccharides present in the seed coat. Seeds contain monosaccharides, disaccharides, and trisaccharides. The outer seed coat contains carbohydrate polymers that swell in contact with water and form mucilage with high viscosity. These polysaccharides are composed of xylose, arabinose, galactorunic acid, glucuronic acid, rhamnose, galactose, and glucose (10).

The aim of the present study is to investigate the suitability of *Plantago major* seed mucilage for a matrix-forming agent and propranolol hydrochloride has been chosen as a model drug. As hydroxypropyl methylcellulose (HPMC) is one of the widely used hydrophilic polymers in matrix formulations (11), the present study also compares the release, swelling and erosion data obtained for matrices containing *Plantago major* seed mucilage to those of matrices containing HPMC.

EXPERIMENTAL

Materials

Propranolol hydrochloride (Rouz-daru Co., Iran) was received as a free sample. HPMC K4M (Colorcon, UK), tragacanth, NaOH, KCl, HCl, magnesium stearate (Merck, Germany) and potassium dihydrogen phosphate (Fluka, Switzerland) were used as supplied.

Swelling factor

To determine the swelling factor, *Plantago major* seeds (1 g) were put into graduated stoppered cylinders that were later filled with distilled water at room temperature up to the 25 mL mark. Except for intermittent agitation, the cylinders were left undisturbed for 24 h and the volume of swollen seed layer was then recorded by observation of the water gel boundary. The test was done in triplicate and the results are shown as mean values (12).

Extraction of mucilage

Plantago major seed mucilage was extracted according to the Sharma and Koul method (12). Ten milliliters of 0.1 mol L^{-1} hydrochloride was heated to boiling in a 100-mL Corning flask. The flask was removed from the flame and a 1-g test sample of dry seed was added to it. Heating was resumed and the process of dissolution of the seed husk was monitored. When all seeds had changed color, the flask was finally removed from the flame and the solution was filtered through a clean muslin cloth while still hot. In order to separate residual traces of mucilage, the seeds were washed twice in 5 mL of hot water and the solution obtained each time was filtered. The combined filtrate, containing dissolved mucilage, was mixed with 60 mL of 95 % ethyl alcohol, stirred and allowed to stand for 5 h. Finally, the supernatant liquid was decanted and the beaker containing the precipitate was dried in an oven maintained at 50 °C. The weight of dry precipitate was taken to represent the total mucilage content (12).

Viscosity determination

Dried and finely powdered *Plantago major* seed mucilage (2 g) was suspended in 75 mL of distilled water for 24 h. Distilled water was added up to 100 mL to produce a concentration of 2 % (*m/V*). The mixture was homogenized with a mechanical stirrer for 2 h and its viscosity was determined using a Brookfield viscometer, spindle –LV2 (Brookfield LV-II, USA) at 20 rpm and 25 °C.

Preparation of matrix tablets

A series of formulations containing a fixed amount of propranolol hydrochloride (80 mg), and several amounts of *Plantago major* seed mucilage powder (drug to mucilage ratios 1:0.5, 1:1, 1:2) or HPMC K4M, tragacanth (drug to polymer ratios 1:0.5, 1:1, 1:2) were thoroughly blended for 10 min. Magnesium stearate (1 %, *m/m*) was then added, followed by further mixing for 2 min. The resultant powder mixture was compressed into tablets using a single punch tableting machine (Korsch, Germany), with a 10-mm diameter flat punch. All matrices were stored in a desiccator for at least 3 days to allow tablet relaxation before use. Compositions of all formulations are listed in Table I.

Evaluation of tablets

Tablet properties (crushing strength, mass variation, and friability) were determined by the standard procedure (13). The tensile strength (T) of tablets, which is a measure of the stress necessary to cause diametric fracture of the compact, was determined from the mean data obtained from the hardness test carried out on tablets (n = 10) using an Erweka hardness tester (TBH 30MD, Germany). The T values were computed from the equation below (7):

$$T = \frac{2P}{\pi Dt} \qquad \textit{Eq. (1)}$$

where P is the load applied on the tablet that causes diametric fracture of the tablet of diameter, D, and t is tablet thickness. Content uniformity of the drug in tablets was confirmed based on the British Pharmacopoeia method (14).

Table I. Formulation composition of investigated propranolol hydrochloride matrix tablets

Formulation code	Formulation composition					Total mass (mg)
	Propranolol hydrochloride (mg)	*Plantago major* mucilage (mg)	HPMC K4M (mg)	Tragacanth (mg)	Mg-stearate (mg)	
F1	80	40	–	–	1.2	121.2
F2	80	80	–	–	1.6	161.6
F3	80	160	–	–	2.4	242.4
F4	80	–	40	–	1.2	121.2
F5	80	–	80	–	1.6	161.6
F6	80	–	160	–	2.4	242.4
F7	80	–	–	40	1.2	121.2
F8	80	–	–	80	1.6	161.6
F9	80	–	–	160	2.4	242.4

In vitro *release studies*

The United State Pharmacopoeia (USP) basket method was used for all *in vitro* dissolution studies. In this method, distilled water containing hydrochloric acid 0.2 mol L^{-1} (pH 1.2) and phosphate buffer pH 7.4 without enzyme were used as dissolution media. The dissolution profile of propranolol hydrochloride was determined according to the USP basket method at 100 rpm, in 900 mL maintained at 37.0 ± 0.5 °C in a dissolution tester (Caleva 8ST, Germany). The amount of propranolol hydrochloride was 80 mg in all formulations. The matrices were placed in 900 mL of distilled water containing hydrochloric acid (pH 1.2) for 2 h. The samples were withdrawn at predetermined time intervals (0.5, 1, 1.5, and 2 h), filtered and assayed spectrophotometrically at 289 nm using a UV/Visible spectrophotometer (Varian, Australia). After 2 h, the dissolution medium pH was changed from 1.2 to 7.4 using phosphate buffer. The samples were withdrawn at predetermined time intervals (3, 4, 5, 6, 7, and 8 h) and analyzed by the mentioned method. The mean of four determinations was used to calculate drug release from each of the formulations.

Drug release kinetics

Various mathematical equations have been proposed for kinetic analysis of drug release from the evaluated formulations. The zero order rate *Eq. 2* describes the systems where the drug release is independent of its concentration. The first order rate *Eq. 3* describes drug release from systems where the release is concentration dependent. According to the Higuchi model *Eq. 4*, drug release from the insoluble matrix is directly proportional to the square root of time and is based on Fickian diffusion (15):

$$Q_t = k_0 t \quad (2)$$

$$ln\ Q_t = ln\ Q_0 - k_1 t \quad (3)$$

$$Q_t = k_H t^{1/2} \quad (4)$$

where Q_t is the amount of drug released at time t, Q_0 is the initial amount of drug in the tablet and k_0, k_1 and k_H are release rate constants for the zero order, first order and Higuchi models, respectively.

In order to define a model that will represent a better fit for the formulations, dissolution data can be further analyzed by the Peppas and Korsemayer equation:

$$M_t / M_\infty = K_p\ t^n \quad (5)$$

where M_t corresponds to the amount of drug released at time t, M_∞ is the total amount of drug that must be released at infinite time, K_p is a constant and n is the release exponent indicating the type of drug release mechanism. The value of n for a cylinder is < 0.45, for Fickian release > 45 and < 0.8 for non-Fickian release, 0.89 for the case II release and > 0.89 for the super case II type release (16). Criteria for selecting the most appropriate model were based on the best goodness of fit and smallest sum of squared residuals.

Matrix swelling studies

Swelling of the matrices can be measured by their ability to absorb water and swell. The study was carried out in a USP/NF dissolution apparatus No. 1 (Caleva 8ST, Germany). Dry polymer matrices were accurately weighed, placed in dissolution baskets, and immersed in 900 mL of phosphate buffer (pH 7.4) maintained at 37 °C in dissolution vessels. At regular intervals, the pre-weighed basket-matrix system was withdrawn from the dissolution vessel, lightly blotted with a tissue paper to remove excess test liquid and reweighed. The percent water uptake, *i.e.*, degree of swelling due to absorbed test liquid, was estimated at each time point as the mean of three determinations (17).

Matrix erosion studies

A standard USP/NF dissolution apparatus No. 1 (Caleva 8ST, Germany) was used for this purpose. Dry matrices were weighed, placed in dissolution baskets, and subjected to dissolution in 500 mL of 0.05 mol L^{-1} phosphate buffer (pH 7.4), maintained at 37 °C, with the basket rotating at 100 rpm. At regular intervals, basket-matrix assemblies were removed from the dissolution vessels and dried to a constant weight in a hot air oven at 50 °C (17). The percentage matrix erosion (%*E*) at time *t*, was estimated as mean of three determinations.

Differential scanning calorimetery (DSC)

Thermograms of samples (*P. major* mucilage, propranolol hydrochloride, and powdered tablet containing 1:1 of drug/mucilage) were recorded on a DSC-60 (Perkin Elmer). Samples (3–5 mg accurately weighed to 0.01 mg) were placed in aluminum pans and the lids were crimped using a Perkin Elmer crimper. Thermal behavior of the samples was investigated at a scanning rate of 10 °C min^{-1}, covering a temperature range of 30–300 °C. The instrument was calibrated with an indium standard.

FT-IR spectroscopy

Fourier-transform infrared spectroscopy (FT-IR) was obtained on a Perkin Elmer Spectrum one FT-IR system (Perkin Elmer, USA) using the KBr disk method. Samples (*P. major* mucilage, propranolol hydrochloride, and powdered tablet containing 1:1 of drug/mucilage) were mixed with KBr and compressed to 10 mm discs using a hydraulic press at a pressure of 100 kN for 30 s. The IR scanning range was 450–4000 cm^{-1} and the resolution was 2 cm^{-1}.

Statistical analysis

ANOVA followed by Tukey's test was used to determine significant differences between groups and $p < 0.05$ was considered significant.

RESULTS AND DISCUSSION

Evaluation of mucilage

The swelling factor of 1 g of *P. major* seeds was 14.8 ± 1.08 mL (643.5 ± 46.9 %) according to the above method. Sharma and Koul reported 8.33 and 12.0 mL swelling factors for *P. major* seeds in their study (12). The yield of mucilage extraction from *P. major* seeds was 22.1 % and the viscosity of its 1 % aqueous dispersion was 0.482 Pa s.

Evaluation of prepared matrices

Table I shows the composition of formulations. Mg-stearate (1 %) was added to every formulation as lubricant. Table II compares the properties of propranolol hydrochloride matrix tablets with *P. major* mucilage (F1-F3) and HPMC K4M and tragacanth (F4-F9). The content uniformity test showed that the drug content was between 98.71–101.09 %. The values of hardness (from 3.91 ± 0.18, 4.32 ± 0.24, and 4.78 ± 0.23 kg cm^{-2} in F1, F2 and F3, respectively) increased with an increase in the mucilage. This increase in F1 and F2, and between F2 and F3, was not significant ($p = 0.064$ and $p = 0.118$, respectively), but comparison of F1 and F3 showed a significant increase ($p = 0.005$) in hardness with an increase in mucilage. The tensile strength of tablets increased as the concentration of *P. major* mucilage increased (from 0.44 ± 0.03, 0.51 ± 0.06, and 0.58 ± 0.06 MN m^{-2} in F1, F2 and F3, respectively), indicating good compactibility of mucilage powders. A significant difference was observed between F1 and F3 ($p = 0.047$). Friability decreased with an increase in mucilage concentration (from 1.34 ± 0.08, 1.12 ± 0.06, and 0.96 ± 0.05 % (*m/m*) in

Table II. Characteristics of propranolol hydrochloride tablets prepared with different amounts of P. major mucilage, HPMC K4M, and tragacanth

Formulation	Hardness[a,b] (kg cm^{-2})	Friability[a,b] (%)	Tensile strength[a,b] (MN m^{-2})	Assay[a,c] (%)
F1	3.91 ± 0.18	1.34 ± 0.08	0.44 ± 0.03	99.14 ± 3.42
F2	4.32 ± 0.24	1.12 ± 0.06	0.51 ± 0.06	101.09 ± 2.14
F3	4.78 ± 0.23	0.96 ± 0.05	0.58 ± 0.06	98.94 ± 3.17
F4	4.82 ± 0.31	0.92 ± 0.05	0.62 ± 0.07	99.34 ± 2.47
F5	5.19 ± 0.34	0.87 ± 0.07	0.67 ± 0.06	98.71 ± 3.04
F6	5.31 ± 0.34	0.75 ± 0.06	0.71 ± 0.05	100.78 ± 2.95
F7	3.11 ± 0.29	1.29 ± 0.05	0.38 ± 0.07	99.51 ± 2.16
F8	3.45 ± 0.31	1.11 ± 0.07	0.47 ± 0.05	100.67 ± 2.64
F9	3.57 ± 0.35	0.93 ± 0.05	0.52 ± 0.06	99.28 ± 2.11

[a] Data are shown as mean ± SD.

[b] $n = 10$; [c] $n = 20$.

F1, F2 and F3, respectively) for tablets prepared by direct compression ($p < 0.02$). Nokhodchi *et al.* observed the same results in propranolol hydrochloride matrix tablets prepared with fenugreek mucilage as an excipient for controlling drug release (18). Comparing the crushing strength of mucilage matrices with HPMC K4M matrices at similar drug to polymer ratios revealed that the tensile strength of matrices containing HPMC was greater than the strength of matrices containing carbohydrate polymer extracted from *P. major*. This comparison shows a similar crushing strength in tragacanth containing formulations ($p > 0.05$). The content of HPMC did not significantly affect the hardness, tensile strength, and friability of tablets ($p > 0.05$).

Drug release studies

The comparative dissolution profile (Fig. 1–3) showed that an increase in the percentage of *P. major* mucilage from 40 mg (formulation F1) to 160 mg (formulation F3) resulted in a decrease in the release rate of propranolol ($p < 0.001$). Drug release was slower from the HPMC K4M containing tablets compared to the mucilage containing matrices, and drug release rates in formulations containing tragacanth were higher than the drug release from matrices containing *P. major* mucilage ($p < 0.001$ for all investigations). Odeku and Fell reported that an increase in the percentage of Khaya gum from 60 to 90 % (*m/m*) mucilage containing matrices resulted in a significant decrease in the release rate of paracetamol (13). Similar results were observed in glimepiride matrix tablets containing dried mucilage of *Aloe barbadensis* as a release retardant excipient (19).

The results show that drug release was generally linear, especially 1–3 hours after the initial release for all formulae. Such linear drug release from hydrophilic matrices was attributed to synchronization between swelling and erosion of the polymer in main-

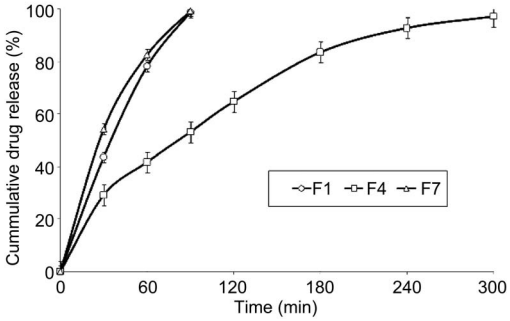

Fig. 1. Comparison of the release behavior of propranolol hydrochloride from matrices containing 1:0.5 of drug/mucilage, HPMC K4M or tragacanth (n = 4).

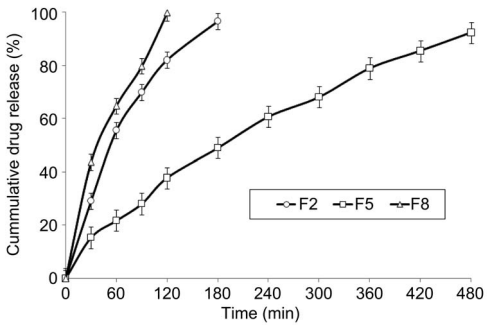

Fig. 2. Comparison of the release behavior of propranolol hydrochloride from matrices containing 1:1 of drug/mucilage, HPMC K4M or tragacanth (n = 4).

taining a constant gel layer. During dissolution studies, the outer layer of tablets appeared to be hydrated after being placed in the dissolution medium. There was a progressive increase in the size of this hydrated layer, followed by a gradual loss in integrity resulting from the hydrodynamic stress induced by agitated dissolution medium (20). Samuelsen *et al.* identified the composition of *P. major* mucilage. Seeds contained the monosaccharides glucose, fructose, xylose and rhamnose as well as the disaccharide sucrose and the trisaccharide planteose. Lyophilized mucilage contained about 76 % carbohydrate. Only traces of proteins were detected by their method. The outer seed coat contained polysaccharides that swelled in contact with water and formed a gel layer of high viscosity (10, 21). The hydrated gel layer persisted for a considerable part of the dissolution process. This could be attributed to an increase in the viscosity of the hydrated layer with the increase in mucilage concentration, which thus improved its resistance to erosion and release.

Drug release data showed that the dissolution rate in F2 (containing 80 mg mucilage) was faster ($p < 0.000$) than F4 (containing 40 mg HPMC K4M), but the increase in the amount of *P. major* mucilage in F3 (containing 160 mg mucilage) showed a slower

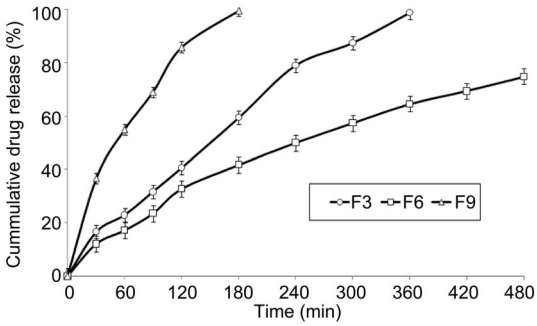

Fig. 3. Comparison of the release behavior of propranolol hydrochloride from matrices containing 1:2 of drug/mucilage, HPMC K4M or tragacanth (n = 4).

dissolution rate in comparison with F4 ($p < 0.000$). Similar results were observed in aminophylline matrix tablets containing *Adansonia digitata* mucilage. The drug release retardation efficiency of the *Adansonia digitata* mucilage tablets at an equal polymer concentration was lower than that of HPMC (22).

Dissolution rate data were analyzed based on the listed equations and the results are given in Table III. The results show that in formulations containing *P. major* mucilage as a controlling-release agent (F1-F3), release kinetics changed with an increase in the amount of mucilage. These results show that in F1 (containing 1:0.5 drug/mucilage), the highest correlation coefficient was achieved with the Higuchi model. The release rate was so fast that kinetic analysis could not be fitted accurately in the Peppas model. Increasing the amount of *P. major* mucilage in F2 (containing 1:1 drug/mucilage) changed the kinetics of release and the best fit was observed in the Peppas model. The value of n in the Peppas model was 0.932 (> 0.89) and showed the super case II type release (16). The results of kinetic analysis show that in F3 (containing 1:2 drug/mucilage), the highest correlation coefficient was achieved with the zero order model. Jani and Shah studied the mucilage of *Hibiscus rosasinensis* as a release retardant excipient in diclofenac sodium matrix tablets. Drug release kinetics from these formulations corresponded best to zero-order kinetics (8). Nokhodchi *et al.* reported that drug release in propranolol hydrochloride matrices containing fenugreek mucilage was related to mucilage content. The same release rate was observed in formulations containing drug/fenugreek mucilage ratio 1:1 and F1 in this study. The results of release kinetics from matrices composed of varying amounts of fenugreek mucilage showed the best fit in the Peppas model and the release exponent (n) remained almost unchanged whereas in formulations containing *P. major* mucilage, the release kinetic changed with an increase in mucilage amount (18).

Ford *et al.* proved that the sum of squares of errors involves values that can be used to determine the most appropriate model for a data set. The sum of squares of errors is a measure of discrepancies between the observed data and the values that would have been predicted by a particular model (23). In formulations containing HPMC K4M (F4-F6), the highest correlation coefficients were achieved with Peppas, Higuchi, and first order models, respectively. The lowest sums of squares of errors were observed in the Peppas model in F4-F6 containing HPMC K4M. The values of n in the Peppas model in F4-F6

Table III. Kinetics of propranolol hydrochloride release from tablets prepared with different amounts of Plantago major *mucilage, HPMC K4M, and tragacanth*

Formulation	Zero-order model			First-order model			Higuchi model			Peppas model			
	k_0 (% min^{-1})	R^2	ss	k_1 (min^{-1})	R^2	ss	k_H (% min$^{-1/2}$)	R^2	ss	k_p (% min^{-n})	n	R^2	ss
F1	0.0092	0.979	2425	–0.066	0.918	10211	0.1389	0.995	8126	–	–	–	–
F2	0.0043	0.925	9668	–0.020	0.967	4578	0.0846	0.979	4493	0.0122	0.9321	1.000	0.0
F3	0.0026	0.988	6032	–0.011	0.847	34733	0.0650	0.984	46058	0.0138	0.7095	0.974	253
F4	0.0026	0.941	18791	–0.012	0.984	1581	0.0612	0.985	597	0.0459	0.5422	0.998	3.9
F5	0.0017	0.984	14831	–0.005	0.964	2453	0.0488	0.995	425691	0.0145	0.6753	0.989	153
F6	0.0014	0.974	15606	–0.003	0.999	1617	0.0397	0.996	19692	0.0105	0.7046	0.991	189
F7	0.0075	0.978	6486	–0.068	0.912	4175	0.1131	0.995	306	–	–	–	–
F8	0.0061	0.938	5981	–0.058	0.712	13598	0.0991	0.943	2460	–	–	–	–
F9	0.0044	0.950	10152	–0.031	0.905	11013	0.0845	0.973	2245	–	–	–	–

k_0 – zero-order release rate constant, k_1 – first-order release rate constant, k_H – Higuchi model release rate constant k_p – Peppas model release rate constant, n – release exponent in Peppas model, R^2 – coefficient of determination, ss – sum of squares of errors.

were 0.542, 0.675, and 0.705, respectively. These values indicated that release mechanisms were similar and were based on anomalous transport of the drug from the matrix. Similar values of *n* of around 0.6 were found for propranolol hydrochloride release from hydroxypropyl methylcellulose K4M matrices (24). Kinetic analysis of drugs released from matrices containing tragacanth (F7-F9) showed the best fit with the Higuchi model. Rasul *et al.* evaluated the kinetics of metoprolol release from matrices containing tragacanth. The results show that the best fit was observed in the Higuchi model (25).

Swelling and erosion behavior of matrix tablets

Swelling and erosion studies were carried out on all formulations. The results of these tests in phosphate buffer (pH 7.4) are provided as the percentage weight change and the percentage remaining of tablet mass, as shown in Figs. 4 and 5. The swelling behavior indicated the rate at which this formulation absorbed water from dissolution media and swelled. The changes in weight, characteristic of water uptake and swelling, started from the beginning and continued until 300 min of experiment, with the exception of F1 and F2 which disintegrated after 3 and 4 hours, respectively. Matrices containing a lower proportion of mucilage showed a lower degree of mass gain with time ($p < 0.000$). The percent swelling of formulations containing HPMC K4M was found to be higher than that of formulations containing *P. major* mucilage ($p < 0.000$). Formulations containing tragacanth showed the lowest swelling in comparison with other formulations ($p < 0.01$).

Matrix erosion measured the mass loss from matrix tablets immersed in dissolution media as a function of time. The remaining percentage of matrices is shown in Fig. 5 and reflects the amount of polymer dissolved and erosion of the matrix during the dissolution process. Mass loss from the tablets increased progressively with the erosion. The extent of erosion in formulations containing *P. major* mucilage (F1-F3) was higher than for HPMC matrices (F4-F6) and lower than for tablets containing tragacanth ($p < 0.001$). There was a significant ($p < 0.000$) increase in the remaining percent of the tablet with increased *P. major* mucilage concentrations (formulations F1-F3). These erosion profiles confirm the release pattern of propranolol hydrochloride from the *P. major* mucilage containing matrix tablets. Singh *et al.* studied the *Mimosa pudica* seed mucilage as a sustained release excipient in diclofenac sodium matrix tablets. The swelling and erosion studies revealed that as the proportion of mucilage in tablets was increased, there was a corresponding increase in percent swelling and decrease in percent erosion of tablets (26).

There was an initial rapid uptake of water by dry matrices during the first 0.5–1 h, followed by a leveling off of wet weights due to the increasing rate of erosional release. This proceeded until the rate of erosion exceeded the rate of water uptake, with a resultant decrease in weight with time. Similar results were observed in the xanthan gum containing tablets (27).

Interaction between drug and mucilage

It has been shown that polymorphic changes of the drug are important factors that may affect the dissolution rate and bioavailability. On the other hand, the importance of polymorphism for the therapeutic effectiveness of a drug and the pharmaceutical implication of the presence of metastable crystalline forms in the bulk powder are well

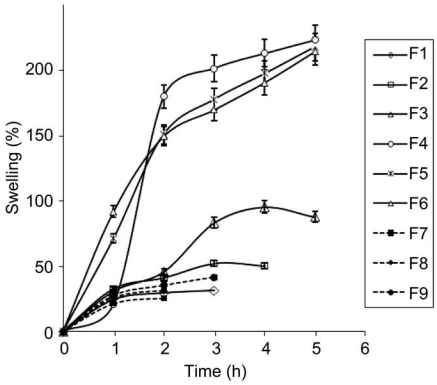

Fig. 4. The percentage of swelling (weight change) of different formulations of propranolol hydrochloride matrices containing *P. major* mucilage or HPMC K4M and tragacanth (n = 3).

known. It has also been shown that the crystal structure could affect tablet porosity and density, the mechanism of disintegration and aggregation, as well as the plastic and elastic properties of solid dosage forms (28). It is therefore important to study polymorphic changes of propranolol hydrochloride in matrix tablets containing *P. major* mucilage as a release retardant excipient. Bartolomei *et al.* reported that (*R, S*) propranolol hydrochloride existed in two crystalline forms, designated I and II (28).

The results of DSC thermograms are shown in Fig. 6. The *P. major* mucilage thermogram exhibits a very broad endothermic peak at 95.2 °C, which is associated with loss of water from the carbohydrate polymer. Further, an exothermic transition was recorded above 223.7 °C, which is indicative of mucilage degradation. The DSC profiles of forms I and II, recorded at a heating rate of 10 °C min^{-1}, showed rather sharp fusion endotherms: form I with an onset temperature of 163.0 ± 0.2 °C (peak temperature: 166 ± 0.5 °C), while

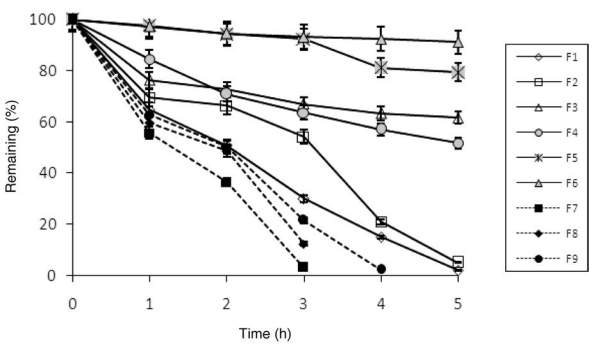

Fig. 5. The remaining percentage of different formulations of propranolol hydrochloride matrices containing *P. major* mucilage or HPMC K4M and tragacanth (n = 3).

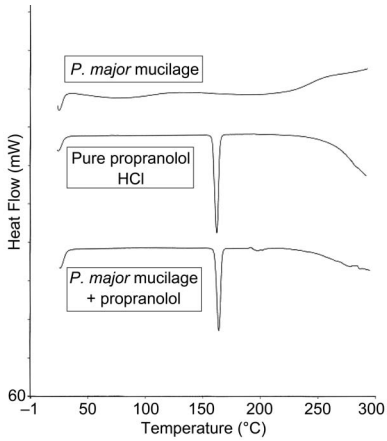

Fig. 6. Differential scanning calorimetry of *P. major* mucilage, propranolol hydrochloride, and matrix tablet containing 1:1 of drug/mucilage ratio.

form II showed an onset temperature of 161.8 ± 0.1 °C (peak temperature: 163.6 ± 0.2 °C). According to Fig. 6, propranolol hydrochloride showed an endothermic peak around its melting point (164.2 ± 0.1 °C). The matrix tablet containing the drug/mucilage ratio 1:1 showed the same peak in this area, which indicates that there was no interaction between the drug and *P. major* mucilage during the formulation process. From the above finding it can be concluded that the delayed dissolution rate of propranolol hydrochloride was

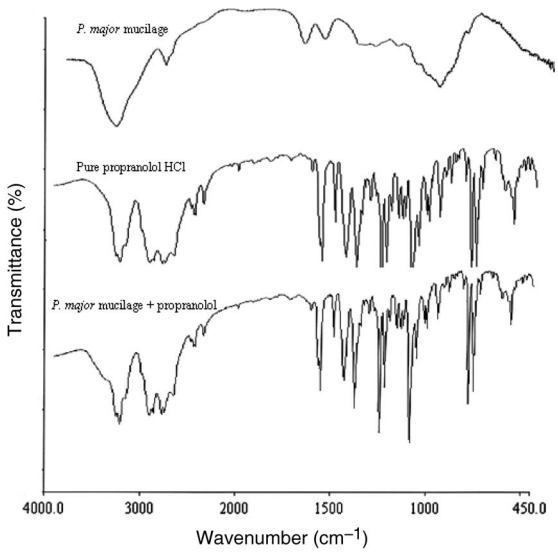

Fig. 7. FTIR spectra of *P. major* mucilage, propranolol hydrochloride, and matrix tablet containing 1:1 of drug/mucilage ratio.

not due to the formation of a complex between the drug and *P. major* mucilage or changes in drug crystallinity.

FT-IR spectral studies (Fig. 7) confirmed the above conclusion. In case of pure *P. major* mucilage, a broad band appearing around 3437.5 cm^{-1} corresponds to OH stretching, wave number 1742.9 cm^{-1} depicts the stretching zone of C=O, and 1040.1 cm^{-1} depicts the stretching vibration of the C-O group, which is characteristic of polysaccharides (3). The FT-IR spectrum of propranolol hydrochloride revealed the presence of peaks at 2964.9 cm^{-1} due to the presence of a secondary amine group, peaks at 3280.6 cm^{-1} due to the hydroxyl group (secondary), the aryl alkyl ether displayed a stretching band at 1267.8 cm^{-1} and the peak at 979.9 cm^{-1} was due to α-substituted naphthalene. In the spectra of the mucilage and drug blend, major characteristic peaks of both propranolol hydrochloride individually and *P. major* mucilage were retained. This confirms that there were no physical or chemical interactions amongst the components of the formulation and compatibility of the drug with the natural carbohydrate polymer.

CONCLUSIONS

This study has demonstrated the potential of *P. major* mucilage to act as a release retardant excipient in matrix formulations. An increase in the concentration of mucilage in binary drug-mucilage mixtures resulted in an increase in the crushing strength of tablets. Release kinetics showed that the mechanism was related to the mucilage content and at a concentration of about 66 % (*m/m*) the best fitting was observed in the zero-order model. The present study has demonstrated that *P. major* mucilage has great potential for being used as a controlled release excipient.

Acknowledgment. – This work was supported by a grant from the research council of the Mazandaran University of Medical Sciences.

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