Iranian Journal of Pharmaceutical Sciences
2014: 10 (3): 1- 18
www.ijps.ir

Original Article

Evaluation of Buccoadhesive Propranolol Hydrochloride Formulations Containing *Plantago psyllium* Seed Mucilage and Carbopol 934P

Majid Saeedi [a,b*], Jafar Akbari[a,b], Katayoun Morteza-Semnani[b,c], Ali Azarashk[a]

[a] Department of Pharmaceutics, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran.[b] Pharmaceutical Sciences Research Centre, Mazandaran University of Medical Sciences, Sari, Iran.[c] Department of Medicinal Chemistry, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

Abstract

Drug delivery via buccal mucosa by means of buccoadhesive formulations offer distinct advantages over peroral administration. Recently, plant gums and exudates have been screened for their use as pharmaceutical adjuvants. The aim of this study is to evaluate matrix tablets containing *Plantago psyllium* seed mucilage in addition to carbopol as a mucoadhesive agent, and propranolol hydrochloride as a model drug. Mucoadhesive tablets of propranolol were prepared using *Plantago psyllium* mucilage and Carbopol 934P. The swelling, erosion, mucoadhesion force, *in vitro* drug release were studied. Interaction between drug and polymers were investigated by DSC thermograms and FT-IR spectroscopy. The bioadhesion strength of formulations containing mucilage and carbopol was more than that of the tablets containing mucilage alone. The results also showed that bioadhesive strength increased with increase in the amount and viscosity of polymers. As the amount of mucilage increased from 6.25% per tablet (F1) to 43.75% (F7) drug release was increased. Combination of *Plantago psyllium* mucilage and Carbopol 934P modified the release rate and kinetic. The kinetic of drug release has changed by increase in amount of mucilage in these formulations. DSC and FT-IR studies showed no interaction between drug and formulations macromolecules. The use of *Plantago psyllium* mucilage and carbopol can optimize the drug release in propranolol HCl buccoadhesive tablets.

Keywords: bioadhesion, buccoadhesive, Carbopol 934P, mucilage, *Plantago psyllium*, releas

Corresponding Author: Majid Saeedi, Department of Pharmaceutics, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran and Pharmaceutical Sciences Research Centre, Mazandaran University of Medical Sciences, Sari, *Iran.*
Tel: +98-11-33543082
E-Mail: majsaeedi@gmail.com
Cite this article as: Saeedi M, Akbari J, Morteza-Semnani K, Azarashk A, Evaluation of Buccoadhesive Propranolol Hydrochloride Formulations Containing *Plantago psyllium* Seed Mucilage and Carbopol 934P.Iranian Journal of Pharmaceutical Sciences, 2014, 10(3): 1-18.

1. Introduction

Mucoadhesion consists of the attachment of a natural or synthetic polymer to a biological substrate. It is an applicable method of drug immobilization or localization and an important new aspect of controlled drug level. Buccal mucoadhesive controlled-release formulations could optimize the effectiveness of a drug by maintaining the drug concentration between the effective and toxic levels, limiting the dilution of the drug in the body fluids, and facilitating targeting and localization of a drug at a specific site [1]. In recent years interest in mucoadhesive polymers for drug delivery has increased [2, 3]. The main advantages of buccal drug delivery systems are: ease of administration and termination of drug action, localization or retention of drug to specific areas of oral cavity, rapid onset of action, high blood supply, and avoidance of first pass effect and limiting exposure of drug to gastrointestinal tract [4, 5].

Plantago psyllium or Isabgol is a 10-45 cm short-stemmed annual herb of the Plantaginaceae family. Leaves are born in rosettes addressed to the soil surface or alternately on the stem. Leaf count per plant varies from 40 to 86. Leaves are strap shaped recurved, linear 6.0-25 cm long and 0.3-1.9 cm broad. The surface of the leaves is glabrous or slightly downy. Spikes measure 0.6-5.6 cm and are ovoid or cylindrical. Flowers are arranged in four spiral rows on the spike. Petals are four, glabrous, reflexed and white in colour and sepals are four, free, concave, glabrous and elliptic. Placentation is axile and the ovary is bilocular with single ovule per locule. The capsule is ovate or ellipsoid, dehiscing along the ring of abscission tissue which is developed around the capsule. Isabgol seeds are translucent, concavo-convex in shape, cymbiform, and their color is pinkish-gray, brown or pinkish-white with a brown streak in color. Seed contains mucilage, fatty oil, large quantities of albuminous matter, the pharmacologically inactive glucoside, namely Aucubin ($C_{13}H_{19}O_8H_2O$) and a plantiose

sugar [6, 7]. Isabgol seed husk absorbs and retains water which accounts for its utility in stopping diarrhoea. It could alleviate kidney and bladder complaints as a diuretic, stop gonorrhea, arthritis, and hemorrhoids [8].

Carbomers are synthetic high-molecular-weight polymers of acrylic acid that are crosslinked with either allyl sucrose or allyl ethers of pentaerythritol. They contain between 52% and 68% of carboxylic acid (COOH) groups calculated on the dry basis. The molecular weight of carbomer is theoretically estimated at 7×10^5 to 4×10^9. In tablet formulations, carbomers are used as controlled release agents and/or as binders. In contrast to linear polymers, higher viscosity does not result in slower drug release with carbomers. Lightly crosslinked carbomers (lower viscosity) are generally more efficient in controlling drug release than highly crosslinked carbomers (higher viscosity). However, the presence of cationic salts may accelerate drug release rates and reduce bioadhesive properties [9]. Carbomer polymers have also been investigated in oral mucoadhesive controlled drug delivery systems [10-12].

In this study, formulations of propranolol hydrochloride as a model drug containing different proportions of *P. psyllium* mucilage and carbopol were evaluated for their release, swelling, erosion and bioadhesvie properties.

2. Materials and Methods

2.1. Materials

Propranolol hydrochloride (Rouz-daru Co., Iran) was received as a free sample. Carbopol 934P (B.F.Goodrich USA) and *Plantago psyllium* seed (Sari herbal market, Iran) were used as bioadhesive polymers. Other chemicals such as NaOH, HCl, magnesium stearate, and potassium di-hydrogen phosphate (Merck, Germany) were used as supplied.

2.2. Swelling Factor

The *Plantago psyllium* seeds (1 g by weight) were put in to graduate 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 triplicate and result showed in mean [13].

2.3. Extraction of Mucilage

Plantago psyllium seed mucilage was extracted according to the Sharma and Koul method [13]. 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 [13].

2.4. Preparation of Bioadhesive Matrix Tablets

The materials for each tablet (Table 1) were weighed, and were sufficiently blended) for 10 min. Magnesium stearate (1% w/w) 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.

2.5. Evaluation of Tablets

The tablet properties (crushing strength, mass variation, and friability) were determined by standard procedure [14]. The content uniformity of drug in tablets was confirmed based on British pharmacopoeia method [15].

2.6. In Vitro Release Studies

The dissolution tests were performed to the basket method (USP pharmacopoeia 24). A dissolution apparatus (Caleva 8ST, Germany)

was employed with a stirring rate of 100 rpm. The dissolution medium was 900 ml phosphate buffer (pH=6.4). Samples of the solution were withdrawn at definite time intervals. The dissolution media was then replaced by fresh dissolution fluid to maintain a constant volume. The solution was passed through a filter (Watman, USA) and then the concentration of propranolol hydrochloride in solution was measured with an ultraviolet spectrophotometer (Varian, Australia) at a wavelength of 289 nm after suitable dilution with the dissolution medium when necessary (n=3).

2.7. Drug Release Kinetics

In order to describe the kinetics of drug release from mucoadhesive tablets, various mathematical equation models (zero-order, first-order, Higuchi) were tested.

$Q_t = k_0 t$ Eq. (1)

$LnQ_t = LnQ_0 - K_1 t$ Eq. (2)

$Q_t = K_H t^{1/2}$ Eq. (3)

Where Q_t is the amount of drug released in time t, Q_0 is the initial amount of drug in tablet and k_0, k_1 and k_H are release rate constant for zero order, first order and Higuchi model, respectively. In order to define a model, which will represent a better fit for the formulations, dissolution data can be further analyzed by Peppas and Korsemayer equation.

$M_t/M_\infty = K_p t^n$ Eq. (4)

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, Kp 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, > 0.45 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.

2.8. Determination of Bioadhesive Strength

To evaluate the bioadhesion strength, a tensile tester apparatus was designed similar to a tensile tester apparatus (Instron model 4301) and the bioadhesive strength of the tablets was

measured according to previously published method by a tensile tester apparatus [17].

2.9. 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, Ger-many). 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 [18].

2.10. 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 [18]. The percentage matrix erosion (%E) at time t, was estimated as mean of three determinations.

2.11. Differential Scanning Calorimetery (DSC)

Thermograms of samples (*P. psyllium* mucilage, propranolol hydrochloride, and powdered tablet containing drug, mucilage and carbopol) were recorded on a DSC-60 (PerkinElmer). 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 were investigated at a scanning rate of 10oC min–1, covering a temperature range of 30–300oC. The instrument was calibrated with an indium standard.

2.12. 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. psyllium mucilage, propranolol hydrochloride, and powdered tablet containing drug, mucilage and carbopol) were mixed with KBr and compressed to 10 mm discs using a hydraulic press at a pressure of 100 kN for 30s. The IR scanning range was 450–4000 cm–1and the resolution was 2 cm^{-1}.

2.13. Statistical Analysis

ANOVA followed Tukey test was used to determine significant differences between groups and "P<0.05" was considered significant.

3. Results and Discussion

The swelling factor of 1 g of *P. psyllium* was 14.3 ± 1.06 mL (637.2 ± 43.9%) according to the aforementioned method. Saeedi et al. reported 14.8 ± 1.08 mL (643.5 ± 46.9%) swelling factor for *P. major* seeds in their study (15). The yield percentage of the mucilage extraction from *P. major* seeds was 19.8% and the viscosity of its 1% aqueous dispersion was 0.432 Pa.s.

Table 1 shows the composition of formulations and their physical characteristics. The results shows that hardness and friability of formulations F_1 to F_7 decreased by increase in the amount of mucilage in comparison with carbopol content (P < 0.01). In mucilage containing formulations (F_8 to F_{10}) friability increased by increase in the amount of mucilage, while in carbopol containing formulations (F_{11} to F_{13}) low amounts of friability with the same pattern was observed. In previous studies on the effect of *Plantago major* mucilage, an increase in the amount of mucilage resulted in an increase of hardness and decrease in friability of tablets [15, 17]. The content uniformity test showed that the drug content was between 97.5-101.75%.

The release rate of propranolol from matrix tablets containing different ratios of both polymers as a function of time is shown in Fig. 1 and Fig. 2. Dissolution rate data were analyzed based on Eqs. (1-4) and their results are listed in Table 2.

The results shows that as the drug release increased by increase in amount of *P. psyllium* seed mucilage in polymer mixture in formulations containing mucilage and carbomer (P < 0.01). The drug release was slower from

the carbopol containing tablets compared to the mucilage containing matrices ($P < 0.01$). The lowest release rate was observed with formulation F13 containing Carbopol 934P alone.

The kinetic study showed that the type and amount of polymer have effect on the release kinetic of propranolol HCl from buccoadhesive tablets. In formulations F1 and F2, the highest correlation coefficient was achieved with the

Table 1. Characteristics of propranolol hydrochloride tablets prepared with different ratios of *P. psyllium* mucilage and carbopol.

	Total Mass [a,b]				
Formulation Code	***P. psyllium* mucilage (mg)**	**Carbopol 934P (mg)**	**Hardness***	**Content Uniformity***	**Friability***
F1	10	70	165.2±2.168	79.7±1.4	1.2±0.011
F2	20	60	146±3.808	80.1±1.5	1.0±0.006
F3	30	50	121.6±2.074	79.6±2.8	1.11±0.06
F4	40	40	130.4±4.506	80.2±2.1	0.318±0.002
F5	50	30	83.4±2.881	78.8±0.8	0.24±0.07
F6	60	20	64±1.871	79.5±0.7	0.209±0.001
F7	70	10	82.2±2.95	81.4±0.81	0.11±0.001
F8	40	-	29.16±1.88	78±1.2	0.842 ± 0.05
F9	80	-	34.74±2.69	81.1±0.83	0.979±0.06
F10	160	-	40.96±2.21	78.9±1.7	1.012±0.07
F11	-	40	91.69±0.054	79.3±0.8	0.19±0.05
F12	-	80	234.38±0.232	80.2±1.3	0.31±0.07
F13	-	160	250.07±0.242	79.4±0.6	0.48±0.05

a The amount of propranolol hydrochloride in each formulation was 80mg.

b The amount of Mg stearate in each formulation was 1% of the total mass.

* Data are shown as Mean ± SD

Table 2. The kinetics data of propranolol hydrochloride release from investigated mucoadhesive tablets.

Formulation	Zero Order Model			First-order model			Higuchi model			Peppas model			
	K_0 (%.min)	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	0.0008	0.9839	12246	-0.0011	0.9922	5396	0.0223	0.9925	33005	0.0049	0.724	0.9966	135
F2	0.0008	0.9321	34293	-0.0013	0.9660	20662	0.0233	0.9887	1240	0.0301	0.4719	0.9901	172
F3	0.0014	0.9949	9035	-0.0026	0.9450	3178	0.0378	0.9542	41239	0.0103	0.6656	0.9801	579
F4	0.0014	0.9956	14474	-0.0031	0.9309	2898	0.0395	0.9634	15855	0.0198	0.5688	0.9916	138
F5	0.0014	0.9945	21446	-0.0034	0.9321	3417	0.0395	0.9802	3212	0.0337	0.4958	0.9834	169
F6	0.0020	0.9952	11601	-0.0061	0.8690	5764	0.0520	0.9873	22433	0.0158	0.6642	0.9991	11
F7	0.0027	0.9831	12505	-0.0093	0.9411	2508	0.0622	0.9975	7264	0.0253	0.6367	0.9971	13
F8	0.0014	0.8816	36561	-0.0046	0.9920	5342	0.0404	0.9629	2178	0.0296	0.6154	0.9982	7
F9	0.0014	0.9252	30573	-0.0037	0.9909	5654	0.0401	0.9835	216	0.0305	0.5653	0.9982	11
F10	0.0012	0.9777	25318	-0.0023	0.9990	8388	0.0334	0.9972	846	0.0266	0.5295	0.9936	92
F11	0.0033	0.9256	13795	-0.0283	0.8097	20277	0.0727	0.9761	2713	-	-	-	-
F12	0.0010	0.9162	19318	-0.0016	0.9468	8041	0.0292	0.9694	12964	0.0100	0.6630	0.9795	668
F13	0.0005	0.9915	22531	-0.0006	0.9963	17089	0.0131	0.9940	2407	0.0089	0.5494	0.9948	118

k_0: zero order release rate constant; k1: first order release rate constan;kH: Higuchi model release rate constant;kp: Peppas modelrelease rate constant; n: release exponent in Peppas model; r^2: definition coefficient;ss : sum of squares of errors.

Higuchi model. Increasing the amount of *P. psyllium* mucilage in F3 to F5 changed the kinetic of release and the best fitted model was observed with Zero-Order Model. Kinetic of Release for F6 and F7 were best fitted with Peppas and Higuchi model, respectively. For formulations F8 and F9, Peppas model showed the best fitting for kinetic of release. Drug

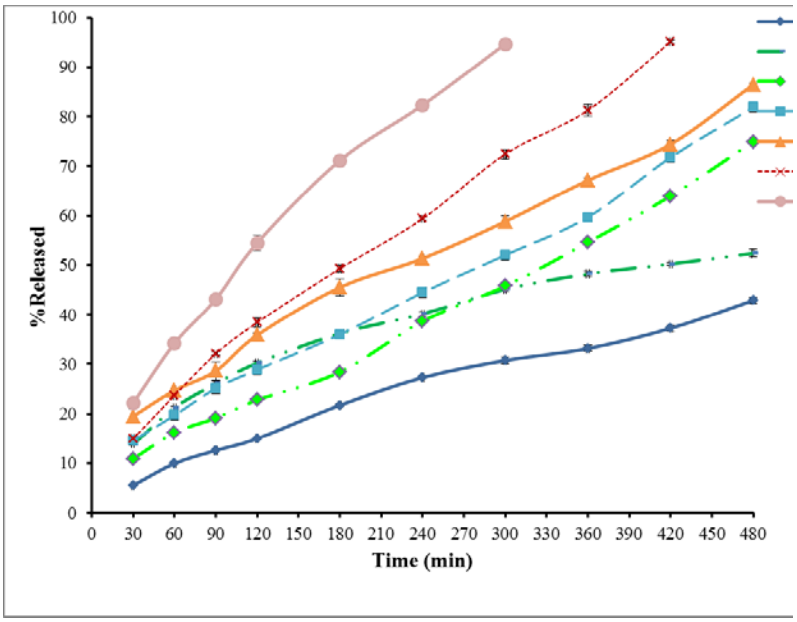

Figure 1. Comparison of release behaviour of propranolol HCl from matrices containing different ratios of both polymers.

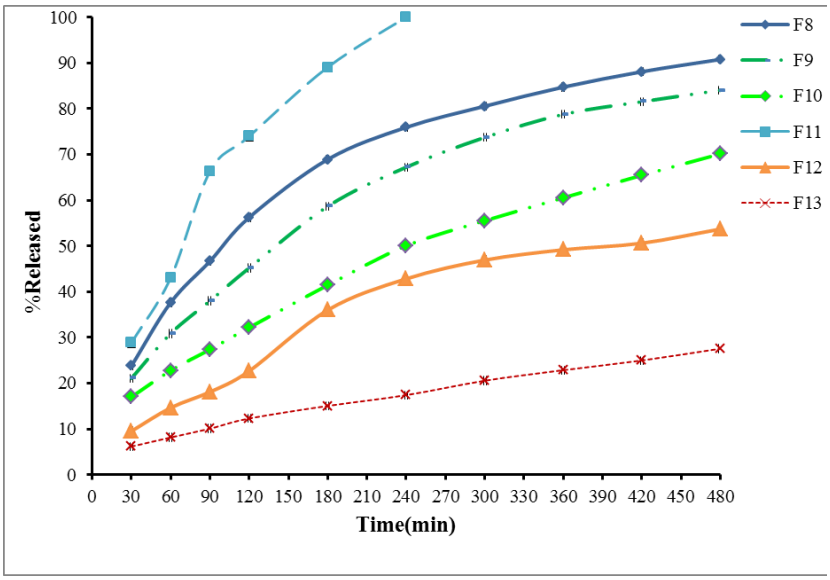

Figure 2. Comparison of release behavior of propranolol HCl from matrices containing different ratios of either polymers.

release in F10 and F11 were fitted in Higuchi model. The values of n in formulations F6, F8, F9 and F12 which followed Peppas model, showed the diffusion type release in all cases [16].

Much interest has been expressed in the use of oral cavity membranes as sites of drug

administration. Both the buccal and sublingual sites offer advantages compared with other routes, namely rapid onset of action, high blood levels, avoidance of the first-pass effect and possible degradation of drug as a consequence of exposure to the gastrointestinal tract. Moreover, there is easy access and the drug could be applied, localized and removed easily [20]. Odeku and Fell observed a significant decrease in the release rate of paracetamol following an increase in the percentage of Khaya gum from 60% to 90% w/w mucilage containing matrices [14]. Similar results were reported in glimepiride matrix tablets containing dried mucilage of *Aloe barbadensis* as a release retardant excipient [21]. The same results were reported in aminophyline matrix tablets containing *Adansonia digitata* mucilage, as the drug release retardation efficiency of the tablets containing *Adansonia digitata* mucilage were less than HPMC containing tablets [22]. Perez-Marcos et al. reported that an increase in amounts of carbopol 974 decreases the release rates of propranolol hydrochloride from matrix tablets and the

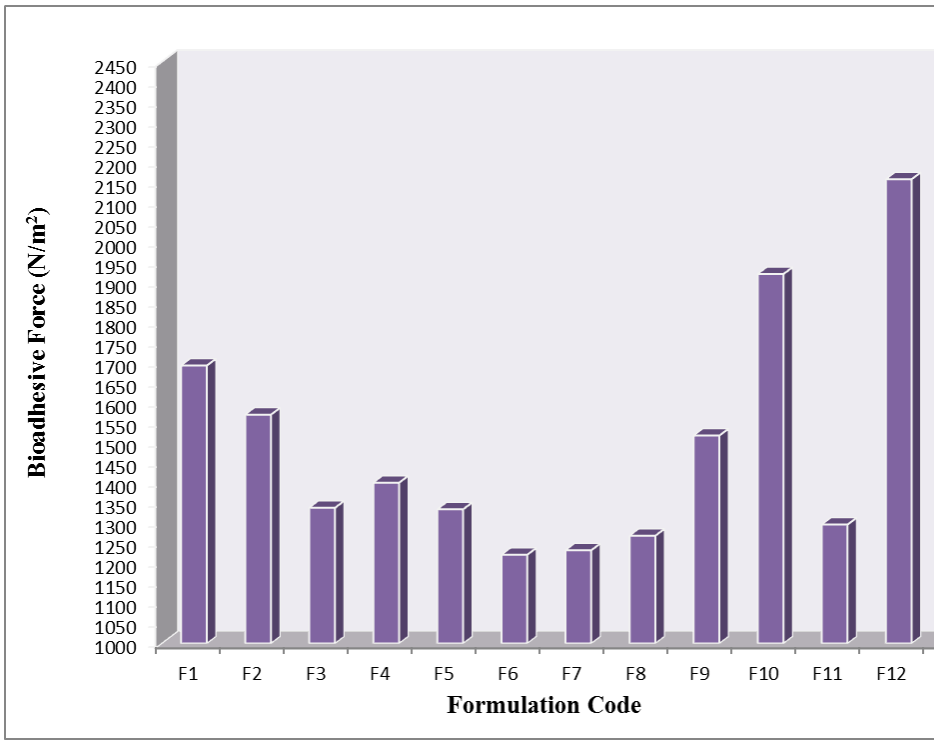

Figure 3. Comparison of bioadhesive force (N/m2) of matrices.

kinetics of release in all cases followed Zero-Order kinetics [23]. Saeedi et al. reported that an increase in *P. psyllium* amounts results in a decrease in drug release and kinetic of release best fitted First-Order and Peppas models in different formulations [24].

The bioadhesion strength of mucoadhesive tablets were evaluated by method that described by Akbari et al. [17]. The bioadhesion strengths of these tablets are shown in Fig. 3. Maximum bioadhesion strength was seen with Carbopol 934P. The bioadhesive force increased by increase in the amount of Carbopol 934P in tablets (F1-F7) containing mucilage and carbomer (P<0.05).

electrostatic, hydrophobic, hydrogen bonding, and Van der waals interactions (adsorption and electronic theories) [27]. Bioadhesion studies showed that adhesive force in formulations containing both carbopol and mucilage (F1 to F7) is more than formulations contain mucilage alone and less than formulations containing carbopol. Bioadhesion strength significantly increased by increase in the amount of mucilage in F8 to F10 and Carbopol in F11 to F13 (P<0.001). A prerequisite for extensive and longer mucoadhesion is formation of hydrogen bonds between the hydrophilic functional groups of the mucoadhesive polymers and the mucosal surface. The amount of the polymer also shows

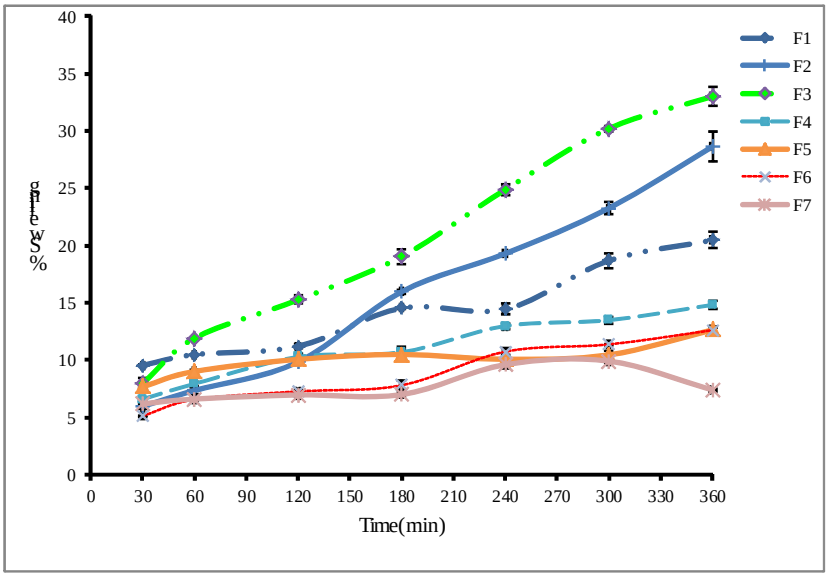

Figure 4. Comparison of swelling of matrices F1 to F7.

Clarithromycin using Carbopol 974P, HPMC K15M and HPMC K4M. They found that high molecular weight and high viscosity polymers exhibited hier adhesion. HPMC K15M and Carbopol 974P showed great mucoadhesive strength. Carbopol possesses carboxy groups required for bioadhesion [30].

In this study the swelling of formulations with different ratios of both polymers (F1 to F7) were investigated. The percent of swelling of the tablets were determined by the method described previously (Fig. 4). The matrix erosion measured by the weight loss from matrix tablets immersed in dissolution media as a function of time (Fig. 5). Erosion and swelling studies showed an asymmetrical process. In F1 to F4, the amount of swelling significantly increases ($P<0.05$), then decreases and remains constant. The increase in erosion was observed in these formulations, F1-F7, ($P<0.05$). Singh et al. observed that with increase in the amounts of *Mimosa pudica* mucilage, swelling increases

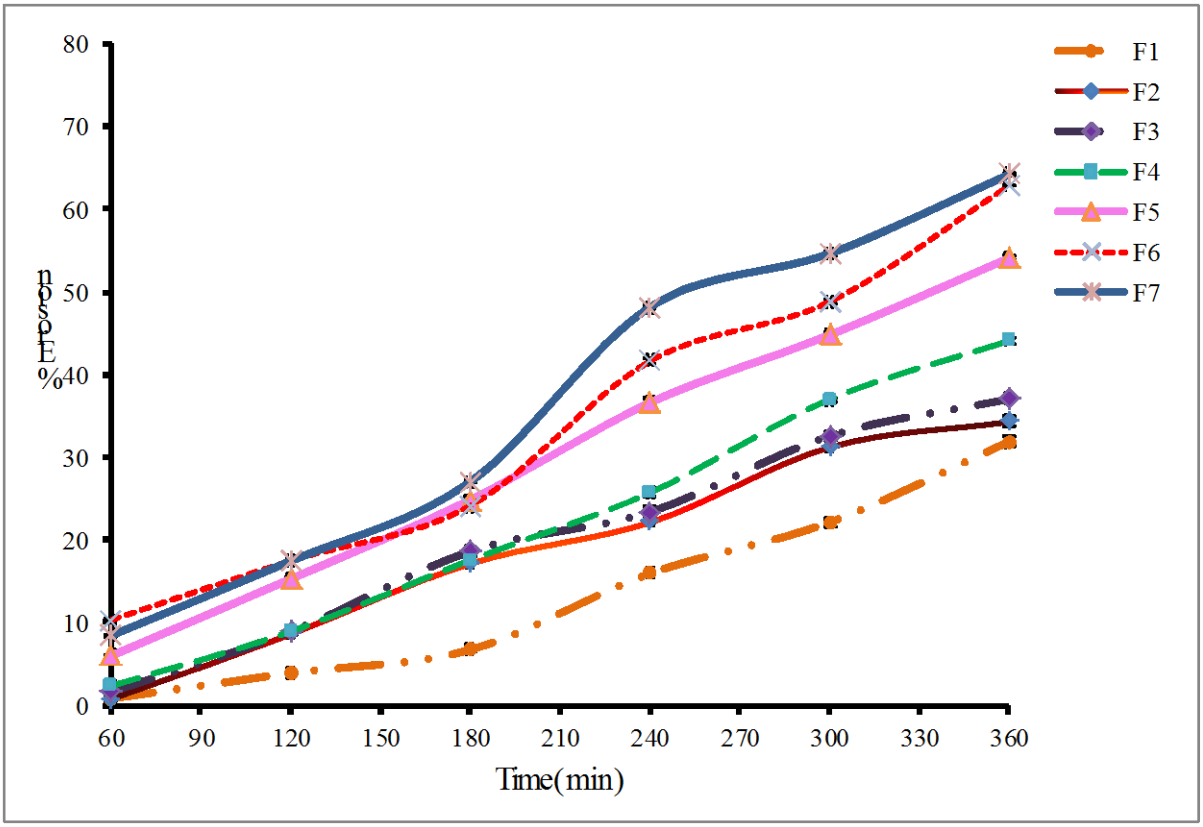

Figure 5. Comparison of erosion of matrices F1 to F7.

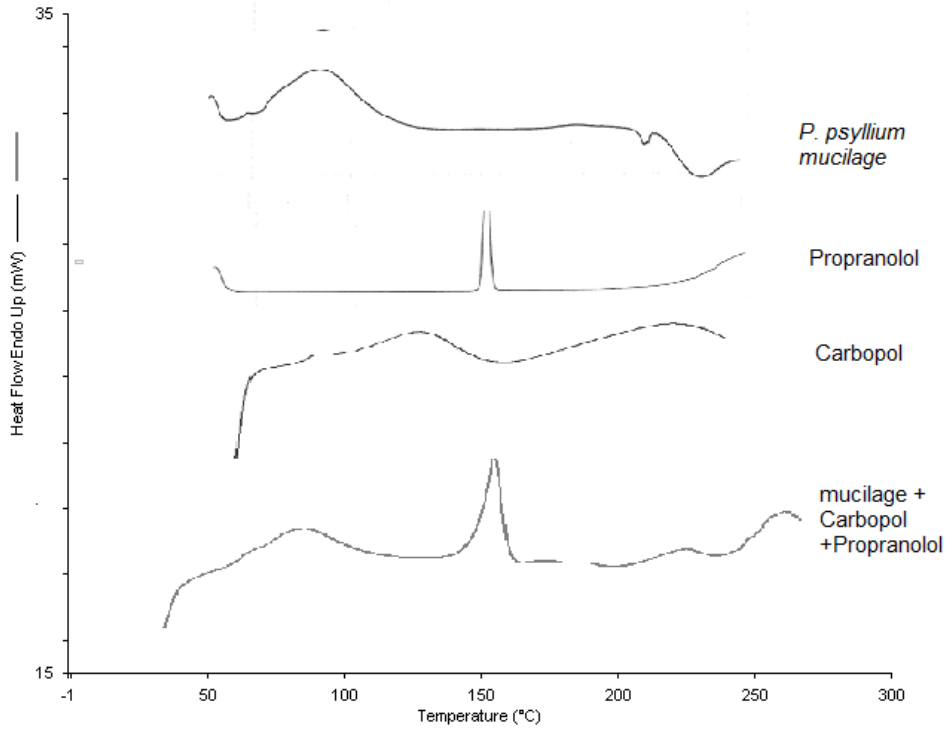

Figure 6. DSC thermograms of *P. psyllium* mucilage, carbopol, propranolol hydrochloride, and matrix tablet.

while erosion decreases [25].

Polymorphic changes of the drug are regarded as one of the significant factors that may affect the dissolution rate, bioavailability and therapeutic effectiveness of a drug. It has also been shown that the crystal structure could influence porosity of tablets, density, mechanism of disintegration and aggregation, besides the plastic and elastic properties of solid dosage forms [19]. Thus, it is important to study polymorphic changes of propranolol hydrochloride in matrix tablets containing *P. psyllium* mucilage as a release retardant excipient. Bartolomei et al. reported that (R, S) propranolol hydrochloride exist in two crystalline forms, designated I and II [19].

In order to investigate any possible interaction between propranolol and the used polymers, DSC and FT-IR tests were conducted as previously discussed. The results of DSC thermograms are shown in Fig. 6. The results of FTIR spectral studies are also shown in Fig. 7.

As previously discussed, polymorphic changes of the drug may influence the dissolution rate and bioavailability. Bartolomei et al. reported that (R, S) propranolol

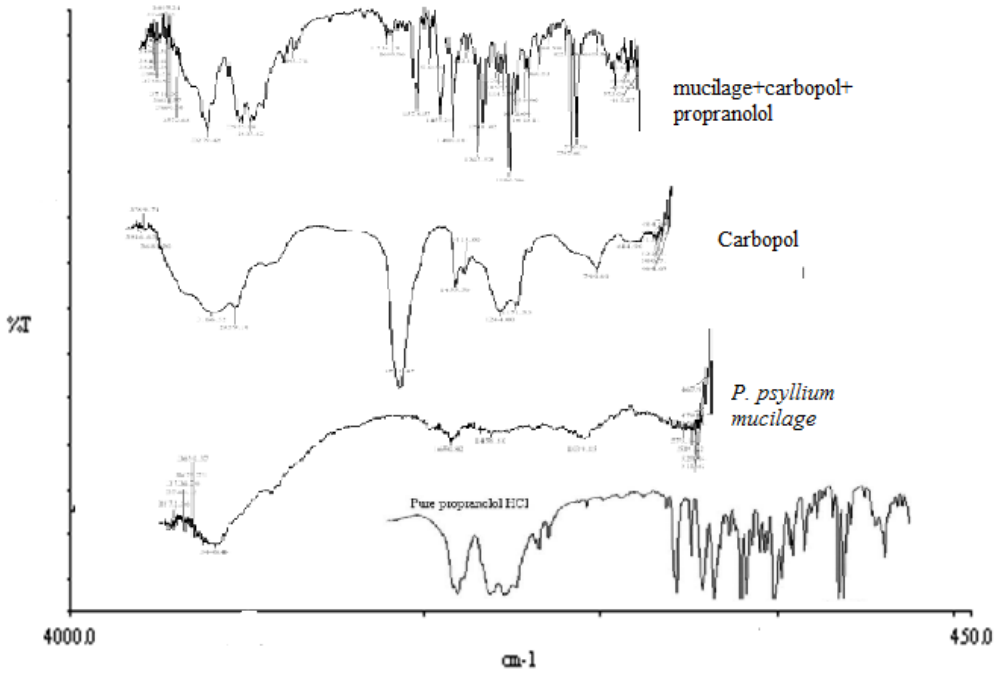

Figure 7. FTIR spectra of *P. psyllium* mucilage, carbopol, propranolol hydrochloride, and matrix tablet.

hydrochloride existed in two crystalline forms, designated I and II. *P. psyllium* mucilage thermogram exhibits a very broad endothermic peak at 93^{o}C which is associated with the loss of water from the carbohydrate polymer and an exothermic peak at 190^{o}C which is associated with mucilage degradation. Carbopol thermogram shows a peak at 140^{o}C associated with polymer's melting point. Propranolol hydrochloride showed an endothermic peak around its melting point (164.2±0.1^{o}C). Both matrix tablets and physical mixtures showed the same peak in this area, which indicates that there is no interaction between drug, Carbopol and *P. psyllium* mucilage during the formulation process [15, 19].

FT-IR spectral confirms the above conclusion. In case of pure *P. psyllium* mucilage, a broad band appeared around 3437 cm^{-1} corresponding to OH stretching, wave number 1742 cm^{-1} depicts the stretching zone of C=O, and 1040.1 cm^{-1} depicts the stretching vibration of C-O group which was characteristics of polysaccharides. The FT-IR spectrum of carbopol, showed OH stretching of carboxylic acid group at 3166 cm^{-1} and C=O

stretching of carboxylic acid group at 1712 cm^{-1} and 2959 cm^{-1} wave number depicts C-H stretching. 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 797 cm^{-1} was due to α-substituted naphthalene [31, 32]. The FT-IR spectrum of the blend of mucilage, carbopol and drug, major characteristic peaks of propranolol hydrochloride were retained. This confirmed no physical or chemical interactions amongst the components of the formulation and compatibility of the drug with the natural carbohydrate polymer.

4. Conclusion

The aim of this study was to evaluate matrix tablets containing *Plantago psyllium* seed mucilage in addition to carbopol as a mucoadhesive agent, and propranolol hydrochloride as a model drug. This mucilage as a natural compound offers some advantages like oral safety, and inexpensiveness. This study has demonstrated the suitability of *Plantago psyllium* seed mucilage in addition to carbopol to act as a controlled release excipient and bioadhesive agent in matrix formulations. An increase in amount of mucilage in comparison with carbopol in different ratios of the mixtures of drug, carbopol and mucilage resulted in an increase in drug release from tablets. The kinetics of release showed that the best fitting was observed in Higuchi model for F1, F2 and F6; Zero-Order model in F3 to F5 formulations and Peppas model in F7. The present study demonstrated that *P. psyllium* mucilage has major potential for use as a bioadhesive and controlled release excipient.

Acknowledgment

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

References

[1] Huang Y, et al. Molecular aspects of muco-and bioadhesion: Tethered structures and site-specific surfaces. *J. Control. Rel. (2000)* 65(1): 63-71.

[2] Duchene D, Touchard F, Peppas N. Pharmaceutical and medical aspects of bioadhesive systems for drug administration. *Drug Dev. Ind. Pharm. (1988)* 14(2-3): 283-318.

[3] Peppas NA, Buri PA. Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues. *J. Control. Rel. (1985)* 2: 257-275.

[4] Lehr CM, et al. An estimate of turnover time of intestinal mucus gel layer in the rat in situ loop. *Int. J. Pharm. (1991)* 70(3): 235-240.

[5] Pather SI, Rathbone MJ, Senel S. Current status and the future of buccal drug delivery systems. *Expert Opin. Drug Del. (2008)* 5(5): 531.

[6] Karimzadeh G, Omidbaigi R. Growth and Seed Characteristics of isabgol (*Plantago ovata* Forsk) as Influenced by some Environmental Factors. *J. Agric. Sci. Technol (2004)* 6: 103-110.

[7] Parsa A. Flore de l'lran. Danesh, Tehran, Iran (1951).

[8] Ansari S, Ali M. Chemical, pharmacological and clinical evaluation of Plantago ovata Forsk. *Hamdard Med. (1996)* 39: 58-63.

[9] Rowe RC. Carbomer, In: *Handbook of Pharmaceutical Excipients*. Pharmaceutical Press: London (2009) 113-115.

[10] Ikinci G, et al. Development and in vitro/in vivo evaluations of bioadhesive buccal tablets for nicotine replacement therapy. *Die Pharmazie (2006)* 61(3): 203-207.

[11] Labot JM, Manzo RH, Allemandi DA. Drug release from carbomer: carbomer sodium salt matrices with potential use as mucoadhesive drug delivery system. *Int.J. Pharm.(2004)* 276(1): 59-66.

[12] Singla AK, Chawla M, Singh A. Potential applications of carbomer in oral mucoadhesive controlled drug delivery system: a review. *Drug Dev. Indus. Pharm.(2000)*. 26(9): 913-924.

[13] Sharma P, Koul A. Mucilage in seeds of Plantago ovata and its wild allies. *J. Ethnopharmacol. (1986)* 17(3): 289-295.

[14] Odeku OA, Fell JT. Effects of the method of preparation on the compression, mechanical, and release properties of khaya gum matrices. *Pharm. Dev. Technol. (2006)* 11(4): 435-441.

[15] Saeedi M, Morteza-Semnani K, Sagheb-Doust M. Evaluation of *Plantago major* L. seed mucilage as a rate controlling matrix for sustained release of propranolol hydrochloride. *Acta Pharm. (2013)* 63(1): 99-114.

[16] Peppas N. Analysis of Fickian and non-Fickian drug release from polymers. *Pharm. Acta Helv. (1984)* 60(4): 110-111.

[17] Akbari J, et al. Development and evaluation of buccoadhesive propranolol hydrochloride tablet formulations: effect of fillers. *Il Farmaco (2004)* 59(2): 155-161.

[18] Sriamornsak P, Thirawong N, Korkerd K. Swelling, erosion and release behavior of alginate-based matrix tablets. *Eur. J. Pharm Biopharm. (2007)* 66(3): 435-450.

[19] Nagai T. Machida Y. Buccal delivery systems using hydrogels. *Adv. Drug Del. Rev. (1993)* 11(1): 179-191.

[20] Ahad HA, et al. Formulation and evaluation of Aloe barbadensis Miller mucilage based controlled release matrix tablets of glimepiride. *Asian J. Chem. (2009)* 21(8): 6271-6276.

[21] Builders P, Okeke U, Egieye A. Evaluation of the controlled release potential of Adansonia digitata mucilage: a super gel forming polymer. *J. Phytomed. Therap. (2007)* 12: 22-30.

[22] Perez-Marcos B, et al. Release of propranolol hydrochloride from matrix tablets containing hydroxypropylmethylcellulose K4M and Carbopol 974. *Int.J. Pharm. (1994)* 111(3): 251-259.

[23] Saeedi M, et al. Evaluation of binding properties of Plantago psyllium seed mucilage. *Acta Pharm.(2010)* 60(3): 339-348.

[24] Choi HG, Kim CK. Development of omeprazole buccal adhesive tablets with stability enhancement in human saliva. *J. Control. Rel.(2000)* 68(3): 397-404.

[25] Alladi KK, et al. Formulation and characterization of clarithromycin controlled released bioadhesive tablets. *J. Chem. Pharm. Res. (2011)* 3(2): 684-690.

[26] Roy S, et al. Polymers in mucoadhesive drug-delivery systems: a brief note. *Designed Monomers Pol. (2009)* 12(6): 483-495.

[27] Maniyar AH, et al. Mucoadhesion: A new polymeric controlled drug delivery. *Int. J. Pharm. Sci. Rev. Res.(2011)* 8(2): 54-60.

[28] Chandira M, Sachin DB, Jayakar B. Formulation and evaluation of mucoadhesive oral tablet of Clarithromycin. *Pharm. Res. (2009)*. 2: 30-42.

[29] Singh K, et al. Evaluation of Mimosa pudica seed mucilage as sustained-release excipient. *AAPS Pharm. Sci. Tech. (2009)* 10(4): 1121-1127.

[30] Bartolomei M, et al. Physico-chemical characterisation of the modifications I and II of (R, S) propranolol hydrochloride: solubility and dissolution studies. *J. Pharm.Biomed. Anal. (1999)* 21(2): 299-309.

[31] Allawadi D, et al. Propranolol hydrochloride loaded nanospheres: Development and Characterization. *Int. J. Pharm. Sci. Res. (2013)* 4(7): 2639-2647.

[32] Vino S, et al. Formulation and characterization of Propranolol HCl loaded casein microparticles. *J. Pharm. Res. (2010)* 3(7): 1634-1636.