ISSN 0976 – 3333

Available Online at www.ijpba.info

International Journal of Pharmaceutical & Biological Archives 2011; 2(4):1282-1290

ORIGINAL RESEARCH ARTICLE

Formulation and *In-vitro* Evaluation of Microcrystalline Chitosan Based Buccoadhesive Bilayered Tablets of Repaglinide

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Received 18 May 2011; Revised 07 Aug 2011; Accepted 11 Aug 2011

ABSTRACT

The buccoadhesive tablets of Repaglinide were prepared with the objective of avoiding the first pass metabolism as well as to evaluate the sustained release component of microcrystalline chitosan and compared with the carbopol. The buccoadhesive tablets were prepared by direct compression method using different composition of microcrystalline chitosan as a primary polymer, and secondary polymer like HPMC K4M, Sodium CMC and Karaya gum. The formulations were evaluated for the hardness, thickness, weight variation, content uniformity, surface pH, swelling index, *in-vitro* bioadhesion, *in-vitro* mucoadhesion retention time, *in-vitro* drug release kinetics. The modified physical balance was used to measure the *in-vitro* bioadhesion strength, using fresh goat buccal mucosa as a model tissue. The best mucoadhesive performance and *in-vitro* drug release profile were exhibited by the tablet containing microcrystalline chitosan and Sodium CMC in the ratio of 1:1. The mechanism and order of drug release from the tablets were non-Fickian diffusion (values of n between 0.5 to 1.0) and first order kinetics, respectively. The formulation containing 1:1 ratio of microcrystalline chitosan and Sodium CMC, showed good bioadhesion strength (33.21±4.48), mucoadhesion time (399±4.76) and controlled release property (95.3% after 8 h) as well as acceptable surface pH (5.9±0.4) to the buccal mucosa. The stability studies of buccoadhesive tablets were evaluated for their physico-chemical parameters such as colour, shape, thickness and drug contents which exhibit no changes, suggesting the satisfactory stability of buccal tablets in human saliva.

Key words: Buccoadhesive bilayered tablets, Microcrystalline chitosan, Buccoadhesive strength, Mucoadhesion time, Repaglinide.

1. INTRODUCTION

Repaglinide is selected as a drug candidate for this study as its bioavailability is low and half-life of 1 hour necessitating frequent administration so as to maintain adequate plasma level of drug. Repaglinide is well absorbed following oral administration and shows low oral bioavailability due to extensive first pass metabolism. First pass metabolism can be avoided by designing proper drug delivery system. This could be achieved by formulating and developing buccal mucoadhesive drug delivery systems which will not only lower the first-pass metabolism but also provide constant drug plasma level for prolonged duration [1,2].

The transmucosal route utilizes sublingual and buccal mucosa as absorption sites with two different therapeutic goals. In particular, the sublingual route is generally employed for the delivery of drugs characterized by a high permeability across the mucosa and used in the treatment of acute disorders, whereas the buccal route is generally used in the treatment of chronic disorders when a prolonged release of the active substance is required.

There are many drug substances have been administered by the buccal route which include peptides like TRH (thyrotropin-releasing hormone) (Li et al., 1997b), calcitonin (Heiber et al., 1994), buserelin (Hoogstraate et al., 1996a), Oxytocin (Li et al., 1997a), and octreotide (Wolany et al., 1990); steroids such as testosterone and its various esters (Voorspoels et al., 1996); analgesics such as morphine (Hoskin et al., 1989), buprenorphine (Kuhlman et al., 1996); antihypertensives such as nifedipine (Kondo and Sugimoto, 1987); and vasodilators such as nitroglycerin (Dellborg et al., 1991). Buccal drug delivery necessitates the use of mucoadhesive polymers as these dosage forms should ideally

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adhere to the mucosa and withstand salivation, tongue movement, and swallowing for a significant period of time. Examples of mucoadhesive polymers include sodium carboxymethyl cellulose, Carbopol 934, Carbopol 940, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, acacia, microcrystalline chitosan, karaya gum, gelatin etc[3].

The hydrophilic polymer matrix system consists of hydrophilic polymer, drug, and other excipients distributed throughout the matrix. HPMC (hydroxy propyl methyl cellulose), sodium carboxy methyl cellulose and carbopol are hydrophilic, possess water swellable property and also show the bioadhesive property. Chitosan is a mucoadhesive agent due to either secondary chemical bonds such as hydrogen bonds or ionic interactions between the positively charged amino groups of chitosan and the negatively charged sialic acid residues of mucus glycoproteins or mucins. So these polymers are selected because of their ease of manufacturing, relatively low cost, favourable *in-vivo* performance and versatility in controlling the release of drugs with a wide range of physiochemical properties. Polycarbophil and hydroxypropylmethylcellulose (HPMC) are suitable polymers for the formulation of bioadhesive tablets. These polymers in addition of bioadhesion effects, decrease release rate and change kinetic of drug release from mucoadhesive tablets [4,5].

Chitosan has found a number of applications in several drug delivery systems, by virtue of its high biocompatibility, biodegradability and lack of toxicity associated with gel- and film forming abilities, bioadhesiveness, dissolution and transmucosal penetration enhancer properties [6,7]. The pH sensitivity, coupled with the reactivity of the primary amine groups, make chitosan a unique polymer for oral drug delivery applications [8]. The buccal bilayered devices (bilaminated films, palavered tablets) using a mixture of drugs (nifedipine and propranolol hydrochloride) and chitosan, with or without anionic crosslinking polymers (polycarbophil, sodium alginate, gellan gum) has promising potential for use in controlled delivery in the oral cavity[9].

2. MATERIALS AND METHODS

2.1 MATERIALS

Repaglinide was obtained as a gift sample from Sun Pharmaceuticals Pvt. Ltd, Mumbai, India. Hydroxypropylmethylcellulose K4M was obtained from Colorcon Asia Pvt. Ltd, Goa. Sodium carboxy methyl cellulose was obtained from Loba Chemie, Mumbai. Microcrystalline chitosan P652 was obtained from Mahtani Chemicals, Mumbai, India. Karaya gum was obtained from Nutriroma Chemicals, Chennai. All other materials used are analytical grade.

2.2 METHODOLOGY

2.2.1 PREPARATION OF BUCCOADHESIVE BILAYERED TABLETS

Bilayered buccal mucoadhesive tablets were prepared by direct compression method using two steps (Derle *et al.*). Various batches were prepared by varying the ratio and combination of polymers shown in (**Table 1**). The mucoadhesive polymer/ drug mixture was prepared by homogenously mixing the drug and polymers in a polybag for 15 minutes. The mixture (155 mg) was then compressed using a 9 mm diameter die in a single punch tablet machine. The upper punch was raised and the backing layer of ethyl cellulose (45 mg) was placed on the above compact; the two layers were compressed into a mucoadhesive bilayered tablet [10].

2.2.2 EVALUATION OF BUCCOADHESIVE BILAYERED TABLETS

2.2.2.1 EVALUATION OF PHYSICAL PARAMETERS

The prepared tablets were evaluated for their diameter, thickness, hardness, friability, drug content uniformity and weight variation [11-16]. The diameter and thickness were determined by Vernier callipers where as hardness by Monsanto hardness tester in triplicate. Twenty tablets were weighed individually and the average weight was determined. Percentage deviation was calculated and checked for weight variation. Ten tablets from each formulation were taken, crushed and mixed. From the mixture 4 mg of drug equivalent of mixture was extracted thoroughly with 100 ml of methanol. The amount of drug present in each extract was determined using UV spectrophotometer at 242 nm. This procedure was repeated thrice and the average values were recorded. Friability test was performed by using Roche friabilator (**Table 2**). The surface pH [17] of the tablets was determined in order to investigate the possibility of any side effects in-vivo. As an acidic or alkaline pH may cause irritation to the buccal mucosa, hence attempt is made to keep the surface pH close to the neutral as possible. The buccal mucoadhesive tablets (n=3) were made in contact with 1 ml of distilled water and allowed to swell for 2 hours at room temperature. The pH

was measured by bringing the pH meter electrode in contact with the surface of the tablet and allowing it to equilibrate for 1 min (**Table 3 & Fig 3**).

2.2.2.2 *IN-VITRO* SWELLING STUDIES

The swelling properties and the erosion characteristics of tablets were evaluated by determination of the percentage of hydration. The percent values were calculated according to the following equation: % of Hydration = $[(W_2-W_1)/W_1]$ X 100. Each tablet was weighed (W1) and immersed in a simulated salivary fluid[11] at pH 6.8 for predetermined times (0.5, 1, 2, 4, 8, and 24 hours). After immersion, excess surface water was removed from the tablets using filter paper and weighed (W2). This experiment was performed in triplicate[18-20] (**Table 4**).

2.2.2.3 *IN-VITRO* BIOADHESION STUDIES

A modified balance method (**Fig 2**) was used for determining the *ex-vivo* mucoadhesive strength. Fresh goat buccal mucosa was used as model mucosal membrane. The mucosal membrane was separated by removing underlying fat and loose tissues. The goat buccal mucosa was cut into pieces and washed with phosphate buffer pH 6.8. A piece of buccal mucosa was tied to the glass vial, which was filled with phosphate buffer. The glass vial was tightly fitted into a glass beaker (filled with phosphate buffer pH 6.8, at 37°C ± 1°C) so that it just touched the mucosal surface. The buccal tablet was stuck to the lower side of a rubber stopper with cyanoacrylate adhesive. The two sides of the balance were made equal before the study, by keeping a 5 g weight on the right-hand pan. A weight of 5 g was removed from the right-hand pan, which lowered the pan along with the tablet over the mucosa. The balance was kept in this position for 5 minutes contact time. The water (equivalent to weight) was added slowly with the help of burette to the right-hand pan until the tablet detached from the mucosal surface. Then the equivalent to weight of water was calculated by using its density which gave detachment force as well as mucoadhesive strength of the buccal tablet in grams [21-23] (**Table 3 & Fig 4**).

Force of adhesion (N) = (Bioadhesive strength/1000) X 9.81

2.2.2.4 *IN-VITRO* MUCCOADHESION/ RETENTION TIME DETERMINATION

The *in-vitro* retention time is one of the important physical parameter of buccal mucoadhesive tablet. The mucoadhesion time was performed (n = 3) after application of the buccal tablet on freshly cut goat buccal mucosa. The fresh goat buccal mucosa was tied on the glass slide, and a mucoadhesive core side of each tablet was wetted with 1 drop of phosphate buffer pH 6.8 and pasted to the goat buccal mucosa by applying a light force with a fingertip for 30 seconds. The glass slide was then put in the beaker, which was filled with 200 mL of the phosphate buffer pH 6.8, and was kept at 37ºC ± 1ºC. After 2 minutes, a 50 rpm stirring rate was applied to simulate the buccal cavity environment, and tablet adhesion was monitored for 12 hours. The time for the tablet to detach from the goat buccal mucosa was recorded as the mucoadhesion time[24-25](**Table 3 & Fig 5**).

2.2.2.5 *IN-VITRO* RELEASE STUDY

USP type II rotating paddle method was used to study the drug release from the bi-layer tablet (**Fig 1**). The dissolution medium consisted of 900 ml of phosphate buffer pH 6.8. The release study was performed at 37 ± 0.5°C, with a rotation speed of 50 rpm. The backing layer of the buccal tablet was attached to the glass slide with cyanoacrylate adhesive. The glass slide was placed at the bottom of the dissolution vessel. 10 ml samples were withdrawn at predetermined time intervals (1 hour) and replaced with fresh medium. The samples were filtered through Whatman filter paper no.42 and analyzed after appropriate dilution by UV Double beam spectrophotometer at 282 nm. The percentage drug release was calculated using PCP disso software [16, 26-29](**Table 5**).

2.2.2.6 STABILITY STUDIES

Stability studies of buccal tablets were performed for optimized formulation (F4) using normal human saliva. The saliva was collected from humans (age 23-34 years) and filtered through Whatman (0.2 µm) filter paper. Buccal tablets were placed in separate Petri dishes containing 5 ml of human saliva and placed in a temperature-controlled oven (Biocraft Scientific, Agra, UP) at 37 ± 0.2°C for 6 hours. At regular time intervals (0, 1, 2, 4 and 6 h), the buccal tablets were taken out and examined for changes in its appearance, such as colour and shape, and its drug (repaglinide) content[30].

The selected tablets of repaglinide (F4) were sealed in aluminium foil packaging coated inside with polyethylene and were stored in humidity chamber at accelerated (40 ± 2°C/ 75 ± 5% RH) and ambient (25 ± 2°C/ 60 ± 5% RH) conditions for 60 days. Samples were withdrawn at 0, 15, 30 and 60 days periods and were analyzed for active drug content, hardness, friability, bioadhesive

strength, adhesion time, weight gain/ loss and in- vitro dissolution[30-31].

Table-I: ***Composition of buccal mucoadhesive tablets.***

Formulation Code	Drug (mg)	HPMC K4M (mg)	Sod. CMC(mg)	Karaya Gum(mg)	Microcrystalline Chitosan(mg)
F1	4	60	-	-	60
F2	4	40	-	-	80
F3	4	80	-	-	40
F4	4	-	60	-	60
F5	4	-	40	-	80
F6	4	-	80	-	40
F7	4	-	-	60	60
F8	4	-	-	40	80
F9	4	-	-	80	40

Table 2: Physical parameters of buccoadhesive tablets.

Formulation Code	Weight Uniformity (mg) (n=20)	Thickness (mm) (n=10)	Hardness (Kg/cm^2) (n=3)	% Friability (n=3)	% Drug Content (n=3)
F1	201 ± 1.7	3.6 ± 0.1	6.54 ± 0.65	0.55 ± 0.05	97.84 ± 0.6
F2	198 ± 1.9	3.7 ± 0.4	6.70 ± 0.24	0.54 ± 0.08	102.7 ± 0.5
F3	197 ± 1.4	3.8 ± 0.3	6.35 ± 0.32	0.52 ± 0.06	98.8 ± 0.3
F4	200 ± 0.6	3.6 ± 0.2	7.32 ± 0.30	0.32 ± 0.04	100.3 ± 0.2
F5	199 ± 1.2	3.6 ± 0.1	7.50 ± 0.22	0.52 ± 0.08	99.6 ± 0.9
F6	201 ± 0.2	3.6 ± 0.3	6.80 ± 0.58	0.45 ± 0.06	100.5 ± 0.3
F7	199 ± 1.2	3.6 ± 0.4	5.25 ± 0.74	0.49 ± 0.03	97.72 ± 0.4
F8	198 ± 1.4	3.7 ± 0.2	5.60 ± 0.56	0.45 ± 0.06	99.12 ± 0.9
F9	197 ± 1.3	3.8 ± 0.1	5.20 ± 0.24	0.36 ± 0.03	97.56 ± 0.6

Mean ± SD (n)

Table 3: Surface pH, bioadhesive strength, adhesion force and mucoadhesion time of buccoadhesive tablets

Formulation Code	Surface pH*	Bioadhesive Strength (gm)*	Adhesion Force (N)*	Mucoadhesion Time (min)*
F1	6.8 ± 1.3	27.52 ± 3.65	0.269	409 ± 7.56
F2	6.6 ± 1.2	29.81 ± 8.59	0.291	412 ± 5.64
F3	6.7 ± 1.5	30.29 ± 6.97	0.296	415 ± 8.81
F4	5.9 ± 0.4	33.21 ± 4.48	0.324	399 ± 4.76
F5	5.8 ± 0.6	32.78 ± 5.92	0.320	397 ± 8.53
F6	5.7 ± 0.7	31.69 ± 5.84	0.310	394 ± 6.34
F7	5.9 ± 0.9	23.54 ± 6.63	0.230	368 ± 7.56
F8	6.3 ± 1.1	22.94 ± 7.75	0.224	349 ± 5.42
F9	5.9 ± 1.5	21.29 ± 5.58	0.208	352 ± 6.34

Mean ± SD (n=3)

Table 4: Percentage swelling index of different formulations

Time(hrs)	% Swelling Index								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	73.28	81.16	64.93	78.42	61.17	96.27	62.26	69.25	78.24
2	92.19	105.48	99.17	172.25	117.19	109.25	128.57	112.38	96.25
4	128.78	121.82	142.95	199.17	178.39	186.75	146.85	164.59	123.54
6	201.7	175.54	208.49	223.27	198.13	209.48	187.94	143.45	174.24

Table 5: Release kinetics of buccoadhesive tablets.

Formulation Code	Zero Order (R^2)	First Order (R^2)	Higuchi (R^2)	Korsmeyer-Peppas	
				(n)	(R^2)
F1	0.811	0.986	0.966	0.56	0.539
F2	0.896	0.964	0.956	0.57	0.547
F3	0.895	0.990	0.989	0.59	0.559
F4	0.880	0.996	0.939	0.75	0.539
F5	0.873	0.993	0.984	0.67	0.567
F6	0.896	0.992	0.987	0.57	0.478
F7	0.793	0.987	0.963	0.67	0.462
F8	0.725	0.962	0.930	0.64	0.485
F9	0.759	0.958	0.942	0.59	0.495

Fig 1: Schematic representation of in-vitro dissolution apparatus

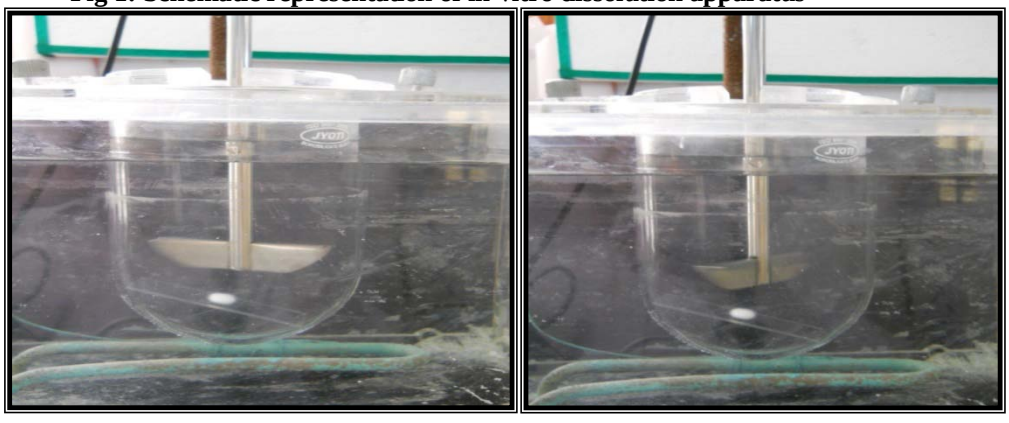


Fig 2: Schematic representation of modified physical balance

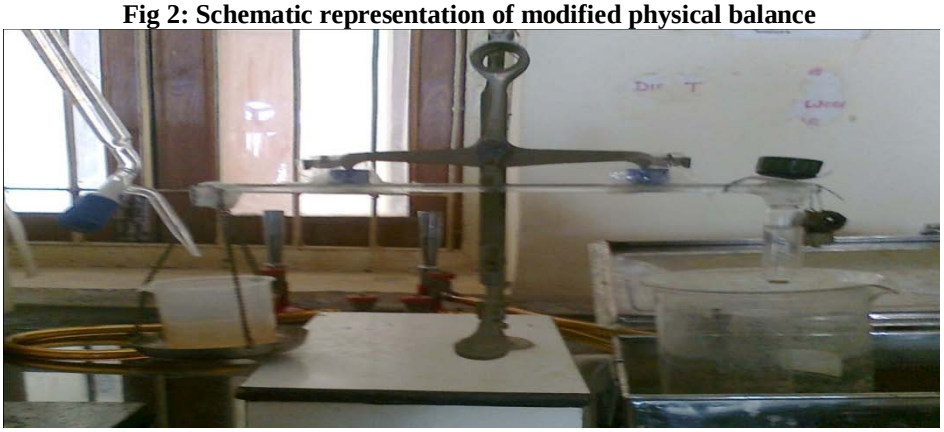


Fig 3: Surface pH of different formulations

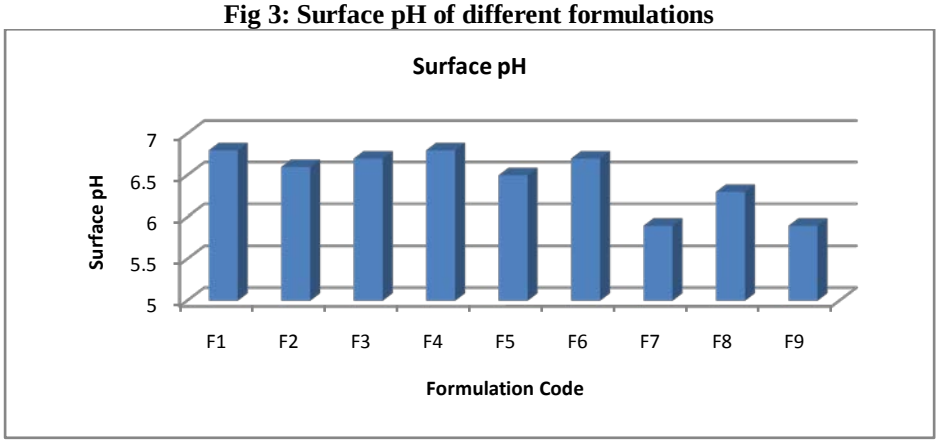


Fig 4: Bioadhesive strength of different formulations

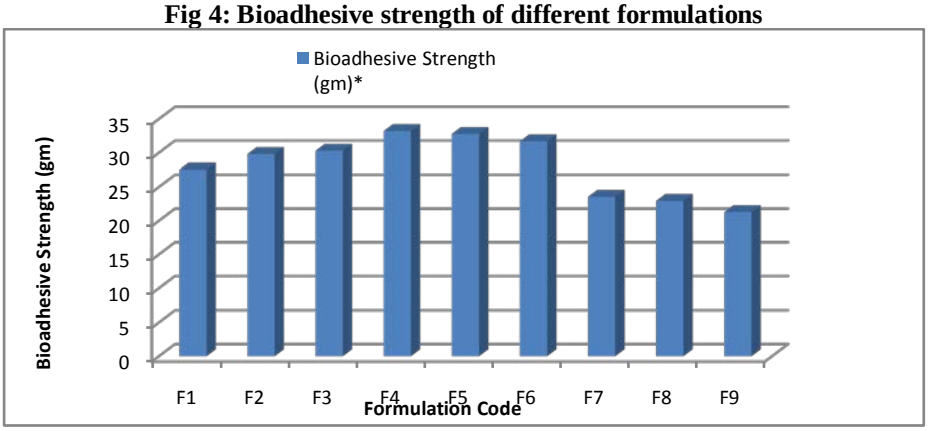
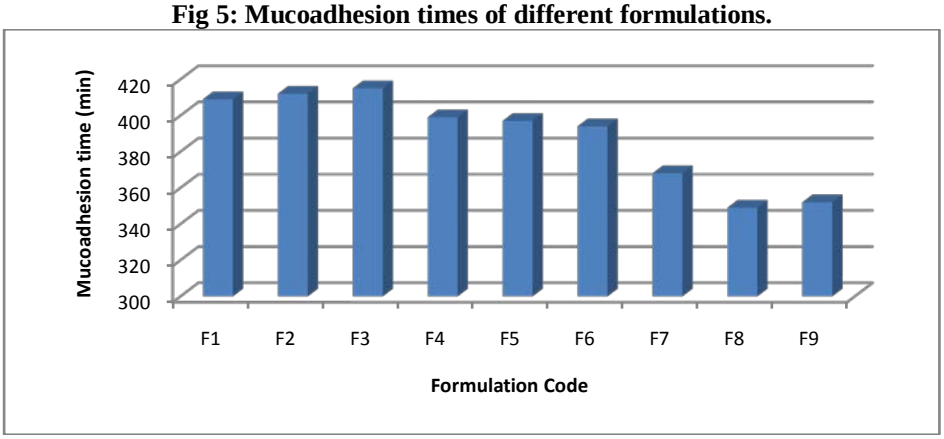


Fig 5: Mucoadhesion times of different formulations.



3. RESULTS AND DISCUSSION

The variation in weight was found in the range of ± 5% complying with Indian Pharmacopoeial specification. All formulations showed weight throughout in the range of 197 ± 1.3 to 201 ± 1.7 mg. The prepared buccoadhesive tablets showed uniform thickness throughout, in the range of 3.6±0.1 to 3.8±0.1 mm. The drug contents in the

buccoadhesive tablets were also within the limit of 97.56 ± 0.6 to 102.7 ± 0.5% which is complying with Pharmacopoeial specification. The loss in total weight of the tablet due to friability was within the limits, ranging from 0.32 ± 0.04 to 0.55 ± 0.05% which is within the limits of convention oral tablets reported in Indian Pharmacopoeia (1996). Buccoadhesive tablets showed hardness in the range of 5.20±0.24 to 7.50±0.22 Kg/cm^3 and it depended on secondary polymers concentration like HPMC, Sod.CMC & Karaya gum. The hardness of the tablets containing Karaya gum was much lower, ranging from 5.20 ± 0.24 to 5.80 ± 0.30 Kg/cm^3 where as the tablets containing Sodium CMC and Microcrystalline chitosan were much high, ranging from 7.50 ± 0.22 to 6.80 ± 0.58 Kg/cm^3. The differences in the tablets hardness are reported not to affect the release of drug from hydrophilic matrices. Because the drug is released by diffusion through the gel layer and/ or erosion of this layer and was therefore independent of the dry state of the tablet [30].

Tablets of all the formulations had shown a surface pH values in the range of 5.7 ± 0.7 to 6.8 ± 1.3 that indicates no risk of mucosal damage or irritation. Tablets of formulation F4, F5 & F6 had shown lower surface pH which is due to presence of carboxylic acid in Sod.CMC. These observations reflect that higher conc. of Sod.CMC cannot be incorporated in the designing of buccoadhesive tablets.

The swelling index test was performed according to the method reported by Nakhat *et al*. The swelling index increased as the weight gain by the tablets increased proportionally with rate of hydration. The swelling indices of the tablets with HPMC and Sod.CMC (F1-F3 & F4-F6) increased with increasing amounts of Microcrystalline chitosan, respectively. Due to water absorbing capacity and molecular weight, and thus hydration increases with an increasing the concentration of HPMC, in buccal tablets [32]; and due to hydrophilic nature of HPMC and Sodium CMC, it's swell rapidly when contact to aqueous environment. Maximum swelling was seen with the formulation F4 containing Sod.CMC and Microcrystalline chitosan. Since, Sodium CMC and deacetylated chitosan have higher rate of hydration, absorbed water rapidly. The swelling indices of the tablets containing HPMC (F1 to F3) increased with increasing amounts of HPMC due to hydrophilic nature.

The bioadhesion characteristics were found to be affected by the nature and proportions of the bioadhesive polymers used. The highest adhesion force i.e. highest strength of mucoadhesive bond was observed with the formulations F1-F3 containing Microcrystalline chitosan & HPMC, and F4-F6 formulations containing Microcrystalline chitosan & Sod.CMC. The reason for such findings might be due to HPMC at salivary pH leads to improved attachment of the device to mucosal surface and for formulations F4-F6 is that chitosan is cationic polymer and Sod.CMC is anionic polymer, thus result in formation of ionic complex which further adhere with mucin as well as chitosan covalently bind with the mucin of buccal mucosa. Adhesion force decreased as another polymer is mixed with MCCh. Tablets of formulation F7-F9 containing Karaya gum showed least adhesion force than tablet of all other formulations, which might be due to low viscosity of the Karaya gum. These observations indicate that the bioadhesive strength had higher values of formulations containing MCCh and Sod.CMC (F4>F5>F6) as well as formulations containing MCCh and HPMC (F3>F2>F1). HPMC formed the hydrogen bond due to their hydrophilic properties, resulted in increased of mucoadhesion. This high bioadhesion strength is due to the formation of secondary bioadhesion bonds with mucin and interpenetration of the polymer chains in the interfacial region, while other having low bioadhesion is because they only undergo to superficial bioadhesion.

In- vitro mucoadhesion time for bilayered tablets F1 to F9 varied from 5 to more than 7 hours. The optimized bilayered tablets (F4) showed 6 hrs 39 min of mucoadhesion time. The difference could be attributed due to the combination of various amounts of the polymers, which affected the mucoadhesion. Moreover, sodium CMC (F4 to F6), due to erosion and faster fragmentation, resulted in lower mucoadhesion time, but much lower mucoadhesion time was found in formulations containing Karaya gum (F7 to F9) because of rapid water uptake by karaya gum which leads to dispersed as colloidal solution. In fact, with bilayered tablets containing a higher proportion of MCCh and HPMC (F1 to F3), mucoadhesion time was found to be increased. Due to hydrophilic nature of HPMC, they probably formed the hydrogen bond with mucus membrane as well as HPMC having gel forming property and cross-linking, when attached, they don't detached from the mucus membrane, easily. Since microcrystalline chitosan is cationic in

nature and mucin of mucus membrane anionic nature, they formed the covalent bond; as a result their mucoadhesion time was increased.

The release rate of Repaglinide decreased with increasing concentration of HPMC K4M (F1 to F3). These finding are in compliance with the ability of HPMC to form complex matrix network which leads to delay in release of drug from the device. Another finding is that the HPMC retard the drug release, its increases in totuosity as a result of swelling in contact with aqueous fluid, increases the path length available for the drug to diffuse out from the swollen matrix. The rate of drug release increased with increasing the amount of hydrophilic polymer. Formulations F4 to F6 showed relatively high rate of release of Repaglinide which is due to rapid swelling and erosion of Sodium CMC. Further, the increase in rate of drug release could be explained by the ability of the hydrophilic polymers to absorb water, thereby promoting the dissolution, and hence the release of drug. Moreover, the hydrophilic polymers have tendency to leach out and therefore, they created more pores and channels for the drug to diffuse out from the device. The formulations containing karaya gum (F7 to F9) showed relatively high rate of drug release because of its property to swell rapidly and diffused into the fragments which leads to loss of its integrity.

In-vitro drug release data of all the buccal tablet formulation was subjected to goodness of fit test by linear regression analysis according to zero order equation, Higuchi's and Korsmeyer-Peppas models to ascertain the mechanism of drug release. Data of the *in-vitro* release was fit into different equations and kinetic models to explain the release kinetics of buccal tablets.

As observed from the (Table 5), the regression correlation coefficient (r^2) values of first order drug release was more than (r^2) values of zero order drug release in all formulations. So drug release from tablets followed first order drug release kinetics. Drug release mechanisms of the repaglinide were evaluated by using the Koresmeyer-Peppas model. In this model, the value of 'n' identifies the release mechanism of drug.

If n < 0.45 corresponds to a Fickians diffusion mechanism, n is 0.45- 0.89 to non-Fickians transport and n=0.89 to case II (relaxational) transport and n > 0.89 to super case II transport. From the Table-IV, the calculated exponents (n) values indicated that all the formulations are within the limits of non-Fickian diffusion mechanism.

Buccoadhesive bilayered tablets did not exhibit change in colour and shape, suggesting the satisfactory stability of the drug and buccal device in human saliva. Physical properties of bilayered tablets like thickness and diameter increased slightly owing to swelling of system in human saliva. Whereas, tablets did not collapsed in the human saliva until the end of the study, confirming the sufficient strength of bilayered tablets. The result obtained, suggested that the tablets were stable at room temperature and there was no significant changes in hardness, friability, bioadhesive strength, adhesion time, % drug content, weight gain/loss and % drug release. There was no significant reduction in the active drug content over a period of 60 days. Results of formulation F13 indicated that it was stable at 40 ± 2ºC & 75 ± 5% Relative humidity as there were no statistically significant differences observed for dissolution and bioadhesion data.

CONCLUSION

In this study we successfully developed optimized buccoadhesive tablets which exhibit a unique combination of bioadhesion and drug release pattern. So, formulation F4 (MCCh and Sod. CMC in the ratio of 1:1) was nominated as best formulation. On the basis of above findings we can conclude that the mucoadhesive tablets of Repaglinide may be the best dosage form for buccal drug delivery system.

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