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Mucoadhesive buccal tablets of rabeprazole sodium formulation and *in-vitro* evaluation

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Abstract

The present investigation describes the development of mucoadhesive tablets of Rabeprazole sodium, proton pump inhibitor, designed to prolong the gastric residence time after oral administration. Tablets were formulated using four mucoadhesive polymers namely Carbopol 934P, HPMC K4M, Guar gum and Chitosan. The formulated tablets were characterized for various quality control parameters namely, weight variation, thickness, hardness, content uniformity, swelling index, mucoadhesive force and in-vitro drug release. The swelling index of the formulations maintained for 6h were in the range of 44.3-50.4, 42.8-48.9, 38.3-45.7% for F1-F3, F4-F6, F7-F9 formulations. The in-vitro drug release studies were performed for F1 to F9 formulations and it had revealed that the formulations release was found to be in between 77.5-97.6%. F8 formulation was optimized due highest mucoadhesive strength; surface pH and drug release.

Keywords: Rabeprazole Sodium, Mucoadhesive, Buccal Tablets, Proton Pump Inhibitors, quality control parameters.

INTRODUCTION

Proton-pump inhibitors [1] remains the important class of drugs for treating patients suffering with acid related diseases, also used to treat gastroesophageal reflux disease (GERD), duodenal ulcer, and gastric ulcer. They are more safe and effective, accumulate and activate in an acid environment at the secretory canalicular surface of the parietal cell [2]. Proton-pump inhibitors are among the most widely prescribed drugs around the world, and in the United States, they holds the third position with the sales turnover of sales of $13.9 billion annually[3].

Rabeprazole sodium is used to treat gastric ulcer disease which is a proton pump inhibitor and it is prepared as mucoadhesive tablet. Many preparations are used for treatment of gastric ulcers like proton pump inhibitors, antacids etc.[4]. The drug is selected because it exhibits potent and long lasting inhibition of gastric acid secretion and it is formulated as mucoadhesive delivery system because its oral absorption is very low by oral route administration (<50%) due to hepatic metabolism. Thus various oral dosage forms of Rabeprazole such as enteric-coated granules, enteric-coated tablet and inclusion complex with cyclodextrin have been developed to improve its bioavailability [5]. Formulating into novel dosage form such as mucoadhesive systems, Rabeprazole sodium can sustain the release for longer period than

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the immediate release dosage forms and polymers used in this research work control over the rate and amount of drug release by showing the therapeutic efficacy of bioadhesive drug delivery system [6]. In this work Rabeprazole mucoadhesive tablet is aimed d to overcome the problem of frequent dosing due to its shorter half-life. Increased bioavailability and modified release of the drug leads to significant reduction in the dose and hence dose related side effects[7] .In this research work, an attempt was made to formulate mucoadhesive buccal tablet by Rabeprazole using different mixture of polymers in order to avoid first pass metabolism, degradation in the stomach and for prolonged effect.

Materials and Methods

Materials

The drug Rabeprazole sodium was the gift sample given by HETERO drugs Pvt. Ltd., Hyderabad; polymers were gift samples from Nishka Laboratories, Hyderabad.

Method of preparation

Mucoadhesive tablets of Rabeprazole sodium was prepared by direct compression method[8-9]. Drug, polymers and excipients were initially passed through sieve 40. Then the required quantities of drug, polymers and excipients were blended for 15mins. Then 1% magnesium stearate was added to the blend and again mixed for another 5mins. The produced blend was compressed into tablets using 8 stations Cadmach rotary compression machine with 8mm punches.

Table 1: Composition of various Mucoadhesive tablets of Rabeprazole

Ingredients(mg/tab)	Formulation Code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Rabeprazole sodium	10	10	10	10	10	10	10	10	10
Carbopol934P	40	50	60	40	50	60	40	50	60
Guar gum	20	30	40	-	-	-	-	-	-
Chitosan	-	-	-	20	30	40	-	-	-
HPMCK4M	-	-	-	-	-	-	20	30	40
PEG4000	60	60	60	60	60	60	60	60	60
Microcrystalline cellulose	20	20	20	20	20	20	20	20	20
Lactose Monohydrate	92.75	72.5	52.5	92.75	72.5	52.5	92.75	72.5	52.5
Magnesium stearate	5	5	5	5	5	5	5	5	5
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total Weight (mg)	250	250	250	250	250	250	250	250	250

Evaluation of mucoadhesive buccal tablets

Mucoadhesive buccal tablets of Rabeprazole sodium were characterized for various quality control parameters [10].

Weight variation and thickness

10 tablets from each formulation were weighed and average weight of ten tablets and standard deviation were calculated. Thick ness of each formulation was measured using vernier caliper[11].

Content uniformity: Tablets were taken and crushed, from this 20mg of mixture containing drug was taken and extracted in 100ml of methanol, then extract was taken to find out the amount of drug using UV spectrophotometer at 284 nm.

Surface pH

This test was done to determine whether surface is alkaline or acidic pH which may cause irritation to the buccal mucosa and to keep surface pH as close to neutral as possible [12]. A combined glass electrode was used for this purpose. Tablet was allowed to swell by keeping it in contact

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with 1 ml of distilled water (pH 6.5 ± 0.05) for 2 h at room temperature. The pH was measured by bringing the electrode in contact with the surface of the tablet and allowing it to equilibrate for 1 min.

Bioadhesive strength

The tablet is placed in balance and kept in this position for 5 min contact time. The water (equivalent to weight) was added slowly with an infusion set (100 drops/ min) to the right-hand pan until the tablet detached from the mucosal surface [13]. This detachment force gave the mucoadhesive strength of the buccal tablet in grams.

In vitro dissolution studies

The USP XXIII rotating paddle method was used to study the drug release from the tablets. The phosphate buffer pH 6.8 was taken as dissolution medium[14]. The release was performed at 37°C ± 0.5°C, with a rotation speed of 50 rpm. The backing layer of buccal tablet was attached to the glass disk with instant adhesive (Cyanoacrylate adhesive). The disk was allocated to the bottom of the dissolution vessel. 5 ml sample were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered and analyzed after appropriate dilution by UV spectrophotometry at 284 nm.

Results and Discussion

Weight variation and thickness

The minimum and maximum average weight of the tablet was found to be 248.2±1.3 to 251.3±1.6mg and thickness of the tablet 2.92±0.1 to 3.04±0.2 which was showed in Table 2. Thickness of the tablet will affect side flow of the drug from the formulation, so it should be as small as possible.

Drug content

The drug content from all the formulations was found to be 97.46±0.4 to 99.58±0.14 and showed in Table 2. The results were within the limit of USP standards.

Surface pH

The surface pH from all the formulations was
found to be 5.8±0.1 to 6.1±0.1, showed in Table 3.The results reveal that all the formulations provide an acceptable pH in the range of 5.5 to 7.0. Hence, they may not produce any local irritation to the mucosal.

Bio-adhesive strength

The bioadhesive strength of the tablets depends on the concentration of polymer used in the preparation. The tablets with carbopol and guargum have bioadhesive strength in between the 20.4±0.4g to 24.1±0.56g. The tablets with the carbopol and chitosan have bioadhesive strength 21.2±0.42g to 26.5±0.51g. The tablets with carbopol and HPMCK4M have bioadhesive strength in between the 23.5±0.63 g to 31.44 g. The tablets with the HPC have bioadhesive strength in between the 27.37g to 30.7±0.63g. The increase in concentration of polymer increases the bioadhesive strength showed in Table 3.

***In-vitro* drug dissolution studies**

In-vitro release for Rabeprazole sodium mucoadhesive tablets were obtained for formulation F1 to F9. The cumulative drug release of F1-F3,F4-F6 and F7-F9 were found to be 88.2%, 89.5%, 84.5% in 6,7,8hrs, 93.5%, 96.2%, 77.5% in 5, 6 hours and 92.5%,97.6% ,77.5% in 7, 8h respectively showed in Figure 1 & 2. It was concluded that increasing polymer concentration like Carbapol 934P, Guargum, and HPMC K4M release the drug slower for a longer period.

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Table 2. Evaluation of Rabeprazole mucoadhesive tablets

Code	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Weight variation	Drug content (%)
F1	5.0±0.3	2.94±0.1	0.68±0.04	249.2±1.6	98.21±0.37
F2	4.7±0.2	2.92±0.1	0.73±0.01	250.5±1.3	99.47±0.17
F3	4.3±0.3	2.94±0.2	0.73±0.04	249.1±1.4	97.46±0.4
F4	4.7±0.5	2.96±0.3	0.6±0.02	251.2±1.3	98.63±0.32
F5	4.8±0.1	2.96±0.1	0.57±0.005	250.8±1.6	98.31±0.16
F6	5.2±0.1	2.96±0.4	0.52±0.06	249.3±1.2	97.51±0.18
F7	5.3±0.4	3.02±0.4	0.5±0.01	248.2±1.3	98.97±0.11
F8	6.1±0.4	3.04±0.2	0.47±0.02	250±1.5	99.58±0.14
F9	6.2±0.1	3.04±0.1	0.44±0.03	251.3±1.6	98.49±0.31

Table 3. Bioadhesive strength and surface pH of Rabeprazole mucoadhesive tablets

Formulation code	Bioadhesive strength(gm)	Surface pH
F1	20.4±0.4	6.1±0.1
F2	23.2±0.42	5.98±0.2
F3	24.1±0.56	6.1±0.1
F4	21.2±0.42	6.0±0.1
F5	24.7±0.52	5.8±0.1
F6	26.5±0.51	6.0±0.1
F7	23.5±0.63	5.84±0.2
F8	27.6±0.77	5.92±0.2
F9	30.7±0.63	5.9±0.4

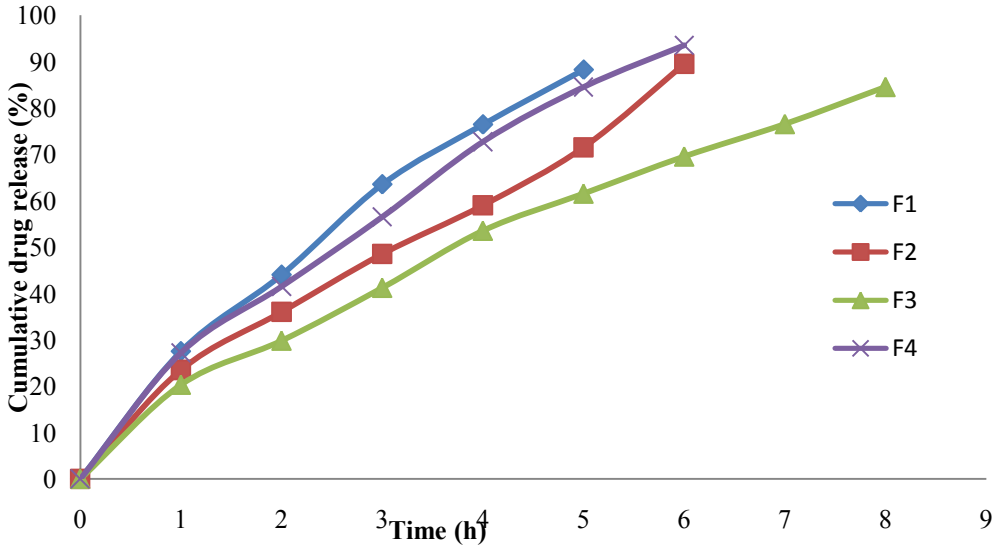

Figure 1. (F1-F4) : *In-Vitro* drug release profile of Rabeprazole mucoadhesive tablets

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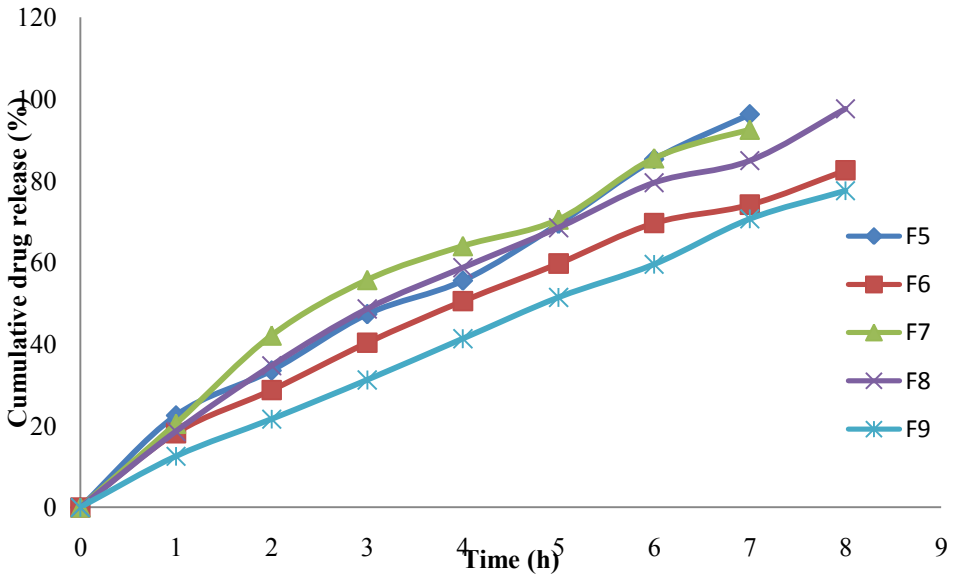

Figure 2. (F5-F9) : *In-Vitro* drug release profile of Rabeprazole mucoadhesive tablets

Conclusion

Muchoadhesive tablets of Rabeprazole Solidum tablets were successfully formulated and characterized for the various quality control parameters. From the study results, it was concluded that mucoadhesive tablets of Raberprazole can release the drug over a prolonged period of time. Formulation F8 considered as the optimized formulation based on mucoadhesve strength, surface pH, Swelling index and *In-vitro* drug release studies.

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