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Research Article

Design and evaluation of buccoadhesive bi-layer tablet of atenolol

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ABSTRACT

The aim of the study was to prepare and characterize buccoadhesive tablets of atenolol using different mucoadhesive polymers such as carbopol 971P, sodium alginate and HPMC K100M incombination. The bilayered buccoadhesive tablets were prepared by direct compression technology. The prepared tablets were evaluated for physicochemical parameters such as hardness, thickness uniformity, weight variation, surface pH and swelling studies. Also prepared tablets were evaluated for bioadhesive strength and in vitro drug release. *In vitro* bioadhesive strength studies showed that formulations containing combination of carbopol 971P and HPMC K100M were more bioadhesive than sodium alginate. In vitro dissolution studies revealed that all the formulations exhibited non-fickian release kinetics. The optimized formulations F1 and F5 showed 90% release in 8 hr in vitro dissolution studies.

Keywords: Buccal drug delivery; Atenolol; carbopol 971P; sodium alginate.

INTRODUCTION

Oral drug administration has been one of the most suitable and widely accepted by the patients for the delivery of most therapeutically active drugs. Various dosage forms like tablets, capsules and liquid preparations have been administered by oral route. But, due to some unsuitable physiological conditions of the gastro-intestinal tract like relatively poor absorption, presence of various digestive enzymes of the gastro-intestinal lumen and epithelium, poor absorption efflux (i.e. by P-glycoprotein, etc.) and first pass metabolism by hepatic enzymes, the administration of some drugs is affected1. Mucoadhesive formulations have been researched for delivery to the buccal cavity, generally with the addition of permeation enhancers. Also, it may be necessary to hide the taste of drugs or excipients by the incorporation of taste masking agents (Jain 2002, McConville 2005).

Carbopol 971P and sodium alginate are anionic polymers, which have excellent bioadhesive strength but their mucoadhesive properties are just satisfactory when used alone. Therefore, it is needed to combine the anionic polymers with HPMC K100M so that it will increase mucoadhesion period and drug permeation across buccal mucosa (Saini *et al.,* 2005).

Atenolol, a ß-blocker, is prescribed widely in diverse-cardiovascular diseases, e.g. hypertension, angina pectoris, arrhythmias, and myocardial infarction. Administration of conventional tablets of atenolol has been reported to exhibit fluctuations in the plasma drug levels, resulting in manifestation of side effects or reduction in drug concentration at the receptor site. Atenolol have poor membrane permeability in the gastro-intestinal tract due to its hydrophilic nature. Also it is sparingly soluble in water, having low partition coefficient. Hence, large fraction of the drug is excreted in an unchanged form and leads to incomplete absorption (Singh *et al.,* 2006; Marcos *et al.,* 1991; Jacobsen *et al.,* 2001; Patel *et al.,* 2007; Patel *et al.,* 2007). Atenolol is selected as a model drug candidate for administration by buccal route. Because, it's short half-life (6-8 hrs), low molecular weight; low dose (25-50mg) makes it a suitable candidate for administration by buccal route. Previous studies have reported that atenolol can be successfully delivered through various controlled release systems like hydrophilic systems, osmotic pumps and transdermal drug delivery systems (Marcos 1991; Jacobsen 2001; Metia 2008)

MATERIAL AND METHODS

Materials

Atenolol was obtained as a gift sample from CiplaLtd., Mumbai. Carbopol 971P, Ethyl cellulose, hydroxypropylmethylcellulose K100M were obtained from Glenmark pharmaceuticals Ltd. Sodium alginate was obtained from Lobachemicals, Mumbai. All other ingredients used in formulations were of analytical grade.

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Methods

Preparation of buccoadhesive tablets

All the ingredients including drug, polymers and excipients weighed accurately according to their batch size (Patel 2007). All the ingredients except PEG 6000 were mixed in an ascending order and blended for 20 minutes. After uniform mixing of ingredients, PEG 6000 was added and again mixed for 2 min. The prepared blend of each formulation was subjected to flow properties of granules. 100 mg of powder bed was precompressed, on the single station tablet-punching machine (Cadmach Ahemdabad, India) at a pressure of 0.5 ton for 30 seconds to form single layered flat-faced tablets of 8 mm diameter. Then, 50 mg of ethyl cellulose powder was added and final compression was done at apressure of 3.5 tons for 30 seconds to get bilayer tablet. Composition of bilayer tablets is given in table 1.

Physical properties of tablets

It includes hardness, thickness, weight uniformity of tablets in a similar manner as stated for conventional oral tablets.

Swelling studies

Three tablets from each formulation were placed in empty baskets and the total weight of basket with tablet noted (W1). The tablets containing baskets were fixed to a six-station dissolution apparatus. Baskets immersed in a 500 ml dissolution medium (phosphate buffer pH 6.6), at 37 0C and at 50 rpm. At regular interval of one hour, the baskets were detached from the dissolution apparatus and blotted with tissue paper to remove excess surface water. Then the weight of basket containing swollen tablet was taken and reported as (w2). The graph of swelling index Vs time was plotted for each formulation (Patel 2007).

$$\text{Swelling Index (SI)} = \frac{W2-W1}{W1} \times 100$$

Where W1 – Dry weight of weight

W2 – Wet weight of swollen tablet

Content uniformity

Drug content uniformity was determined by dissolving the tablets in ethyl alcohol and filtering with Whattman filter paper (0.45 m). The filtrate was evaporated and the drug residue dissolved in 100 ml phosphate buffer pH 6.8. The 5 ml solution was then diluted with phosphate buffer pH 6.8 up to 20 ml, filtered through Whattman filter paper and analyzed at 225nm using a UV Double beam spectrophotometer (Shimadzu 2501 PC, Japan) (Kemken 1991). The experiments were performed in triplicate and average values reported.

In-vitro mucoadhesion time

Adhesion time of formulations were determined by using rotating cylinder method USP type VI apparatus (Disso Lab India, India) at 37 ± 0.50 C at 100 rpm using phosphate buffer pH 6.8 (Gupta 1992). The goat buccal mucosa was adhered to the cylinder by using cynoacrylate glue. The disk was pressed on the mucosa gently with the finger for 1 minute. The time of disk adhered to mucosa was measured and results are given in Table 2.

Surface pH study

The surface pH of the buccal tablets was determined.

In-vitro drug release

USP type II rotating paddle method was used to study the drug release from the bi-layer tablet. The dissolution medium consisted of 600 ml of phosphate buffer Ph 6.8. The release study was performed at 37 ± 0.50^0C, with a rotation speed of 50 rpm. The backing layer of the buccal tablet was attached to the glass slide with cyanoacrylate adhesive. The disk was placed at the bottom of the dissolution vessel. 5 ml samples were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through 0.2µm Whatman filter paper and analyzed after appropriate dilution by UV Double beam spectrophotometer at 225 nm (Kemken 1991).

RESULT AND DISCUSSION

CP and Na-alginate were selected as the bioadhesive polymers because of their excellent bioadhesive properties (Walle 1978; Chidambaram 1995; Guo 1996). EC has recently been reported to be an excellent backing material, given its low water permeability, hydrophobicity, and moderate flexibility (Peppas 1985), so it was

Table 1: Formulation of buccal adhesive tablet

S. No.	Ingredients Mg/tab	F1	F2	F3	F4	F5
			Adhesive layer			
1	Atenolol	25	25	25	25	25
2	Sodium alginate	32.3	31.4	30.0	28.0	24.7
3	Carbopol 971P	4.7	5.6	7	9	12.3
4	HPMC K100M	28.0	28.0	28.0	28.0	28.0
5	Perlitol	8	8	8	8	8
6	PEG6000	2	2	2	2	2
			Backing layer			
7	Ethyl cellulose	50	50	50	50	50
	Total	150	150	150	150	150

Table 2: Ex-vivo mucoadhesion time of formulation

Formulation	Adhesion time Hours ± SD
F1	8 ± 0.19
F2	10 ± 1.08
F3	9 ± 0.31
F4	7 ± 0.52
F5	11 ± 0.63

Table 3: Evaluation of tablet parameter

Formulation	Weight Variation (mg)	Thickness (mm)	Hardness (Kg/cm2)	% friability	% Drug content
F1	148 ± 0.13	2.60 ± 0.03	4.01 ± 0.16	0.67 ± 0.04	96.73 ± 0.32
F2	149 ± 0.45	2.53 ± 0.31	3.93 ± 0.11	0.92 ± 0.02	99.17 ± 0.09
F3	148 ± 0.61	2.59 ± 0.23	3.81 ± 0.07	0.87 ± 0.05	100.3 ± 0.14
F4	150 ± 0.21	2.50 ± 0.08	3.97 ± 0.14	0.69 ± 0.01	95.98 ± 0.23
F5	152 ± 0.17	2.52 ± 0.16	3.83 ± 0.04	0.59 ± 0.03	98.13 ± 0.14

chosen as an impermeable backing layer. Perlitol and HPMC K100M were used to improve the release of drug from polymer matrices, and the concentration was optimized during the preliminary trial to find the best formulation of bi-layer buccal tablets as shown in Table 1. Tablets were found to be satisfactory when evaluated for weight variation (149 ± 0.32%), thickness (2.54 ± 0.16 mm), hardness (3.91±0.14kg/cm2), friability (0.78± 0.03%), and drug content (98.06 ± 0.18%). The surface pH of all the tablets was within a range of 5-6 as shown in the Table 3, close to neutral pH (Bottenberg 1991; Kemken 1991). Appropriate swelling behavior of a buccal adhesive system is essential for uniform and prolonged release of the drug and effective mucoadhesion (Ilango 1997). The swelling study indicated that the rate of swelling was proportional to the Na-alginate content and inversely proportional to the CP content of the tablets in the initial study up to 1 hour. This finding may have been because of the fast swelling property of Na-alginate compared with CP. The maximum swelling index was found in batch F1 (48±1.23), containing a higher proportion of Na-alginate, and the lowest in F5 (22±0.23). Tablets did not show any appreciable change in their shape and form during the 8 hours they were kept on the 2% agar gel plate (De Vries 1991). This finding is owing to the hydrophilic nature of Na-alginate; it is hydrated easily with less contact time and forms a strong gel that entangles tightly with the mucin molecules. Tablets containing Na-alginate and CP in the ratio of 5:1 (F 2) had the (98.21%) maximum percentage of *in vitro* drug release without disintegration in 12 hours.

CONCLUSION

The mucoadhesive buccal tablets of atenolol can help to bypass extensive hepatic first-pass metabolism and hence improve bioavailability. The buccal bi-layer tablets showed a mucoadhesion time of more than 12 hours.

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