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Formulation and evaluation of mouth dissolving tablets of atenolol

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Abstract

Attempts were made to prepare mouth-dissolving tablets of atenolol by direct compression method with a view to enhance patient compliance. The two super disintegrants used in this study were croscarmelose sodium and sodium starch glycolate. The prepared batches of tablets were evaluated for uniformity of weight, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time and dissolution study. Using the same excipients, the tablets were also prepared, without disintegrants and were evaluated in the similar way. From the results obtained, it can be concluded that the tablet formulation (A4) showed the promising formulation. Also the hardness, friability, disintegration time and dissolution rate of prepared tablets were found to be acceptable according to standard limits.

Keywords: Mouth dissolving tablets, Atenolol, In-vitro evaluation.

Introduction

The tablet is the most widely used dosage form because of its convenience in terms of self- administration, compactness, and ease in manufacturing. For the past one decade, there has been an enhanced demand for more patient- friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually. Since the development cost of a new drug molecule is very high, efforts are now being made by pharmaceutical companies to focus on the development of new drug dosage forms for existing drugs with improved safety and efficacy together with reduced dosing frequency, and the production of more cost- effective dosage forms[1].

However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as " melt in mouth" or " mouth dissolve (MD)" or sometimes " dispersible" tablets. These are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bed- ridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market[2].

Atenolol, a beta-blocker used in the treatment of hypertension and angina pectoris. It is incompletely absorbed from the gastrointestinal tract[3] and has an oral Bioavailability of only 50%, while the remaining is excreted unchanged in feaces. This is because of its poor absorption in lower gastrointestinal tract. It undergoes hepatic first pass metabolism and its elimination half-life is 6 to 7 hours [4]. Atenolol results in poor Bioavailability when administered in the form of conventional tablets because of hepatic first pass metabolism and exhibit fluctuation in the plasma drug level resulting in reduction in drug concentration at receptor site. In the present study, an attempt was made to develop mouth-dissolving tablets of atenolol and to improve its bioavailability.

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Material and methods

Atenolol was a gift from Flamingo Pharmaceuticals, Mumbai. Croscarmelose sodium used was analytical reagent grade procured from Loba Chemie, Mumbai and Sodium Starch Glycolate used was procured from Merck Limited, Mumbai. All other reagents and chemicals used were of analytical grade.

Preparation of mouth dissolving tablets of Atenolol

All the materials were passed through 60 # screens prior to mixing. Atenolol, Croscarmellose sodium, Sodium Starch Glycolate, and Mannitol were mixed using a glass mortar and pestle. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using concave face round tooling on a 16-station rotary tablet machine. The compositions of the batches are shown in Table 1.

Evaluation of atenolol mouth dissolving tablets

Weight variation test[5]

Weight variation test was done by weighing 20 tablets individually, by using Sartorious balance (Model CP- 224 S). Calculating the average weight and comparing the individual tablet weight to the average weight.

Tablet thickness[5]

The thickness was measured by placing tablet between two arms of the Varnier calipers. 5 tablets were taken and their thickness was measured.

Tablet hardness[5]

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Tablet friability[5]

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W0) or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. Determination was made in triplicate.

$$\% \text{ Friability} = \frac{W_0 - W}{W_0} \times 100$$

Wetting time[6]

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water- containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

Water absorption ratio (%)[7, 8]

A piece of tissue paper folded twice was placed in a small petridish (Internal Diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was determined using the following equation.

$$R = \frac{W_a - W_b}{W_b} \times 100$$

Where, Wb is the weight of the tablet before water absorption and Wa is the weight of the tablet after water absorption.

In-vitro disintegration test[5]

The test was carried out on 6 tablets using Tablet disintegration tester ED-20 (Electrolab, Mumbai, India) distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

In-vitro dissolution study[9]

The release rate of atenolol from mouth dissolving tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 as a dissolution medium, at 37±0.5^{0}C and 50 rpm. A sample (10 ml) of the solution was

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withdrawn from the dissolution apparatus at 5, 10, 15, 20, 25, 30, 35 and 40 min. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 276 nm using a Shimadzu UV-1700 UV/VIS spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

Results and Conclusion

The present investigation was undertaken to formulate and evaluate mouth-dissolving tablets of atenolol by direct compression method using croscarmellose sodium and sodium starch glycolate as a superdisintegrants. The use of superdisintegrants for preparation of mouth dissolving tablets is highly effective and commercially feasible. The results of tablets were evaluated for uniformity of weight, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time and dissolution study and results were shown in Table 2. Using the same excipients, the tablets were also prepared, without superdisintegrants (Control). The absorption of water results in breaking of tablets due to swelling of superdisintegrants and disintegration property of microcrystalline cellulose therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well. Prepared mouth-dissolving tablet gets dispersed in the mouth quickly and releases the drug early as compared to its formulated conventional tablet. Figure 1 show the cumulative percentage of atenolol released from formulated tablet with different concentration of crosscarmellose sodium and Sodium starch glycolate. It is clear that the dissolution of atenolol has improved considerably in formulation A4 as compared to formulation A1, A2, A3 and A5 (Control). The tablets of the batch A4 showed good dissolution efficiency and rapid dissolution.

It can be concluded that disintegration time and dissolution rate of atenolol can be enhanced to a great extent by direct compression technique with the addition of combination of superdisintegrants. Further investigations are needed to confirm the *in-vivo* efficiency.

Table 1: Formulation of Atenolol MDT

Ingredients	**Formulation Code**				
	A1	**A2**	**A3**	**A4**	**A5**
Atenolol	50	50	50	50	50
Sodium starch glycolate	09	15	--	--	--
Crosscarmellose sodium	--	--	09	15	--
MCC	30	30	30	30	--
Mannitol	99	93	99	93	138
Aspartame	6	6	6	6	6
Magnesium stearate	3	3	3	3	3
Talc	3	3	3	3	3
Total (mg)	200	200	200	200	200

Table 2: Evaluation of Atenolol MDT

Formulation parameters	**Formulation Code**				
	A1	**A2**	**A3**	**A4**	**A5**
Weight variation (%)	201±1.44	200±1.25	201±1.17	198±1.11	202±1.31
Thickness (mm)	3.2	3.2	3.1	3.2	3.3
Hardness (kg/cm2)	3.1±0.15	3.0±0.10	3.3±0.30	3.6±0.21	2.9±0.12
Friability (%)	0.48	0.31	0.53	0.40	0.53
Wetting time (sec)	43±1.33	35±1.54	41±1.35	33±1.28	86±2.11
Water absorption ratio (%)	87.35	90.38	89.58	91.56	80.29
Disintegration time (sec)	33±2.8	28±3.2	31±2.4	27±4.4	82±2.5

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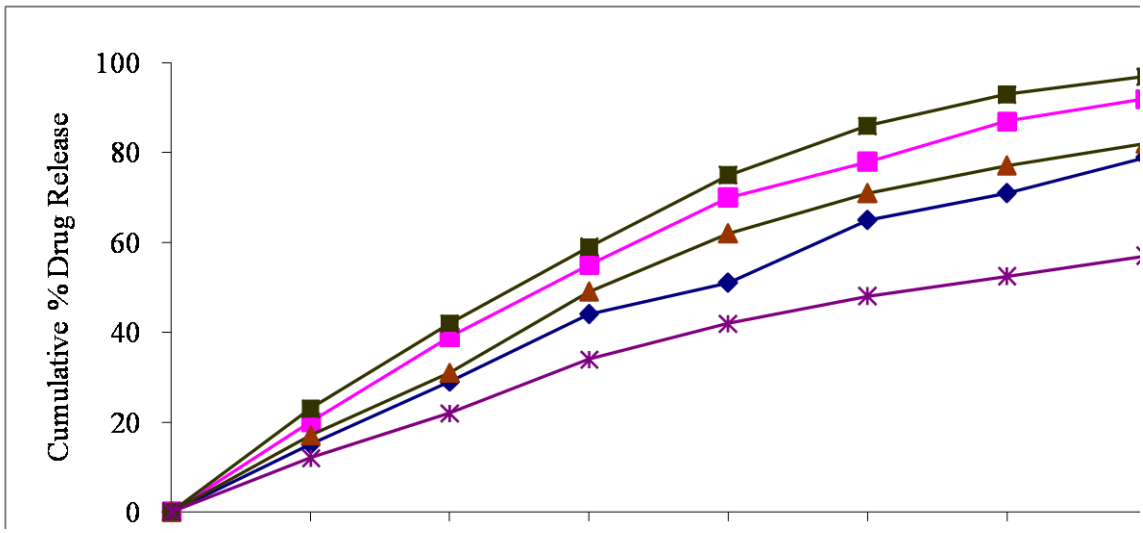

Fig. 1: Drug release profile of Atenolol MDT from various batches

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