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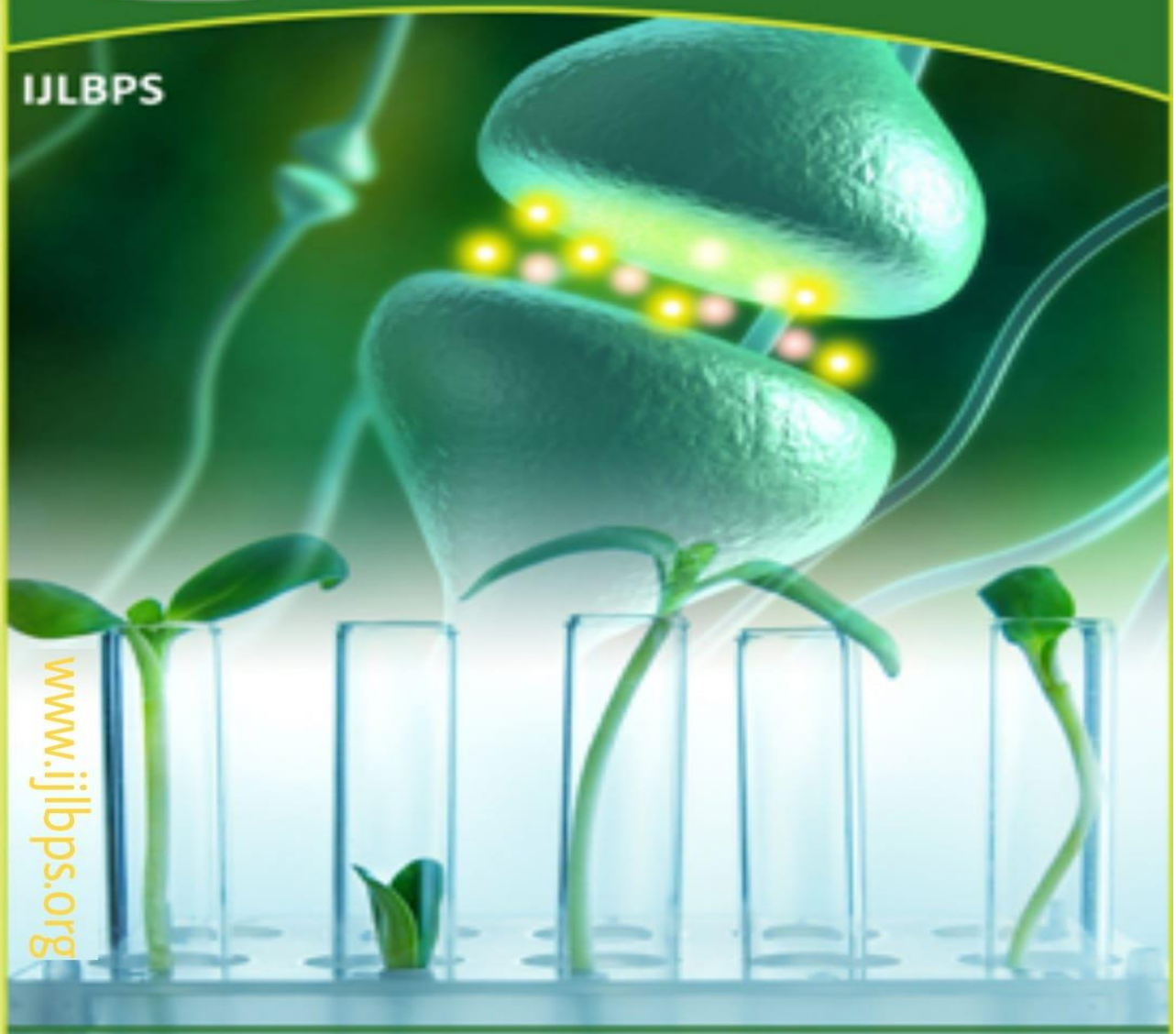

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Dissolvable atenolol tablet formulation and efficacy assessment

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Abstract

In an effort to improve patient adherence, direct compression technique atenolol pills were developed. Croscarmelose sodium and sodium starch glycolate were the two super disintegrants tested here. Tablets were tested for consistency in weight, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time, and dissolution studies after being manufactured in batches. The tablets were likewise manufactured using the identical excipients, but were tested without dis integrants. Based on the data, it seems that tablet formulation (A4) is the most viable option. Standard limitations were also met for the tablets' hardness, friability, disintegration time, and dissolution rate during preparation.

Atenolol, orally disintegrating pills, and in vitro testing are some of the keywords here.

Introduction

Due to its portability, small size, and simple production process, the tablet has quickly become the most popular dosage form. There has been a growing need for convenient and patient-friendly dose forms during the last decade. This has resulted in a steadily rising yearly need for R&D in cutting-edge technology. Pharmaceutical companies are shifting their research and development priorities away from creating entirely new drug molecules and toward creating new dosage forms for existing drugs that improve safety However, elderly and young patients have trouble taking regular medications, which maylow levels of patient compliance. Innovative drug delivery technologies, such as " melt in mouth" or " mouth dissolve (MD)" or even " dispersible" tablets, have been developed to address this shortcoming.

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Tablets like this are cutting edge since they dissolve or scatter in the mouth. They are well suited for both elderly and young patients because of their convenient administration characteristics, such as not requiring water and being taken at any time. Patients without ready access to water, those with mental illness, and those confined to a bed may all benefit from using them. Tablets are widely used because of the advantages they provide in terms of patient compliance, speed of beginning of action, enhanced bioavailability, and excellent stability.

Atenolol is a beta-blocker used for high blood pressure and angina. It has a low oral Bioavailability of 50% and is eliminated mostly unaltered in the feces because to its poor absorption from the GI tract3

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The reason for this is because it is poorly absorbed in the lower intestines. Its elimination half-life is between 6 and 7 hours 4 due to its first-pass metabolism in the liver. Due to hepatic first pass metabolism and fluctuations in the plasma drug level, typical tablet administration of atenolol leads in limited Bioavailability and low drug concentration at the receptor site. In the current investigation, researchers sought to enhance the bioavailability of atenolol by creating mouth-dissolving pills

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 andtheir thickness was measured.

Tablet hardness[5]

The tablet hardness, which is the force required to break a tablet in a diametric compressio n 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.

$$\% \text{ Friability} = \frac{W0 - W}{W0} \times 100$$

Wetting time[6]

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue pap ers 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 requiredfor 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.

$$R = \frac{Wa - Wb}{Wb} \times 100$$

Where, Wb is the weight of the tablet before water absorption and Wa is the weight of th e 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

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 froma standard curve

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Results and Conclusion

The goal of the current study was to develop and assess a direct compression technique for making atenolol mouth dissolving tablets with the aid of croscarmellose sodium and s odium starch glycolate as superdisintegrants. Superdisintegrants may be used to make effective and marketable mouth dissolving tablets. Table 2 shows the findings of an evaluation of tablet uniformity with respect to weight, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time, and a dissolution study. The tablets were likewise produced using the identical excipients, but without the addition of superdisintegrants (Control). Tablets quickly disintegrate after being exposed to water owing to the swelling of superdisintegrants and the disintegration characteristic of microcrystalline cellulose. It has been observed that this break down also affects the way the substance dissolves in water. The medicine is released from the prepared mouth-dissolving tablet sooner than it would from the conventionally prepared tablet. As can be seen in Figure 1, tablets containing varying amounts of crosscarmellose sodium and sodium starch glycolate result in varying rates of atenolol release. Formulation A4 clearly shows much better atenolol solubility compared to formulations A1, A2, A3, and A5 (Control). Dissolution efficiency and rate were both high for tablets from batch A4.

It can be concluded that direct compression approach with the inclusion of combination of superdisintegrants greatly improves disintegration time and dissolving rate of atenolol. More research is required to verify the effectiveness in living organisms.

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

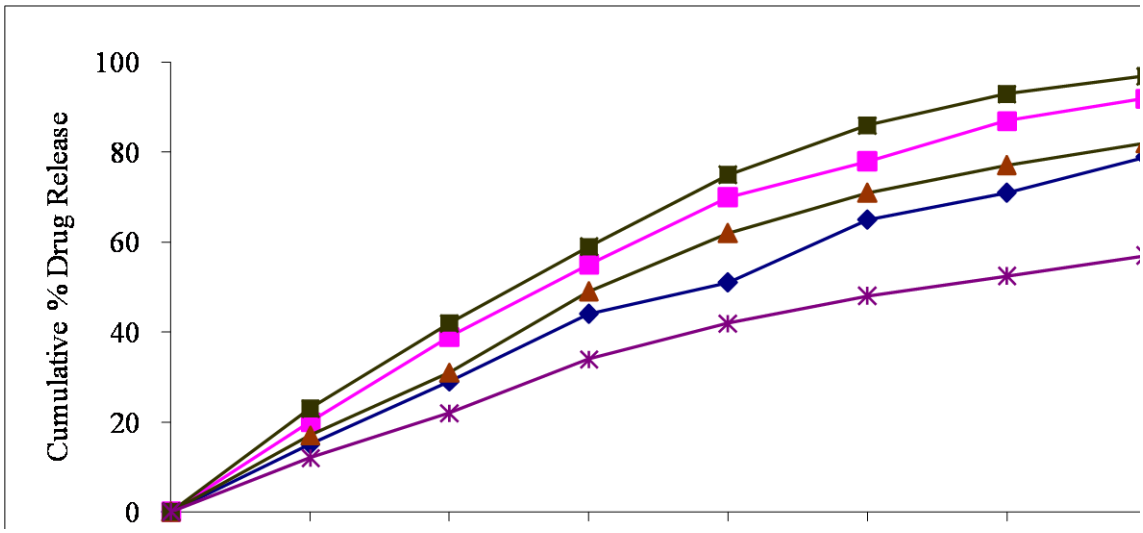

Fig. 1: Drug release profile of Atenolol MDT from various batches

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