ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Formulation and Evaluation of Mouth Dissolving Tablets of Metoprolol tartrate by new Co-processed Technique

Vijaya Suman Reddy B*[1], Ramesh Y[2], Parameshwar K[3], Jhansi reddy K[4]

[1]Department of Pharmacology, Sri krishnadavaraya University, Ananthapur, A.P, India
[2]Department of Pharmaceutics, Rao's College of Pharmacy, Chemmuduguntla, Nellore, A.P, India
[3]Department of Medicinal chemistry , K.L.E University, Bangalore, A.P, India
[4]Department of Pharmaceutics, NIPER, Bala Nagar, Hyderabad, A.P, India.

ABSTRACT

Metoprolol tartrate is effective β-blocker which is having antianginal properties and used in the treatment of myocardial infarction. Oral bioavailability of Metoprolol tartrate is around 40%. In present work an attempt has been made to prepare mouth dissolving tablets of Metoprolol tartrate by direct compression method with a view to enhance patient compliance. The two superdisintegrants used in this study were Croscarmellose 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 prepared, without disintegrants and were evaluated in the similar way. From the results obtained, it can be concluded that the tablet formulation (M5) 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: Metoprolol tartrate, Mouth dissolving tablets, In vitro evaluation, Superdisintegrants.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Metoprolol tartrate is a selective beta1- adrenoreceptor blocking agent. Chemically Metoprolol tartrate is (±)-1-(isopropyl amino)-3-[p- (2-methoxyethyl) phenoxy]-2-propanol (2:1) dextro-tartrate salt used in Essential hypertension, prevention after a myocardial infarction, tachycardia, coronary heart disease (prevention of angina attacks), treatment of heart failure. Oral bioavailability of Metoprolol tartrate is around 40% and having half life 3 to 5 hrs [1].

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 [2].

Literature survey revealed that delivery of Metoprolol tartrate oral, intranasal route but no systematic previous report available on mouth dissolving tablet formulation. 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 [3]. These are novel types of tablets tha 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.

MATERIALS AND METHODS

Metoprolol tartrate was a gift from Mann Pharmaceutical Industries (Mehsana, India). Croscarmellose sodium (Ac-Di-Sol) used was analytical reagent grade procured from Loba Chemicals, Mumbai and Sodium Starch Glycolate (Explotab) used was procured from Merck Limited, Mumbai. All other reagents and chemicals used were of analytical grade.

Preparation of mouth dissolving tablets of Metoprolol tartarate [4]

All the Excipients (or) materials were passed through 60 # screens prior to mixing. Metoprolol tartrate, 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 (Table 1).

ISSN: 0975-8585

TABLE 1: Formulation of Metoprolol tartrate MDT

Ingredients	Formulation Code				
	M1	M2	M3	M4	M5
Metoprolol tartrate	100	100	100	100	100
Crosscarmellose sodium	20	10	20	-------	20
Sodium starch sodium	45	40	34	-------	34
Lactose	30	46	40	194	40
Mannitol	94	94	94	94	94
Aspartame	6	6	6	6	6
Magenesium stearate	3	3	3	3	3
Talc	3	3	3	3	3
Total (mg)	300	300	300	300	300

Weight variation test

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 [5].

Tablet thickness

The thickness of the tablet was measured by placing tablet between two arms of the Varnier calipers. 5 tablets were taken and their thickness was measured [6].

Tablet hardness

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 applied force to the tablet diametrically with the help of an inbuilt spring [7].

Tablet friability

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (Wo) 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[8]. The weight loss should not be more than 1 %. Determination was made in triplicate.

$$\% \text{ Friability} = 100 (Wo - W) / Wo$$

Wetting time

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 [9].

Water absorption ratio (%)

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[10]. The water absorption ratio (R) was determined using the following equation.

$$R = 100 (Wa - Wb) / Wb$$

Where,

Wa is the weight of the tablet after water absorption.

Wb is the weight of the tablet before water absorption and

In-vitro Disintegration test [11]

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

The release rate of Metoprolol tartrate 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±0.50C and 50 rpm[12]. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus at 2.5, 5, 7.5, 10, 15, 20, 25, 30, 35 and 40min. The samples were filtered through a 0.45 membrane filter. Absorbance of these solutions was measured at 223 nm using a Shimadzu UV-1700 UV/VIS spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve. (Fig 1)

RESULTS AND DISCUSSION

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 (Table 2). Using the same excipients, the tablets were prepared, without these superdisintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment [14]. The absorption of water

ISSN: 0975-8585

results in breaking of tablets and 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.

TABLE 2: Evaluation of Metoprolol tartrate MDT

Ingredients	Formulation Code				
	M1	M2	M3	M4	M5
Weight variation (%)	301±1.23	298±1.22	269±2.45	312±1.34	301±2.27
Thickness(mm)	4.9	4.2	4.1	4.3	4.1
Hardness (kg/cm^2)	3.5±0.16	3.2±0.22	3.6±0.45	3.3±0.35	3.7±0.19
Friability (%)	0.39	0.40	0.33	0.39	0.32
Wetting time (sec)	43±1.22	45±0.90	47±2.70	38±1.35	38±1.35
Water absorption ratio (%)	90.71	92.45	90.23	57.32	93.45
Disintegration time (sec)	38±3.6	32±2.8	34±3.6	28±2.7	69±3.7

Values in parenthesis are standard deviation (±SD)

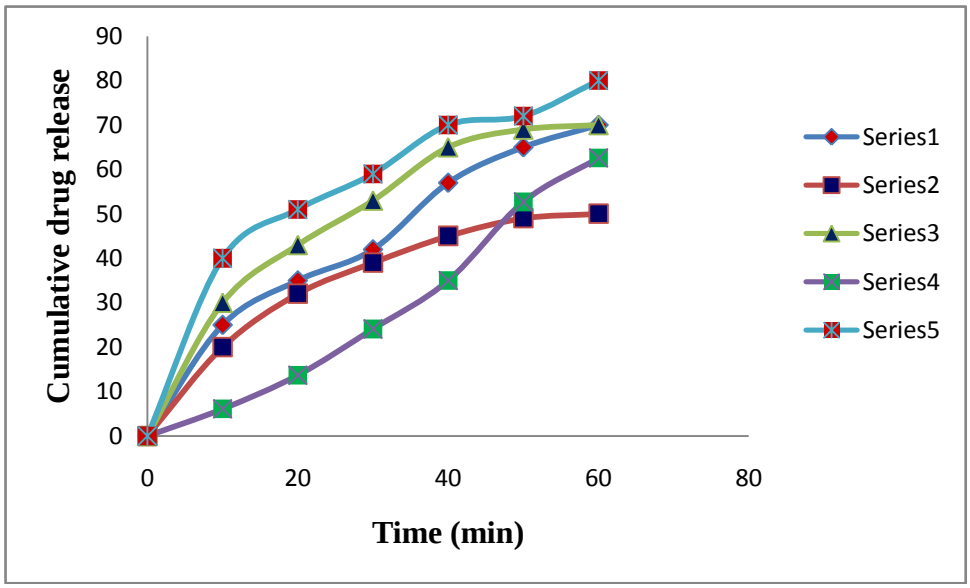

Fig 1: Drug release profile of Metoprolol tartarate MDT from various batches

Figure 1 show the cumulative percentage of Metoprolol tartrate released from formulated tablet with different concentration of Crosscarmellose sodium and Sodium starch glycolate. It is clear that the dissolution of Metoprolol tartrate has improved considerably in formulation M5 as compared to formulation M1, M2, M3 and M4 (Control). The tablets of the batch M5 showed good dissolution efficiency and rapid dissolution.

CONCLUSION

The was finally concluded that mouth dissolving tablets of Metoprolol tartrate showing enhanced dissolution will lead to improved bioavailability and enhanced to a great extent by

direct compression technique with the addition of combination of superdisintegrants and M5 best promising formulation.

ACKNOWLEDGEMENT

The authors are thankful to from Mann Pharmaceutical Industries, Mehsana, India for providing the gift sample of Metoprolol tartarate and also thankful to Sri Krishnadavaraya University, Ananthapur, for the providing the all facilities for carried out this research work.

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