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Formulation and Evaluation of Atenolol Mouth Dissolving Tablet

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Abstract: An attempt has been made to formulate & evaluate Atenolol mouth dissolving using direct compression technique. Three superdisintegrants (Croscarmellose sodium, Crospovidone and Sodium starch glycolate) were used alone as well as in combination. Fifteen formulations were prepared with different concentration level of superdisintegrant to assess their efficiency. Physical properties, in-vitro release characteristics, wetting time and stability profile of optimized formulation were evaluated. Formulation with Croscarmellose sodium, Crospovidone combination found to be best among the three alone as well as other combinations of superdisintegrant.

Keywords: Mouth dissolving tablets (MDTs), Atenolol, Superdisintegrant, Direct compression

Introduction

Atenolol is a β_1 selective antagonist without membrane stabilizing activity. It is acting selectively and competitively on adrenoreceptors, block the action of catecholamines. It can be administered once daily 50 to 100 mg orally as an antihypertensive agent [1]. Mouth dissolving tablets are novel solid oral dosage form, which disintegrates and dissolves rapidly in saliva without the need for drinking water when administered [4]. Market studies indicates that more than half of the patient population prefers MDTs to other dosage forms and most consumers would ask their doctors for MDTs (70%), purchase MDTs (70%), or prefer MDTs to regular tablets or liquids >80%[5]. Geriatric patients may have difficulties in swallowing and chewing the tablets, resulting in patient noncompliance and ineffective therapy [6]. They overcome the problem of swallowing and chewing [7]. These in turn provides convenience of administration, greater patient compliance and quick onset of action. Thus present drug chosen as a suitable candidates for formulation of mouth dissolving dosage form.

Materials and Methods

Atenolol was obtained as gift sample from IPCA Laboratories Ltd, Mumbai. Sodium starch glycolate, Croscarmellose sodium (Ac-Di-Sol), Crospovidone, Mannitol, Starch, Aspartame, Magnesium stearate, Talc and all other chemicals/solvents were obtained from college laboratory and were of analytical grades.

Preparation of mixed blend of drug and excipients

All the ingredients were passed through mesh no. 60. Required quantity of each ingredient was taken for each specific formulation and all the ingredients were cogrounded in a mortar and pestle. Finally magnesium stearate and talc were added and mixed. The powder blend was evaluated for flow properties like bulk density, compressibility index and angle of repose for each formulation.

Preparation of Mouth Dissolving Tablet

The mixed blend of drug and excipients was compressed using single punch tablet machine, weighing 200 mg each with a diameter of 8 mm. Fifteen formulations with varying percentage of croscrmellose sodium 2, 4, and 6 %w/w (formulations coded as A1, A2, and A3), with varying percentage of sodium starch glycolate 2, 4, and 6 %w/w (formulations coded as B1, B2 and B3), with varying percentage of crospovidone 2, 4 and 6 %w/w (formulations coded as C1, C2 and C3), with varying combination of croscarmellose sodium : crospovidone 1:1, 2:1, 3:1, 4:1, and 5:1 respectively (formulation coded as A1C, A2C, A3C, A4C and A5C) and with starch 4 %w/w (formulation coded as N) were prepared. Formulations are shown in **Table 1**.

Table 1: Formulation of Atenolol mouth dissolving tablets

S. No.	Formulation code	Ingredients (mg/tab.)								
		Atenolol	Mannitol	CCS	SSG	CP	Aspartame	Starch	Mg-stearate	Talc
1.	A1	50	128	04	-	-	02	08	03	05
2.	A2	50	124	08	-	-	02	08	03	05
3.	A3	50	120	12	-	-	02	08	03	05
4.	N	50	132	-	-	-	02	08	03	05
5.	B1	50	128	-	04	-	02	08	03	05
6.	B2	50	124	-	08	-	02	08	03	05
7.	B3	50	120	-	12	-	02	08	03	05
8.	C1	50	128	-	-	04	02	08	03	05
9.	C2	50	124	-	-	08	02	08	03	05
10.	C3	50	120	-	-	12	02	08	03	05
11.	A1C	50	128	02	-	02	02	08	03	05
12.	A2C	50	126	04	-	02	02	08	03	05
13.	A3C	50	124	06	-	02	02	08	03	05
14.	A4C	50	122	08	-	02	02	08	03	05
15.	A5C	50	120	10	-	02	02	08	03	05

CCS: Croscarmellose sodium, CP: Crospovidone, SSG: Sodium starch glycolate. Total weight of each tablet is 200mg.

Evaluation

The dimensional specification was measured using screw gauge. Weight variation test was performed as per specification of IP. Hardness test was performed by using a Pfizer hardness tester. The friability test was performed using a Roche friabilator. Disintegration time and wetting time were critical parameter for optimization, determined as per procedure given in IP. Buffer pH 6.2 was used as a medium. Disintegration time and wetting time are shown in **Table 2**.

Table 2: Disintegration and wetting time of various formulations

S. No.	Formulation Code	Disintegration Time (sec)*	Wetting Time (sec)*
1.	A1	92.3±2.52	22.3±2.52
2.	A2	45±5.0	16±3.61
3.	A3	107.3±2.5	26±1.0
4.	N	117±2.5	27±1.0
5.	B1	96±3.6	22±2.0
6.	B2	115±5.0	22±1.0
7.	B3	116.6±7.6	20.6±1.5
8.	C1	69.3±6.03	18±1.0
9.	C2	106±3.6	16.3±1.5
10.	C3	94±3.6	18±4.3
11.	A1C	33±2.65	16±1.0
12.	A2C	30.3±3.5	16±1.0
13.	A3C	20.3±2.52	13±1.0
14.	A4C#	15.3±2.5	10±1.5
15.	A5C	30±5.0	17±1.0

*n=3, #Formulation A4C shown least disintegration as well as wetting time.

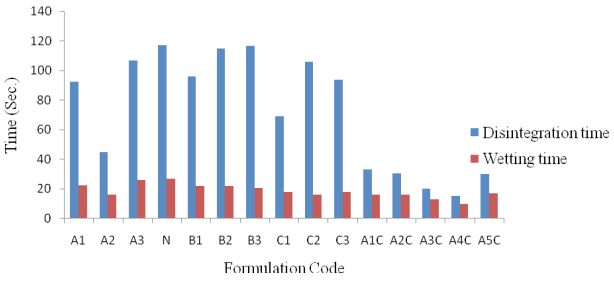

Fig.1: Disintegration time of different Batches

Content uniformity

Powder equivalent to 50mg of Atenolol was dissolved in buffer pH 6.2. Solution was filtered and absorbance of resulting solution was measured at 276nm using UV/VIS spectrophotometer (UV-1700, Shimadzu). The amount of drug present in the given tablet was calculated from absorbance.

In-vitro drug release

Dissolution studies were carried out by USP paddle method, media was buffer pH 6.2 maintained at 37±1^{0}C with stirring speed of 50 rpm. Absorbance of filtered sample at different time intervals were measured at 276nm in a UV spectrophotometer (UV-1700, Shimadzu) and cumulative release was calculated.

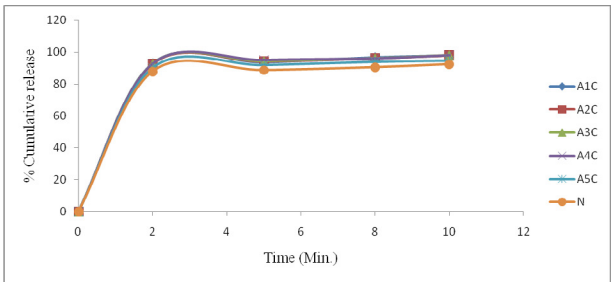

Fig. 4: In-vitro drug release profile of formulation A1C, A2C, A3C, A4C, A5C & N in buffer pH6.2

In-vitro drug release stability study

Tablets of optimized batch (A4C) were packed in tightly closed plastic container stored at 40^{0}c/75% RH for one month. The product was analyzed after 30 days storage and drug release profile was found out and compared with release obtained immediately after compression.

Result and Discussion

Mouth dissolving tablets are mainly preferred by geriatric & pediatric patients, these dosage forms overcome the problem of swallowing of medicaments. MDT has the advantage of quick onset of action; no need of water & in some cases bioavailability may be increased. Extensive literature survey showed the potential of such a drug delivery system to achieve the desired goal.

The present study was carried out to investigate the possibility of formulating stable mouth

dissolving tablet of Atenolol. In order to determine the effect of formulation component, croscarmellose sodium, sodium starch glycolate and crospovidone were chosen as excipients. The disintegration time and in-vitro release studies of formulation prepared with different concentration of superdisintegrants were also explored in order to assess the possible disintegration & release of drug.

Characterization of Mouth Dissolving Tablet

All formulations were characterized to assess the MDT using Direct compression method. All formulations were showed to contain disintegrants as well as superdisintegrants, which is present in different concentration in formulations. The tablets were white or colorless, round, bi-convex. The diameter of all formulation was found to be 8 mm, the average thickness was found in the range of 2.63 - 3.60 mm and mean content uniformity was in the range of 94 – 104.2% (under specified limit), weiht variation was also under specified limit. Friability of all formulation was < 1%, showed that there is no problem during handling, packaging & transportation of dosage form. Hardness of all formulations was kept 2.5 – 3.2 kg/cm^2.

The disintegration time of MDT is critical parameter, which was found in range of 12.3 – 157 seconds. Batch A4C showed the least disintegration time and may be due to swelling & wicking action of croscarmellose sodium & crospovidone respectively or both. Wetting time of all formulation was in the range of 10 – 27 seconds.

In-Vitro release study

All the formulations were subjected to in-vitro release study using USP paddle apparatus, dissolution media was phosphate buffer (pH 6.2) and rotation speed was 50 rpm. In-vitro dissolution studies of various formulations at different time intervals are obtained. Formulation A4C showed maximum dissolution rates with 98% of drug release in 10 min.

When caparison were made for disintegration time and in-vitro release of all formulation, result shown that formulation A4C was best among all rest formulation because it have least disintegration time as well as acceptable in-vitro release data. Formulation A4C has to be optimized on the following basis.

In-Vitro release stability study

In-vitro release stability study was carried out for selected formulation (A4C) by storage at 40^{0}c/75%RH for one month, then the formulation was subjected to dissolution test and the result shown that there is no stability problem for selected formulation i.e. stability study showed that the formulation stable at pre defined stability condition.(**Table 3)**

Table 3: Data showing % cumulative release after storage for 30 days

S. No.	Time (min)	Batch code A4C	
		% Cumulative Release	
		0 Day	30 Day
1.	2	92.8	90.6
2.	5	95.2	93.0
3.	8	96.2	96.2
4.	10	98.2	97.8

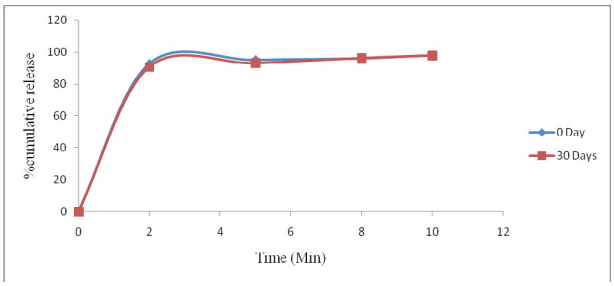

Fig. 5: In-vitro release stability study of optimized formulation A4C in buffer pH 6.2.

Conclusion

Mouth dissolving tablet can provide quick onset of action, relief for any disease can be found in less time as compared to conventional tablet. The real issue in the development of mouth dissolving tablet is not increase the bioavailability or prevention of pre systemic metabolism, but to found the quick onset of action or fast disintegration of dosage form. In present study, it may conclude that the fast disintegrating Atenolol tablets can be prepared by direct compression method using combination of superdisintegrants. Croscarmellose sodium: crospovidone combination was found to be the best among the other concentration of superdisintegrants. Croscarmellose sodium: crospovidone combination showed the least disintegration time of 15.3±2.5 seconds and the highest release of more than 98% of drug in 10 minutes. Further in-vivo studies need to be performed to confirm the result obtained from in-vitro studies.

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