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Novel Tactic in Designing Mouth Dissolving Atenolol tablets

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Abstract

Mouth dissolving drug delivery systems has faster onset of action, classiness, ease of admin, ease of engineering, easy to store and carrying. A different tactic has been made to develop mouth dissolving tablets of Atenolol by incorporating clove oil as flavor and local anesthetic on taste buds. Atenolol tablets were made by direct compression method. The prepared tablets were checked for Pre compression and post compression parameters and they were found to be satisfactory. The prepared tablets found to have better drug releasing characteristics, mouth feel and enhanced drug obtain ability with better patient acquiescence.

Keywords: Mouth dissolving, Atenolol tablets, direct compression, superdisintegrants, Clove oil.

Contents

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1. Introduction

Atenolol is beta blocker [1]. Mouth dissolving tablets endure dissociation in mouth and forms a suspension which can be is easily swallowed. Aged patients and children, have trouble in swallowing solid dosage forms [2-4]. To assist in such cases, a wide range of mouth dissolving drug delivery systems were developed. Mouth dissolving tablets dissolve quickly in mouth without the water. The present design is to prepare Atenolol mouth dissolving tablets using super disintegrants, sweetener (stevia leaf powder) and local anesthetic flavor (Clove oil) in different proportions [5-7].

2. Materials and Methods

Materials

Atenolol was a gift sample from Sun Pharmaceuticals, Mumbai, India. Stevia leaf powder was obtained from the medicinal garden of Balaji College of Pharmacy, Ananthapuramu, India and authenticated by the Pharmacognosy department. Mannitol, Clove oil, talc, micro crystalline cellulose, Croscarmellose sodium, Crospovidone, magnesium stearate and talc were purchased from S.D. Fine Chemicals, Mumbai, India. All other chemicals, solvents and reagents were used of either pharmacopoeial or analytical grade.

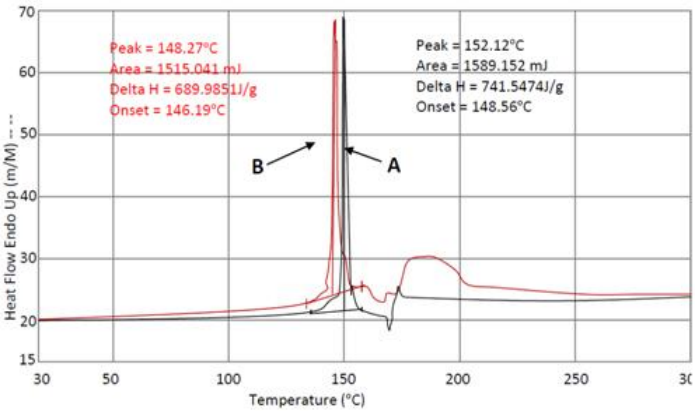

Figure 1: DSC of Pure drug (A) and blend (B)

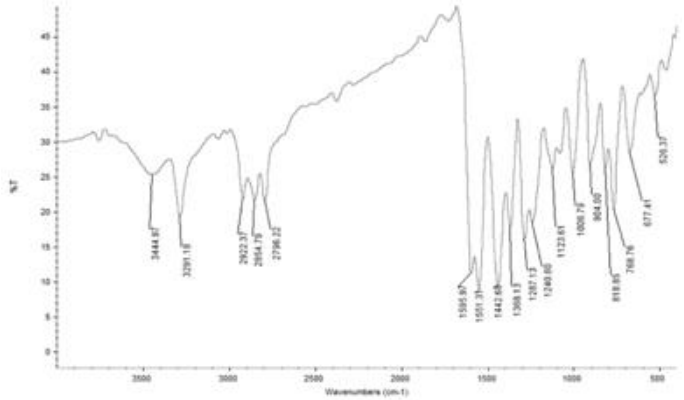

Figure 2: FTIR of Pure drug

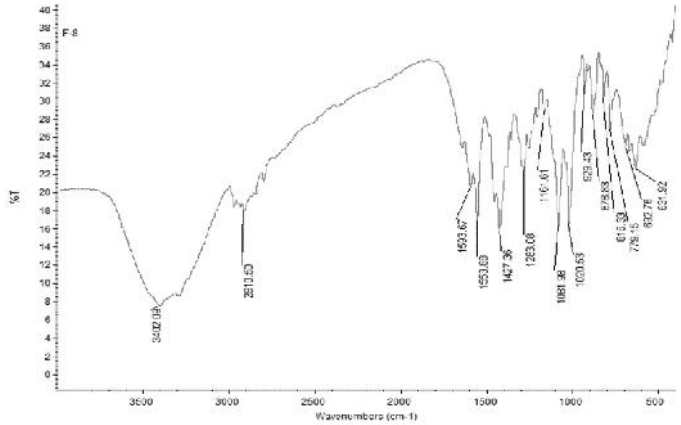

Figure 3: FTIR of drug and excipient blend

Preparation of Mouth Dispersible Tablets:

All the ingredients were passed through sieve No. 60. Atenolol, mannitol, Micro Crystalline Cellulose and stevia leaf powder were triturated in a glass mortar. Micro crystalline cellulose, Croscarmellose sodium, Crospovidone were incorporated in the powder mixture and finally magnesium stearate and talc were added [8-10]. The mixed blend was then compressed with 10mm flat face surface punches using hydraulic press single tablet punching machine.

Pre-compression parameters

Compatibilities study: The compatibility of drug and polymers under experimental condition was conducted using DSC and FTIR studies.

Flow properties of the blend

Angle of repose:

The Angle of repose can be mathematically calculated by the following equation [11-13].

$\tan(\theta) = h / r$

Where
θ = Angle of repose,
h = Height of heap,
r = Radius of pile.

Loose Bulk density and Tapped Bulk Density

Mathematically loose bulk density (LBD) and Tapped bulk Density (TBD) were calculated by the following equations [11-13].

LBD = M / Vb

Where M = Weight of powder, Vb = Bulk volume

TBD = M / Vt

Where V t = Volume after tapping

Carr's index

Mathematically carr'sindex can be calculated by the following equation [11-13].

I = [(Vb - Vt) / Vb] x 100

Where Vb = Bulk volume, Vt = Tapped volume

Hausner ratio

Mathematically Hausner's ration was calculated by the following equation [11-13].

Hausner ratio = TBD / LBD

Where TBD = Tapped bulk density, LBD = Loose bulk density

Preparation Tablets

Tablets were made from blends by direct compression method. All the ingredients (Table 1) were passed through mesh no. 60. All the ingredients were ground in a pestle motor. Finally talc and magnesium stearate were added and mixed. The mixed blend of excipients was compressed using a single punch machine to produce convex faced tablets weighing 300 mg with 3 mm thickness and 10 mm in diameter [14-16].

Post compression parameters

Thickness: The thickness of the tablets was determined using a thickness screw gauge (Mitutoyo, New Delhi, India). Five tablets from each batch were used and average values were calculated.

Hardness test

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and analyzed for hardness. The mean and standard deviation values were also calculated [17].

Friability test: The friability of tablets was determined using Roche Friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions. The % friability was then calculated by the following equation [18].

$$F = W_{initial} - W_{final} / W_{initial} X\ 100 \quad \ldots\ldots\ldots\ldots\ldots (1)$$

Where

F= friability (%), $W_{initial}$ = initial weight, W_{final} = Final weight

Weight variation test

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Denver APX-100, Arvada, Colorado) and the test was performed according to the official method [19].

Drug content uniformity

20 tablets were weighed and powdered. The blend equivalent to 25 mg of Atenolol was weighed and dissolved in phosphate buffer solution (PH 6.8). The solution was filtered through Whatmann filter paper (no.41), suitably diluted with PBS (pH 6.8) and assayed at 224.2 nm [20], using a UV-Visible double beam spectrophotometer (UV-1700 Shimadzu).

Wetting time

The tablet was placed in a petridish of 6.5 cm in diameter, containing 10 ml of water at room temperature, and the time for complete wetting was recorded. To check for reproducibility, the measurements were carried out six times and the mean value calculated [21].

Water absorption ratio: A small piece of tissue paper folded twice and placed in a petridish containing 6ml of distilled water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined by the following equation [21].

$$R = 10\ X\ \frac{(Wa - Wb)}{Wb}$$

Where,

Wb = weight of the tablet before water absorption

Wa = weight of the tablet after water absorption

Three tablets from each formulation were analysed performed and standard deviation was also determined.

***In vitro* dispersion time**

Tablet was placed in 10 ml phosphate buffer solution, pH 6.8±0.5^{o}C. Time required for complete dispersion of a tablet was measured [22-24].

***In vitro* disintegration time**

The *in vitro* disintegration time of a tablets were performed by placing one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 (simulated saliva fluid) maintained at 37±2^{0}C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 37±2^{0}C. The time taken for the complete disintegration of the tablet with no palpable mass remaining in the basket was measured and recorded [22-24].

Mouth feel: To know mouth feel of the tablets, selected human volunteers were given placebo tablets and the taste sensation felt was evaluated [23].

***In vitro* dissolution studies:**

In vitro dissolution studies were carried out using dissolution test apparatus USP XXIII. The following procedure was employed throughout the study to determine the *in vitro* dissolution rate for all the formulations [23]. The parameters *in vitro* dissolution studies were tabulated in Table 4.

Accelerated Stability studies: The promising formulation (F5) were tested stability for a period of 3 months at accelerated conditions of a temperature 40^{0}C and a relative humidity of 75% RH, for their drug content [25].

3. Results and Discussion

Preformulation studies:

The DSC spectrum showed in fig.1. The FTIR spectrums were showed in fig 2 and 3. These data indicates that Atenolol is compatible with the excipients used.

Evaluation of powdered blend:

The formulated blend was evaluated for various parameters such as angle of repose, loose bulk density, tapped bulk density, compressibility index, hausner ratio. The values were within the official limits with less standard deviation. The results of angle of repose indicate good flow properties. Loose bulk density, tapped bulk density, compressibility indexand hausner ratio values indicate that the formulated powder blend shows satisfactory flow property. All these values were represented in Table 2.

Evaluation of tablets

The prepared tablets were found to have uniformity in thickness. The hardness of formulated tablets was more than 4kg/cm^{2} and the loss in friability was less than 1% indicates that the formulated tablets have good mechanical strength. All the tablets have uniformity in weight as per the pharmacopoeial limits. The Wetting Time indicates that all the formulated tablets have quick wetting, this may be due to ability of swelling and also capacity of absorption of water. The water absorption ratio favors the wetting of the tablet in saliva. The disintegration time was within the pharmacopoeial limits aided with the presence of Croscarmellose sodium and Crospovidone, in direct compression method results in hydrophilicity and swelling which in turn causes rapid disintegration.

The human volunteers felt good taste in all the formulations. As the formulation was not bitter due to the presence of stevia leaf powder (as it is 400 times sweeter than sucrose) and the Euginol in clove oil which acts as both flavoring and local anesthetic agent to block the sensation of taste buds. In oral disintegration all the formulations showed rapid disintegration in oral cavity. All these values were represented in Table 3. In all the formulations the drug release was nearer to 100% within 6 min. This rapid dissolution might be due to fast breakdown of particles of superdisintegrants. The *in vitro* dissolution profile of formulated tablets was shown in Fig.4. The dissolution parameters were shown in table 4. The optimized formulation F5 was subjected to accelerated stability studies and the tablets possessed the same parameters even after the stressed storage conditions.

Table 1: Composition of Mouth Dissolving Tablets of Atenolol

Ingredients (mg)	**Formulations**				
	F1	**F2**	**F3**	**F4**	**F5**
Atenolol	25	25	25	25	25
Mannitol	50	50	50	50	50
Croscarmellose sodium	10	20	30	40	50
Cross povidone	10	20	30	40	50
Stevia leaf Powder	5	5	5	5	5
Micro crystalline cellulose	189	169	149	129	109
Magnesium stearate	3	3	3	3	3
Talc	3	3	3	3	3
Clove oil (Flavoring agent and local anesthetic)	5	5	5	5	5
Total weight of the tablet 300mg					

Table 2: The physicochemical properties of powdered blend

Formulations	Angle of Repose (¯)	Compressibility Index (%)	Hauser's Ratio
F1	27.26±0.10	17.18±0.02	1.148±0.02
F2	25.21±0.55	20.22±0.06	1.215±0.01
F3	28.55±0.22	13.02±0.09	1.125±0.01
F4	28.28±1.52	13.35±0.16	1.041±0.02
F5	29.22±0.19	12.96±0.12	1.043±0.01
All values mentioned as mean ±SD; Number of trials (n)=3			

Table 3: Evaluation parameters of Tablets

Formulation	Thickness (mm)	Hardness (kg/cm^3)	Friability (%)	Wetting Time (sec)	Water absorption ratio(g)	Disintegration Time (sec)
F1	3.03±0.02	6.55±0.07	0.25±0.02	99±0.98	14.25±0.02	36±0.25
F2	3.01±0.01	8.10±0.05	0.55±0.01	93±1.52	15.56±0.12	38±1.55
F3	2.99±0.15	7.25±0.05	0.26±0.01	95 ±1.95	16.25±0.14	30±0.88
F4	3.02±0.01	6.05±0.01	0.22±0.01	99±1.64	16.75±0.02	28±0.25
F5	3.00±0.01	5.85±0.02	0.41±0.01	99±1.28	17.26±0.05	32±1.61
All values mentioned as mean ±SD; Number of trials (n)=3						

Table 4: Tablet dissolution apparatus parameters

Parameter	value
Dissolution medium	900 ml of 0.1N HCl
Temperature	37±0.5^{0}C
RPM	50
Tablet taken	One tablet (Known drug content).
Volume withdrawn	5 ml every 2 min
Volume made up to	5 ml
λ_{max}	224.2 nm
Beer's range	1-10 µg/ml
Dilution factor	10

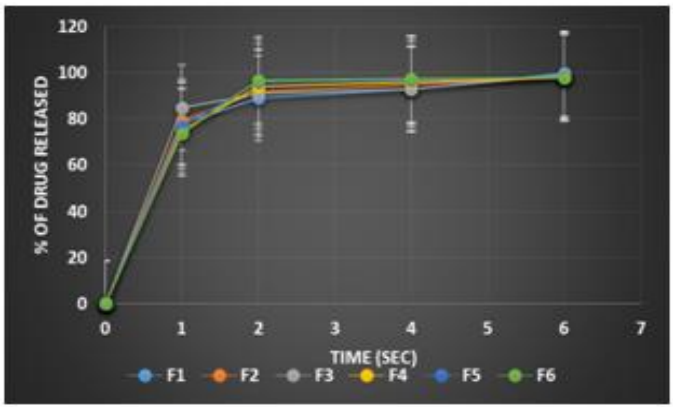

Figure 4: *In vitro* drug dissolution profile

4. Conclusion

This study concludes that mouth dissolving tablets of Atenolol can be developed by incorporating clove oil as flavor and local anesthetic on taste buds.

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