International Journal of Chemistry and Pharmaceutical Sciences

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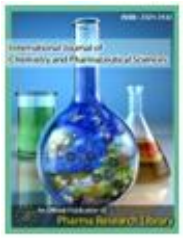

Research Article **Open Access**

Preparation and *In-Vitro* Characterization of Asenapine Maleate Fast Dissolving Sublingual Tablets

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A B S T R A C T

The present study was carried out on Asenapine Maleate Sublingual tablets using direct compression method. In this study super disintegrants were crospovidone, croscarmellose sodium, starch glycolate and remaining exciepients Magnesium stearate, Talc and mannitol were also used. The aim of the present study was to prepare and evaluate sublingual tablets by using Crospovidone, Croscarmellose sodium, Sodium Starchglycolate as super dissintegrants prepared by wet granulation method. The FT-IR confirmed no interaction between the drug and polymers. Thickness, Weight variations, hardness, friability, drug content estimation, wetting time, Water absorption ratio, *in vitro* dispersion time, *in vitro* disintegration time, *in vitro* dissolution studies of methanol were found to be uniform and reproducible.

Keywords: Asenapine Maleate, crospovidone, croscarmellose sodium, starch glycolate.

A R T I C L E I N F O

CONTENTS

Article History: Received 05 November 2016, **Accepted** 18 December 2016, **Available Online** 27 January 2017

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PAPER-QR CODE

Citation: D. Anudeep Reddy. Preparation and *In-Vitro* Characterization of Asenapine Maleate Fast Dissolving Sublingual Tablets. *Int. J. Chem, Pharm, Sci.*, 2017, 5(1): 06-10.

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1. Introduction

Drugs have been applied to the mucosa for topical application for many years. However, recently there has been interest in exploiting the oral cavity as a portal for delivering drugs to the systemic circulation. Notwithstanding the relatively poor permeability characteristics of the epithelium, a number are offered by this route of administration. Foremost among these are the avoidance of first pass metabolism, ease of access to the delivery site, and the opportunity of sustained drug delivery predominantly via the buccal tissues.

Oral mucosal drug delivery is an alternative method of systemic drug delivery that offers several advantages over both injectable and enteral methods. Because the oral mucosa is highly vascularised, drugs that are absorbed through the oral mucosa directly enter the systemic circulation, by passing the gastrointestinal tract and first-pass metabolism in the liver. For some drugs, this results in rapid onset of action via a more comfortable and convenient delivery route than the intravenous route. Not all drugs, however, can be administered through the oral mucosa because of the characteristics of the oral mucosa and the physicochemical properties of the drug.

The sublingual route usually produces a faster onset of action than orally ingested tablets and the portion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes. The main mechanism for the absorption of the drug in to oral mucosa is via passive diffusion into the lipoidal membrane. The tablet must dissolve quickly allowing the API to be absorbed quickly. It is designed to dissolve in small quantity of saliva. After the tablet is placed in the mouth below the tongue, the patient should avoid eating, drinking, smoking and possibly talking in order to keep the tablet in place. Swallowing of saliva should also be avoided since the saliva may contain dissolved drug. Bland exciepients are used to avoid salivary stimulation. Various techniques can be used to formulate rapidly disintegrating or dissolving tablets

Advantages

- Ease of administration to patients who refuse to swallow a tablet, such as pediatric, geriatric patients and psychiatric patients.
- Convenience in administration of drug and accurate dosing as compared to liquid formulations.
- Water is not required for swallowing the dosage form, which is convenient feature for patients who are traveling and do not have immediate access to water.
- Good mouth feels property helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
- Fast dissolution of medicament and absorption which will leads to rapid, onset of action.
- Some drugs are absorbed from the mouth pharynx and esophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- It provides advantages of liquid formulations in the form of solid dosage form.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

Disadvantage

- Since sublingual administration of drugs interferes with eating, drinking, and talking, this route is generally considered unsuitable for prolonged administration.
- Although this site is not well suited to sustained-delivery systems.
- Sublingual medication cannot be used when a patient is uncooperative or unconscious.
- The patient should not smoke while taking sublingual medication, because smoking causes vasoconstriction of the blood vessels. This will decrease the absorption of the medication.

2. Materials and Methods

Evaluation Parameters

Pre compression parameters

Angle of Repose:

It is performed to determine the flow rate of powder done by the funnel method. The powder was poured into a funnel which is fixed from height of 2cm of the plane surface. Circumference was drawn with a pencil on the graph paper and the radius of base of a pile was measured at 5 different points and average was taken for calculating Angle of repose using following formula:

$\Theta = \tan^{-1} H/R$

Θ=angle of repose

H=height of powder cone,

R=radius of powder cone

Angle of Repose less than 30^0 shows the free flowing property of the material.

Bulk Density (BD):

Bulk density was obtained by dividing the mass of powder by the bulk volume in cm^3. The sample of about 50 cm^3 of powder, previously been passed through a standard sieve no. 20, was carefully introduced into a 100 ml graduated cylinder. The cylinder was dropped at 2 second intervals on to hard wood surface three times from a height of 1 inch. The bulk density of each formulation was then obtained by dividing the weight of sample in grams by the final volume in cm^3 of the sample contained in the cylinder. It was calculated by using equation given below

$Df = M / Vp$

Where, Df = bulk density

M = weight of sample in grams

Vp = final volume of powder in cm^3

Tapped density (TD):

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times if the difference between these two volumes is less than 2%. If it is more than 2%, tapping was continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by

$Do = M / Vp$

Where,

Do = Tapped density,

M = weight of sample in grams

Vp = final volume of powder after tapping in cm^3

Carr's index:

The Carrs index is an indication of the compressibility of a powder. This is calculated by the formula

$$C = \frac{(\rho b - \rho t)}{\rho b} \times 100$$

Where, ρ_b is the bulk density ,
ρ_t is the tapped bulk density
A Carrs index greater than 25 is considered to be an indication of poor flow ability, and below 15, of good flow ability.

Hausners ratio:

The Hausners ratio is a number that is correlated to the flowability of a powder or granular material. The Hausner ratio is calculated by the formula
$H = \rho_t / \rho_b$
Where, ρ_b is the bulk density
ρ_t is the tapped density
Hausners ratio greater than 1.25 is considered to be an indication of poor flow ability.

Post compression parameters:

Weight variation test:

The tablets were selected randomly from each formulation and weighed individually to check for weight variation.

Thickness:

Randomly 5 tablets were taken from formulation batch and their thickness (mm) was measured using a Digital micrometer.

Hardness test:

The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in Kg/cm^2. 3 tablets were randomly picked from each formulation.

Friability test:

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche friabilator (Lab India, FT 1020). It is expressed in percentage (%). Ten tablets were initially weighed [$W_{(initial)}$] and transferred into friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions. The tablets were weighed again [$W_{(final)}$]. The percentage friability was then calculated by,

$$F = \frac{[W(initial) - W(fina\ )]}{W(initial)} \times 100$$

Drug Content estimation:

3 tablets were randomly selected, weighed and finely powdered and quantity of powder equivalent to one tablet was added to 100 ml of pH 6.8 Phosphate buffer in a volumetric flask. A volumetric flask was then placed on a rotary shaker. An aliquot of solution was filtered. Absorbance was measured using U.V Visible double beam spectrophotometer at respective wavelength against pH 6.8 Phosphate buffer as blank.

Wetting Time:

A piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A water-soluble dye phenolphthalein was added to the petridish. The dye solution was used to identify the complete wetting of the tablet surface. A tablet was carefully placed on the surface of tissue paper in the petridish at room temperature.
The time required for water to reach the upper surface of the tablets and completely wet them was noted as the wetting time. To check for reproducibility, the measurements were carried out in triplicates (n=3). The wetting time was recorded using a stopwatch.

Water absorption ratio (r):

The weight of the tablet before keeping in the petridish was noted (W_b) using digital balance. The wetted tablet from the petridish was taken and re weighed ($W_{a'}$) using the same. The Water absorption ratio, R, was determined according to the following equation:
$R = (W_a - W_b) / W_b * 100$
W_a= Weight of the tablet after absorption
W_b= Weight of the tablet before absorption

In vitro dispersion time:

In vitro dispersion time was determined by placing one tablet in a beaker containing 10 ml of pH 6.8 Phosphate buffer at 37±0.5°c and the time required for complete dispersion was determined.
To check for reproducibility, the measurements were carried out in triplicates (n=3). The dispersion time was recorded using a stop watch.

In vitro disintegration time:

In-vitro disintegration time was determined using Disintegration test apparatus (Lab india DT 1000). 3 tablets were randomly selected and disintegration test was performed in pH 6.8 phosphate buffer.

In vitro dissolution studies:

Apparatus used : USP II Lab India DS 8000
Dissolution Medium : 0.1N HCL
Dissolution Medium volume : 900ml
Temperature : 37^0C
Speed of paddle: 50rpm
Sampling Intervals: 5, 10, 15, 20, 30, 45 and 60 min
Sample withdrawn: 5ml

3. Results and Discussion

Drug and excipient compatability studies

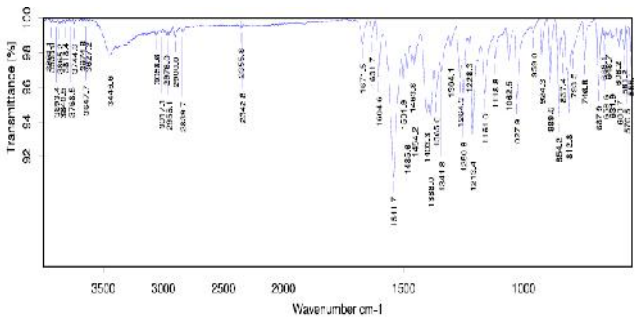

Figure 1: FTIR of pure drug of Asenapine Maleate

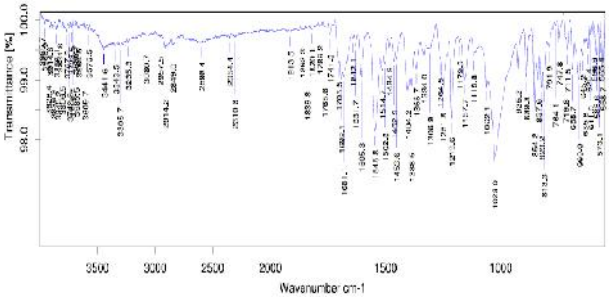

Figure 2: FTIR of optimized formulation

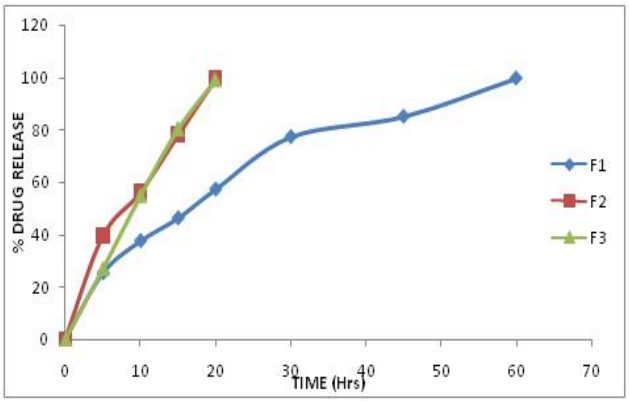

Figure 3: Dissolution profile of formulations prepared with Crospovidone as super disintegrate

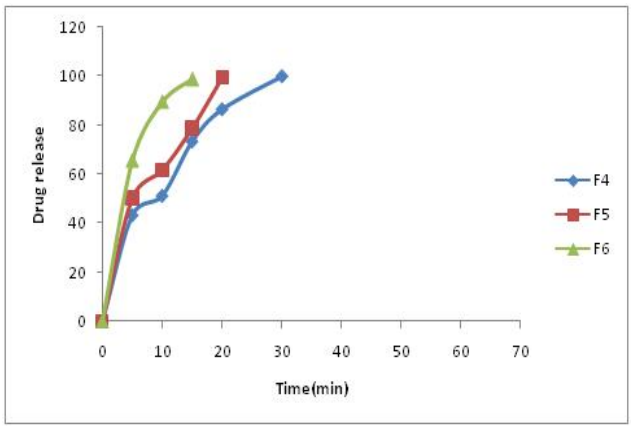

Figure 4: Dissolution profile of formulations prepared with Crosscarmellose sodium as super disintegrate

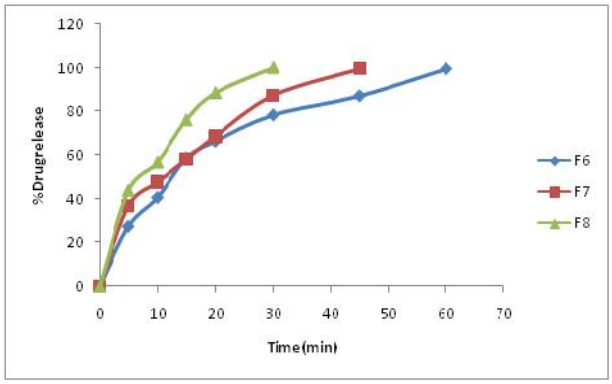

Figure 5: Dissolution profile of formulations prepared with Sodium starch glycolate as super disintegrate

4. Conclusion

The present study was carried out on Asenapine Maleate Sublingual tablets using direct compression method. In this study superdisintegrants were crospovidone, croscarmellose and sodium starch glycolate and remaining exciepients Magnesium stearate, Talc and mannitol were also used. Those all ingredients weighed and blended properly and compressed directly using rotary tablet compression machine using 6mm punches. All the pre and post compression parameters such as bulk density, tapped density, carrs index, hausners ratio, weight variation, thickness, hardness, friability, disintegration, drug content were found to be within limits. In vitro dissolution data revealed that, among all formulations F6 formulation containing croscarmellose sodium was shown maximum drug release at 15 min. Hence it was concluded as optimised formulation.

Table 1: Post compression parameters and post compression parameters

Formulation code	Weight variation (mg)	Thickness (mm)	Hardnes (kg/cm^2)	Friabiliy (%)	In-vitro disintegration time (sec)	Drug Content (%)
F1	99.6 ± 0.36	3.59 ± 0..01	2.5 ± 0.02	0.69 ± 0.05	19.33 ± 0.03	101.16 ± 0.84
F2	100.7 ± 0.44	3.56 ± 0.02	2.4 ± 0.03	0.54 ± 0.04	16.00 ± 0.08	99.25 ± 0.11
F3	99.9 ± 0.37	3.52 ± 0.02	2.5 ± 0.01	0.44 ± 0.03	14.00 ± 0.07	98.57 ± 0.154
F4	100.1 ± 0.29	3.58 ± 0.04	2.6 ± 0.01	0.57 ± 0.03	23.00 ± 0.04	99.34 ± 0.11
F5	99.4 ± 0.34	3.59 ± 0.01	2.5 ± 0.01	0.49 ± 0.04	18.33 ± 0.06	98.16 ± 0.16
F6	98.5 ± 0.41	3.64 ± 0.03	2.4 ± 0.02	0.54 ± 0.02	13.66 ± 0.04	99.55 ± 0.98
F7	100.01 ±0.12	3.59 ± 0.01	2.5 ± 0.02	0.53 ± 0.02	25.33 ± 0.05	99.23 ± 0.09
F8	99.32 ± 0.08	3.64 ± 0.03	2.4 ± 0.04	0.54 ± 0.01	20.66 ± 0.06	99.55 ± 0.12
F9	100.4 ± 0.21	3.59 ± 0.02	2.5 ± 0.03	0.49 ± 0.04	17.33 ± 0.07	100.16 ± 0.82

Table 2: *In-Vitro* Dissolution Data

Time (Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	25.3	39.5	26.91	43.16	50.23	65.48	27.4	36.7	43.8
10	37.6	56.3	54.91	51.03	61.57	89.33	40.6	47.5	56.72
15	46.3	78.2	80.45	73.15	78.61	98.56	58.6	57.9	76.16
20	57.3	99.8	99.23	86.28	99.21		66.3	68.4	88.4
30	77.3			99.72			78.4	87.1	100.02
45	85.1						87.1	99.3	
60	99.7						99.6		

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