Preparation and Characterization of Oral Fast Dissolving Tablet of Enalapril Maleate using Fenugreek Mucilage as a Superdisintegrant

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Abstract: There are various natural products which can be used for the formulation of various formulations. The current study was carried out by using the fenugreek mucilage as a natural superdisintegrant. The present study was carried out to enhance the drug absorption by dissolving the formulation in the oral cavity itself so that no drug gets metabolized. The prepared tablet was formulated by using fenugreek mucilage as well as sodium starch glycolate in different ratios. The results of pre-compression parameters were found to be satisfactory. The prepared tablet showed the disintegration time in the range of 56-120 sec, average weight was found to be 123-125mg, the average wetting time was found to 19.5 seconds, the thickness was found to be in the range of 2.1-2.9 mm, the hardness was found to be in the range of 2.6-3.5 kg/cm², the % friability was in the range of 0.48-0.65%, the % drug content was found to be in the range of 99.67-100.22 %, the % drug release was found to be above 90% in 30 minutes. From the study it was concluded that the fast oral dissolving tablet of enalapril maleate was formulated successfully with using natural superdisintegrant.

Keywords: Fast dissolving tablet, Fenugreek mucilage, Antihypertensive drug, Superdisintegrant, Oral dispersible tablet etc.

1. Introduction

The oral route of administration is taken into account because the most generally accepted route due to its convenience of self-administration, compactness and easy manufacturing. But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, resulting in patients incompance particularly just in case of pediatric and geriatric patients, but it also applies to people that are ill in bed and to those active working patients who are busy or travelling, especially those who have no access to water. [1]

Oral drug delivery system is the most convenient delivery system which does not needs to administer drugs with expertise in administration. Oral fast dissolving tablets are the one in which the tablet is dissolved in the mouth cavity and releases the drug in oral cavity which will increase the absorption. [2]

Enalapril is a prodrug belonging to the angiotensin-converting enzyme (ACE) inhibitor drug class that works on the renin-angiotensin-aldosterone system, which is responsible for the regulation of blood pressure and fluid and electrolyte homeostasis. Enalapril is an orally-active and long-acting nonsulphydryl antihypertensive agent that suppresses the renin-angiotensin-aldosterone system to lower blood pressure. It was developed from a targeted research programmed using molecular modeling. Being a prodrug, enalapril is rapidly biotransformed into its active metabolite. Enalapril is a prodrug belonging to the angiotensin-converting enzyme (ACE) inhibitor drug class that works on the renin-angiotensin-aldosterone system, which is responsible for the regulation of blood pressure and fluid and electrolyte homeostasis. Enalapril is an orally-active and long-acting nonsulphydryl antihypertensive agent that suppresses the renin-angiotensin-aldosterone system to lower blood pressure. It was developed from a targeted research programmed using molecular modeling. Being a prodrug; enalapril is rapidly biotransformed into its active metabolite, enalaprilat, which is responsible for the pharmacological actions of enalapril. The active metabolite of enalapril competitively inhibits the ACE to hinder the production of angiotensin II, a key component of the renin-angiotensin-aldosterone system that promotes vasoconstriction and renal reabsorption of sodium ions in the kidneys. Ultimately, enalaprilat works to reduce blood pressure and blood fluid volume, which is responsible for the pharmacological actions of enalapril. The active metabolite of enalapril competitively inhibits the ACE to hinder the production of angiotensin II, a key component of the renin-angiotensin-aldosterone system that promotes vasoconstriction and renal reabsorption of sodium ions in the kidneys. Ultimately, enalaprilat works to reduce blood pressure and blood fluid volume.
The present study was carried out in order to increase the drug absorption by preparing the fast dissolving tablet using fenugreek mucilage as a natural superdisintegrant. The tablet of enalapril maleate was prepared to bypass the hepatic first pass metabolism and to increase the concentration of drug in blood.

2. Methods and Materials

2.1. Materials:

Enalapril maleate was procured from yarrowchem, Mumbai, sodium starch glycolate, magnesium stearate, mannitol, vanillin, talc, and microcrystalline cellulose was procured from s.d.fine chemicals, Mumbai, and all other chemicals used were of analytical grade.

2.2. Extraction of Fenugreek Mucilage:

Fenugreek seed were collected from the local market and dried after that they were soaked in water for 2 hours. After that they were heated at 60 c and stirred by electrical stirrer at 500 rpm. Viscous liquid is formed. This liquid is filtered by muslin cloth. After that this process is repeated again

2.3. Isolation of Fenugreek Mucilage:

Acetone was added to the filtrate to suppress the mucilage from the viscous fluid then the suppressed mucilage is then filtered and dried gum is now ready to use as the natural disintegrants.

2.4. Preparation of tablet: The oral fast dissolving tablet of enalapril maleate was prepared using fenugreek mucilage as a natural super disintegrants by direct compression technique. The required quantity of drug was taken in a mortar pestle by adding the other ingredient in the ascending order of their weight. The mixer was triturated properly to get a free flowing powder and was passed through sieve #10. The mixture which was passed through the sieve was compressed on a nine station tablet punching machine. [3, 4, 5] The prepared tablet were collected and stored in a desiccator for further evaluation.

Table 1: Formulation Chart

<table>
<thead>
<tr>
<th>Ingredients (mg)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
<th>F10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril Maleate</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Fenugreek Mucilage</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Sodium Starch Glycolate</td>
<td>10</td>
<td>9</td>
<td>8</td>
<td>7</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
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<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Talc</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
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<td>5</td>
</tr>
<tr>
<td>Vanillin</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Micro Crystalline Cellulose</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>Total Weight</td>
<td>125</td>
<td>125</td>
<td>125</td>
<td>125</td>
<td>125</td>
<td>125</td>
<td>125</td>
<td>125</td>
<td>125</td>
<td>125</td>
</tr>
</tbody>
</table>

2.5 Evaluation parameters

2.5.1 Determination of Pre-compression Parameters

2.5.1.1 Bulk Density: It is the quantitative relation between a given mass of a powder and its bulk volume. Bulk density of the formulated powder was calculated by pouring about 2 g of formulated powder in a clean measuring cylinder, and initial volume was measured [4]. The bulk density was calculated by the subsequent equation.

\[
\text{Bulk Density} = \frac{\text{Mass}}{\text{Bulk volume}}
\]

2.5.1.2 Tap Density: The bulk density of a material is ratio of the mass to the volume of untapped powder sample.

\[
\text{Tap Density} = \frac{\text{Weight of powder}}{\text{Minimum volume occupied after tapping}}
\]

2.5.1.3 Carr’s Index: The cars index is an indication of the compressibility of a powder
Carr’s Index = \[
\frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}}
\]

2.5.1.4 **Hauser’s Ratio:** It is the number that is co-related to the flow ability of a powder or a granular material.

\[
\text{Hauser’s Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}
\]

2.5.1.5 **Wetting time:** Tablet is placed on a bit of tissue folded twice and kept during a petri dish containing 6 ml water, and therefore the time for compete wetting is measured. [5]

2.5.1.6 **Water absorption ratio:** This test is performed as like wetting time.

\[
R = 10 \left( \frac{W_a}{W_b} \right)
\]

Where, R = water absorption ratio, Wa = weight of tablet after water absorption, Wb = weight of tablet before water absorption.

2.5.2. **Determination of Post compression Parameters.**

2.5.2.1. **% drug content:** The films were tested for drug content uniformity by UV-spectrophotometric method. Each tablet was placed in 10 ml volumetric flask and diluted with phosphate buffer 6.8 up to 10 ml. The absorbance of the solution was measured at 216nm using UV visible spectrophotometer (shimadzu UV-1800). The percentage of drug content was determined.

2.5.2.2. **% Friability:** Friability is the tendency to break. This tendency is normally confined to uncoated tablet and surfaces during handling or subsequent storage.

\[
\% \text{ Friability} = (1 - \frac{W_0}{W}) \times 100
\]

Where, WO= weight of tablet before the test, W= weight of the tablet after the test

2.5.2.3. **% Drug release:** The process by which the drug loaded in the body through diffusion, dissolution of the matrix releasing the drug in solution.

2.5.2.4. **Dissolution / % Cumulative Drug Release:** The dissolution of enalapril maleate oral fast dissolving tablet was studied in USP XXIV dissolution test apparatus 900ml phosphate buffer 6.5 solutions was used as dissolution medium. The stirrer of apparatus was adjusted to rotate at 50 pm. The temperature of the dissolution medium was maintained at 37oC throughout the experiment. One film was used in each test. Samples after the dissolution medium (5ml) were withdrawn using syringe. The solution was filtered was with whatman filter paper. Samples were withdrawn after 2, 5, 10, 15, 20, 25, 30-minute intervals of time and analyzed for drug release by measuring the absorbance at 216nm. [6]. The volume withdrawn at whenever interval was replaced was replace with a fresh quantity of dissolution medium cumulative percent enalapril maleate was calculated and plotted against the clock.

3. **Results:**

3.1 **Drug Excipient Interaction Studies:** From the study carried out by Fourier transform infrared spectroscopy and from the results it was found that there was no chemical or physical interaction seen. Therefore, it was concluded that there is no drug excipient incompatibility. **Method 1: Drug excipient compatibility:**

3.1.1 **Fourier transform infrared spectroscopy**

The FTIR spectroscopy was employed to further characterize the possible interaction between drug and excipient in the solid state on the infrared spectrophotometer (Shimadzu Affinity-I) by conventional KBr plate method. 1:1 ratio of drug and KBr. IR spectrum of drug was recorded in the frequency range of 400-4000 cm\(^{-1}\). The important peaks were recorded from the data and were matched with standard readings of FTIR. [7]
Figure 1: FTIR of Enalapril Maleate

Figure 2: FTIR of Enalapril Maleate + Fenugreek Gum Powder
3.2 Standard calibration curve - From the standard calibration curve the equation follows the beer’s lamberet law. And the equation was found to be \( y = 0.0131x + 0.0064 \) and the value of \( R^2 = 0.9989 \)

From solution having concentration 100 µg / ml aliquots of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 ml were pipette out into volumetric flasks. The volume was made up to the mark with phosphate buffer 6.8 to get final concentration of 10, 20, 30, 40, 50, 60, 70, 80, 90 and 100 µg /ml respectively. The absorbance of every concentration was measured at 216.00nm. [8]

3.3 Percent Cumulative Drug Release - The drug release study was carried out and the results were found to be that the drug gets release in the expected period of time i.e. more than 50% of drug was released in less than 20 minutes. The % cumulative drug release of F1- F10 was found to be in the range of 98.35-99.67 % in 30 minutes. The cumulative drug release time was found to be less than 30 minutes for the total drug release from the prepared formulation.
Table 2: Evaluation parameters

<table>
<thead>
<tr>
<th>Batch No.</th>
<th>Average Weight (mg)</th>
<th>Thickness (mm)</th>
<th>Hardness $^2$ (kg/cm²)</th>
<th>Friability (%)</th>
<th>Drug Content (%)</th>
<th>Disintegration Time (Sec)</th>
<th>% Drug Release (After 30min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>123.01</td>
<td>2.1</td>
<td>2.6</td>
<td>0.48</td>
<td>99.82</td>
<td>56</td>
<td>99.12</td>
</tr>
<tr>
<td>F2</td>
<td>123.2</td>
<td>2.15</td>
<td>2.5</td>
<td>0.51</td>
<td>99.67</td>
<td>58</td>
<td>98.35</td>
</tr>
<tr>
<td>F3</td>
<td>124.2</td>
<td>2.28</td>
<td>2.4</td>
<td>0.42</td>
<td>99.14</td>
<td>57</td>
<td>99.47</td>
</tr>
<tr>
<td>F4</td>
<td>123.8</td>
<td>2.24</td>
<td>2.5</td>
<td>0.52</td>
<td>99.14</td>
<td>59</td>
<td>99.12</td>
</tr>
<tr>
<td>F5</td>
<td>124</td>
<td>2.21</td>
<td>2.6</td>
<td>0.57</td>
<td>99.50</td>
<td>64</td>
<td>99.08</td>
</tr>
<tr>
<td>F6</td>
<td>124.2</td>
<td>2.35</td>
<td>2.7</td>
<td>0.51</td>
<td>100</td>
<td>56</td>
<td>99.67</td>
</tr>
<tr>
<td>F7</td>
<td>124.5</td>
<td>2.41</td>
<td>3.2</td>
<td>0.59</td>
<td>99.71</td>
<td>61</td>
<td>99.38</td>
</tr>
<tr>
<td>F8</td>
<td>125.8</td>
<td>2.6</td>
<td>3.5</td>
<td>0.61</td>
<td>100</td>
<td>60</td>
<td>99.47</td>
</tr>
<tr>
<td>F9</td>
<td>125.4</td>
<td>2.8</td>
<td>3.4</td>
<td>0.64</td>
<td>99.85</td>
<td>63</td>
<td>99.29</td>
</tr>
<tr>
<td>F10</td>
<td>125.6</td>
<td>2.9</td>
<td>3.5</td>
<td>0.65</td>
<td>99.68</td>
<td>57</td>
<td>99.24</td>
</tr>
</tbody>
</table>

Table No. 3: Pre compression evaluation parameter of optimize batch

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulk density</td>
<td>1.42</td>
</tr>
<tr>
<td>Tapped density</td>
<td>1.66</td>
</tr>
<tr>
<td>Carr’s index</td>
<td>14.45</td>
</tr>
<tr>
<td>Hausner’s ratio</td>
<td>1.16</td>
</tr>
<tr>
<td>Wetting time</td>
<td>2 min 50 sec</td>
</tr>
<tr>
<td>Water absorption ratio</td>
<td>60</td>
</tr>
</tbody>
</table>

4. Discussion: The prepared oral fast dissolving tablets of enalapril maleate were prepared by direct compression and were evaluated for the different parameters which shows that the F6 as the optimized formulation as it shows minimum disintegration time and maximum drug content with the fastest drug release as compared with other formulation.

The pre compression parameters of the tablet show satisfactory results. And the post compression factors are as follows, the % drug content was found to be 99.67, the disintegration time was 56 seconds, average weight was found to be 124.4mg, thickness was found to be 2.35mm, hardness was found to be 2.7, the % friability was found to be 0.51%, and the % drug release was found to be 99.67% in 20 minutes.

The oral fast dissolving tablet of enalapril maleate was prepared by using fenugreek mucilage and sodium starch glycolate as a superdisintegrant in various ratios in order to increase the bioavailability of the drug so that maximum amount of drug reaches the blood. The study shows satisfactory results and the drug release was more than 50% in less than 10 minutes. The % drug content
was found to be satisfactory and the % drug release was found to be maximum in the formulation F6 therefore it was found to be optimum as compared to other formulations.

5. Conclusion:

The prepared oral fast dissolving tablets of enalapril maleate was prepared in order to increase the bioavailability of the drug and therefore this work was proved to increase the drug release at a faster rate and also to increase the bioavailability. The fenugreek mucilage was proved to be a better disintegrating agent than the sodium starch glycolate. So the study was completed with the result that the fenugreek mucilage can be a better alternative than the other disintegrants.

References:


