FORMULATION CHARACTERIZATION AND EVALUATION OF MOUTH DISSOLVING TABLET OF LISIONPRIL BY USING DEHYDRATED BANANA POWDER AS A NATURAL POLYMER

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ABSTRACT

The purpose of this research was to introduce and evaluate natural excipient that has versatile property in the oral disintegrant and immediate release formulations. This natural excipient was used as disintegrant in the formulation of orodispersible tablets of some model drugs such as lisinopril, Physicochemical studies such as swelling power and solubility, particle size distribution and some other physical evaluations was done on the natural excipient to ensure the suitability to incorporate for such formulation. Five formulations of each drug were formulated in different ratios of natural excipient and Croscaramellose (Superdisintegrant) and the final formulation of all drug used natural excipient alone as binder, diluent and disintegrant. All the formulations are subjected for invitro evaluations such as wetting time, water absorption ratio, invitro dispersion time and disintegration time, etc. Almost same results were obtained on formulations with or without the super disintegrant. Therefore, we conclude that the natural excipient proposed can be used as binder, diluent and disintegrant in oral disintegrating tablets and immediate release dosage forms. Mainly the natural excipient used is biocompatible, cost effective and provides as nutrition supplements.

KEYWORDS: Natural excipient, Patient friendly dosage form, Diluent, Disintegrant, Binder, In vitro stu.

INTRODUCTION

Recent advances in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is fast dissolving tablets. LISONOPRIL is a drug of
the angiotensin converting enzyme (ACE) inhibitor class that is primarily used in treatment of hypertension, congestive heart failure, heart attacks and also in preventing renal and retinal complications of diabetes. The present study involved the comparison between various synthetic superdisintegrants in combination Dehydrated banana powder (DBP). Banana is also called Plantain. DBP is prepared from the variety of banana called Ethan and nenthran (nenthra vazha) belonging to the family Musaceae. It contains vitamin A so used in the treatment of gastric ulcer and diahorrea. It also contains vitamin B6 release rate of drug from the tablet formulation increases and used in the treatment of chronic disorder at the initial stage of chronic attack. The unripr fruit contains tannins. the enzymes present in the banana is amylase, invertase, protease, catalase, peroxidase because of non-toxicity and are renewable source. If the natural source is abundantly available then the resultant excipients is also economical. With this view, the research was undertaken in the area of natural excipients.

MATERIALS AND METHODS

Lisinopril were obtained as a gift sample from Modern Lab., Indore (M.P). Croscarmellose sodium, crospovidone, sodium starch glycolate, mannitol, magnesium stearate were purchased from S.D. Fine Chemicals, India.

Materials

Table No. 1: List of Materials.

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Material</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Lisinopril dihydrate</td>
<td>Meckloides, pharma.</td>
</tr>
<tr>
<td>2.</td>
<td>Dehydrated banana powder</td>
<td>Tiruanantapuram Karanataka.</td>
</tr>
<tr>
<td>3.</td>
<td>Sodium starch glycolate</td>
<td>Meckloides pharma.</td>
</tr>
<tr>
<td>4.</td>
<td>Mannitol</td>
<td>Loba Chemie, Mumbai</td>
</tr>
<tr>
<td>5.</td>
<td>Microcrystalline Cellulose</td>
<td>Loba Chemie, Mumbai</td>
</tr>
<tr>
<td>6.</td>
<td>Magnesium Stearate</td>
<td>Pure Chem Laboratories, Pune</td>
</tr>
<tr>
<td>7.</td>
<td>Sodium Saccharine</td>
<td>Research Laboratories Fine Chem Industry, Mumbai</td>
</tr>
</tbody>
</table>

METHODS

Direct compration method is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. Directly compressed tablet’s disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agent.
Drug excipients interaction study\(^3\)

Infra red spectrometry is a useful analytical technique utilized to check the chemical interaction between the drug and the other excipients used in the formulations. The samples (drugs blended with DBP and stored at room temperature for a week) were powdered and intimately mixed with dry powdered potassium bromide. The powdered mixture was taken in a diffuse reflectance sampler and the spectra recorded by scanning in the particular wavelength region (4000 – 400 cm\(^{-1}\)) using Shimadzu FTIR spectrometer. The IR spectrum of drug was compared with that of the physical mixture of the drug and excipients used to check for any possible drug-excipients interaction.
Figure: FTIR spectra of dehydrated banana powder.

Figure: DSC Thermogram of Physical Mixture Formulation of mouth dissolving tablet (10 mg) Preparation of fast disintegrating tablets.

Punch diameter: 8 mm
Average tablet weight: 250 mg
Punch shape: Flat

Tablet batches were prepared by using direct compression method. All the product and process variables like mixing time and hardness are kept as practically constant. Quantity of drug, microcrystalline cellulose, sodium starch glycolate, banana powder, sodium saccharine and mannitol were accurately weighed and mixed by gentle triturating with magnesium stearate. Then blend was compressed into tablets using flat faced punches of 9mm diameter by keeping hardness in between 2 to 3 kg/cm².
Table No. 2: Formula for mouth dissolving tablet of lisinopril.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>P4</th>
<th>P5</th>
<th>P6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Banana powder</td>
<td>60</td>
<td>70</td>
<td>80</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SSG</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Mannitol</td>
<td>120</td>
<td>110</td>
<td>100</td>
<td>173</td>
<td>171</td>
<td>168</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Sodium saccharine</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

EVALUATION PARAMETERS

Evaluation of the tablets

All prepared matrix tablets were evaluated for its uniformity of weight, hardness, friability and thickness according to official methods.

Hardness

The crushing strength of the tablets was measured using a Monsanto hardness tester. Three tablets from each formulation batch were tested randomly and the average reading noted.

Friability

Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula, Percentage friability = Initial weight – Final weight x 100 Initial weight.

Weight Variation

Randomly, twenty tablets were selected after compression and the mean weight was determined. None of the tablets deviated from the average weight by more than ±7.5% (USP XX).

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 20mg of Lisinopril was dissolved in 100ml of 0.1N hydrochloric acid, filtered, diluted suitably and analyzed for drug content at 246nm using UV-Visible spectrophotometer (UV 160 Shimadzu, Japan).
Wate abssorption ratio (R)
The weight of the tablet prior to placement in the petri dish was noted (\(wb\)) utilizing a Shimadzu digital balance. The wetted tablet was removed and reweighed (\(wa\)). Water absorption ratio, \(R\), was then determined according to the following equation.

Invitro dispersion time\(^{[18]}\)

*Invitro* dispersion time was measured by dropping a tablet in a 10ml measuring cylinder containing was cerried out.

In vitro disintegration time

10 ml of water at 25°C was placed in a petri dish of 10 cm diameter. The tablet was then carefully positioned in the center of the petri dish and the time required for the tablet to completely disintegrate into fine particles was noted.

<table>
<thead>
<tr>
<th>Batch Parameter</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angle of repose (°)</td>
<td>35.71 ± 0.49</td>
<td>34.74 ± 0.54</td>
<td>36.52 ± 0.58</td>
<td>36.39 ± 0.71</td>
<td>35.71 ± 0.49</td>
<td>34.74 ± 0.54</td>
</tr>
<tr>
<td>Bulk density (g/ml)</td>
<td>0.7855 ± 0.01</td>
<td>0.784 ± 0.008</td>
<td>0.804 ± 0.009</td>
<td>0.805 ± 0.007</td>
<td>0.7855 ± 0.01</td>
<td>0.784 ± 0.008</td>
</tr>
<tr>
<td>Tap density (g/ml)</td>
<td>0.844 ± 0.01</td>
<td>0.843 ± 0.012</td>
<td>0.845 ± 0.012</td>
<td>0.849 ± 0.016</td>
<td>0.844 ± 0.01</td>
<td>0.843 ± 0.012</td>
</tr>
<tr>
<td>Carr’s index (%)</td>
<td>4.853 ± 0.25</td>
<td>4.721 ± 0.025</td>
<td>4.877 ± 0.019</td>
<td>4.906 ± 0.031</td>
<td>4.853 ± 0.25</td>
<td>4.721 ± 0.025</td>
</tr>
<tr>
<td>Hausner’s ratio</td>
<td>1.07 ± 0.08</td>
<td>1.057 ± 0.16</td>
<td>1.19 ± 0.20</td>
<td>1.193 ± 0.20</td>
<td>1.07 ± 0.08</td>
<td>1.057 ± 0.16</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Hardness Kg/cm(^2) ± S.D.</th>
<th>Thickness (mm) ± S.D.</th>
<th>Weight variation (mg) ± S.D.</th>
<th>% Friability</th>
<th>%Drug Content ± S.D.</th>
<th>In-vitro DT (Min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>2.16 ± 0.2886</td>
<td>2.896 ± 0.015</td>
<td>5.44</td>
<td>0.512 ± 0.014</td>
<td>99.51 ± 0.56</td>
<td>1.75 ± 0.147</td>
</tr>
<tr>
<td>F2</td>
<td>2.16 ± 0.2886</td>
<td>2.896 ± 0.015</td>
<td>2.29</td>
<td>0.227 ± 0.014</td>
<td>100.51 ± 0.56</td>
<td>1.54 ± 0.147</td>
</tr>
<tr>
<td>F3</td>
<td>2.16 ± 0.2886</td>
<td>2.896 ± 0.015</td>
<td>2.92</td>
<td>0.251 ± 0.014</td>
<td>98.51 ± 0.56</td>
<td>1.45 ± 0.147</td>
</tr>
<tr>
<td>F4</td>
<td>2.16 ± 0.2886</td>
<td>2.896 ± 0.015</td>
<td>2.45</td>
<td>0.245 ± 0.014</td>
<td>99.51 ± 0.56</td>
<td>1.74 ± 0.147</td>
</tr>
<tr>
<td>F5</td>
<td>2.16 ± 0.2886</td>
<td>2.896 ± 0.015</td>
<td>5.35</td>
<td>0.212 ± 0.014</td>
<td>99.46 ± 0.56</td>
<td>1.68 ± 0.147</td>
</tr>
<tr>
<td>F6</td>
<td>2.16 ± 0.2886</td>
<td>2.896 ± 0.015</td>
<td>5.78</td>
<td>0.312 ± 0.014</td>
<td>99.92 ± 0.56</td>
<td>1.51 ± 0.147</td>
</tr>
</tbody>
</table>
**Invitro drug release studies**

*In-vitro* drug release rate of lisinopril mouth dissolving tablets were carried out using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus (Paddle method). The dissolution test was carried out using 900 ml of 6.8 pH phosphate buffer, at 37±.50C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 1, 2, 3, 4, 5, 6, 7 and 8 min. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through Whatman filter paper No 40 and analyzed for lisinopril after appropriate dilution by UV spectrophotometer at 215 nm. The percentage drug release was calculated using an equation obtained from the calibration curve. The results are presented in figures. The dissolution testing was carried out in triplicate.

![Invitro drug release of the tablet](image)

**Figure:** *In-vitro* dissolution study of lisinopril in PBS pH 6.8.

**SEM Images of Musa paradisiaca L. (SP2) Powder.**

**SUMMERY AND CONCLUSION**

**9.2 SUMMERY**

Fast dissolving tablets get dissolved or disintegrated in mouth quickly. This characteristics feature is useful for patient compliance. The time required for complete wetting was few seconds hence tablets disintegrate rapidly in oral cavity. Thus the release rate of lisinopril can be significantly enhanced by super disintegrating agent. lisinopril is an Angiotensin II receptor blocker, used in treatment of moderate to severe hypertension. It is white crystalline powder and practically soluble in water it is reported to be rapidly and fully absorbed following oral administration but lisinopril t<sub>max</sub> is achieved at about 12 hrs with oral administration suggesting a need for a delivery system with rapid achievement of t<sub>max</sub>. The present research work deals with the investigation of dehydrated banana powder as a natural
superdisintegrants. This natural excipient was used as disintegrant in the formulation of orodispersible tablets of some model drugs such as lisinopril. Physicochemical studies such as swelling power and solubility, and some other physical evaluations was done on the natural excipient to ensure the suitability to incorporate for such formulation. Six formulations batches were formulated in different ratios of natural excipient. SSG (Superdisintegrant) were used for comparison. All the formulations are subjected for \textit{in vitro} evaluations such as wetting time, water the purpose of this research was to introduce and evaluate natural excipient that has disintegrating property in the oral disintegrant and immediate release formulations. Evaluation such as absorption ratio, \textit{in vitro} dispersion time and disintegration time, etc. Almost different results were obtained with natural polymer and synthetic polymer.

9.2 CONCLUSION
The F1, F2 and F3 batches were formulated using DBP alone which showed almost equal and better results in terms of the evaluations such as disinterring time, wetting time, water absorption ratio, \textit{in vitro} dispersion time and percent drug release with the formulation contain superdisintegrant (SSG). Swelling and Solubility study showed that the DBP have enough swelling and solubility properties and from the results obtained from the formulations indicated that the DBP can be incorporated alone as disintegrant in the formulation of orodispersible tablets of some model drugs such as lisinopril. Physicochemical studies such as swelling power and solubility, particle size distribution and some other physical evaluations was done on the natural excipient to ensure the suitability to incorporate for such formulation. Six formulations of each drug were formulated in different ratios of natural excipient and SSG (Superdisintegrant). Hence it can be concluded that natural super disintegrants should be preferred as having nutritive value as well as cost benefit in formulation and development of orodispersible tablet than synthetic polymer.

REFERENCE
2. Wallis, TE. Textbook of Pharmacognosy; CBS publishers and distributors; New Delhi; 5\textsuperscript{th} Ed., 2005; 51-52.
4. Evans, WC. Trease and Evans Pharmacognosy; Elsevier publication; 15th Ed., 2002; 442.
15. Mere sing prepration and evaluation of powder of unripe fruit of various varitirs of musa paradiasisca as a tablet disintegrants, 3: 113-125.


35. The Merck Index; An encyclopedia of chemicals, drugs and biological; 14th Ed.; published by Merck research laboratory; Division of Merck and company; USA, 2006; 1754.


38. Indian pharmacopoeia; Government of India; Ministry of health and family welfare; The Indian Pharmacopoeial Commission; Ghaziabad, 2010; 2 and 3: 1625, 1633, 1695, 2082, 2135.


40. Indian Pharmacopoeia; Government of ministry of health & family welfare; The Indian Pharmacopoeia Commission, Ghaziabad, 2010; 1: 1593.


42. British Pharmacopoeia; Medicinal and pharmaceutical standards, 2009; 2: 1274, 1287, 1880.


