INTRODUCTION

Orally administered dosages form e.g. tablets, capsules are convenient dosage form for many drugs but they are challenging to formulate if the active substances has poor dissolution or low bioavailability. Polymer coating enables the formulation of mouth dissolving and taste masking of bitter taste drugs thereby giving better patient compliance. Most pharmaceutical forms for oral administration are formulated for direct ingestion, for chewing, for prior dispersion and for dissolution in water; some of them are absorbed in mouth (sublingual or buccal tablets). Elderly individuals have difficulty in swallowing when prescribed in conventional tablet and capsule form. The problem of swallowing is also evident in pediatrics, psychiatric as well as traveling patients who may not have ready access to water. The rapidly disintegrating tablet in mouth or orodispersible tablets overcome all the above problems and thus offer an alternate form of oral medication, which provide patients with a more convenient means of taking their medication and other excipients at optimum concentration.

KEYWORDS: Crosspovidone, Fast disintegrating tablet, Lisinopril, Superdisintegrants, Wetting time.

MATERIALS AND METHODS

Materials

Lisinopril was gifted from Dr.Reddy's Laboratories (Hyderabad, India). Crosspovidone, Croscarmellese sodium were obtained from SD Fine Chem. LTD (Mumbai). Micro crystalline cellulose was purchased from (S.D. Fine Chemicals, Mumbai). Magnesium stearate and talc were obtained from (Loba Chemicals, Mumbai). All other ingredients used were of analytical grade.

Taste masking and Preparation of fast disintegrating tablets of Lisinopril by kneading technique.

Required quantity of lisinopril was weighed and sifted through # 40 ASTM SS sieve. Complexation with beta-cyclodextrin was done. Initially, Drug: beta-cyclodextrin ratio was 1:5. Slurry of beta-cyclodextrin was prepared by taking beta-cyclodextrin: water (5 gm: 5 ml), stirred for 30 minutes. Drug was added, stirred for 2 hours, dried it. Mixed the above powder base with sifted avicel, crosspovidone, croscarmellese sodium and other excipients by tumbling. All the ingredients were mixed thoroughly for not less than 5 minutes and until to get uniform mixed powder. Finally compressed the lubricated powder base on 10 station rotary tabletting machine.

Table 1: Composition of different batches of fast disintegrating Lisinopril tablets

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Formulation code F-1</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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<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>B- Cyclodextrin</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Avicel</td>
<td>79</td>
<td>69</td>
<td>69</td>
<td>69</td>
<td>69</td>
<td>69</td>
</tr>
<tr>
<td>Lactose</td>
<td>79</td>
<td>69</td>
<td>69</td>
<td>69</td>
<td>69</td>
<td>69</td>
</tr>
<tr>
<td>Starch powder</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Crosscarmellese sodium</td>
<td>05</td>
<td>05</td>
<td>05</td>
<td>05</td>
<td>05</td>
<td>05</td>
</tr>
<tr>
<td>Crosspovidone</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sodium saccharin</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
</tr>
<tr>
<td>Vanillin</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
</tr>
<tr>
<td>Talc</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
<td>02</td>
</tr>
</tbody>
</table>

**Keywords**: Crosspovidone, Fast disintegrating tablet, Lisinopril, Superdisintegrants, Wetting time.
Evaluation of granules

The angle of repose was measured by using funnel method\(^{12}\), which indicates the flowability of the granules. Loose bulk density (LBD) and tapped bulk density (TBD) \(^{14}\) were measured using the formula:

\[
\text{LBD} = \frac{w_b}{V_b}, \quad \text{TBD} = \frac{w_b}{V_b},
\]

where \(w_b\) is the weight of the powder / volume of the packing. TBD = weight of the powder / tapped volume of the packing. Compressibility index \(^{14}\) of the granules was determined by using the formula: CI (%) = \(\left[\frac{(\text{TBD} - \text{LBD})}{\text{TBD}}\right] \times 100\).

The physical properties of granules were shown in Table 2.

### Table 2: Data for blend evaluation of formulation (F-1 to F-6)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Formulation code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F-1</td>
</tr>
<tr>
<td>Angle of repose (°)</td>
<td>25.59 ± 0.41</td>
</tr>
<tr>
<td>Loose bulk density (g/ml)</td>
<td>0.397 ± 0.27</td>
</tr>
<tr>
<td>Tapped bulk density (g/ml)</td>
<td>0.563 ± 0.48</td>
</tr>
<tr>
<td>Compressibility index (%)</td>
<td>14.78 ± 0.53</td>
</tr>
</tbody>
</table>

### Evaluation of the tablets

All prepared matrix tablets were evaluated for its uniformity of weight, hardness, friability and thickness according to official methods \(^{15}\), shown in Table 3.

#### 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.

\[
\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100
\]

#### 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 20 mg of Lisinopril was dissolved in 100 ml of 0.1 N hydrochloric acid, filtered, diluted suitably and analyzed for drug content at 246 nm using UV-Visible spectrophotometer (UV 160, Laabodia, Mumbai, India).

#### Wetting time

A piece of tissue paper (12 cm x 10.75 cm) folded twice was placed in a petri dish and the time required for the tablet to completely disintegrate into fine particles was noted.

#### Water absorption 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 (\(w_a\)). Water absorption ratio, \(R\) was then determined according to the following equation.

\[
R = \frac{\text{w_a} - \text{w_b}}{\text{w_b}} \times 100
\]

#### In-vitro dispersion time

In-vitro dispersion time was measured by dropping a tablet in a 10 ml measuring cylinder containing 6 ml of 0.1 N hydrochloric acid.

#### 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.

#### In-vitro drug release studies

In-vitro drug release studies of all the formulations were carried out using tablet dissolution test apparatus (USP XXII type II Electrolab, Mumbai, India) at 50 rpm. 0.1 N hydrochloric acid was used as the dissolution media with temperature maintained at 37±1°C. Samples were withdrawn at different intervals, diluted suitably and analyzed by 246 nm for cumulative drug release using an ultraviolet visible spectrophotometer (Labindia, Mumbai, India). The study was performed in triplicate.

### Table 3: Thickness, hardness, friability, drug content, weight variation, wetting time, water absorption ratio, in vitro dispersion time, in vitro disintegration time of Lisinopril fast disintegrating tablets

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Formulation code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F-1</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>2.18 ± 0.14</td>
</tr>
<tr>
<td>Hardness (kg/cm²)</td>
<td>3.248 ± 1.7</td>
</tr>
<tr>
<td>Friability (%)</td>
<td>0.487 ± 0.541</td>
</tr>
<tr>
<td>Drug content (%)</td>
<td>97.9 ± 0.18</td>
</tr>
<tr>
<td>Weight variation (mg)</td>
<td>201.35</td>
</tr>
<tr>
<td>Wetting time (sec)</td>
<td>52</td>
</tr>
<tr>
<td>Water absorption ratio</td>
<td>93</td>
</tr>
<tr>
<td>In vitro dispersion time (sec)</td>
<td>63</td>
</tr>
<tr>
<td>In Vitro disintegrating time (sec)</td>
<td>58</td>
</tr>
</tbody>
</table>
Stability studies

Short term stability studies on the optimum formulation (F6) were carried out by storing the tablets (in amber colored rubber stoppered vials) at 40°C/75% RH for 3 weeks. At every 1 week intervals, the tablets were examined for physical changes, properties, drug content and in vitro release studies. 

![In-vitro release profile of formulations F-1 to F-6.](image1)

**Fig. 1:** Comparison of *In-vitro* release profile of Lisinopril from formulations F-1 to F-6.

![Fourier transform infrared spectra of A: Pure Lisinopril](image2)

**Fig. 2:** Fourier transform infrared spectra of A: Pure Lisinopril

B: Lisinopril tablet (From top to bottom)

![Process of disintegration of F-6 FDTS](image3)

**Fig. 2:** Process of disintegration of F-6 FDTS
RESULTS AND DISCUSSION

The supplied drug passed the various tests of identification and analysis. The pure drug Lisinopril and the solid admixture of drug and various excipients used in the preparation of fast dispersible tablet formulations were characterized by FT-IR spectroscopy to know the comparability, figure-2. The FT-IR study did not show any possibility of interaction between Lisinopril and superdisintegrants used in the fast dispersible tablets. Since the flow properties of the powder mixture are important for the uniformity of the mass of the tablets, the flow of the powder mixture was analyzed before compression of the tablets. The results of angle of repose and compressibility index (%) ranged from (24.65 ± 0.72 to 28.49 ± 0.23) and (14.72 ± 0.87 to 17.4 ± 0.28), respectively. The results of bulk loose density and tapped bulk density ranged from (0.397 ± 0.27 to 0.562 ± 0.43) and (0.563 ± 0.48 to 0.692 ± 0.31), respectively. The results of angle of repose (<30°) indicate good flow mechanical strength, acceptable taste and smaller disintegration time. The wicking type of disintegration of crospovidone tablets may be attributed due to the wicking type of crospovidone F‐4 to F‐6. The disintegration time of crospovidone tablets are not significant change when compared with zero day of formulation dissolution profile of oral disintegrating tablets. FTIR studies revealed that there was no shift in peaks, indicating there is no interaction between Lisinopril and other ingredients used. Among two superdisintegrants used cross povidone showed better performance in disintegration time when compared to croscarmellose sodium. In the in vitro dissolution study of F-6 shows 35.25% release of drug in less than two minutes and 99.46% with in 60 minutes So the formulation of F6 was found to be best among all other formulations, because it has exhibited faster wetting time, good taste and faster disintegration time when compared to all other formulations.

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REFERENCES