Introduction

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. For the past one decade, there has been an enhanced demand for more patient-friendly and compliant dosage forms. However, this form of dosage has some limitation like motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, but one important drawback is ‘dysphagia’ or difficulty in swallowing. Particularly, the difficulty is experienced by paediatric and geriatric patients in swallowing conventional tablets, which lead to poor patient compliance. Mouth dissolving tablets have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance.

Tolperisone hydrochloride is a centrally acting muscle relaxant having half life of 1.5 to 2.5 h, bioavailability of 20% and more stable in acidic than basic media with high solubility in water. It is recently prescribed by physician for the treatment of back pain, arthritis of large joints (degeneration of cartilage tissue in joints), spastic muscle cramps, paralysis, and muscle pain. Tolperisone hydrochloride has a short elimination half-life; it is rapidly and completely absorbed from the gastrointestinal tract. Conventional Tolperisone tablet available in the market are not suitable for acute pain and inflammatory conditions where quick onset of action of drug is required. The rapidly disintegrating tablets in oral cavity can be swallowed with a small amount of water or saliva. Hence, an attempt was made to improve the dissolution of Tolperisone through the formulation of mouth-dissolving tablets with appropriate mechanical strength, which would disintegrate in oral cavity, in less than 30 seconds, and would provide an immediate relief from pain due to its faster dissolution in gastrointestinal tract.

Materials and Methods

2.1 Materials

Tolperisone was obtained from Aristo Pharma Ltd. Baddi (H.P.). Crospovidone and sodium starch glycolate were obtained as gift samples from Micro Labs, Bangalore.

2.2 Methods

2.2.1 Preparation of mouth dissolving tablets

Tablets of Tolperisone were prepared by direct compression method using Crospovidone and Sodium starch glycolate. Tablets blends were evaluated for loose bulk density, tapped bulk density, compressibility index and angle of repose, shows satisfactory results. The compressed tablets were then evaluated for various physical tests like thickness, friability, hardness, weight variation, wetting time, water absorption ratio and disintegration test by using standard procedures. The results of all these tests were found to be satisfactory. The in-vitro dissolution study was carried out for 14 min using paddle method in phosphate buffer (pH 6.8) as dissolution media. The data of in-vitro dissolution of tablets revealed that 78 to 100% of drug release from various formulations at 14 min.

The formulation T7 exhibited better results as compared to other formulations.
2.2.2 Evaluation of pre-compression characteristics of powder blend\textsuperscript{6-10}

Powder blend prepared were evaluated for various rheological properties like bulk density, tapped density, Hausner's ratio, angle of repose by using standard procedures. All these properties were carried out in triplicate (n=3) and average values were reported.

2.2.3 Bulk density

Bulk density was determined by placing the powders blend in a measuring cylinder and the total volume is noted. The weight of powder bed was determined by using digital weighing balance. Bulk density was calculated using the following formula:

\[
\text{Bulk Density} = \frac{\text{Weight of the powder}}{\text{Volume of the powder}}
\]

2.2.4 Tapped density

Tapped density was determined by taking the dried powders in a measuring cylinder and measures the volume of powders after 100 tapping's and take weight of the total powders.

\[
\text{Tapped Density} = \frac{\text{Weight of the powder}}{\text{Tapped Volume of the powder}}
\]

2.2.5 Angle of repose

Angle of repose was determined by measuring the height and radius of the heap of the powder bed. A cylindrical two side open tube of 6 cm length is place on graph paper. Powders are placed in the tube and slowly removed the tube vertically. With the help of scale the height and radius of the heap were measure and note.

\[
\theta = \tan^{-1} \frac{h}{r}
\]

Where, \(h\) = height of heap of granular bed, \(r\) = radius of heap of granular bed.

2.2.6 Hausner’s ratio

It is expressed in percentage and is expressed by

\[
H = \frac{D_t}{D_b}
\]

Where \(D_t\) is the tapped density of the powder

\(D_b\) is the bulk density of the powder.

2.2.7 Evaluation of compression characteristics of mouth dissolving tablets\textsuperscript{11-14}

The prepared tablets were evaluated for their thickness, friability, hardness, weight variation and dissolution test by using standard procedures.

2.2.8 Weight variation test

20 tablets are taken and their weight is determined individually and collectively on a digital weighing balance. The average weight of one tablet is determined from the collective weight. Note more than 2 of the individual weights may deviate from the average weight by more than the percentage deviation given in the monographs and none should deviate by more than twice that percentage given in the monographs.

2.2.9 Thickness test

The tablets were evaluated for their thickness using a venier caliper measured in terms of micrometer. Averages of three readings were taken and the results were tabulated (n = 3).

2.2.10 Hardness test

Prepared tablets were evaluated for their hardness by using Monsanto hardness tester. The hardness was measured in terms of kg/cm\textsuperscript{2}. Triplicate readings were taken and average was determined.

2.2.11 Friability test

Roche friabilator was used for testing the friability of the tablets. For this test, 20 tablets were weighted accurately and placed in the friabilator chamber and rotated at 25 rpm for a period of 4 min. Tablets were again weighted and the percentage weight loss was determining by using formula given below.

\[
\% \text{ Friability} = \frac{(W_1 - W_2) \times 100}{W_1}
\]

Where,

\(W_1\) = Weight of tablet before test

\(W_2\) = Weight of tablet after test.

2.2.12 Drug content

Three tablets were weighed and ground in a mortar with pestle to get fine powder. Powder equivalent to the mass of one tablet was dissolved in pH 6.8 phosphate. This solution was diluted with pH 6.8 phosphate buffer. The absorbance of diluted sample of Tolperisone was measured at 260 nm in UV-Visible Spectrophotometer and drug content was calculated using equation obtained from a standard calibration curve.

2.2.13 Wetting time

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of purified water, then a tablet was placed on the paper and the time required for complete wetting was measured.

Wetting time corresponds to the time taken for the tablet to disintegrate when placed gently on the tissue paper in a Petridish. Less wetting time indicates more porous tablets.
2.2.14 Water absorption ratio

A piece of tissue paper folded twice was placed in a small petri plate containing 6 ml 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 calculated using equation.

\[ R = 100 \times \frac{(W_a - W_b)}{W_b} \]

Where, \( W_a = \) weight of the tablet after water absorption
\( W_b = \) weight of the tablet before water absorption

2.2.15 In-vitro disintegration time

The process of breakdown of a tablet into smaller particles is called as disintegration. The in vitro disintegration time of a tablet was determined using disintegration test apparatus as per IP specifications. Place 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 °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 °C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

2.2.16 In-vitro drug release study

In vitro release study was performed using tablet dissolution test apparatus USP XXIII, apparatus I. The dissolution medium consists of 900 mL phosphate buffer pH 6.8 maintained at 37 ± 1°C rotated at 50 rpm. At different interval of time 10 mL sample was withdrawn and replaced with fresh medium. 10 mL sample was diluted to 100 mL phosphate buffer pH 6.8, the aliquots were assayed spectrophotometrically at 260 nm for Tolperisone.

3 Results and Discussion

3.1 Evaluation of pre-compression characteristics of powder blend

The powders were evaluated for bulk density, tapped density, Hausner’s ratio and angle of repose and consistency in data obtained as indicated by their standard deviation values shown in table 2.

Bulk density and tapped density of different formulations were calculated. The result of bulk density range from 0.473 to 0.574 and tapped density from 0.565 to 0.698. Hausner’s ratio was found to be in between 1.14 to 1.23; and Compressibility index from 12.74 to 19.34. Angle of repose showed good to excellent flow properties of the powdered blend (Table 2).

The tablet dimension includes diameter and thickness of tablets. Thickness of all formulations was found to be between 3.21 to 3.62 (Table 3). No significant difference was observed in the thickness of individual tablet from the average value. No significant difference was observed in the weight of individual tablets form the average weight.

From table 3 it has been observed that tablet weights of all batches were found with in recommended USP limits, between 305 ± 1 mg. Hardness of tablets of all batches are in between 3.05 to 3.73 (Kg/cm²) which is acceptable limits, which shows in the literature. Friability of all the formulation showed % friability less than 1% that indicates ability of tablets to withstand shocks, which may encountered. The data of uniformity of content which was performed by UV spectroscopy indicated that tablets of all batches had drug content within USP limits i.e. between 97.61 to 99.25 %. In guidance of industrial scientist different parameter of tablet like flow property, dimension hardness, drug content etc. were studied which results in successful trials.

The wetting time and water absorption ratio were found to be 17.79 to 35.07 seconds and 39.24 to 73.38 seconds (Table 4), respectively. The disintegration time of mouth dissolving tablets ranges from 38.21 to 22.36 seconds (Table 4).

From above result it has been observed that T7 formulation exhibited excellent wetting time, water absorption ratio and disintegration time as compared to other formulations. Moreover the T8 formulation exhibited lowest wetting time and disintegration time; and highest water absorption ratio. This parameter enhances due to gelling and its subsequent viscosity producing effects.

3.2 In vitro drug release studies

Figure 1 displayed in-vitro dissolution of tablets, it revealed that 78 to 100% of drug release from various formulations. The 50% of the drug was released from the T7 and T8 within 4 minutes. The rapid drug dissolution might be due to easy breakdown of particle by superdisintegrant action. From in vitro dissolution data, it was observed that 98.16% of Tolperisone released in 14 minutes indicates that the tablet complies as per IP specifications, that is, 85%–110%. The dissolution rate was found to increase linearly with increase in the concentration of superdisintegrant. Mechanism it followed was wicking and swelling with minimum gelling. It was observed that T8 formulation released 65.62% drug in 12 minutes. This formulation has maximum amount of superdisintegrant that may cause tablets fragile.
### Table 1: Formulation of mouth dissolving Tolperisone tablet

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>T5</th>
<th>T6</th>
<th>T7</th>
<th>T8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolperisone</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
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<td>150</td>
</tr>
<tr>
<td>Crospovidone</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Sodium starch glycolate</td>
<td>7</td>
<td>9</td>
<td>11</td>
<td>13</td>
<td>7</td>
<td>9</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Mannitol</td>
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<td>112</td>
<td>110</td>
<td>108</td>
<td>112</td>
<td>110</td>
<td>108</td>
<td>106</td>
</tr>
<tr>
<td>Mg. Stearate</td>
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<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Talc</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Aspartame</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Theoretical Weight</td>
<td>305</td>
<td>305</td>
<td>305</td>
<td>305</td>
<td>305</td>
<td>305</td>
<td>305</td>
<td>305</td>
</tr>
</tbody>
</table>

### Table 2: Data of pre-compression characteristics of Tolperisone powder blend

<table>
<thead>
<tr>
<th>Parameters</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>T5</th>
<th>T6</th>
<th>T7</th>
<th>T8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Angle of repose* ± S.D.</td>
<td>36° 25' ± 0.02</td>
<td>29° 36' ± 0.11</td>
<td>31° 28' ± 0.05</td>
<td>30° 57' ± 0.08</td>
<td>29° 91' ± 0.09</td>
<td>31° 43' ± 0.13</td>
<td>34° 72' ± 0.21</td>
<td>38° 14' ± 0.05</td>
</tr>
<tr>
<td>Mean Apparent bulk density* (g/cm³) ± S.D</td>
<td>0.473 ± 0.02</td>
<td>0.565 ± 0.04</td>
<td>0.547 ± 0.06</td>
<td>0.574 ± 0.01</td>
<td>0.519 ± 0.06</td>
<td>0.538 ± 0.04</td>
<td>0.558 ± 0.02</td>
<td>0.558 ± 0.02</td>
</tr>
<tr>
<td>Mean Tapped bulk density* (g/cm³) ± S.D</td>
<td>0.565 ± 0.03</td>
<td>0.689 ± 0.04</td>
<td>0.672 ± 0.06</td>
<td>0.621 ± 0.01</td>
<td>0.698 ± 0.04</td>
<td>0.625 ± 0.02</td>
<td>0.645 ± 0.02</td>
<td>0.672 ± 0.02</td>
</tr>
<tr>
<td>Compressibility Index* (%)</td>
<td>12.74</td>
<td>15.09</td>
<td>17.11</td>
<td>17.39</td>
<td>14.89</td>
<td>15.36</td>
<td>16.59</td>
<td>19.34</td>
</tr>
<tr>
<td>Hausner’s Ratio*</td>
<td>± 0.01</td>
<td>± 0.02</td>
<td>± 0.04</td>
<td>± 0.02</td>
<td>± 0.05</td>
<td>± 0.02</td>
<td>± 0.05</td>
<td>± 0.03</td>
</tr>
</tbody>
</table>

*Value shown in tables is mean of three determinations

### Table 3: Evaluation of Tolperisone mouth dissolving tablets

<table>
<thead>
<tr>
<th>Parameters</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>T5</th>
<th>T6</th>
<th>T7</th>
<th>T8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uniformity of weight (mg)*</td>
<td>305.20±1.12</td>
<td>304.17±1.07</td>
<td>304.84±2.01</td>
<td>305.07±1.81</td>
<td>304.6±1.92</td>
<td>305.51±1.25</td>
<td>304.30±1.58</td>
<td>305.42±1.34</td>
</tr>
<tr>
<td>Thickness (mm)*</td>
<td>3.21±0.01</td>
<td>3.50±0.04</td>
<td>3.10±0.03</td>
<td>3.34±0.02</td>
<td>3.17±0.01</td>
<td>3.27±0.05</td>
<td>3.41±0.03</td>
<td>3.62±0.04</td>
</tr>
<tr>
<td>Friability (%)*</td>
<td>0.28±0.02</td>
<td>0.19±0.01</td>
<td>0.24±0.03</td>
<td>0.27±0.01</td>
<td>0.29±0.05</td>
<td>0.22±0.06</td>
<td>0.20±0.02</td>
<td>0.25±0.01</td>
</tr>
<tr>
<td>Tablet Hardness (Kp)*</td>
<td>3.29±0.01</td>
<td>3.18±0.03</td>
<td>3.51±0.06</td>
<td>3.05±0.04</td>
<td>3.62±0.07</td>
<td>3.21±0.05</td>
<td>3.73±0.03</td>
<td>3.42±0.04</td>
</tr>
<tr>
<td>Assay (%)</td>
<td>98.37±0.15</td>
<td>99.25±0.72</td>
<td>98.74±0.12</td>
<td>99.18±0.34</td>
<td>97.61±0.53</td>
<td>98.24±0.79</td>
<td>99.15±0.47</td>
<td>98.05±0.25</td>
</tr>
</tbody>
</table>

*Average of three times measure
Table 4: Evaluation of wetting time, water absorption ratio and in-vitro disintegration time of mouth dissolving tablets

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Wetting time (sec)</th>
<th>Water absorption ratio (sec)</th>
<th>In-vitro disintegration time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>35.07±0.02</td>
<td>39.24±1.01</td>
<td>38.21±0.08</td>
</tr>
<tr>
<td>T2</td>
<td>30.52±0.05</td>
<td>46.83±1.24</td>
<td>35.18±0.12</td>
</tr>
<tr>
<td>T3</td>
<td>28.36±0.12</td>
<td>52.64±0.78</td>
<td>34.52±0.07</td>
</tr>
<tr>
<td>T4</td>
<td>25.73±0.19</td>
<td>64.71±1.37</td>
<td>29.73±0.08</td>
</tr>
<tr>
<td>T5</td>
<td>28.46±0.08</td>
<td>50.57±1.29</td>
<td>31.61±0.19</td>
</tr>
<tr>
<td>T6</td>
<td>23.91±0.17</td>
<td>61.27±0.97</td>
<td>28.45±0.09</td>
</tr>
<tr>
<td>T7</td>
<td>21.32±0.09</td>
<td>68.19±1.07</td>
<td>27.58±0.10</td>
</tr>
<tr>
<td>T8</td>
<td>17.79±0.13</td>
<td>73.38±1.15</td>
<td>22.36±0.05</td>
</tr>
</tbody>
</table>

Value shown in tables is mean of three determinations

Fig 1: In-vitro drug release profile of Tolperisone mouth dissolving tablets

4 Conclusion

It was concluded that mouth dissolving tablets of Tolperisone can be successfully prepared by direct compression techniques using various superdisintegrants for the better patient compliance and effective therapy. It was also found that the superdisintegrants are effective at an optimum concentration, on increasing the ratio of Crospovidone and Sodium starch glycolate concentration above their optimum concentration this enhance the gelling effects of formulation. The formulation T7 exhibited better results as compared to other formulations. Further these formulations can be select for in vivo study.

5 References

