FORMULATION AND EVALUATION OF FAST DISINTIGRATING MELOXICAM TABLETS AND ITS COMPARISON WITH MARKETED PRODUCT

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ABSTRACT
The present investigation deals with the formulation of fast disintegrating tablets of Meloxicam that disintegrate in the oral cavity upon contact with saliva and there by improve therapeutic efficacy. Meloxicam is a newer selective COX-1 inhibitor. The tablets were prepared by wet granulation procedure. The influence of superdisintegrants, crosspovidone, croscarmellose sodium on disintegration time, wetting time and water absorption ratio were studied. Tablets were evaluated for weight and thickness variation, disintegration time, drug content, in vitro dissolution, wetting time and water absorption ratio. The in vitro disintegration time of the best fast disintegrating tablets was found to be 18 sec. Tablets containing crosspovidone exhibit quick disintegration time than tablets containing croscarmellose sodium. The fast disintegrating tablets of Meloxicam with shorter disintegration time, acceptable taste and sufficient hardness could be prepared using crosspovidone and other excipients at optimum concentration.

Keywords: Crosspovidone, Fast disintegrating tablet, Meloxicam, Superdisintegrants, Wetting time.

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 drugs thereby giving better patient compliance. Most pharmaceutical forms for oral administration are formulated for direct ingestion, for chewing, for prior dispersion and/or 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. Addition of super disintegrating agent in the formulation is one of the approaches to formulate orodispersible tablets. Orally disintegrating tablets contain wide variety of pharmaceutical active ingredients covering many therapeutic categories. The time for disintegration of orally disintegrating tablets are generally considered less than one minute. Orally disintegrating tablets are characterized by high porosity, low density and low hardness. When administered, an in-situ suspension is created in the oral cavity as the tablet disintegrates and is subsequently swallowed.

Meloxicam is a nonsteroidal anti-inflammatory drug of the oxicam class, used to relieve the symptoms of arthritis, primary dysmenorrhea, fever and as an analgesic, especially where there is an inflammatory component. Meloxicam inhibits cyclooxygenase (COX) synthesis.

This enzyme is responsible for converting arachidonic acid into prostaglandin H2. This is the first step in the synthesis of prostaglandins, which are mediators of inflammation. Meloxicam has been shown, especially at its low therapeutic dose, selectively to inhibit COX-2 over COX-1. A primary advantage of the oxicam family of drugs is their long half-life which permits once-day dosing. In gastric disease, lower dose of meloxicam is required 7.5 mg/day. Meloxicam is safer than other NSAID’s. Hence in present study an attempt was made for preparation of fast disintegrating tablets of meloxicam with aim of providing faster onset of action.

MATERIALS AND METHODS

Materials
Meloxicam was gifted from Dr. Reddy’s Laboratories (Hyderabad, India). Crosspovidone, Croscarmellose 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.

Preparation of Meloxicam orally disintegrating tablets
The prepared β-Cyclodextrin complex and the excipients were granulated using starch mucilage (10% solution), to form cohesive masses, then were passed through sieve # No 22. The formed granules were dried in hot air oven at 60°C for 2-3 hours. The dried granules were passed through sieve # No 22 and again passed through sieve # No 100. The blend was compressed into tablets using 10 station rotary tabletting machine.

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

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Formulation code</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F-1</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>7.5</td>
</tr>
<tr>
<td>B-Cyclodextrin</td>
<td>18</td>
</tr>
<tr>
<td>Micro crystalline cellulose</td>
<td>107.5</td>
</tr>
<tr>
<td>Dextrose</td>
<td>40</td>
</tr>
<tr>
<td>Starch powder</td>
<td>05</td>
</tr>
<tr>
<td>Croscarmellose sodium</td>
<td>14</td>
</tr>
<tr>
<td>Crosspovidone</td>
<td>-</td>
</tr>
<tr>
<td>Sodium saccharin</td>
<td>02</td>
</tr>
<tr>
<td>Vanilla</td>
<td>02</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>02</td>
</tr>
<tr>
<td>Talc</td>
<td>02</td>
</tr>
</tbody>
</table>

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

LBD = 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:
\[
CI (\%) = \left(\frac{TBD-LBD}{TBD}\right) \times 100
\]

The physical properties of granules were shown in Table 2.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Formulation code</th>
<th>F-1</th>
<th>F-2</th>
<th>F-3</th>
<th>F-4</th>
<th>F-5</th>
<th>F-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angle of repose</td>
<td></td>
<td>26.79 ± 0.32</td>
<td>28.34 ± 0.53</td>
<td>24.83 ± 0.24</td>
<td>26.45 ± 0.19</td>
<td>27.32 ± 0.39</td>
<td>26.85 ± 0.48</td>
</tr>
<tr>
<td>Loose bulk density (LBD) (g/ml)</td>
<td></td>
<td>0.487 ± 0.34</td>
<td>0.532 ± 0.385</td>
<td>0.5182 ± 0.17</td>
<td>0.470 ± 0.29</td>
<td>0.514 ± 0.28</td>
<td>0.527 ± 0.49</td>
</tr>
<tr>
<td>Tapped bulk density (TBD) (g/ml)</td>
<td></td>
<td>0.580 ± 0.48</td>
<td>0.675 ± 0.48</td>
<td>0.522 ± 0.27</td>
<td>0.592 ± 0.71</td>
<td>0.583 ± 0.16</td>
<td>0.514 ± 0.29</td>
</tr>
<tr>
<td>Compressibility index (%)</td>
<td></td>
<td>13.92 ± 0.36</td>
<td>15.71 ± 0.83</td>
<td>14.72 ± 0.67</td>
<td>17.68 ± 0.19</td>
<td>16.41 ± 0.18</td>
<td>17.09 ± 0.35</td>
</tr>
</tbody>
</table>

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

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 20mg of Meloxicam was dissolved in 100ml of pH 7.4 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 273nm using UV-Visible spectrophotometer (UV 160 Shimadzu, Japan).

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). Water absorption ratio, R, was then determined according to the following equation.
\[
R = \frac{\text{wb} - \text{w}}{\text{w}} \times 100
\]

In vitro dispersion time\(^{16}\)
In vitro dispersion time was measured by dropping a tablet in a 10ml measuring cylinder containing 6ml of buffer solution (pH 7.4).

In vitro dispersion 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 Electro lab, Mumbai, India) at 50 rpm. Phosphate buffer pH 7.4 was used as the dissolution media with temperature maintained at 37±1°C. Samples were withdrawn at different intervals, diluted suitably and analyzed at 363nm 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 Meloxicam fast disintegrating tablets

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Formulation code</th>
<th>F-1</th>
<th>F-2</th>
<th>F-3</th>
<th>F-4</th>
<th>F-5</th>
<th>F-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickness (mm)</td>
<td></td>
<td>2.45 ± 0.04</td>
<td>2.83 ± 0.15</td>
<td>2.52 ± 0.27</td>
<td>2.79 ± 0.16</td>
<td>2.59 ± 0.12</td>
<td>2.34 ± 0.29</td>
</tr>
<tr>
<td>Hardness (kg/cm(^2))</td>
<td></td>
<td>3.752 ± 1.2</td>
<td>3.461 ± 1.8</td>
<td>3.392 ± 1.5</td>
<td>3.541 ± 2.6</td>
<td>3.621 ± 1.4</td>
<td>3.674 ± 1.2</td>
</tr>
<tr>
<td>Friability (%)</td>
<td></td>
<td>0.341</td>
<td>0.529</td>
<td>0.476</td>
<td>0.421</td>
<td>0.571</td>
<td>0.526</td>
</tr>
<tr>
<td>Drug content (%)</td>
<td></td>
<td>99.5 ± 0.12</td>
<td>98.1 ± 0.17</td>
<td>97.9 ± 0.23</td>
<td>98.6 ± 0.53</td>
<td>97.8 ± 0.31</td>
<td>99.1 ± 0.38</td>
</tr>
<tr>
<td>Weight variation (mg)</td>
<td></td>
<td>202.15</td>
<td>200.18</td>
<td>201.86</td>
<td>199.98</td>
<td>200.29</td>
<td>200.45</td>
</tr>
<tr>
<td>Wetting time (sec)</td>
<td></td>
<td>63</td>
<td>52</td>
<td>35</td>
<td>56</td>
<td>44</td>
<td>21</td>
</tr>
<tr>
<td>Water absorption ratio</td>
<td></td>
<td>71</td>
<td>82</td>
<td>94</td>
<td>116</td>
<td>125</td>
<td>132</td>
</tr>
<tr>
<td>In vitro dispersion time (sec)(^{*})</td>
<td></td>
<td>67</td>
<td>54</td>
<td>41</td>
<td>47</td>
<td>39</td>
<td>32</td>
</tr>
<tr>
<td>In Vitro disintegrating time (sec)</td>
<td></td>
<td>86</td>
<td>79</td>
<td>58</td>
<td>41</td>
<td>41</td>
<td>25</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 stopped vials) at 40°/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\(^{17}\).
RESULTS AND DISCUSSION

The supplied drug passed the various tests of identification and analysis. The pure drug Meloxicam 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 compatibility, figure-3. The FT-IR study did not show any possibility of interaction between Meloxicam 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 analysed before compression of the tablets. The results of angle of repose and compressibility index (%) ranged from (24.83 ± 0.24 to 28.34 ± 0.53) and (13.92 ± 0.36 to 17.68 ± 0.19), respectively. The results of loose bulk density and tapped bulk density ranged from (0.470 ± 0.29 to 0.532 ± 0.385) and (0.522 ± 0.27 to 0.675 ± 0.48), respectively. The results of angle of repose (<30) indicate good flow properties of granules. This was further supported by lower compressibility index values. The lowest compressibility index is 5-15 % which indicates excellent flow properties (Table 2). The physical properties of different batches of fast dissolving tablets are given in (Table 3).

Tablet mean thickness was almost uniform in all the formulations. The thickness varies between 2.34 ± 0.29 to 2.83 ± 0.15 mm. The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 3.392 ± 1.5 to 3.821 ± 1.4 kg/sq cm. Friability values below 1% were an indication of good mechanical resistance of the tablets. Formulations prepared by sublimation method were found to be more friable. All the tablets
from each formulation passed weight variation test, as the % weight variation was within the pharmacopeial limits of ±7.5% of the weight. The weight variation in all the six formulations was found to be 199.98 to 202.15 mg, which was in pharmacopeial limits of ±7.5% of the average weight. The percentage drug content of all the tablets was found to be between 91.43 ± 0.54 to 99.18 ± 0.32 % of Meloxicam which was within the acceptable limits. The wetting time for all the six formulations was performed in triplicate. The values lie between 21 to 63 sec. In vitro dispersion is a special parameter in which the time taken by the tablet to produce complete dispersion is measured. The time for all the six formulations varied between 32 to 67 sec. Tablets were prepared with croscarmellose sodium F-1 to F-3 and with crospovidone F-4 to F-6. The wetting time, in vitro dispersion time of the tablets were also considerably reduced in tablets containing crospovidone which may be attributed due to the wicking type of disintegrants (crospovidone) formed thus facilitating the disintegrants to bring about faster disintegration. The results of water absorption ratio (%) and in vitro disintegrating time (sec) ranged from (71 to 132) and (18 to 86), respectively.

The in vitro dissolution profile indicated faster and maximum drug release from formulation F6. Stability studies shown that there was no significant change when compared with zero day of formulation (F-6). The disintegration time of crospovidone tablets are comparatively lower than the sodium starch glycolate. The faster disintegration of crospovidone tablets may be attributed to its rapid capillary activity and pronounced hydration with little tendency to gel formation. Thus, these results suggest that the disintegration time can be decreased by using wicking type of disintegrants (crospovidone).

CONCLUSION

The oral disintegrating tablets of Meloxicam with sufficient mechanical strength, acceptable taste and smaller disintegration time were achieved employing suitable superdisintegrants and other excipients at optimum concentration. Stability studies revealed that there was no significant change in drug content and dissolution profile of oral disintegrating tablets. FTIR studies revealed that there was no shift in peaks, indicating there is no interaction between Meloxicam and other ingredients used. Among two superdisintegrants used crospovidone showed better performance in disintegration time when compared to croscarmellose sodium. In the in vitro dissolution comparison study between F6 and marketed product (Muvera) the formulation F6 shows 38.123% release of drug in two minutes and marketed product showed 18% release in the same time. F6 shows 99.189% with in 50 minutes and marketed product shows only 92.456% in 50 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