INTRODUCTION

Mouth dissolving tablets disintegrate or dissolve in saliva and are swallowed without the need for water. They are beneficial to swallowing tablets and capsules. Thus difficulty is particularly experienced by pediatric and geriatric patients. Various techniques such as freeze drying, sublimation, spray drying, molding, mass extrusion and direct compression method have been reported for preparation of mouth dissolving tablets. Metformin HCl is an oral antihyperglycemic agent that improves glucose tolerance in patients with NIDDM, lowering both basal and postprandial plasma glucose. The poor water solubility of the drug gives rise to difficulties in the formulation of dosage form leading to variable dissolution rate. Hence it was selected as a model drug. In the present work an attempt has been made to prepare MDTs of Metformin HCl using superdisintegrants in different concentrations.

MATERIALS AND METHODS

Metformin HCl was received as a gift sample from Aventis Pharmaceuticals Pvt. Ltd., crosподовидоне, croscarmellose, sodium starch glycolate and all other excipients were gift samples from New Neeta Chemicals, Pune.

Preparation of Metformin HCl tablets using direct compression

Weighed the Metformin HCl, superdisintegrants, microcrystalline cellulose, mannitol, magnesium stearate, and talc accurately. All the materials were passed through 60 mesh prior to mixing and transferred to glass mortar and triturated till it was mixed uniformly. The resultant powder mixture was compressed into tablets using single punch tablet machine.

Evaluation of powder blend

Bulk density (Db)\textsuperscript{5,6}

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by:

\[ D_b = \frac{M}{V_b} \]

Where, M is the mass of powder and \( V_b \) is the bulk volume of the powder.

Tapped density (DT)\textsuperscript{7,8}

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by:

\[ D_t = \frac{M}{V_t} \]

Where, M is the mass of powder and \( V_t \) is the tapped volume of the powder.

Angle of repose (θ)\textsuperscript{9}

The friction forces in a loose powder can be measured by the angle of repose (θ). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

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

Where, θ is the angle of repose.

‘h’ is the height in cms
‘r’ is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particles slip and roll over each other through the sides of the funnel.

Carr’s index (or) % compressibility\textsuperscript{10,11}

It indicates powder flow properties. It is expressed in percentage and is given by:

\[ C = \left( \frac{V_t - V_b}{V_b} \right) \times 100 \]
A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37°C. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

In vitro drug release
Release of the drug in vitro, was determined by estimating the dissolution profile.

Dissolution test
USP II Paddle apparatus was used and paddle was allowed to rotate at 50 rpm. 0.1 N HCl (900 ml) was used as a dissolution medium. Determination of amount of drug dissolved from tablets was carried out by UV 1601 spectrophotometer at 234 nm.

RESULT AND DISCUSSION
Evaluation of blend

Table 1: Formulation composition of Metformin HCl mouth dissolving tablets

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Ingredients</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Metformin HCl</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>2</td>
<td>Croscarmellose Sodium</td>
<td>-</td>
<td>-</td>
<td>20</td>
<td>25</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Crospovidone</td>
<td>10</td>
<td>15</td>
<td>-</td>
<td>-</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>Sodium starch glycolate</td>
<td>18</td>
<td>22.5</td>
<td>-</td>
<td>-</td>
<td>18</td>
<td>31.5</td>
</tr>
<tr>
<td>5</td>
<td>Microcrystalline cellulose</td>
<td>-</td>
<td>-</td>
<td>45</td>
<td>67.5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Magnesium stearate</td>
<td>5.4</td>
<td>5.4</td>
<td>5.4</td>
<td>5.4</td>
<td>5.4</td>
<td>5.4</td>
</tr>
<tr>
<td>7</td>
<td>Talc</td>
<td>3.1</td>
<td>3.1</td>
<td>3.1</td>
<td>3.1</td>
<td>3.1</td>
<td>3.1</td>
</tr>
<tr>
<td>8</td>
<td>Mannitol up to 213.5</td>
<td>204</td>
<td>176.5</td>
<td>124</td>
<td>203.5</td>
<td>185</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Total weight</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
</tr>
</tbody>
</table>

Wetting time<sup>5,8,10</sup>
Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

\[
dl/dt = r \gamma \cos \theta / (4 \eta l)
\]

Where \( l \) is the length of penetration, \( r \) is the capillary radius, \( \gamma \) is the surface tension, \( \eta \) is the liquid viscosity, \( t \) is the time, and \( \theta \) is the contact angle.

It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place.

A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37°C. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

In vitro drug release
Release of the drug in vitro, was determined by estimating the dissolution profile.

Table 2: Evaluation of the physical parameters of blend of Metformin HCl

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Hardness (kg/cm²)</th>
<th>Weight variation</th>
<th>Friability (%)</th>
<th>Disintegration time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>2.8±0.1</td>
<td>4.5</td>
<td>0.457</td>
<td>21</td>
</tr>
<tr>
<td>F2</td>
<td>2.6±0.12</td>
<td>4.1</td>
<td>0.524</td>
<td>17.5</td>
</tr>
<tr>
<td>F3</td>
<td>3.2±0.10</td>
<td>5.5</td>
<td>0.435</td>
<td>33.5</td>
</tr>
<tr>
<td>F4</td>
<td>3.8±0.23</td>
<td>4.9</td>
<td>0.463</td>
<td>27</td>
</tr>
<tr>
<td>F5</td>
<td>3.8±0.14</td>
<td>4.7</td>
<td>0.511</td>
<td>25</td>
</tr>
<tr>
<td>F6</td>
<td>2.8±0.8</td>
<td>4.4</td>
<td>0.455</td>
<td>18.5</td>
</tr>
</tbody>
</table>

Table 3: Evaluation of Physical Parameters of MDTs of Metformin HCl

In vitro drug release

Table 2: Evaluation of the physical parameters of blend of Metformin HCl

Dissolution test

Table 3: Evaluation of Physical Parameters of MDTs of Metformin HCl

In vitro drug release

Hausner ratio
Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

\[
\text{Hausner ratio} = \frac{D_t}{D_b}
\]

Where, \( D_t \) is the tapped density of the powder and \( D_b \) is the bulk density of the powder.

EVALUATION OF MOUTH DISSOLVING TABLETS<sup>3,6,12</sup>

Weight variation
20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P.
Friability was found between 0.43 and 0.52%, which were below 1% indicating sufficient mechanical integrity and strength of prepared tablets. From Figure 1, in vitro dissolution studies showed that more than 50% of drug was released from within 5 minutes. The fast dissolving tablet of F2 formulation containing 3% Crospovidone and 5% Sodium Starch Glycolate disintegrated in 17.5 seconds. 62.74% drug was released in 5 minutes and 99.0% drug was released in 25 minutes. The present investigation was undertaken to formulate and evaluate fast dissolving tablets of Metformine hydrochloride by direct compression method using Croscarmellose Sodium, Crospovidone and Sodium Starch Glycolate as superdisintegrants. Superdisintegrants are generally used by formulation scientists for developing fast dissolving tablets or for improvement of solubility for drugs. The amount of Superdisintegrants was optimized in the formulation of fast dissolving tablets. The ten formulations were prepared using different concentration of Croscarmellose Sodium, Crospovidone and Sodium Starch Glycolate to study its effect on Disintegration Time.2,4,7

Percent weight variation was found to be between 4.1 and 5.6, well within the acceptable limit for uncoated tablets as per Indian Pharmacopoeia. It is well known to formulation scientists that the tablets with more hardness show longer disintegration time. Since mechanical integrity is of paramount importance in successful formulations of fast dissolving tablets, hence hardness of tablet was determined and was found to be in the range of 2.6 to 3.8 Kg/cm². (9,10,11) Friability was found between 0.43 and 0.52%, which were below 1% indicating sufficient mechanical integrity and strength of prepared tablets. The Disintegration time for formulation was found to be 17-34 seconds.

CONCLUSION

Fast dissolving tablets of Metformin Hydrochloride were prepared by direct compression method using Croscarmellose Sodium, Crospovidone and Sodium Starch Glycolate as superdisintegrants. The tablets disintegrate rapidly in oral cavity and had acceptable hardness and friability. In vitro drug release from the tablets shows significantly improved drug dissolution. The Crospovidone was taken 3% and Sodium Starch Glucolate was taken 5% showed minimum disintegration time of 17.5 seconds and the 62.74% drug was released in 5 minutes and 99.0% drug was released in 25 minutes.12,13

REFERENCES

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