Design and Development of Aceclofenac Fast Dissolving Tablets by Novel Hole Technology: A Novel Approach to Decrease the Disintegration Time and Increase the patient compliance

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Attempts were made to prepare Aceclofenac fast dissolving tablets by Novel Hole technology. When these fast dissolving tablets contacts with the saliva or gastro intestinal fluids, the saliva or fluid will enters the hole present in the tablet and immediate breaking of the tablet is going to takes place. This fast disintegration of tablets is also influenced by the formation of new absolute area. The prepared FDTs were subjected to various pre and post formulation studies. Its disintegration and dissolution rates were compared with the control formulation (without hole). In-vitro drug release of FDTs (AH) showed almost 99% of the drug was released at 4th minute, whereas the control formulation A, shows the 99% drug release at 18th minute. Overall, this technique is novel and most useful for formulation into fast dissolving tablets.

Key words: Novel Fast Dissolving Tablets, Aceclofenac, Hole technology.

INTRODUCTION

The oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. The reasons that the oral route achieved such popularity may be in part attributed to its ease of administration as well as the traditional belief that by oral administration the drug is as well absorbed as the foodstuffs that are ingested daily. Pharmaceutical products designed for oral delivery and currently available on the prescription and over-the-counter markets are mostly the immediate-release type, which are designed for immediate release of drug for rapid absorption. These fast-dissolving tablets ensure complete solubilization of tablet through surface erosion, resulting in elimination of lag time for disintegration thereby offering faster absorption and rapid onset of action.

Despite increasing interest in controlled-release drug delivery systems, the most Common tablets are those intended to be swallowed whole and to disintegrate and release their medicaments rapidly in the gastro intestinal tract. In more recent years, increasing attention has been paid to formulating not only fast dissolving tablets that are swallowed, but also orally disintegrating tablets that are indented to disolve and disintegrate rapidly in the mouth.

Fast dissolving tablets (FDTs) are solid single-unit dosage forms that are place in the mouth, allowed to disperse/dissolve in the saliva and then swallowed without the need for water.

FDTs are appreciated by a significant segment of the population, particularly children and elderly who have difficulty in swallowing conventional tablets or capsules. The most desirable formulation for use by the elderly is one that is easy to swallow and easy to handle. Since such a tablet can disintegrate in only a small amount of water in the oral cavity, it is easy to take for any age patient, regardless of time or place. For example, it can be taken anywhere at any time by anyone who do not have easy access to water. It is also easy to dose the aged, bed-ridden patients, or infants who have problems swallowing tablets and capsules. Recently, many companies have researched and developed various different types of fast-dissolving tablets by adopting different techniques. However, some of these technologies have disadvantages. New equipment, such as freeze-driers and specially molded tableting machines, were required for their production. Furthermore, these formulations were difficult for the aged to handle because of inadequate strength.

Therefore the objectives of present research investigation were to formulate fast-dissolving tablets with sufficient hardness for handling and be manufactured by commonly used production methods and equipment.

MATERIALS AND METHODS

Aceclofenac was obtained as gift sample from Rantus pharma pvt ltd, Hyderabad, India. Crospovidone and Microcrystalline cellulose (MCC) were obtained from Maple biotech pvt ltd, Pune, India. Mannitol, Talc and Magnesium stearate were purchased from S.D Fine chemicals ltd, Mumbai, India. All other chemicals were of analytical grade.

Preparation of Aceclofenac fast dissolving Tablets:

Step I: Preparation of FDTs containing super disintegrant (Control A).

Tablets (A) containing 100mg of Aceclofenac was taken and then mixed with mannitol, crospovidone and Microcrystalline cellulose (MCC) in a plastic container. Magnesium stearate and talc were passed through sieve # 60 mixed and blend with initial mixer in the plastic container followed by compression in to the tablets.

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Received 20-04-2011; Accepted 22-05-2011
Step II: Preparation of FDTs by Novel technology (AH).

Plain 100mg camphor tablets were prepared by taking plain camphor granules and compressed into tablets. In the next step, Aceclofenac, excipient and super disintegrant were mixed in a plastic container. Magnesium stearate and Talc were passed through sieve # 60 mixed and blend with initial mixer in the plastic container. This mixer is then placed in the die cavity and at the centre of the die cavity, previously compressed camphor tablets were kept then compressed into tablets. These tablets containing tablet in tablet. I.e. Camphor tablet is present in Aceclofenac tablet.

After compression, these tablets were vacuum dried at 60°C by keeping the tablets in a vacuum dryer until complete removal of camphor to make tablets with hole at the center leading to formation of extra absolute surface area. (Fig4)

Evaluation of powder blends

Angle of repose

Angle of repose (θ) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the heap (r) was measured and angle of repose was calculated.

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

Compressibility index

The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility that is calculated as follows:

\[ C = \left( \frac{\rho_t - \rho_b}{\rho_t} \right) \times 100 \]

\( \rho_t \) - Tapped density,
\( \rho_b \) - Untapped bulk density

Hausner's ratio

Hausner's ratio is an index of ease of powder flow; it is calculated by following formula.

\[ \text{Hausner's ratio} = \frac{\rho_t}{\rho_b} \]

\( \rho_t \) - Tapped density,
\( \rho_b \) - Untapped bulk density

Evaluation of Aceclofenac fast disintegrating tablets

Weight variation test:

Weight variation test was done by weighing 20 tablets individually, by using Sartorious balance (Model CP-224 S). Calculating the average weight and comparing the individual tablet weight to the average weight.

Tablet thickness:

The thickness was measured by placing tablet between two arms of the Varnier calipers. 5 tablets were taken and their thickness was measured.

Tablet hardness:

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Tablet friability:

The friability of the tablets was measured in a Roche friabilator (Campbell Electronics, Mumbai). Tablets of a known weight (Wo) or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. Determination was made in triplicate.

\[ \% \text{Friability} = 100 \left( \frac{Wo-W}{Wo} \right) \]
The entire samples were run at a scanning rate of 10 sealed in the same way as the sample was used as a reference. For drug content analysis a total 10 tablets were weighed and powdered. The powder equivalent to Aceclofenac was taken and dissolved in phosphate buffer pH 7.4. After that an aliquot of the filtrate was diluted and analyzed spectrophotometrically (UV 1700 Shimadzu Japan) at 274nm. In dissolution study, 99% of drug release was achieved within 4 minutes in case of formulation AH. The Controlled formulation A was showed the 99% drug release at 18th minute. This enhanced dissolution of formulation AH may be due to the extra availability of absolute surface area of the novel formulation and due the presence of hole in the tablet. During the dissolution of formulation AH, the fluid enters into the whole present in the formulation AH, leads to immediate breaking of the tablet due the wicking action of the crospovidone. Where as in case of formulation A, it also contains crospovidone but due to the absence of the hole, it takes more time to disintegrate in comparison with the formulation AH. From the disintegration, wetting time and wetting time decreased significantly in formulation AH in comparison with the control formulation A.

In wetting time study a piece of tissue paper folded twice was placed in a petridish (with internal diameter 6.5cm) containing 5ml of distilled water. A tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. For drug content analysis a total 10 tablets were weighed and powdered. The powder equivalent to Aceclofenac was taken and dissolved in phosphate buffer pH 7.4. After that an aliquot of the filtrate was diluted and analyzed spectrophotometrically (UV 1700 Shimadzu Japan) at 274nm.

In wetting time study:

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In vitro release studies:

The in vitro dissolution study was carried out in the USP dissolution test apparatus (Electrolab TDT - 08 L Dissolution tester USP) type 2 (paddle). 900 ml of the dissolution medium (Phosphate buffer pH 7.4) was taken in vessel and the temperature was maintained at 37 ± 0.5°C. The speed of the paddle was set at 50 rpm. 5ml of the dissolution medium was withdrawn and the same amount of fresh medium was replenished to the dissolution medium. The sample withdrawn was filtered and diluted with phosphate buffer pH 7.4 prior to analysis in the UV Spectrophotometer (a PG instrument T80 model UV/VIS spectrophotometer) at 274nm.

Characterization of Aceclofenac tablets:

Infrared spectroscopic study:

Fourier transformed (FTIR) spectrum of Aceclofenac, Drug with different subliming agent were obtained on a FTIR (84005 Shimadzu Japan) using the KBr disk method.

DSC Studies:

DSC scans of about 10mg, using an automatic thermal analyzer system performed accurately weighed Aceclofenac and its mixture with camphor (Mettler Toledo, USA). Sealed and perforated aluminum pans were used in the experiments for both the samples. Temperature calibrations were performed using indium as standard. An empty pan sealed in the same way as the sample was used as a reference. The entire samples were run at a scanning rate of 10°C/min from 50-200°C.

RESULTS

The values of pre-compression parameters evaluated were within prescribed limits and indicated a good free flowing property. Results are shown in Table 2.

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Angle of repose (θ) (±SD), n=3</th>
<th>Compressibility (%) (±SD), n=3</th>
<th>Hausner’s ratio (%)±SD, n=3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>23.40(1.20)</td>
<td>12.16(1.25)</td>
<td>1.38(0.04)</td>
</tr>
<tr>
<td>AH</td>
<td>22.30(1.50)</td>
<td>18.18(1.22)</td>
<td>1.22(0.06)</td>
</tr>
</tbody>
</table>

Table 2: Pre-Compressional parameters of Aceclofenac tablets

The post compression parameters such as hardness, friability, thickness, diameter, disintegration time, wetting time, drug content are shown in Table 3.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness (kg/cm²)</td>
<td>A</td>
</tr>
<tr>
<td>± SD, n=3</td>
<td>±0.18</td>
</tr>
<tr>
<td>Friability (g/cm³)</td>
<td>0.52</td>
</tr>
<tr>
<td>± SD, n=3</td>
<td>±0.07</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>4.33</td>
</tr>
<tr>
<td>± SD, n=6</td>
<td>±0.03</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>10.55</td>
</tr>
<tr>
<td>± SD, n=6</td>
<td>±0.08</td>
</tr>
<tr>
<td>Wetting time (Sec)</td>
<td>62.34</td>
</tr>
<tr>
<td>± SD, n=6</td>
<td>±0.54</td>
</tr>
<tr>
<td>Weight variation (%)</td>
<td>598.9</td>
</tr>
<tr>
<td>± SD, n=10</td>
<td>±0.18</td>
</tr>
</tbody>
</table>

In vitro disintegration time:

In the disintegration time study, the tablets were taken and introduced in each tube of disintegration apparatus, and the tablet rack of the disintegration apparatus was positioned into a 1-litre beaker containing 900ml of distilled water and time of disintegration was recorded at 37±0.5°C.

In the wetting time study:

In wetting time study a piece of tissue paper folded twice was placed in a petridish (with internal diameter 6.5cm) containing 5ml of distilled water. A tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. For drug content analysis a total 10 tablets were weighed and powdered. The powder equivalent to Aceclofenac was taken and dissolved in phosphate buffer pH 7.4. After that an aliquot of the filtrate was diluted and analyzed spectrophotometrically (UV 1700 Shimadzu Corporation, Japan) at 274nm.

Table 3: Post-Compressional parameters of Aceclofenac tablets

In all the formulations, the hardness test indicates good mechanical strength. Friability of all formulations was less than 1%, which indicated that the tablets had a good mechanical resistance. Drug content was found to be high (≥ 100%) and uniform in both the formulations. The weight variation results revealed that average percentage deviation of 20 tablets of each formula was less than ± 7.5%, which provides good uniformity. The disintegration time and wetting time decreased significantly in formulation AH in comparison with the control formulation A.

In dissolution study, 99% of drug release was achieved within 4 minutes in case of formulation AH. The Controlled formulation A was showed the 99% drug release at 18th minute. This enhanced dissolution of formulation AH may be due to the extra availability of absolute surface area of the novel formulation and due the presence of hole on the tablet. During the dissolution of formulation AH, the fluid enters into the whole present in the formulation AH, leads to immediate breaking of the tablet due the wicking action of the crospovidone. Where as in case of formulation A, it also contains crospovidone but due to the absence of the hole, it takes more time to disintegrate in comparison with the formulation AH. From the disintegration, wetting time and dissolution studies, it clearly indicates, presence of Hole in the tablet makes lot of difference in response variables.

Infrared spectroscopic study:

The prominent IR absorption peaks of Aceclofenac showed at 3319 and 3267 these broad peaks may be due to OH hydrogen bonding 2970 is NH aromatic stretching, peaks near 2937 including 1921 may be due to CH stretching of CH₂ groups.
carbonyl group vibration at 1770 and 1716. Peaks at 1589, 1577 and 1508 indicates the presence of C=C ring stretching. All these principal IR peaks of Aceclofenac were present in all formulations. This clearly indicates that there is no interaction between drug and carrier.

**ACKNOWLEDGEMENT**

We are thankful to Rantus Labs Hyderabad, Maple Biotech Pune, for providing Aceclofenac drug sample, and crospovidone, MCC.

**REFERENCES**