Formulation and Evaluation of Fast Dissolving Tablets of Diclofenac Sodium by Novel Hole Technology

Renati Damodar1*, Babji Movva1, Mallikarjun PN1, Chaitanya Pasumarthy2, Nishanth Kona3 and Varsha PV4
1Department of Pharmaceutics, Vignan Institute of Pharmaceutical Technology, Visakhapatnam, Andhra Pradesh, India
2Mother Teresa College of Pharmacy, Ghatkesar, Hyderabad, India
3Department of Pharmaceutics, Sree Siddaganga College Pharmacy, Tumkur, Karnataka, India
4Department of Biotechnology, GITAM University, Visakhapatnam, Andhra Pradesh, India

Abstract
Research has done to prepare Diclofenac Sodium quick dissolving tablets by Hole technology. Once these quick dissolving tablets contact with gastro enteric fluids, the fluid can enter the hole within the tablet and immediate breaking of the tablet goes to take place. This quick disintegration of tablets is additionally influenced by the formation of latest absolute space. The ready FDTs were subjected to numerous pre and post formulation studies. Its disintegration and dissolution rates were compared with the management formulation (without hole). In-vitro drug release of FDTs (DH6) showed virtually 100.92% of the drug was discharged at sixth minute, whereas the management formulation D12 shows the 99% drug release at 20th minute. Overall, this method is novel and most helpful for formulation into quick dissolving tablets.

Keywords: Hole technology; Diclofenac sodium; Novel fast dissolving tablets; Hole formation

Introduction
The oral drug delivery has been celebrated for many years because the most generally used route of administration among all the routes that have been explored for the general delivery of drugs via varied pharmaceutical product of different indefinite quantity forms [1]. The explanations that the oral route achieved such popularity could also be partly attributed to its simple administration still because the ancient belief that by oral administration the drug is still absorbed because the foodstuffs that are ingested daily [2]. Pharmaceutical product designed for oral delivery and presently available on the prescription and over-the-counter markets are largely the immediate-release sort, that are designed for immediate unreleased of drug for speedy absorption. These fast-dissolving tablets ensure complete solubilization of tablet through surface erosion, leading to elimination of lag time for disintegration thereby offering quicker absorption and speedy onset of action [1-3].

Despite increasing interest in controlled- unreleased drug delivery systems, the most common tablets are those supposed to be enclosed whole and to disintegrate and unreleased their medicaments quickly within the gastro enteral tract. In additional recent years, increasing attention has been paid to formulating not solely fast dissolving and / or disintegrating tablets that are enclosed, but conjoinly orally disintegrating tablets that are indented to dissolve and/or disintegrate quickly within the mouth [4-6].

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 [7-12].

The Diclofenac sodium is a non steroidal anti inflammatory drug. It comprise a large family of weak acidic drugs whose pharmacological effects result primarily from the inhibition of cyclooxygenase (COX) an enzyme that catalyses the first step in the synthesis of prostaglandins from arachidonic acid and other precursor fatty acids. Since its solubility is very high in upper G.I. and need of fast releasing action in case of acute pain it is formulated as fast dissolving tablet [13-18].

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

Materials
Diclofenac Sodium was obtained as a gift sample from Hetero drugs limited Laboratories, Hyderabad, India. Sodium starch glycolate, cross carmellose sodium, mannitol, sodium saccharine were procured from Yarrow Chem. Products, Mumbai, camphor was procured from Saptagir camphor limited, Anantapur. Potassium dihydrogen phosphate, methanol Reagent was procured from Merck limited.

*Corresponding author: Renati Damodar, Department of Pharmaceutics, Vignan Institute of Pharmaceutical Technology, Visakhapatnam, Andhra Pradesh, India, Tel: +918500932050; E-mail: renatidamodar@gmail.com
Received May 27, 2014; Accepted July 28, 2014; Published July 31, 2014


Copyright: © 2014 Damodar R, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
Mumbai. Lactose, magnesium stearate and talc I.P were procured from Molychem, Mumbai, India. All other chemicals were of analytical grade.

**Preparation of FDTs by novel hole technology**

All the ingredients in Table 1 were accurately, 100mg camphor tablets were prepared by taking plain camphor granules and compressed into tablets. Diclofenac sodium, super disintegrants and exponents were mixed in a container. Talc and Magnesium stearate after passing through sieve # 60 mixed and blended with initial mixer in the container. This mixture 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 then placed in the die cavity and at the centre of the die cavity leading to formation of extra absolute surface area (Figure 1).

**Evaluation of Tablets**

**Pre compression parameters**

Characteristics like tapped density, bulk density, carr’s index, hausner,s ratio were studied for powder blend of formulations which are ready to compress in to tablets [19-35].

**Post compression parameters**

All the prepared tablets were subjected to various physical characteristics like Crushing strength, Friability, Thickness, Diameter, Hole depth, Disintegration time, Wetting time, Weight variation, Drug content (Table 3).

**Weight variation test**

Weight variation test was done by weighing 20 tablets individually, by using electronic balance. Calculating the average weight and comparing the individual tablet weight to the average weight [21-23].

**Tablet thickness**

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

**Table 1:** Formulation chart of Diclofenac Sodium FDT with Hole technology.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Ingredient (mg/tab)</th>
<th>DH1</th>
<th>DH2</th>
<th>DH 3</th>
<th>DH 4</th>
<th>DH 5</th>
<th>DH 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diclofenac Na</td>
<td>75 mg</td>
<td>75 mg</td>
<td>75 mg</td>
<td>75 mg</td>
<td>75 mg</td>
<td>75 mg</td>
</tr>
<tr>
<td>2</td>
<td>Cross carmellose Sodium</td>
<td>10 mg</td>
<td>-</td>
<td>20 mg</td>
<td>30 mg</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Sodium Starch Glycolate</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10 mg</td>
<td>20 mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>4</td>
<td>Lactose</td>
<td>175 mg</td>
<td>175 mg</td>
<td>175 mg</td>
<td>175 mg</td>
<td>175 mg</td>
<td>175 mg</td>
</tr>
<tr>
<td>5</td>
<td>Mannitol</td>
<td>230 mg</td>
<td>220 mg</td>
<td>210 mg</td>
<td>230 mg</td>
<td>220 mg</td>
<td>210 mg</td>
</tr>
<tr>
<td>6</td>
<td>Sodium saccharine</td>
<td>6 mg</td>
<td>6 mg</td>
<td>6 mg</td>
<td>6 mg</td>
<td>6 mg</td>
<td>6 mg</td>
</tr>
<tr>
<td>7</td>
<td>Magnesium stearate</td>
<td>2 mg</td>
<td>2 mg</td>
<td>2 mg</td>
<td>2 mg</td>
<td>2 mg</td>
<td>2 mg</td>
</tr>
<tr>
<td>8</td>
<td>Talc</td>
<td>2 mg</td>
<td>2 mg</td>
<td>2 mg</td>
<td>2 mg</td>
<td>2 mg</td>
<td>2 mg</td>
</tr>
<tr>
<td>9</td>
<td>Camphor</td>
<td>100 mg</td>
<td>100 mg</td>
<td>100 mg</td>
<td>100 mg</td>
<td>100 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>Total weight after sublimation</td>
<td>500 mg</td>
<td>500 mg</td>
<td>500 mg</td>
<td>500 mg</td>
<td>500 mg</td>
<td>500 mg</td>
<td></td>
</tr>
</tbody>
</table>

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 (M/s. Elite Scientific & Equipments.). Tablets of a known weight (W_a) 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.

\[
\% \text{ Friability} = \frac{100 (W_a - W)}{W_a}
\]

**In vitro characterization of prepared tablets**

**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 ± 2°C [23-28].

**In the wetting time study**

In wetting time study a piece of tissue paper folded twice was placed in a petridish (with internal diameter 6.5 cm) containing 5 ml of distilled water. A tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds [36-42].

**Drug content analysis**

Total 10tablets were weighed and powdered. The powder equivalent to Diclofenac Sodium was taken and dissolved in 0.1N HCl. After that an aliquot of the filtrate was diluted and analyzed spectrophotometrically (Elite UV- 150 double beam spectrophotometer.) at 314 nm [43,44].

**In vitro release studies**

The in vitro dissolution study was carried out in the USP dissolution test apparatus (M/s Lab India (Model – DS 8000) type 2 (paddle). 900 ml of the dissolution medium (Phosphate buffer pH 6.8) 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
Compatibility studies

Infrared spectroscopic study: Fourier transformed (FTIR) spectrum of Diclofenac, Drug with different excipients were obtained on a FTIR (Perkin-Elmer) using the KBr disk method. The prominent IR absorption peaks of Diclofenac showed at 3381.57 cm⁻¹ due to N-H stretching of secondary amine. Peak at 1572.66 cm⁻¹ due to C=O stretching of carboxyl ion. Peak at 745.35 cm⁻¹ because of C-Cl stretching. All these principal IR peaks of Diclofenac Sodium were present in all formulations. This clearly indicates that there is no interaction between drug and carrier.

Pre compression parameters

The Bulk density of all the formulations were within the range of 0.51 ± 0.005 to 0.56 ± 0.005 g/ml and Tapped density was found to be in the range of 0.61 ± 0.03 to 0.66 ± 0.03 g/ml (good flow property). The Angle of repose of powder blends of all formulation was found to be in the range of 19.21 ± 0.12 to 29.62° ± 0.2 (good flow property). The values calculated Hausners ratio of all the formulations was found to be in the range of 1.162 ± 0.13 to 1.21 ± 0.03 (good flow property). The calculated Carrs index of all formulations was found to be in the range of 17.74% ± 0.16 (good flow property). The values of pre-compressional parameters evaluated were within the prescribed limits and indicated good free flowing properties.

Post compression parameters

The post compression parameters of all batches were studied and shown in Table 2. The crushing strength of tablets prepared by hole technology were within the range of 3.5 ± 0.25 to 3.5 ± 0.5 kg/cm². The loss of percentage of weight in friability was found to be 0.39 ± 0.08 to 0.53 ± 0.06 which is less than 1% which indicates tablets has good mechanical resistance. The thickness and diameter of prepared tablets was found to be in the range of 3.812 ± 0.02 to 4.0 ± 0.03 mm and 12.80 ± 0.05 to 12.90 ± 0.04 mm respectively. The hole depth of all formulations prepared by hole technology was found to be in the range of 1.66 ± 0.22 to 1.75 ± 0.04 mm. The wetting time of all formulations prepared by hole technology was found to be in the range of 21 ± 0.49 to 44 ± 0.61 sec. The disintegration time of all formulations prepared by hole technology was found to be in the range of 14 ± 0.53 to 33 ± 0.65 sec and was shown in Table 4. The weight variation of all formulations prepared by hole technology was found to be in the range of 497.5 ± 0.19 to 498.5 ± 0.18 mg. The drug content of all formulations prepared by hole technology was found to be in the range of 98.9 ± 1 to 101.5 ± 1.25%.

Stability studies of optimized formulation

Optimized formulation was exposed for accelerated conditions as per ICH guidelines. (40ºC / 75% RH for a period of 3 months. Tablets were evaluated for physicochemical properties, drug release. The Stability studies on optimized formulation of Diclofenac Sodium fast dissolving tablets were conducted according to the ICH guidelines. The various parameters tested during studies of Diclofenac Sodium fast dissolving tablets the formulation were withdrawn at suitable intervals (initial and 1 month) and analyzed visually for physical appearance and evaluated for different tests. The tablets showed no visual differences and compiled with description. The percentage of drug release from the formulation DH6 at different intervals of time is given in Table 5 and was found to be matching with specification. The results were shown in Table 5. From the results DH6 was selected as best formulation since it showed total drug release in 6 minutes.
Drug release kinetics

The drug release profiles of the tablets were studied includes zero order (Figure 2), First order (Figure 3), Higuchi square root of time model (Figure 4), Hixon-Crowell model (Figure 5) and Korsmeyer-Peppas model (Figure 6). From the results it is implying that the release kinetics from the FDT tablet follows zero order kinetics. Especially batch DH6 showed R² value of 0.9948 indicating the drug release followed zero order kinetics. The R² values of all formulations were showed in Table 6.

Table 3: Disintegration and wetting time.

<table>
<thead>
<tr>
<th>Time in min</th>
<th>DH1</th>
<th>DH2</th>
<th>DH3</th>
<th>DH4</th>
<th>DH5</th>
<th>DH6</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>16.07</td>
<td>23.14</td>
<td>27.64</td>
<td>23.78</td>
<td>28.28</td>
<td>30.21</td>
</tr>
<tr>
<td>4</td>
<td>48.85</td>
<td>57.21</td>
<td>48.85</td>
<td>58.5</td>
<td>62.35</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>53.35</td>
<td>83.57</td>
<td>90</td>
<td>86.14</td>
<td>92.57</td>
<td>100.92</td>
</tr>
<tr>
<td>8</td>
<td>83.57</td>
<td>91.28</td>
<td>99.64</td>
<td>88.07</td>
<td>96.42</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>89.35</td>
<td>98.35</td>
<td>100.92</td>
<td>97.71</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>100.28</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 4: Dissolution studies of formulations.

<table>
<thead>
<tr>
<th>S No</th>
<th>Test</th>
<th>Initial</th>
<th>40°C/75%RH After 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Thickness (mm) ± SD</td>
<td>3.95 ± 0.25</td>
<td>3.85 ± 0.0057</td>
</tr>
<tr>
<td>2</td>
<td>Hardness (kg/cm²) ± SD</td>
<td>3.5 ± 0.25</td>
<td>3 ± 0.011</td>
</tr>
<tr>
<td>3</td>
<td>Friability (% W/W) ± SD</td>
<td>0.52 ± 0.07</td>
<td>0.89 ± 0.002</td>
</tr>
<tr>
<td>4</td>
<td>Weight variation (%) ± SD</td>
<td>498.3 ± 0.16</td>
<td>485 ± 0.577</td>
</tr>
<tr>
<td>5</td>
<td>Drug content (%) ± SD</td>
<td>101.5 ± 1.25</td>
<td>97.2 ± 0.115</td>
</tr>
<tr>
<td>6</td>
<td>Wetting time (sec)</td>
<td>33 sec ± 0.49</td>
<td>30 sec ± 0.5</td>
</tr>
<tr>
<td>7</td>
<td>Disintegration time (sec)</td>
<td>25 sec ± 0.63</td>
<td>21 sec ± 0.39</td>
</tr>
<tr>
<td>8</td>
<td>Drug release</td>
<td>100% at 6min</td>
<td>97% at 6min</td>
</tr>
</tbody>
</table>

Table 5: Results for stability studies.

Figure 2: Zero order release kinetics plots.

Figure 3: First order release kinetics.

Figure 4: Higuchi model plots.

Figure 5: Hixon-Crowell model.

Figure 6: Korsmeyer-Peppas model plots.
Acknowledgement

The authors are thankful to Dr. L. Rathahal and Chairman of Lavu Educational Society for providing facility to carry out the above research work.

References


Table 6: Drug release kinetics (R² values of formulations).

Conclusion

The tablets prepared with hole technology showed all the parameters like hardness, friability, weight variation within the limits. All the formulations with increased concentrations of super disintegrants showed better drug release compared to the formulations with less concentration of super disintegrants. The formulation DH6 with 30 mg of SSG showed disintegration in 25 sec and a wetting time of 33 sec and showed better drug release in 6 min. The formulation is effectively useful in treatment of acute pains.


