INFLUENCE OF VARIOUS EXCIPIENTS ON QUALITY CONTROL PARAMETER OF ACECLOFENAC TABLETS CONTAINING SSG

C K Pithawalla Institute of Pharmaceutical Science and Research, Surat, Gujarat, India.

ABSTRACT
Fast dissolving tablets are dissolved /disintegrate without water within few second to few minutes. Aceclofenac, a non-steroid anti inflammatory drug used for pain and inflammation. In the present, study the effect of various excipient on fast dissolving tablets of Aceclofenac. Sodium starch glycolate was used as superdisintegrant. Fast dissolving tablets of Aceclofenac were prepared by direct compression method. All formulations were evaluated for hardness, friability, wetting time, disintegration time, and In vitro dissolution study. Tablets were evaluated for stability testing. Formulation containing microcrystalline cellulose and combination of microcrystalline cellulose-lactose (Batch F3 and Batch F5) shows less disintegration time compared to other batches. It was concluded that microcrystalline cellulose was found to be good excipient as compared to lactose and Di-basic calcium phosphate. It was also concluded that when microcrystalline cellulose used alone or in combination there was no difference in disintegration time and tablets are stable after storage.

Key words: Aceclofenac, FDT, SSG, MCC, Disintegration Time, Direct Compression

INTRODUCTION
A fast dissolving system can be defined as a dosage form for oral administration, which when placed in mouth, rapidly dispersed or dissolved and can be swallowed in form of liquid. Recently fast dissolving formulation is popular as NDDS because they are easy to administer and lead to better patient compliance. Pediatric and geriatric patient have difficulty in swallowing the conventional dosage forms. Fast dissolving and fast dispersing drug delivery system may offer a solution to these problems. Many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription, which results in high incidence of noncompliance and ineffective therapy.\[1\]
Fast-disintegrating tablets are gaining prominence as new drug-delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. Following are the reason for the need of the FDDTS:

- due to patients' poor acceptance and compliance with existing delivery regimes,
- To meet current needs of the industry like improved solubility/ stability, and bioavailability enhancement of poorly absorbed drugs.
- No complex procedure required for the preparation FDDT.
- Pharmaceutical marketing is another reason for the increase in available fast-dissolving/disintegrating products.

Various technologies have been used in the manufacture of FDT includes Freeze drying or lyophilization, Tablet Molding, Direct compression, Spray drying, Sublimation, Taste masking, Mass extraction, and Addition of superdisintegrant. Among the number of NSAIDs available, Aceclofenac (AC) is considered as one of the emerging NSAID. It is a newer derivative of Diclofenac and has less gastrointestinal complications. However, the problems of side effects after long term administration of these drugs, such as irritation and ulceration of the GI mucosa, have arisen in clinical trials. These gastroenteropathies are generally believed to be resulted from the direct contact effect, which can be attributed to the combination of local irritation produced by the free carboxylic group in the molecular structure and by local blockage of prostaglandin biosynthesis in the GI tract. The use of conjugates to provisionally hide the acidic group of NSAIDs has been proposed as an approach to reduce or suppress the GI toxicity due to the direct contact effect. Therefore, the development of new NSAIDs without these side effects has long been awaited.

In present study, the effect of various excipient on FDT of Aceclofenac was studied. Formulation of Aceclofenac tablets containing various excipient, alone or in
combination was carried out. Evaluation of formulated tablets was done using various quality parameters like hardness, friability, wetting time, DT, in vitro dissolution study. Finally, stability study of optimized batches was performed.

MATERIALS AND METHODS

Materials

Aceclofenac was received as a gift sample from Torrent Pharmaceutical Ltd., Ahmedabad, Gujarat, India. Sodium Starch Glycolate (SSG) was gifted from Colorcon Asia Pvt Ltd (Mumbai). Lactose, Di-basic calcium phosphate (DCP), microcrystalline cellulose (MCC), Sucrose and Talc were purchased from S D Fine, India. All other reagents and chemicals used were of analytical grade.

Preparation of Fast dissolving Aceclofenac tablets

Aceclofenac and all other ingredient pass through the sieve no. 60. Aceclofenac, excipient and superdisintegrant are mixed in mortar and mix it well by pestle. To the above mixture talc was added, mix it well. The tablets were prepared by direct compression on a rotary tablet press (Model Rimek-II, Karnavati Engg., Ahmedabad), fitted with concave punches of 9 mm diameter. The turret was rotated at a fixed speed of 30 rpm. The compositions of various batches are shown in Table 1.

### TABLE 1 FORMULATION OF ACECLOFENAC FAST DISSOLVING TABLET

<table>
<thead>
<tr>
<th>Ingredients (mg)</th>
<th>Batch F1</th>
<th>Batch F2</th>
<th>Batch F3</th>
<th>Batch F4</th>
<th>Batch F5</th>
<th>Batch F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aceclofenac</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>SSG</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Lactose</td>
<td>112</td>
<td>-</td>
<td>-</td>
<td>56</td>
<td>56</td>
<td>-</td>
</tr>
<tr>
<td>DCP</td>
<td>-</td>
<td>112</td>
<td>-</td>
<td>56</td>
<td>-</td>
<td>56</td>
</tr>
<tr>
<td>MCC</td>
<td>-</td>
<td>-</td>
<td>112</td>
<td>-</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>Sucrose</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Talc</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>275</td>
<td>275</td>
<td>275</td>
<td>275</td>
<td>275</td>
<td>275</td>
</tr>
</tbody>
</table>
Uniformity of weight

The weights were determined by using Sartorious balance (Model CP-224 S). Weight control is based on a sample of 20 tablets. Determinations were made in triplicate.[7]

Hardness and Friability test

Hardness was measured by Monsanto Hardness Tester. Friability was evaluated as the percentage weight loss of 20 tablets tumbled in a friabilator for 4 min at 25 rpm. The tablets were de-dusted, and the loss in weight caused by fracture or abrasion was recorded as percentage friability.

Disintegration time

The time required for disintegration of 6 tablets per batch was carried out in USP disintegration test apparatus (Model ED2L, Electrolab, Mumbai, India) containing 900 mL phosphate buffer (pH 6.8) at 37±0.5°C. The mean DT was calculated.

Wetting time

A piece of tissue paper folded twice was kept in a culture dish (internal diameter 5.5 cm) containing ~6 mL of purified water. A tablet having a small amount of amaranth powder on the upper surface was placed on the tissue paper. The time required to develop a red color on upper surface of the tablet was recorded as the wetting time.[8]

Dissolution Rate Study

The drug release study was carried out using USP XXIII paddle type dissolution test apparatus (Model TDL-08, Electrolab, Mumbai) at 37±0.5°C and at 50 rpm using 900mL Phosphate Buffer (pH 6.8) as dissolution medium (n=5). Five milliliters sample solution was withdrawn at predetermined time intervals, filtered through a 0.45 micron membrane filter, diluted suitably, and analyzed spectrophotometrically at 276nm using a Shimadzu-1700 UV-Visible double beam spectrophotometer. Equal amounts of fresh dissolution medium were replaced immediately after withdrawal of a test sample. The percentage drug dissolved at different time intervals was calculated using regression equation generated from the standard curve.

Stability Study

To study the effect of storage on DT and hardness, stability study of best formulation (Batch F5) was carried out at 40°C and 75% RH in a humidity oven. Samples
were withdrawn after three-month interval and were evaluated for change in DT and hardness.

RESULT AND DISCUSSION

The use of superdisintegrant for preparation of fast-dissolving tablets is highly effective and commercially feasible. There was a uniformity of weight in tablets for all formulations. The hardness of prepared formulation was found to be 2.5 Kg/cm². Friability of all formulation was also within the range i.e., less than 1% indicating the ability of tablet to withstand abrasion in handling packaging and shipment. Since, the dissolution process of a tablet depends upon wetting followed by disintegration. Wetting time measured give another confirmative test for evaluation of tablets. Wetting time for all the formulation was found to be 3.0-9.0 min.\(^9\)\(^{ -}\)\(^{14}\) Result of evaluation parameter of Aceclofenac tablets are shown in the Table 2.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Batch F1</th>
<th>Batch F2</th>
<th>Batch F3</th>
<th>Batch F4</th>
<th>Batch F5</th>
<th>Batch F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness (Kg/cm²) n = 6, Mean ± SD</td>
<td>2.5 ± 0.10</td>
<td>2.5 ± 0.20</td>
<td>2.5 ± 0.20</td>
<td>2.5 ± 0.20</td>
<td>2.5 ± 0.10</td>
<td>2.5 ± 0.10</td>
</tr>
<tr>
<td>Friability (%) n = 3, Mean ± SD</td>
<td>0.6 ± 0.15</td>
<td>0.8 ± 0.10</td>
<td>0.9 ± 0.20</td>
<td>0.8 ± 0.17</td>
<td>0.9 ± 0.18</td>
<td>0.5 ± 0.10</td>
</tr>
<tr>
<td>Disintegration time (sec) n = 6, Mean ± SD</td>
<td>60 ± 5.00</td>
<td>27 ± 2.00</td>
<td>15 ± 2.00</td>
<td>42 ± 3.00</td>
<td>16 ± 2.00</td>
<td>30 ± 2.50</td>
</tr>
<tr>
<td>Wetting time (min) n = 3, Mean ± SD</td>
<td>9.0 ± 1.50</td>
<td>4.0 ± 1.00</td>
<td>3.0 ± 0.50</td>
<td>8.0 ± 1.50</td>
<td>3.0 ± 1.20</td>
<td>4.0 ± 1.10</td>
</tr>
</tbody>
</table>

The most important parameters that need to be optimized in the development of fast disintegrating tablets are the disintegration time. It was observed from results of DT that as we move from batch F1 to F3, there was decrease in DT from 60 to 15 seconds. This may be due the nature of the excipient. Lactose is hydrophilic in nature while DCP is hydrophobic in nature. MCC is well accepted excipient for fast dissolving tablet. While using combination of different excipient (Batches F4 to F6), it was observed that batch F5 (combination of lactose-MCC) shows lesser DT as compared to other batches (Batch F4 – lactose & DCP, Batch F6 – DCP & MCC). Following are the order observed for the combination of excipient for higher to lower DT: lactose - DCP >
DCP - MCC > MCC - lactose. It was also observed that when MCC used alone (Batch F3) or in combination with lactose (Batch F5), there was a no significant difference for the DT. It was concluded that Batch F5 was considered as optimized batch.\cite{15-18}

The influence of various excipients on the dissolution of Aceclofenac is shown in Fig. 1 & 2. Fig.1 shows dissolution profile of batches F1, F2 and F3. It was observed that after 10 min, % drug release was found to be 24.21, 32.56 and 40.09% respectively. Fig. 2 shows dissolution profile of batches F4, F5 and F6. It was observed that after 10 min, % drug release was found to be 26.22, 41.22 and 37.61% respectively. It was observed that formulation containing MCC (Batch F3) having more % drug release as compared to DCP and lactose (Batches F1 and F2). It was also observed that formulation containing combination of MCC-lactose (Batch F5) having more % drug release as compared to other combination (DCP-lactose and DCP-MCC) (Batches F4 and F6). This may be due to more supporting capacity of MCC (to disintegration and dissolution) as compared to others. It was also observed that when MCC used alone (Batch F3) or in combination (Batch F5), there is no significant difference in % drug release. By considering the cost of MCC and lactose, batch F5 was considered as optimized batch. This rapid disintegration of fast disintegrating tablets was due to the penetration of dissolution medium into the pores of the tablets, which lead to the swelling and wicking of super disintegrants to create enough hydrodynamic pressure for quick and complete disintegration of the tablet.\cite{19-22}

![Figure 1](image)

**Figure 1**
Dissolution Profile of Batch F1, F2, F3 in Phosphate Buffer.
Finally, stability study of optimized batch (Batch F5) was carried out at 40°C and 75% RH in a humidity oven. Samples were withdrawn after three-month interval and evaluated for change in hardness and DT. It was found that there was little softening of tablets, so hardness of tablets were reduced from $2.5 \pm 0.10$ to $2.2 \pm 0.10$ kg/cm$^2$ and some increase in DT from $16 \pm 2.00$ to $19 \pm 2.00$ seconds, respectively. There was a no significant effect of such environment on tablets. It was concluded that tablets of Aceclofenac are stable after stability study.

The areas where further work can be done include using a fluid bed dryer or spray dryer for preparation of modified excipient, using different combinations and ratios with widely accepted super disintegrating agent like crospovidone, SSG and croscarmellose.

**CONCLUSION**

In the present study, the effects of various excipient effects on FDT of Aceclofenac were studies. It was concluded that Aceclofenac tablets passes for hardness, friability, wetting time, DT, and *in vitro* dissolution profile. It was observed that when MCC used alone or in combination there is no major difference in DT and % drug release. It is concluded that, although functionality differences existed between excipients, but
Aceclofenac tablets prepared using MCC. Tablets are stable after stability testing. In future, it can be used with different technique to improve quality control parameters of tablets.

REFERENCES