COMPARATIVE IN VITRO EVALUATION OF COMMERCIAL ACECLOFENAC TABLETS

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ABSTRACT
Aceclofenac (ACL), is a synthetic new NSAID, which has been widely used in treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis with minimum side effects. Since Aceclofenac tablet is not an official product of I. P. and practically insoluble in water, it was thought necessary to carry out in vitro testing of the commercial products with special attention to dissolution rate studies. Three different brands (A, B & c) of Aceclofenac tablets 100 mg manufactured in India were evaluated for nine in vitro parameters, both official and non-official, viz., uniformity of weight, dimensions, hardness test, friability test, disintegration test, dissolution test and assay. The dissolution test was carried out in phosphate buffer pH 7.5.

The study on dissolution profile revealed that product A had faster dissolution rate while product C has slowest dissolution rate. All the products met the requirements as per general specifications of Indian pharmacopoeia for tablet formulation. Assay value lies within the limit of 90% to 110%.

KEY WORDS: Aceclofenac, Evaluation, Dissolution rate, friability, Assay etc.

INTRODUCTION
Aceclofenac is an orally administered phenyl acetic acid derivatives with effects on a variety of inflammatory mediators.
Molecular Weight: 354.2
Molecular Formula: $\text{C}_{16}\text{H}_{13}\text{Cl}_2\text{NO}_4$
Melting Point: 149-153 °C
Content: Aceclofenac contains not less than 99.0% and not more than the equivalent of 101.0% percent of $\text{C}_{16}\text{H}_{13}\text{Cl}_2\text{NO}_4$ calculated on the dried basis.
Description: It is a white or almost white crystalline powder.
Solubility: Practically insoluble in water, Freely soluble in acetone, Soluble in alcohol (95%)
Storage: Stored in air tight container protected from light at room temperature not exceeding 30°C.
Therapeutic Category: Anti-inflammatory; analgesic.
It provides symptomatic relief in a variety of painful conditions & helps to reduce inflammation. It is a cytokine inhibitor. It works by blocking the action of substance in the body called as cyclo-oxygenase. Cyclo-oxygenase is involved in the production of prostaglandins chemicals in the body) which cause pain, swelling & inflammation [1][2]. The main purpose of solid dosage form is to make a drug available to the human body at a certain rate and define amount through the gastro intestinal tract so that the drug can produce pharmacological effects. But studies on bioavailability of drugs from a given dosage form reveled that, in many situations, solid dosage forms did not give the same therapeutic effects. Statistical comparison of dissolution profiles under variety of conditions relating to the formulation characteristics, lot-to-lot & brand-to-brand variation occurs. This is mainly due to the insufficient dissolution and subsequent absorption of the drug from the GIT. So, dissolution analysis of pharmaceutical solid dosage forms is a very important test of product quality [3][4]. Aceclofenac (ACL), is a synthetic new NSAID, which has been widely used in treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis with minimum side effects. ACL tablet is not an official product of I. P. ACL and it is poorly water soluble.
class II drug. Therefore, it’s dissolution is rate-limiting step for it’s absorption. Since ACL tablet is an unofficial product and practically insoluble in water, it was thought necessary to carryout in vitro testing of the commercial products with special attention to dissolution rate studies. Tablets of 100 mg were chosen for the investigation. Quality of pharmaceutical product is the most important for efficacy and safety of product. Quality of product refers to its confining to the standards pre-set to assure the desired purpose.[5]

MATERIALS & METHODS

Reagents & Chemicals
Aceclofenac pure drug, Potassium Dihydrogen Orthophosphate, Sodium Hydroxide, Methanol, Marketed Formulations Of Aceclofenac Tablets 100 mg, Distilled water.

Instruments
Shimadzu UV-Vis spectrophotometer, vernier caliper, Disintegration Test Apparatus, Monsanto Hardness Tester, Friabilator, Dissolution Test Apparatus, Digital Balance, Stop Watch.

Evaluation Tests For Tablets

Official evaluation tests
1 Disintegration Test
Introduce one tablet into each tube & add disc to each tube. Suspend the assembly in the beaker containing the specified liquid & operate the apparatus for the specified period of time [6].

2 Dissolution Test
Place the stated volume of the dissolution medium (Phosphate Buffer pH 7.5), free from dissolved air, into the vessel of the apparatus. Assemble the apparatus & warm the dissolution medium at 36.5-37.5°. Place one tablet in dry basket at the beginning of each test. Lower the basket into position before rotation. Operate apparatus immediately. After appropriate time interval, a sufficient volume of sample was withdrawn and filtered through Whatman filter No. 41. Immediately, same volume of the fresh dissolution medium was transferred to the dissolution flask. Samples were collected at suitable time interval and analyzed spectrophotometrically at 273 nm [6].
3 Uniformity Of weight Test
Weigh individually 20 units of tablets and calculate the average weight. Not more than two of
the individual weights deviates from the average weight by more than the percentage given in
the following table and none deviates by more than twice that percentage.[6]

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Average Weight Of Tablets</th>
<th>Percent Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>80 mg or less</td>
<td>± 10</td>
</tr>
<tr>
<td>2.</td>
<td>More than 80mg or Less than 250mg</td>
<td>± 7.5%</td>
</tr>
<tr>
<td>3.</td>
<td>250mg or more</td>
<td>± 5%</td>
</tr>
</tbody>
</table>

4 Assay
Weigh accurately 20 tablets & powdered. The powder containing 100 mg of Aceclofenac is
transferred to 100 ml volumetric flask & make up the volume to mark with methanol. Filter
the solution through Whatman filter paper No. 41. Transfer 5 ml of the filtrate into 50 ml
volumetric flask & make up the volume to mark with methanol. Determine respective
absorbance at 276 nm against the methanol as blank.[7]

5 Friability test
Friability test can be performed to evaluate the ability of the tablets to withstand abrasion in
packing, handling and transporting. The Friabilator consists of a plastic chamber divided into
two parts and revolves at 25 rpm. 20 of tablets are weighed, placed in the tumbling chamber
and rotated for four minutes of 100 revolutions. During each revolution the tablets fall from a
distance of six inches to undergo shock. After 100 revolutions the tablets are again weighed.
The loss in weight indicates the friability. [9]

Non-official evaluation Tests:
1 Dimensions
With the help of vernier caliper find out the thickness & diameter of 10 tablets [8].

2 Shape
All tablets from single brand should have uniform shape.

3 Appearance
Observe the appearance of tablet. Surface of tablet should be smooth. Three should not be
sign of coating & all tablets have uniform texture.
4 Hardness test

Hardness can be defined as the strength of the tablet to withstand the pressure applied. The tablet to be tested was held between a fixed and a moving jaw of Monsanto Hardness Tester. The force applied to the edge of the tablet was gradually increased by moving the screw knob forward until the tablet breaks. The reading was noted from the scale which indicates the pressure required to break the tablet.[8]

Table 1: Calibration Curve Of Aceclofenac In Phosphate Buffer pH 7.5

<table>
<thead>
<tr>
<th>Concentration Mcg/ml</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.128</td>
</tr>
<tr>
<td>4</td>
<td>0.233</td>
</tr>
<tr>
<td>6</td>
<td>0.337</td>
</tr>
<tr>
<td>8</td>
<td>0.436</td>
</tr>
<tr>
<td>10</td>
<td>0.53</td>
</tr>
<tr>
<td>12</td>
<td>0.633</td>
</tr>
<tr>
<td>14</td>
<td>0.738</td>
</tr>
<tr>
<td>16</td>
<td>0.852</td>
</tr>
</tbody>
</table>

Fig. 1:

RESULTS AND DISCUSSION

Official evaluation tests

1 Disintegration Test

Tablets from brand A was disintegrates within 30 seconds, Tablets from brand B was disintegrates within 85 seconds whereas tablets from brand C was disintegrates within 3 minutes.
All the brands of tablets disintegrated before 15 minutes. It conformed to the I. P. specifications.

2 Dissolution Test
Dissolution test is carried out on 6 tablets of each brand. The release of the drug in dissolution test was observed till 60 minutes. From the data, it was interesting to note that more than 80% drug released from brand A within 40 min, while the product B release were around 73%, product C released 70%. The variation in the dissolution, the profile of this commercial ACL tablet was in the following descending order A > B > C.

Table 2. % Drug Release Of Aceclofenac (Brand A) Tablets.

<table>
<thead>
<tr>
<th>Time In Minutes</th>
<th>Tablet No. 1</th>
<th>Tablet No. 2</th>
<th>Tablet No. 3</th>
<th>Tablet No. 4</th>
<th>Tablet No. 5</th>
<th>Tablet No. 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>42</td>
<td>56.12</td>
<td>48.88</td>
<td>38.82</td>
<td>46.59</td>
<td>47.29</td>
</tr>
<tr>
<td>10</td>
<td>61.76</td>
<td>64.11</td>
<td>65.47</td>
<td>56.29</td>
<td>62.82</td>
<td>68.11</td>
</tr>
<tr>
<td>20</td>
<td>73.94</td>
<td>75.35</td>
<td>79.94</td>
<td>68.65</td>
<td>77.12</td>
<td>78.88</td>
</tr>
<tr>
<td>40</td>
<td>80.71</td>
<td>85.06</td>
<td>86.82</td>
<td>84.06</td>
<td>88.06</td>
<td>89.65</td>
</tr>
<tr>
<td>60</td>
<td>99</td>
<td>99.53</td>
<td>96.53</td>
<td>94.24</td>
<td>98.12</td>
<td>99.53</td>
</tr>
</tbody>
</table>

![Drug Release Profile of Aceclofenac (Brand A Tablets)](image)

Fig.2

For brand A tablets more than 45% drug was dissolved within 5 min. More than 60% drug was dissolved within 10 min. More than 70% drug was dissolved within 20 min. More than 80% drug was dissolved within 40 min. & more than 95% drug was dissolved within 60 min.
Table 3. % Drug Release Of Aceclofenac (Brand B) Tablets.

<table>
<thead>
<tr>
<th>Time In Minutes</th>
<th>Tablet No. 1</th>
<th>Tablet No. 2</th>
<th>Tablet No. 3</th>
<th>Tablet No. 4</th>
<th>Tablet No. 5</th>
<th>Tablet No. 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>34.12</td>
<td>37.12</td>
<td>36.59</td>
<td>38.65</td>
<td>29.71</td>
<td>33.24</td>
</tr>
<tr>
<td>10</td>
<td>48.22</td>
<td>51.55</td>
<td>47.71</td>
<td>53.29</td>
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<td>60.59</td>
<td>62.71</td>
<td>63.47</td>
<td>65.88</td>
<td>59.35</td>
</tr>
<tr>
<td>40</td>
<td>72.06</td>
<td>73.29</td>
<td>74.35</td>
<td>72.41</td>
<td>72.82</td>
<td>73.21</td>
</tr>
<tr>
<td>60</td>
<td>88.29</td>
<td>83.18</td>
<td>87.76</td>
<td>85.29</td>
<td>86.22</td>
<td>88.29</td>
</tr>
</tbody>
</table>

Fig. 3:

For brand B tablets more than 30% drug was dissolved within 5 min. More than 50% drug was dissolved within 10 min. More than 60% drug was dissolved within 20 min. More than 70% drug was dissolved within 40 min. & more than 85% drug was dissolved within 60 min.

Table 4. % Drug Release Of Aceclofenac (Brand C) Tablets.

<table>
<thead>
<tr>
<th>Time In Minutes</th>
<th>Tablet No. 1</th>
<th>Tablet No. 2</th>
<th>Tablet No. 3</th>
<th>Tablet No. 4</th>
<th>Tablet No. 5</th>
<th>Tablet No. 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>30.35</td>
<td>38.88</td>
<td>38.29</td>
<td>40.41</td>
<td>37.59</td>
<td>40.06</td>
</tr>
<tr>
<td>10</td>
<td>46.24</td>
<td>52.94</td>
<td>55.76</td>
<td>51.88</td>
<td>55.41</td>
<td>51.35</td>
</tr>
<tr>
<td>20</td>
<td>60.88</td>
<td>59.53</td>
<td>62.59</td>
<td>63.35</td>
<td>60.24</td>
<td>59.18</td>
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<td>70.29</td>
<td>70.22</td>
<td>68.18</td>
<td>68.12</td>
<td>70.53</td>
<td>69.28</td>
</tr>
<tr>
<td>60</td>
<td>85.53</td>
<td>82.55</td>
<td>86.88</td>
<td>82</td>
<td>84.94</td>
<td>83.82</td>
</tr>
</tbody>
</table>
For brand C tablets more than 30% drug was dissolved within 5 min. More than 50% drug was dissolved within 10 min. More than 60% drug was dissolved within 20 min. More than 70% drug was dissolved within 40 min. & more than 83% drug was dissolved within 60 min.

3 Uniformity Of weight Test:
Uniformity Of weight Test was performed on all brands by using 20 units of tablets from each brand. As per I.P. specifications all brands passes the test.

4 Assay
The value of all ACL tablets were within the range of 90% to 110% of stated amount of ACL.

5 Friability test
The friability was carried out for all the brands of tablets. The friability was less than 0.3% for all the brands. The values of less than 1% are considered to be highly satisfactory evaluation characteristics.

Nonofficial evaluation Tests
1 Dimensions
All three brands of Aceclofenac Tablets have uniform diameter & thickness.

2 Shape
All three brands of Aceclofenac Tablets have round shape.
3 Appearance

All three brands of Aceclofenac tablets passed the test for appearance.

4 Hardness test

Using Monsanto hardness tester, the strength of the tablets were tested. All the tablets showed good strength, which is necessary for safe transportation. Sample C had minimum hardness while A and B have maximum hardness.

CONCLUSION

It is concluded that all three brands of commercial Aceclofenac tablets passes official & non official tests for tablets as per I.P. & have good drug release properties.

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