FORMULATION AND EVALUATION OF ACECLOFENAC SUSTAINED RELEASED TABLET

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ABSTRACT

Aceclofenac is a Non-steroidal Anti Inflammatory drug (NSAIDS). It can show Anti-inflammatory, Antipyretic, and analgesic activity and Aceclofenac is important to Inhibition of Cyclooxygenase (COX I, COX II) Enzyme is responsible for Inhibition of Prostaglandins Synthesis. The Authentication and Preformulation studies associated to pure drug Aceclofenac is conducted for maintaining their standard, quality, purity and stability. The formulation of Aceclofenac Sustained release Tablet is important to give prolonged activity in prolonged drug release in Extended Period of Time for the Long Term Therapeutic activity. The Formulation of Sustained Released Tablet by using Suitable Excipients such as (MCC, PVP K 30, I.P.A., HPMC K 4 M, HPMC K 15 M, Acrypol 934 P, Aerosil and Magnesium Stearate). This Aceclofenac Sustained released tablet is from by Wet Granulation Method. The Prepared sustained released Tablet is Evaluated In terms of bulk density, tapped density, angle of repose, carr’s Index and, hardness test, weight variation test, friability test and in vitro study. The result associated in Optimized batch is good to Satisfactory and having a good free flowing property. The hardness, weight variation, and friability these values are within the pharmacopeia limit. The in vitro Dissolution studies shows Maximum percentage of release of drug (96.18) with in end of 8 hours.

INTRODUCTION
Aceclofenac is a Non-Steroidal Anti-inflammatory drug (NSAIDS). Aceclofenac is important to show the Analgesic as well as anti-inflammatory activity for the prevention of Inflammation. The Basic mechanism action of drug to inhibit the COX I, COX II, (Cyclooxygenase I and Cyclooxygenase II) is Responsible for the Inflammation. The chemically Aceclofenac is known as 2-[(2-[(2, 6-dichlorophenyl) amino] phenyl] acetyl] oxy] acetic acid. It is important to give symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. The half-life of Aceclofenac is about 5 hrs. And the dosing Frequency of Aceclofenac is more than one per day hence Aceclofenac is act as Ideal Candidate of Sustained drug Delivery system. It is important application to reduce the dosing frequency, and give prolonged activity in Longer Period of Time. Aceclofenac is a drug is important to prevent the problem associated in gastric irritation and maintain the stability of GI environment. Aceclofenac is a drug is mainly used for the treatment of of mild, moderate, postoperative pain and it is effective against menstrual pain and endometriosis. [1]

MATERIAL AND METHOD
MATERIAL
Aceclofenac and all Formulation Excipient (MCC, PVP K 30, I.P.A., HPMC K 4 M, HPMC K 15 M, Acrypol 934 P, Aerosil and Magnesium Stearate) was obtained from Pharmaceutics Laboratory of R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur 425405, Maharashtra State, one of the NBA and NAAC accredited and AICTE Approved institutes in India.

METHOD
The parameters of Authentication and Preformulation is carried out by pure drug Aceclofenac for Maintaining their Quality, Purity and Standard.

AUTHENTICATION PARAMETERS
Melting Point Method
Melting Point determination is one of the preformulation property in which the temperature at which it changes state from solid to liquid at atmospheric pressure. At the melting process the solid and liquid can exist equilibrium. The Melting point of diclofenac pure drug is determine by using two types of method one is Conventional method and another is Digital method. [2]
Log P Value

Log p value is determined by using Partition Coefficient Phenomenon. In which The 1 gm of drug is added in separating funnel containing equal portion of 25 ml of Octanol and 25 ml of Water. The separating funnel is shake 20 – 25 min. and stabilized the mixture. After stabilizing the mixture to remove water phase from separating funnel and filter it. Take Absorbance of Filtrate and calculate the log p value.\[^3\]

Solubility Studies

The Term Solubility is defined as maximum amount of solute that can be dissolved in a given amount of solvent to form a homogenous system at specified temperature and Specific Pressure to from Saturated Solution.\[^4\]

Procedure

- To Prepare a different solutions Water, PH 1.2 Acidic Buffer, PH 6.8 Phosphate Buffer, PH 7.4 Phosphate Buffer.
- The drug material is added in to above solutions till Supersaturated Solution is from.
- The Mixture can Placed in Orbital Shaker for 24 hrs. After 24 hrs. Filter the mixture Take Filtrate and Give Absorbance.
- To detect the Concentration of Drug is Soluble in Different Solutions.

Calibration Curve of Aceclofenac

Calibration Curve is determined by using UV Spectrophotometric methods. In which 10 mg drug is added in 100 ml of water (100 μg/ml Solution). To Prepared different Dilutions (0, 2, 4, 6, 8, 10, 12) of above solution (100 μg/ml Solution). Take Absorbance in respective λ_{max} 276 nm.\[^5\]

PREFORMULATION STUDIES

Drug-Excipient Compatibility Studies

Drug is an active part of dosages form and it is mainly responsible for therapeutic value and Excipient substances which are included along with drugs being formulated in a dosage form so as to impart specific qualities to them. It is important for determination of Stability of the dosage and its helps to avoid the surprise problems by performing DECS we can know the possible reaction before formulating final dosage form. It’s also used for development of new drug delivery system as well as investigation of new drug Product.\[^6\]
Procedure
The Equal portion of Drug and Excipient (1:1 ratio) is added in Ampules and the Ampules are placed in Stability Chamber for one Week. After One Week the Drug Excipient Compatibility Study is Determine by using TLC (Thin Layer Chromatography), IR (Infrared Spectroscopy) and DSC (Differential Scanning Colariometry).

METHOD OF FORMULATION
Formulation of Aceclofenac Sustained release tablet is done by using the Wet Granulation Method. In which Aceclofenac, HPMC K 15 M, PVP K-30 and Microcrystalline cellulose are mixed together in mortal and pastel. To prepare binder solution of PVP K 30 in Iso propyl alcohol. The Prepared binder solution is added in the mixture of drug and excipient in mortal and pastel till dough mass is formed. The mass is passed through the mesh 20 sieve to get optimum sized of after drying (5-10 min. in hot air oven) of Granules. Lubrication of granules is done by using Magnesium Stearate and granules are passed into 60 mesh sieve. The Compression is done by using the 8 station signal rotatory tablet punching machine having hardness is 8-9 kg/cm². The all formulation ingredients are reported in Table 1.

EVALUATION PARAMETERS

Bulk density
It is a ratio of Bulk mass and Bulk Volume is known as Bulk Density. Amount of Powder is Weighed Separately and transferred into 100 ml of measuring cylinder, initial volume of Powder Material is measured and calculated bulk density according to following formula.\(^7\)

\[
\text{Bulk density} = \frac{\text{Mass}}{\text{Volume}}
\]

Tapped Density
It is a Ratio of Bulk Mass and Tapped Volume is known as Tapped Density. Tapped density is Important Evaluation Parameter is determined by placing a graduated cylinder containing a known mass of powder Undergoes Tapping in Manually (100 Tapes) as well As Using a Mechanical apparatus under powder bed volume has reached a minimum volume. The Tapped Density is calculated by following Formula.\(^7\)

\[
\text{Tapped density} = \frac{\text{Weight of Powder}}{\text{tapped volume of Powder}}
\]
Compressibility Index or Carr’s Index
The Calculation of Compressibility index is based on the Tapped density and Bulk density. It is a ratio of Tapped density and Bulk Density i.e. Compressibility Index. The Tapped density is minimized by the fluff density, divided by tapped density multiply by the 100, to get the Carr’s Index. Carr’s Index is less than or equal to \(<10\) indicates free flowing properties and Carr’s Index is greater than \(>10\) indicates poor flowing Properties.

Angle of Repose
It defines as the Pile surface of Powder is known as Angle of Repose. In this method of determination of angle of repose in which the angle of repose is to pour the powder a conical on a level, flat surface and measure the included angle. The Following Formula for determination of angle of repose: \(^8\)

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

Where,
\(\theta\) - Angle of repose,
\(h\) - Height of the powder cone,
\(r\) - Radius of the powder cone.

The Angle of repose is less than or equal to \(40^\circ\) indicates free flowing properties. The angle of repose is greater than \(40^\circ\) indicates poor flow of material.

Hardness or Crushing strength
Hardness of Tablet is determined by using Conventional Hardness Tester and Digital Hardness Tester. The Standard range of the hardness of Sustained release tablet is 10 -20 kg/CM\(^2\). \(^8\)

Friability Test
The friability of 20 tablets was determined Using Friability Tester. 20 tablets from each formulation were weighed and tested at a speed of 25 rpm for 4 min. After removing of tablets were re-weighed and friability percentage was calculated. To give a initial weight of 20 tablet Minimized these wt. by friability after the 20 tablet, divided by friability after 20 tablet multiply by 100, to get the appropriate friability of the 20 tablets. \(^9\)
Weight variation test
Weight variation was carried out to ensure that, each of tablets contains the proper amount of drug. The test was carried out by weighing the 20 tablets individually using analytical balance, then calculating the average weight, and comparing the individual tablet weights to the average. The percentage of weight variation is calculated by using the following formula:[9]

Weight variation \(= \left[\frac{X^*}{X}\right] \times 100\)

- X - Actual weight of the tablet
- X -* Average weight of the tablet

In vitro drug release studies
It is a Process in which Solid Material Dissolved in Liquid Medium per Unit Time Period. It is mainly based on Sink Condition. Dissolution of Sustained Release Tablet is determined by Paddle Type of Dissolution Apparatus. The tablet was added into cylindrical vessel containing 900 ml PH 1.2 Acidic media having 75 rpm for next two hours and tem. 37±0.5°C. Dissolution media was changes tablet was added in to PH 6.8 Phosphate buffer for next one hour of interval. After every one hour 5 ml sample was Withdrawn and appropriate quantity of sample take absorbance by using U.V. spectroscopy technique and determine rate of dissolution of tablet. [10]

RESULTS AND DISSCUSION
AUTHENTICATION PARAMETERS
Melting Point Method
The Melting Point of Aceclofenac is determined by Conventional and Digital Method and Melting Point of Aceclofenac is Reported in Table 2.

Log P Value
Log P Value is determined by Partition Coefficient Phenomenon and Log P Value of Aceclofenac is reported in Table 2.

Solubility Studies
The Solubility of Aceclofenac in Given Solution. (Water, PH 1.2 Acidic Buffer, PH 6.8 Phosphate Buffer, PH 7.4 Phosphate Buffer) is Reported in Table 3.
Calibration Curve of Aceclofenac in water
The Calibration Curve of Aceclofenac is determined by using U.V. Spectroscopic Method. In which the Absorbance of Aceclofenac in Different Concentration (0, 2, 4, 6, 8, 10, and 12) is reported in 4. And The Calibration Curve is shown in Figure 1.

PREFORMULATION STUDIES
The Drug and Excipient Compatibility studies determined by TLC (Thin Layer Chromatography) and IR (Infrared Spectroscopy) Method In which The TLC of Drug, Drug and Excipient before Stability Chamber and After Stability Chamber is reported in Table 5. And the IR of Pure drug Aceclofenac is shown in Figure 2. The DSC (differential Scanning Colariometry) in which DSC Thermogram is reported in Figure 3.

EVALUATION PARAMETERS
Bulk density
It is important parameter for determination of Flow characteristic in which the Bulk Density of Aceclofenac is reported in Table 6.

Tapped Density
It is important parameter for determination of Flow characteristic in which the Tapped Density of Aceclofenac is reported in Table 6.

Compressibility Index or Carr’s Index
The compressibility index is determined on the basis of Tapped density and bulk density and it is important for determination of flow characteristic in which the Compressibility Index or Carr’s Index of Aceclofenac is reported in Table 6.

Angle of Repose
It is important flow property for determination of flow of material and the value associated in angle of repose is less than 40° is indicate good flow property in which angle of repose of Aceclofenac tablet is reported in Table 6.

Hardness or Crushing strength
The hardness is determined by using a conventional or digital hardness tester in which the hardness of Aceclofenac tablet is reported in Table No.6.
Friability Test
The Friability of Tablet is always less than 1% and the Friability of Aceclofenac is reported in Table 6.

Weight variation test
All 20 Sustained released tablet is passed the weight variation test as per pharmacopoeial limits. The weight of all 20 tablets is uniform and the weight variation of Aceclofenac is reported in Table 6.

In vitro drug release studies
The In vitro drug release studies of Sustained released tablet is determined in PH 6.8 Buffer, in which 96.18 % drug is releases at the end of 8 Hours And the in vitro drug released of Aceclofenac is shown in Figure 4.

Table 1. Formulation Ingredients

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Formulation ingredient</th>
<th>F₁</th>
<th>F₂</th>
<th>F₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Aceclofenac</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>2</td>
<td>MCC</td>
<td>67</td>
<td>67</td>
<td>49</td>
</tr>
<tr>
<td>3</td>
<td>PVP K - 30</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>I.P.A.</td>
<td>Q.S.</td>
<td>Q.S.</td>
<td>Q.S.</td>
</tr>
<tr>
<td>5</td>
<td>HPMC K 4 M</td>
<td>-</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>HPMC K 15 M</td>
<td>15</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>Acrypol 934 P</td>
<td>10</td>
<td>02</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>Magnesium Stearate</td>
<td>05</td>
<td>08</td>
<td>05</td>
</tr>
<tr>
<td>9</td>
<td>Aerosil</td>
<td>03</td>
<td>03</td>
<td>03</td>
</tr>
<tr>
<td></td>
<td>Total Weight [Mg]</td>
<td>310</td>
<td>310</td>
<td>310</td>
</tr>
</tbody>
</table>

Table 2. Melting Point of Aceclofenac

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Parameters</th>
<th>Experimental Result</th>
<th>Std.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Melting Point (°c)</td>
<td>151 – 152°c</td>
<td>152 – 153°c</td>
</tr>
<tr>
<td>2</td>
<td>Log p Value</td>
<td>2.15</td>
<td>2.17</td>
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</table>

Table 3. Solubility of Aceclofenac in different solvents

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Medium</th>
<th>Concentration of drug Soluble (mg /ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Water</td>
<td>2.01</td>
</tr>
<tr>
<td>2</td>
<td>PH 1.2 Acidic Buffer</td>
<td>2.80</td>
</tr>
<tr>
<td>3</td>
<td>PH 6.8 Phosphate Buffer</td>
<td>4.0</td>
</tr>
<tr>
<td>4</td>
<td>PH 7.4 Phosphate Buffer</td>
<td>4.82</td>
</tr>
<tr>
<td>Result</td>
<td>Class of drug</td>
<td>BCS Class II</td>
</tr>
</tbody>
</table>
Table 4. Calibration of Aceclofenac in Water

<table>
<thead>
<tr>
<th>Conc(µg/ml)</th>
<th>Abs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0.148</td>
</tr>
<tr>
<td>5</td>
<td>0.246</td>
</tr>
<tr>
<td>8</td>
<td>0.434</td>
</tr>
<tr>
<td>10</td>
<td>0.535</td>
</tr>
<tr>
<td>12</td>
<td>0.632</td>
</tr>
<tr>
<td>15</td>
<td>0.808</td>
</tr>
</tbody>
</table>

Table 5. TLC of Drug and Drug and Excipient

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Samples (Pure From of Drug material) (Drug + Excipient Mixture)</th>
<th>Retention factor of drug Before the Stability Chamber</th>
<th>Retention factor of drug After the Stability Chamber</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pure Drug Aceclofenac</td>
<td>0.76</td>
<td>0.79</td>
</tr>
<tr>
<td>2</td>
<td>Aceclofenac + MCC</td>
<td>0.80</td>
<td>0.81</td>
</tr>
<tr>
<td>3</td>
<td>Aceclofenac + PVP K 30</td>
<td>0.74</td>
<td>0.76</td>
</tr>
<tr>
<td>4</td>
<td>Aceclofenac+ HPMC K15 M</td>
<td>0.70</td>
<td>0.72</td>
</tr>
<tr>
<td>5</td>
<td>Aceclofenac+ Acrypol934 P</td>
<td>0.82</td>
<td>0.81</td>
</tr>
<tr>
<td>6</td>
<td>Aceclofenac + Aerosil</td>
<td>0.78</td>
<td>0.76</td>
</tr>
<tr>
<td>7</td>
<td>Aceclofenac + Magnesium Stearate</td>
<td>0.73</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Table 6. Evaluation of Aceclofenac Tablet

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Experimental parameters</th>
<th>F₁</th>
<th>F₂</th>
<th>FOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bulk Density (gm/cm³)</td>
<td>0.65</td>
<td>0.61</td>
<td>0.75</td>
</tr>
<tr>
<td>2</td>
<td>Tapped Density (gm/cm³)</td>
<td>0.72</td>
<td>0.52</td>
<td>0.79</td>
</tr>
<tr>
<td>3</td>
<td>Angle of Repose (θ)</td>
<td>35.11</td>
<td>38.21</td>
<td>24.11</td>
</tr>
<tr>
<td>4</td>
<td>Carr's Index (%)</td>
<td>9.76</td>
<td>14.75</td>
<td>5.06</td>
</tr>
<tr>
<td>5</td>
<td>Hardness Test (kg/cm²)</td>
<td>9-10</td>
<td>10-12</td>
<td>8-9</td>
</tr>
<tr>
<td>6</td>
<td>Friability Test (%)</td>
<td>0.8</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>7</td>
<td>% of Weight variation test</td>
<td>99.86</td>
<td>99.85</td>
<td>99.84</td>
</tr>
<tr>
<td>8</td>
<td>In Vitro Drug Release (%)</td>
<td>94.11</td>
<td>95.12</td>
<td>96.18</td>
</tr>
</tbody>
</table>
Figure 1. Calibration curve of Aceclofenac in Water

Figure 2. IR of Pure drug Aceclofenac

Figure 3. DSC Thermogram of pure drug Aceclofenac
CONCLUSION
Aceclofenac Sustained release Tablet is made by Wet Granulation Method by employing a HPMC K 4 M and HPMC K 15 M is responsible for the slow release of drug and spared over longer period of time up to 12 hrs. The release is mainly depended on the composition of tablet Formulation Material. The result associated in Optimized batch is good to Satisfactory and having a good free flowing property. The hardness, weight variation, and friability these values are within the pharmacopeia limit. The in vitro Dissolution studies shows Maximum percentage of release of drug. The sustained released formulation of Aceclofenac is helpful to overcome the problem associated in patient compliance as well as efficiency of dosage form in eliciting desired therapeutic response related problems associated with the conventional dosage forms. Cost effectiveness and once-daily dose are the plus points along with other benefits. Hence, The Formulation of sustained-release tablet dosage forms for drug therapy.

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REFERENCE


