ABSTRACT
The objective of present investigation study was carried out to modulate the release rate and reduce the dosage frequency of etoricoxib, because frequency of doses causes ulcer in stomach. When doses increase consumption of additives also increase. To minimize the side effect and for getting prolonged effect the study was carried out. In this study hydrophilic and hydrophobic polymers are used for making this formulation. Since etoricoxib is freely soluble in alkaline aqueous solution hydrophilic polymers alone cannot retard the rate of release. So hydrophobic polymer Eudragit RL 100 is selected. HPMC used as a hydrophilic polymer. This extended release tablet s were prepared by direct compression technique. The pre-compressed powder blend was evaluated for various parameters like angle of repose, compressibility index and Hausner’s ratio. So all the parameters were suitable for direct compression. Then the prepared matrix tablets were evaluated for hardness, thickness, friability, weight variation, drug content and invitro release. Dissolution studies revealed that optimized formulation \( F_5 \) release the drug up to 24 hours in sustained manner.

Keywords: Extended Release Tablets, Eudragit RL 100, HPMC, Etoricoxib.

INTRODUCTION
Etoricoxib is mainly used as a non-steroidal anti inflammatory drug which belongs to COX-2 inhibitor. It is used for treatment of rheumatoid arthritis, osteo arthritis, ankylosing spondylitis, low back pain, acute back pain and gout [1, 2]. Etoricoxib is insoluble in water but freely soluble in alkaline aqueous solution [3]. Normally drug reaches intestine after 2 hours. To avoid the fast release of etoricoxib in intestine hydrophobic polymer is added along with hydrophilic polymer [4]. It selectively inhibits 2-cyclo oxygenase and reduces the Prostaglandin from arachidonic acid. Eudragit RL 100 is one of the sustained release polymer which gives release up to 24 hours. Eudragit RL 100 properties are insoluble, high permeability, \( p^H \) independent. Benefits of Eudragit RL 100 are time controlled release of active ingredient therapeutically [5].

MATERIALS AND METHODS
Etoricoxib was procured as gift sample from Ranbaxy pharmaceuticals, Mumbai. HPMC, Eudragit RL, MCC, Talc were procured as gift samples from Hexa analytical laboratory, Chennai.

Evaluation of Powder Blends
For each batch of powder blends the following test were carried out as per IP official methods.

Angle of Repose
Angle of repose was determined using funnel method. Granules angle of repose is estimated by following formula

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

Bulk Density
Bulk density is the ratio of bulk volume of powder to mass of powder.

\[ \rho_b = \frac{V}{m} \]

Tapped Density
Known mass of blend was tapped for a fixed time. Tapped density for granules can be calculated by following formula

\[ \rho_t = \frac{V}{m} \]

Compressibility index
By using tapped density and bulk density, compressibility index can be found out by following formula

\[ I = \frac{\rho_b - \rho_t}{\rho_t} \times 100 \]
Hausner’s ratio
It is the ratio of tapped density and bulk density.
\[
H = \frac{\rho_t}{\rho_b}
\]

Preparation of extended release etoricoxib tablets
Extended release matrix tablets of Etoricoxib were prepared by direct compression methods using 9 mm punches. The active ingredients and additives such as microcrystalline cellulose, HPMC, Eudragit RL100 were passed through 80 sieves. Finally to the blend, aerosol and talc were added and mixed for 10 minutes. Different trials were made with hydrophilic polymer (HPMC) alone and combination of hydrophilic and hydrophobic polymers.

Evaluation of Tablets
For each formulation hardness, friability, thickness, weight variation, drug content were estimated as per I.P official methods.

Swelling studies
Matrix tablets were weighed and placed in metallic baskets. These baskets were immersed in 900 ml phosphate buffer of pH 7.4 and rotated at 75 rpm at 37±0.5°C (USP XXIV basket method). After specified time the tablets were removed lightly blotted with tissue paper to remove excess water and weighed again. The percentage degree of swelling was calculated by using the following formula.

Percent degree of swelling= [(w_t-w_d)/w_d] x100

where, 
\(w_t\) - Weight of swollen matrix
\(w_d\) - Weight of dry matrix

Dissolution study
Dissolution profiles of etoricoxib tablets were determined using the USP 24 Method II with paddle speed at 50 rpm. Dissolution was performed in 900 ml 0.1N HCl maintained at 37±0.5°C. Five milliliters of samples were withdrawn at specified time intervals. The volume of dissolution fluid was adjusted to 900 ml by replacing each 5 ml aliquot withdrawn with 5 ml of 0.1N HCl, pre-warmed at 37±0.5°C. Samples withdrawn were filtered through Whatmann filter paper (no.41), suitably diluted with 0.1N HCl, and analyzed at 233 nm, using UV-Visible double beam spectrophotometer. Like that after 2 hours dissolution was performed by using 900ml pH 7.4 phosphate buffer .samples were withdrawn at specified intervals and diluted with buffer and analysed at 233nm using spectrascopy.

Short Term Stability Studies
The stability study was conducted for F5 optimized formulation. The tablets were packed and kept for 3 months at 4°C, 40°C/ 75% and 60°C/ 80% RH in Stability chamber. At the interval of 15 days tablets were withdrawn and evaluated for physical properties like hardness, diameter, friability, weight variation and content uniformity. In vitro drug release and assay were also carried out.

Mechanism of Drug Release
To find out mechanism of drug release, the drug release data was fitted in Korsemeyer-Peppar model.

\[
\frac{M_t}{M_x} = K t^n
\]

\(M_t\) fraction of drug released at time ‘t’
\(K\) rate constant
\(n\) it is used to characterize different release mechanism

RESULT AND DISCUSSION
In extended release matrix tablets, hydrophilic polymer alone cannot produce better results. Hence the present study was done with hydrophobic polymers like Eudragit RL 100 and resin gum, incorporated in hydrophilic matrix. It controls the rate of release and action should be extended. All the prepared matrix tablets were evaluated for various physical properties. Bulk density for granules ranged between 0.85±0.1 to 2.39±0.3 gm L⁻¹ as determined by tap method. This value indicates good packing character. Compressibility index for all formulation was found to be below 15%, indicate desirable flow properties. Angle of repose for all batches were found between 21.5±0.23 to 25.51±0.41. The value indicates good flow property with both the polymers. After compression all the tablets were subjected to evaluation test. Average weight, hardness and thickness of tablets were 300±0.2 mg, 5.1 ±0.01kg/cm²± 0.25, and 3.7mm±0.2 respectively. Hardness test and Friability indicates good handling properties. The drug content uniformity in extended matrix tablets was 98.9%±0.15.

In first two trials F1 and F2 hydrophilic polymers produce initial burst effect. In vitro release study revealed there was no desired rate of release. Both trials release medicament within 10 hours. F1c, F2 trials showed that hydrophilic polymer alone cannot give sustained effect for 24 hours. In next two trials addition of Eudragit RL 100 acts as a release retardant polymer, because of its hydrophobic nature and Eudragit presence on the surface of tablets so the rate of release for F3 and F4 was extended upto 12 hours only . But F3 formulation dissolution studies revealed that both HPMC and Eudragit RL100 are suitable candidates.
for making optimized 24 hours extended release etoricoxib tablets

CONCLUSION
From this investigation and aforementioned discussion Hydrophilic polymer alone cannot give the extended release effect for etoricoxib. Incorporation of HPMC in Eudragit RL100 (1:1) is the best technique for getting extended release of etoricoxib for 24 hours. This F3 optimized formulation will useful for further studies in future.

Table 1: Composition of Matrix Tablets

<table>
<thead>
<tr>
<th>INGREDIENTS</th>
<th>FORMULATION CODE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F1 (mg)</td>
</tr>
<tr>
<td>HPMC:EU</td>
<td>0.3:0</td>
</tr>
<tr>
<td>Etoricoxib</td>
<td>120</td>
</tr>
<tr>
<td>HPMC</td>
<td>25</td>
</tr>
<tr>
<td>Eudragit RL</td>
<td>150</td>
</tr>
<tr>
<td>MCC</td>
<td>3</td>
</tr>
<tr>
<td>Talc</td>
<td>300</td>
</tr>
<tr>
<td>Average Wt.</td>
<td>300</td>
</tr>
</tbody>
</table>

Table 2: Physical and Chemical Parameters of Optimized Etoricoxib Tablet

<table>
<thead>
<tr>
<th>Weight variation (mg) ± S.D</th>
<th>Thickness (mm) ± S.D</th>
<th>Friability (%) ± S.D</th>
<th>Hardness (Kg/cm²) ± S.D</th>
<th>Drug content (%) ± S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>300±0.2</td>
<td>3.7±0.2</td>
<td>0.75±0.01</td>
<td>5±0.01</td>
<td>98.9±0.15</td>
</tr>
</tbody>
</table>

![In vitro Release of F5 Formulation(Optimized)](image)

REFERENCES
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release matrix tablet of Zidovudine, Influence of Combination of both polymers AAPS Pharm Sci Tech. Vol.7, No: 1 E1-E9