FORMULATION AND EVALUATION OF COLON TARGETED NAPROXEN MICROPARTICLES
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KEYWORDS:
Naproxen, colon targeted, pH sensitive delivery system, Eudragit S 100.

ABSTRACT
Naproxen is a non steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties, used for rheumatoid arthritis, osteoarthritis Juvenile arthritis. It has major side effect like gastric irritation, stomach ulcer etc. The objective of this work was to understand the influence of different formulation variables on the optimization of pH-dependent, colon-targeted Naproxen microparticles which restrict the drug release at upper portion of GI track and maximize the drug release at colonic region. Naproxen microparticles were developed by using pH dependent enteric polymer Eudragit S 100 and Ethyl cellulose by o/w emulsification solvent evaporation method. Formulation variables study included, drug to polymer ratio, stirring rate, concentration of emulsifying agent while various evaluation parameter % yield, average particle size, drug entrapment, drug loading and cumulative % of drug release was evaluated. Formulation N3 was shown better physical characteristics of microparticles and the value of $f_2$ was observed 70.08 for the formulation N3 which was the maximum among all the formulation. It was considering that the formulation N3 has shown more identical dissolution profile as targeted than other formulations. The release mechanisms were explored and explained with zero order, first order, Higuchi and Korsmeyer-Peppas models. The correlation-coefficient values of the trend lines of the graphs showed that the formulations were best fitted with Korsmeyer-Peppas release pattern.
INTRODUCTION:
The oral route is considered to be most convenient for the administration of drugs to patients. Where drug normally dissolves in the gastro-intestinal (GI) fluids and is absorbed from these regions of the gastro-intestinal tract (GIT), and both process depends upon the physicochemical properties of the drug. Drugs that are destroyed by the acidic environment of the stomach or metabolized by pancreatic enzymes are only slightly affected in the colon & can be absorbed from colon so colon targeted drug delivery will be useful for these drugs. Sustained colonic delivery of the drug can be useful in the conditions in which diurnal rhythm is evident like nocturnal asthma, angina & arthritis. Treatment of ulcerative colitis, Crohn’s disease, & colorectal cancer is more effective with the direct delivery of the drugs to the colon. Due to the distal location of the colon in the GI tract, a colon specific drug delivery system should prevent drug release in the stomach and small intestine. It also affects an abrupt onset of drug release upon entry into the colon. Overall, the physiological changes along the GI tract can be generally characterized as a continuum, with decrease in enzymatic activity, motility and fluid content and an increase in pH as we move from oesophageal end to the rectum. The pH-dependent systems exploit the generally accepted view that pH of the human GIT increases progressively from the stomach (pH 1-2 which increases to 4 during digestion), small intestine (pH 6-7) at the site of digestion and it increases to 7-8 in the distal ileum.

Microparticles Systems

Single unit colon targeted drug delivery formulations may suffer from the unintentional disintegration of the formulation due to manufacturing deficiency or unusual gastric physiology that may lead to drastically compromised systemic drug bioavailability or loss of local therapeutic action in the colon. Drug carrier systems larger than 200 μm possess very low gastric transit time due to physiological condition of the bowel in colitis.

Recently, much emphasis is being laid on the development of microparticles dosage forms in comparison to single unit systems because of their potential benefits like,

- Microparticles systems enabled the drug to reach the colon quickly and were retained in the ascending colon for a relatively long period of time and hence increased bioavailability.
- Microparticles are less dependent on gastric emptying, resulting in less inter and intra-subject variability in gastrointestinal transit time. They are also better distributed and less likely to cause local irritation.

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• Moreover, microparticles systems tend to be more uniformly dispersed in the Gastrointestinal tract and also ensure more uniform drug absorption.
• Reduced risk of systemic toxicity, reduced risk of local irritation and predictable gastric emptying.

Recently much emphasis is being laid on the development of microparticles dosage forms in preference to single unit systems because of their potential benefits such as increased bioavailability, reduced risk of systemic toxicity, reduced risk of local irritation and predictable gastric emptying.

MATERIALS AND METHODS
Naproxen was collected as a gift sample from Zydus Cadila Healthcare Limited, Ahmadabad. Eudragit S100 and Ethyl cellulose were collected as a gift sample from Alembic limited, Vadodara.

**Preparation of naproxen microparticles by emulsification solvent evaporation**

O/W Emulsification Solvent Evaporation Method

In O/W Emulsification Solvent Evaporation Method distilled water selected as external phase which is aqueous in nature and ethyl acetate selected as internal phase which is oily in nature. Tween 80 was selected as o/w emulsifying agent. The selected drug and polymers (Eudragit S100 and Ethyl Cellulose) were dissolved in the internal phase and the resultant solution was introduced into external aqueous medium at room temperature while stirring at 800 rpm using mechanical stirrer equipped with 3-blade propeller. Agitation provided by stirrer to break the poured polymeric solution into fine droplets to form o/w emulsion. The fine droplets of drug and polymeric solution were solidified due to the evaporation of ethyl acetate. The solidified microparticles were washed with distilled water and recovered by filtration. Recovered microparticles were stored at 50°C by hot air oven for 1h to completely dry.

**Table 1:** Formulation of colon targeted microparticles.

<table>
<thead>
<tr>
<th>SN</th>
<th>INGREDIENTS</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>N4</th>
<th>N5</th>
<th>N6</th>
<th>N7</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Naproxen(g)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>EC(g)</td>
<td>0.5</td>
<td>1</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>3</td>
<td>ES100(g)</td>
<td>0.5</td>
<td>1</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>4</td>
<td>EA (ml)</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>Tween80(%)</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.04</td>
<td>0.06</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>6</td>
<td>DW (ml)</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>7</td>
<td>RPM</td>
<td>1000</td>
<td>1000</td>
<td>1000</td>
<td>1000</td>
<td>1000</td>
<td>800</td>
<td>1200</td>
</tr>
</tbody>
</table>

Note: EC=Ethyl cellulose, ES 100 = Eudragit S100, EA= Ethyl acetate

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Solubility of Naproxen\textsuperscript{6,7,8}

The solubility of Naproxen was evaluated as the procedure specified in IP 2007. The solubility of Naproxen was determined by using the solvents having different pH of solvents i.e. 0.1 N HCL, Phosphate buffer pH 6.8 and phosphate buffer pH 7.4. The results of solubility has shown in results.

Drug Excipient Compatibility Study

Compatibility is an important part of understanding the role of inactive ingredients in product quality. It should be based on the mechanistic understanding of the API, its impurities, excipient and their impurities, mechanism of degradation and potential process conditions for drug product manufacture. A scientifically sound approach should be used in constructing the compatibility studies. Evaluation of binary mixtures is one of many potential empirical approaches.

Chemical Compatibility Study (By FTIR)

The pure drug i.e. Naproxen and mixture of it excipient powder was mixed separately with KBr and corresponding pellets were prepared by applying 10 tons of pressure in the hydraulic press. The FTIR spectrum of Naproxen was measured by KBr disk method by Shimadzu (FTIR-8300) instrument. The drug-KBr pellets were scanned over a wave number range of 400 to 4000 cm. FTIR Spectra have been shown in figure 1-4

Percentage yield

The prepared microparticles of all batches were accurately weighed. The weight quantity of prepared microparticles was divided by the total amount of all the excipients and drug used in the preparation of the microparticles, which give the total percentage yield of microparticles. It was calculated by using following equation,

\[
\text{Percentage yield} = \frac{\text{Total weight of prepared microsphere (g)}}{\text{Theoretical weight of microsphere (g)}} \times 100
\]

Average particle size

The prepared microparticles from different formulations were studied for appearance and size using optical microscopy. Images of microparticles were acquired using an optical microscope equipped with digital camera. The particle size was measured with optical microscope using a calibrated eye piece micrometer. A small amount of dry microparticles was suspended in purified water. Small drops from the obtained suspension were placed on a clean glass slide. The slide containing the microparticles
suspension was mounted on the microscope and 100 particles were measure using the calibrated ocular micrometer.

\[ \text{Particle size} = \frac{\Sigma nd}{\Sigma n} \]

where,
\[ n = \text{No. of particles}, d = \text{Frequency} \]

**Percentage drug Entrapment and drug loading**
The amount of drug present in prepared microparticles was determined to check the drug entrapment efficiency and drug loading capacity. Microparticles were crushed in to fine powder by using a mortar and pestle. Accurately weighed amount of crushed microparticles equivalent to 100mg of drug and added into 100 ml of phosphate buffer till whole quantity was dissolved. Then, the solution was filtered and suitable dilutions were made which was estimated for drug content U. V. Spectrophotometrically at 228nm. Theoretical drug loading and experimental drug loading in prepared microparticles was estimated by using the following formula,

\[ \text{Theoretical Drug Loading (\%)} = \frac{\text{Theoretical amount of drug in microsphere (mg)}}{\text{Total amount of microsphere (mg)}} \times 100 \]

\[ \text{Experimental Drug Loading (\%)} = \frac{\text{Actual amount of drug in microsphere (mg)}}{\text{Total amount of microsphere (mg)}} \times 100 \]

The Entrapment efficiency of prepared microparticles is calculated by using the following formula,

\[ \text{Entrapment Efficiency (\%)} = \frac{\text{Experimental Drug Loading}}{\text{Theoretical Drug Loading}} \times 100 \]

**In vitro dissolution study**
The *In-vitro* dissolution study for the microparticles of each formulation was conducted as per United States Pharmacopoeia type I apparatus. The rotating basket method was used to study the drug release. In vitro drug release studies were carried out at 37 ±0.5°C rotated at constant speed of 100 rpm using 900ml of 0.1N HCl as the dissolution medium for first 2 hrs and after 2 hrs media was replaced by pH 6.8 phosphate buffer. Dissolution was carried out for further 2 hr with same sample and after than 2 hrs media was replaced by in phosphate buffer pH 7.4 up to 12 hrs. Microparticles weight equivalent to
100mg of Naproxen should be used in each test. An aliquot of the sample was periodically withdrawn at suitable time intervals and the sample volume is replaced with fresh dissolution medium in order to maintain the sink condition. The sample was analyzed spectrophotometrically at predetermined λmax. Then, the cumulative percentage amount of drug released at each time interval was calculated using the formula,

**Cumulative amount of drug release = C × DF × DM**

Where,
- C = Concentration of drug at each time interval (µg/ml)
- DF = Dilution Factor is 1.
- DM = Dissolution Medium (900 ml)

**Comparison of dissolution profiles**

Model independent method for comparison of two dissolution profile is based on determination of difference factor (f1) and similarity factor (f2)

\[
\text{Difference factor (f1)} = \left( \frac{\sum_{t=1}^{n} (R_t - T_t)}{\sum_{t=1}^{n} R_t} \right) * 100
\]

If the difference factor is 0 than dissolution profile is identical, and if f1 is 15 ≤ than similarity or equivalent of two profiles.

The similarity factor (f2) given by SUPAC guidelines for modified release dosage form was used as a basis to compare dissolution profile. The dissolution profiles of developed dosage form are considered to be similar with theoretically developed profile when F2 value is 50 to 100.

The dissolution profiles of products were compared using a similarity factor (f2). This similarity factor is calculated by following formula,

\[
F_2 = 50 \times \log \left\{ [1 + \frac{1}{n} \sum_{t=1}^{n} R_t - T_t] \right\} - 0.5 \times 100
\]

When n is the number of dissolution time and R_t and T_t are the reference and test dissolution values at time t. Two dissolution profiles are considered similar when the f2 value is 50 to 100.

**RESULT AND DISCUSSION**

**Solubility of Naproxen**

Solubility of naproxen in different solvents having different pH was evaluated as per IP 2007 and the results were shown in table 2.
Table 2: Solubility of Naproxen in different pH of solvent

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 N HCL</td>
<td>27.012 ml/mg</td>
</tr>
<tr>
<td>6.8 PH Phosphate buffer</td>
<td>2.14 ml/mg</td>
</tr>
<tr>
<td>7.4 PH Phosphate buffer</td>
<td>1.20 ml/mg</td>
</tr>
</tbody>
</table>

From the results shown in table 6.2, it was revealed that the solubility of Naproxen was greatly affected by pH of solvents because higher solubility was shown in the phosphate buffer pH 7.4 than 0.1N HCL and phosphate buffer pH 6.8. It was suggesting that the solubility of Naproxen increased as the pH of solvent increased.

**Drug Excipient Compatibility Study**

Excipient are integral components of almost all pharmaceutical dosage forms thus it is mandatory to detect any possible physical or chemical interaction of the drug with the excipients since the excipients can affect the bioavailability and stability of the drug.

The drug and the excipients must be compatible with one another to produce a product that is stable, efficacious, attractive, easy to administer and safe. If the excipients are new and have not been used in formulations containing the active substance, the compatibility studies have a considerable importance.

In the present investigation for the development of Naproxen colon targeted microparticles, Naproxen was selected as a model drug and its anti-inflammatory property has been reported. Polymers i.e ethyl Cellulose, Eudragit S 100 were selected to develop the colon targeted formulation.

Fourier Transform Infrared Spectrophotometer (FTIR) technique is commonly used to investigate the compatibility between the drug and the various excipient used in the formulation. So, preliminary compatibility study was performed on the selected drug and polymers by FTIR.

**FTIR**

The spectra of FTIR are shown in Figure1 to Figure4. There was no considerable difference observed in IR spectrum of pure drug and IR spectrum of drug with the different polymer mixture. Naproxen contains one O=H one C=O, one C-O, aromatic ring C=C-C, aryl–O and alkyl C-O which have characteristic peak values range around 3214 cm\(^{-1}\), 1227.71cm\(^{-1}\), 1729 cm\(^{-1}\), 1604.8 and 1510–1450cm\(^{-1}\) and 1264.36 cm\(^{-1}\), 1090.76 cm\(^{-1}\) respectively. IR spectra was shown that characteristic peak was observed at 3210.5(O=H) one 1238.6(C=O), one1724.45(C-O), 1612 (aromatic ring C=C-C),1295(aryl–O) and 1090.4 alkyl C-O in
all spectra while new band or shift in characteristic band were not seen in the mixtures. So, it was revealed that there was not chemical incompatibility between the selected drug and polymers.

**Figure 1: IR spectra of Naproxen**

**Figure 2: IR spectra of Naproxen and Ethyl cellulose**

**Figure 3: IR spectra of Naproxen and Eudragit S100**
Figure 4: IR spectra of Naproen, Ethyl Cellulose and Eudragit S100

Table 3: Physical Characterization of the colon targeted naproxen Microparticle.

<table>
<thead>
<tr>
<th>SN</th>
<th>Parameter</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>N4</th>
<th>N5</th>
<th>N6</th>
<th>N7</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Physical Nature</td>
<td>Uniform and free flowing spheres</td>
<td>Uniform and free flowing spheres</td>
<td>Uniform and free flowing spheres</td>
<td>Uniform and free flowing spheres</td>
<td>Uniform and free flowing spheres</td>
<td>Uniform and free flowing spheres</td>
<td>Uniform and free flowing spheres</td>
</tr>
<tr>
<td>2</td>
<td>Y(%)</td>
<td>61.52</td>
<td>68.71</td>
<td>73.63</td>
<td>73.38</td>
<td>73.52</td>
<td>73.31</td>
<td>76.44</td>
</tr>
<tr>
<td>3</td>
<td>D (µm)</td>
<td>308.7</td>
<td>328.32</td>
<td>382.78</td>
<td>378.42</td>
<td>362.41</td>
<td>462.88</td>
<td>302.54</td>
</tr>
<tr>
<td>4</td>
<td>EE (%)</td>
<td>65.06</td>
<td>71.23</td>
<td>75.86</td>
<td>72.96</td>
<td>72.84</td>
<td>76.76</td>
<td>75.36</td>
</tr>
<tr>
<td>5</td>
<td>TDL (%)</td>
<td>50</td>
<td>33.33</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>ADL (%)</td>
<td>32.53</td>
<td>23.74</td>
<td>18.96</td>
<td>18.24</td>
<td>18.21</td>
<td>19.19</td>
<td>18.84</td>
</tr>
</tbody>
</table>

Y = yield, D = Average diameter, EE = Entrapment efficiency,    TDL = Theoretical drug loading, ADL = Actual drug loading

PHYSICAL CHARACTERIZATION OF THE MICROPARTICLE

The physical appearance, mean particle size, yield, and encapsulation efficiency of the prepared formulations are presented result Table

Microparticle Prepared with Varying Drug to polymer ratio [N1-N3]

To determine the drug to polymer ratio sufficient to prevent premature drug release in the pre colonic stages of the in vitro release studies, formulations (N1–N3) with different drug to polymer ratios were prepared and characterized. It was revealed that increase drug: polymer ratio from 1:1 (N1) to 1:2 (N7) to 1:3 (N8) resulted in a significant increase in yield (61.52, 68.71, 73.63) particle size (308.7, 328.78, 382.78) and encapsulation efficiency (65.06, 71.23, 75.86) respectively. Encapsulation efficiency of microparticles is affected by drug: polymer ratio. When the amount of the polymer is decreased, there is no sufficient polymer in the media to produce microparticles for the entire drug. Consequently, greater amount of the drug is lost, resulting in the formation of the microparticles with lower drug content.
Microparticle Prepared With Different concentration of emulsifying agent [N3-N5]
Formulation N3, N4, N5 was developed by varying the concentration of tween 80 which was 0.2, 0.4 and 0.6 percentage of distilled water. This formulation was developed to see the effect of the concentration of emulsifying agent on the physical properties of microparticles. The composition has been shown in Table 1.

It was observed that product yield, drug entrapment, drug loading was not significantly affected but particle size of developed microsphere was slightly reduced with the increased the concentration of emulsifying agent.

Microparticle Prepared with Different Rotation Speed [N5-N6-N7]
Formulation N5, N6, N7 was developed to check the effect of the stirring speed in rotation per minute (rpm) on the characteristics of Microparticles of Naproxen which was kept at 800, 1000 and 1200 respectively. The composition has been shown in Table 1.

From the results, the average diameter of formulation N5, N6, N7 were 382.78, 462.88, 302.54 micrometer respectively. It was suggesting that the average size of the microsphere of Naproxen was greatly affected. The average size of developed micro particle was reduced as the stirring speed was increasing because the formulation N6 was developed by keeping stirring rate at 800 rpm while N7 was developed by keeping stirring rate at 1200 rpm.

It might be observed due to the smaller droplet formed from the drug polymeric solution when it poured in continuous phase for emulsification at higher stirring speed. And because of the reduced diameter of developed micro particle, drug entrapment efficiency and drug loading capacity was reduced due to the reducing the surface area for the entrapment.

The Stirring rate was also affecting the product: Product yield was found to be high in formulation N7 than N6 and it was suggesting the high stirring rate was found higher product yield.

Reduction in diameter of microsphere was also influencing the percentages of Entrapment and it was increased with the increase size of micro particles.
IN VITRO RELEASE STUDIES

Table 4: cumulative % of drug release of the colon targeted naproxen Microparticle.

<table>
<thead>
<tr>
<th>SN</th>
<th>Time (hr)</th>
<th>Dissolution Media</th>
<th>Cumulative % of Drug Release</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>N1</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>0.1 N HCl</td>
<td>2.93</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Phosphate Buffer pH 6.8</td>
<td>4.81</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Phosphate Buffer pH 6.8</td>
<td>7.31</td>
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<td>4</td>
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<td>10.42</td>
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<tr>
<td>5</td>
<td>5</td>
<td>Phosphate Buffer pH 6.8</td>
<td>15.28</td>
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<td>6</td>
<td>6</td>
<td>Phosphate Buffer pH 7.4</td>
<td>25.11</td>
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<td>7</td>
<td>7</td>
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<td>8</td>
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<td>Phosphate Buffer pH 7.4</td>
<td>57.86</td>
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<td>9</td>
<td>Phosphate Buffer pH 7.4</td>
<td>69.45</td>
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<td>10</td>
<td>Phosphate Buffer pH 7.4</td>
<td>80.43</td>
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<td>Phosphate Buffer pH 7.4</td>
<td>87.42</td>
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<td>12</td>
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<td>14</td>
<td>14</td>
<td>Phosphate Buffer pH 7.4</td>
<td>95.88</td>
</tr>
<tr>
<td>15</td>
<td>15</td>
<td>Phosphate Buffer pH 7.4</td>
<td>96.41</td>
</tr>
<tr>
<td>16</td>
<td>16</td>
<td>Phosphate Buffer pH 7.4</td>
<td>96.87</td>
</tr>
</tbody>
</table>

S=Theoretical standard, $f_1$=dissimiliarity factor, $f_2$=similiarity factor

![Graph of % cumulative drug release of drug](image)

**Figure 5:** Graph of % cumulative drug release of drug for N1-N7

In the in vitro release studies, pH condition was chosen in an attempt to approximately GI conditions without enzymes. The pH condition used was pH 1.2 for a period of 2 h (stomach), pH 6.8 for 2 h (duodenum) followed by pH 7.4 (distal ileum and colon) for the remaining period of the study. The successful formulation of a colon-targeted delivery system requires minimum release of the drug during its transit in the stomach and the upper small intestine to ensure maximum dose reaches the colon.
Accordingly, the amount of drug released after 4 h, representing the passage of the formulation in the upper GI tract, must be reduced and considered as a parameter for the evaluation of the prepared formulation.

**Microparticle Prepared with Varying Drug to polymer ratio [N1-N3]**

From the Table 4 and Figure 5, it was found that drug release rate was higher than it was targeted. It might be improve by altering the ratio of drug to polymer 1:1 (N1) to 1:2 (N2) to 1:3 (N3). From the result it was shown that as the ratio of drug: polymer increased, release rate in 0.1 N HCL was reduced and increased the similarity value in pH7.4 phosphate buffer. So, Formulation N3 was shown release profile similar to the therapeutic release profile shown in Table 4.

The in vitro drug release profiles showing the effect of varying Naproxen to polymer ratio. Naproxen release profiles showed Naproxen release in upper portion of gastrointestinal track is limited. After 4hr it reach to lower part of intestine where there was release the drug as shown in Table 4.

**Microparticle Prepared With Different concentration of emulsifying agent [N3-N5]**

Formulation N3, N4, N5 was developed by varying the concentration of tween 80 which was 0.2, 0.4 and 0.6 percentage of distilled water. This formulation was developed to see the effect of the concentration of emulsifying agent on the physical propertied of microparticles. The composition has been shown in Table 4.

As the concentration of emulsifying agent was increasing drug release rate was increasing but not minor differences was observed.

**Microparticle Prepared with Different Rotation Speed [N5-N6-N7]**

The results were in Table 4 and Figure 5 indicated that, in-vitro drug release rate from micro particle was higher from the micro particle prepared at higher stirring rate (1200) because at higher speed there was a decreased the particle size, So there was increased effective surface area but there was at lower speed of rotation (800) increased particle size so, decreased the drug release rate. But at 1000 rpm rotation speed there was observed optimum drug release rate.

The value of $f_2$ was found to be more than 50 which consider the similar drug release profile as targeted. The value of $f_2$ was observed 70.08 for the formulation N3 which was the maximum among all the formulation. It was considering that the formulation N3 has shown more identical dissolution profile as targeted than other formulations.
RESULT AND DISCUSSION FOR TREATMENT OF DISSOLUTION DATA USING DIFFERENT KINETIC MODELS

The dissolution profile of N1 to N7 was fitted to different equations and kinetic models to explain the release kinetics of drug from the tablets.

Table 5: Kinetic treatments to dissolution profile for each formulation N1 to N7

<table>
<thead>
<tr>
<th>Code</th>
<th>Zero Order</th>
<th>First Order</th>
<th>Hixon Crowell</th>
<th>Korsemeyer Peppas</th>
<th>Higuchi Plot</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(R²)</td>
<td>K₀</td>
<td>(R²)</td>
<td>K₁</td>
<td>(R²)</td>
</tr>
<tr>
<td>N1</td>
<td>0.941</td>
<td>8.371</td>
<td>0.701</td>
<td>0.251</td>
<td>0.874</td>
</tr>
<tr>
<td>N2</td>
<td>0.969</td>
<td>8.180</td>
<td>0.792</td>
<td>0.259</td>
<td>0.906</td>
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<td>8.160</td>
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<td>0.265</td>
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<tr>
<td>N4</td>
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</table>

The results of kinetic treatment of dissolution profile are shown in Table 5. These results were suggested that the drug release profile was follow zero order release pattern and release mechanism was fitted to korsemeyer peppas kinetic model for all the formulation. It was also found that the drug release from the dosage form was follow super case II transport mechanism and non-Fickian diffusion because the value of n was less then or equal 0.89. The results were also suggested that the type of dosage form was swelling and erodible matrix type.
CONCLUSION

Eudragit S 100 can be an excellent candidate for encapsulating naproxen which has successfully been established throughout this research work. The FTIR revealed the compatibility between the drug and the polymer. Microparticle were prepared by emulsification solvent evaporation technique which was found to be reproducible and also may be an ideal method to prepare microparticle. The value of $f_2$ was observed 70.08 for the formulation N3 which was the maximum among all the formulation. It was
considering that the formulation N3 has shown more identical dissolution profile as targeted than other formulations. It was also found that the drug release from the dosage form was follow super case II transport mechanism and non-Fickian diffusion because the value of \( n \) was less then or equal 0.89. The results were also suggested that the type of dosage form was swelling and erodible matrix type.

REFERENCES


