INTRODUCTION

Targeted drug delivery into the colon is highly desirable for local treatment of a variety of bowel diseases such as ulcerative colitis, crohn’s disease, amoebiosis, colonic cancer, local treatment of colonic pathologies, and systemic delivery of protein and peptide drugs\(^1\). The colon specific drug delivery system (CDDS) should be capable of protecting the drug en route to the colon i.e. drug release and absorption should not occur in the stomach as well as the small intestine, and neither

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**ABSTRACT**

The aim of the study was to develop colon targeted film coated tablets of Ornidazole using HPMC K4M, HPMC K100 and Eudragit S100 as carriers. Ornidazole is used for the treatment of amoebiasis. The different approaches are designed based on prodrug formulation, pH-sensitivity, time-dependency (lag time), microbial degradation and osmotic pressure etc to formulate the different dosage forms like tablets, capsules, multiparticulates, microspheres, liposomes for colon targeting. The tablets are prepared by using compression method. The prepared tablets are evaluated in terms of their precompression studies, hardness test, thickness test, weight variation test, friability test, \textit{in vitro} study and stability studies. The results of the study showed that formulation FOT-3 is most likely to provide targeting of Ornidazole for local action in the colon. The most satisfactory formulation was stable during stability studies conducted for 60 days as per ICH guidelines. It showed no significant changes in the physicochemical parameters and in vitro release of drug.

**KEYWORDS**

Ornidazole, Film coated tablets, Colon targeted drug delivery, Carriers, \textit{In vitro} study and Stability studies.

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the bioactive agent should be degraded in either of
the dissolution sites but only released and absorbed
once the system reaches the colon. Ornidazole is
the nitroimidazole or analogs compound and it is
used for the treatment of amoebiasis. Ornidazole is
readily absorbed after oral administration and
bioavailability approaches 90%.

MATERIAL AND METHODS
Materials
Ornidazole was obtained from Arati Chemicals Ltd,
Mumbai. HPMC K4M, HPMC K100 and Eudragit
S100 were gifted from Apex Pharmaceutical Pvt.
Ltd, Chennai. Di basic calcium phosphate, Talc and
Magnesium Stearate were purchased from
Qualigens fine chemicals, Mumbai, India. All other
chemicals and ingredients were used for study are
of Analytical grade.
Method
Method of preparation of colon targeted
ornidazole tablets
Ornidazole, HPMC K4M, HPMC K100, Eudragit
S100 and Dicalcium phosphate were taken in
required quantities mixed and passed through #60
sieves, lubricated with magnesium stearate and talc
then was compressed into tablets in 9 mm die cavity
of rotary tablet punching machine. Then film
coating is done by 6% w/v solution of Eudragit
S100 in isopropyl alcohol using 2% PEG-400 as
plasticizer in coating pan.

Evaluation Parameters

Pre-formulation Studies
Fourier Transform Infrared Spectroscopy
The Fourier transform infra-red analysis was
conducted for the structure characterization. FTIR
spectra of the pure drug, polymers and formulations
were recorded by using BOMEN MB SERIES
FTIR instrument. Approximately 5mg of samples
were mixed with 50mg of spectroscopic grade KBr,
samples were scanned in the IR spectroscopy.

Pre-compression studies of tablet powder

Bulk density
3gm of powder were weighed separately and
transferred into 100ml measuring cylinder, initial
volume was measured and calculated according to
the formula

Formula

Bulk density = Mass / Volume

Tapped density
Tapped density is determined by placing a
graduated cylinder containing a known mass of
powder and mechanical tapper apparatus, which is
operated for a fixed number of taps until the powder
bed volume has reached a minimum volume. Using
the weight of the powder in the cylinder and this
minimum volume, the tapped density may be
computed.

Formula

Tapped density = Weight of Powder / Tapped
volume of Powder

Angle of Repose
The manner in which stresses are transmitted
through a bead and the beads response to applied
stress are reflected in the various angles of friction
and response. The most commonly used of this in
angle of repose, which may be determined
experimentally by number of methods. The method
used to find the angle of repose is to pour the
powder a conical on a level, flat surface and
measure the included angle with the horizontal.

Formula

θ = Tan⁻¹(h/r)

Where,
θ = Angle of repose, h = Height of the powder cone,
r = Radius of the powder cone.

Compressibility Index or Carr’s Index
Carr’s Index is measured using the values of bulk density
and tapped density.

The following equation is used to find the Carr’s
Index,

CI = \frac{(TD-BD)}{TD} \times 100

Where, TD = Tapped density BD = Bulk density.

Hausner’s Ratio
It indicates the flow properties of the powder and
ratio of Tapped density to the Bulk density of the
powder.
Hausner’s Ratio = Tapped density/Bulk density

**Post compression studies of Ornidazole tablets**

**Hardness or Crushing strength Test**

Hardness of the tablet was determined using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

The force required to break the tablet is measured in kilograms and a crushing strength of 4Kg is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4 to 10 kg; however, hypodermic and chewable tablets have a hardness of 3 kg and some sustained release tablets have a hardness of 10 -20 kg.

**Thickness Test**

The thickness of the tablet is mostly related to the tablet hardness can be used as an initial control parameter. Ten tablets were randomly selected from each tablet thickness was determined using a Venire caliper and the reading was recorded in millimeters.

**Friability Test**

The pre-weighed tablets were placed in the friabilator (EF-2, Electro lab, Mumbai) which was then operated for 100rpm, then dusted and reweighed. The compressed tablets that lose less than 0.5-1.0% of their weight are generally considered acceptable.

\[
\text{Friability index} = \frac{I - F}{I} \times 100
\]

Where,

I - Initial weight
F - Final weight

Weight variation test

Weights of 20 individual tablets were noted and their mean weight also calculated. The percentage deviation was calculated by using the following formula,

\[
\text{Percentage deviation} = \frac{[X - X^*]}{X} \times 100
\]

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

**Estimation of Drug Content**

An accurately weighed amount of powdered Ornidazole (100 mg) was extracted with water and the solution was filtered through 0.45 µ membrane filter paper. The absorbance was measured at 312 nm after suitable dilution.

**Calculation**

The amount of Ornidazole present in tablet can be calculated using the formula

\[
A_t/As \times S_w/100 \times 100
\]

Where,

\[A_t = \text{Absorbance of sample preparation}\]
\[A_s = \text{Absorbance of Standard preparation}\]
\[S_w = \text{weight at Ornidazole working standard (mg)}\]

**In vitro drug release studies**

The dissolution was carried out using rotating basket method (USP dissolution testing apparatus I); freshly prepared 0.1N Hcl (pH 1.2) (900 ml) was placed in dissolution flask and allowed to obtain temperature at 37±0.5°C and 100 rpm for first 2 h. Then replaced with 6.8 pH phosphate buffer and continued for 24 h. Aliquot volume of 10 ml was withdrawn at regular intervals and replaced with fresh buffer diluted. The samples were replaced with fresh dissolution medium. After filtration, the sample is measured the absorbance at 312 nm by using UV Spectrometer. The dissolution data obtained were plotted as percentage drug release versus time.

**Stability Studies**

To assess the drug and formulation stability, the stability studies were carried out of the most satisfactory formulation (FOT-3) as per ICH guidelines. The formulation is sealed in aluminum packaging and kept in humidity chamber maintained at 30 ± 2°C /65 ± 5% RH and 40 ± 2°C / 75 ± 5% RH for 60 days. At the end of studies, samples were analyzed for the drug content, in vitro dissolution, and other physicochemical parameters.

**RESULTS AND DISCUSSION**

**Compatability studies (Fourier Transform Infrared Spectroscopic studies)**

The fourier transform infra-red analysis was conducted for the surface structure characterization. FTIR spectrum of the formulated tablets, pure drug
and different polymers was recorded. The tablets were taken in a KBr pellet by using BOMEN MB SERIES FTIR instrument. The Fourier Transform Infrared Spectroscopy study reveals that there is no interaction between the different polymers and pure drug. Then all the functional groups are found in the IR spectrum of pure drug and different polymers.

**Bulk density**
The packing properties of the drugs and their formulations widely depend upon bulk density. It has been stated that bulk density values less than 1.2gm/cm$^3$ indicate good flow and values greater than 1.5 gm/cm$^3$ indicate poor flow. From the results it can be seen that the bulk density values are less than 1.2gm/cm$^3$. This indicates good flow characteristics of the powders. Values showed Table No.2.

**Tapped density**
From the results it can be seen that the Tapped density values indicate good flow characteristics of the powders. Values showed Table No.2.

**Angle of Repose**
Angle of repose is less than or equal to 40$^\circ$ indicates free flowing properties of the powders. However angle of repose is greater than 40$^\circ$ indicates poor flow of material. It can be observed that the angle of repose for various batches of the powders is found to be less than 40$^\circ$, it indicates good flow properties of the powders. Values showed Table No.2.

**Compressibility Index or Carr’s Index**
Carr’s Index is less than or equal to <10 indicates free flowing properties of the powders. However Carr’s Index is greater than <10 indicates poor flow of material. It can be observed that the Carr’s Index for various batches of the powders is found to be less than >10; it indicates good flow properties of the powders. Values showed Table No.2.

**Hausner’s Ratio**
Hausner’s Ratio is less than or equal to 1.069 indicates free flowing properties of the powders. However Hausner’s Ratio is greater than 1.35 indicates poor flow of material. It can be observed that the Hausner’s Ratio for various batches of the powders is found to be less than 1.35; it indicates good flow properties of the powders. Values showed Table No.2.

**Post Compression studies**

**Hardness Test**
The hardness of the tablet various batches were determined. The various batches of the tablets of hardness values are found within limits and it indicates good strength of the tablets. Values showed Table No.3.

**Thickness Test**
The thicknesses of tablets were almost uniform in the all formulations and were found to be in the range of 0.48mm. Values showed Table No.3.

**Friability Test**
The tablets friability values are found to be less than 1% in all cases and considered to be satisfactory. Values showed Table No.3.

**Weight variation test**
All this tablets passed weight variation test as the % weight variation was within the pharmacopoeia limits. The weight of the all tablets was found to be uniform with low standard deviation values. Values showed Table No.3.

**Estimation of Drug Content**
Drug content of all the batches are within the acceptable range which shows the proper mixing of the drug and excipients. Values showed Table No.3.

**In vitro drug release studies**
Among all the batches FOT-3 formulations showed the better in vitro release of drug (Table No.4 and Figure No.1).

**Stability studies**
Stability studies were carried out of the most satisfactory formulation FOT-3 at 30 ± 2 °C / 65 ± 5 % RH and 40 ± 2 °C / 75 ± 5 % RH for two months as per ICH guidelines. At various time intervals of 30 days and 60 days end, samples were evaluated. There was no major change in the various physicochemical parameters evaluated.
Table No.1: Formulation of different batches of Ornidazole colon targeted tablets

<table>
<thead>
<tr>
<th>S.No</th>
<th>Ingredients</th>
<th>FOT-1</th>
<th>FOT-2</th>
<th>FOT-3</th>
<th>FOT-4</th>
<th>FOT-5</th>
<th>FOT-6</th>
<th>FOT-7</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ornidazole 200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
</tr>
<tr>
<td>2</td>
<td>HPMC K4M 120 mg</td>
<td>-</td>
<td>-</td>
<td>60 mg</td>
<td>-</td>
<td>60 mg</td>
<td>7.0 mg</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>HPMC K100M 60 mg</td>
<td>120 mg</td>
<td>-</td>
<td>60 mg</td>
<td>60 mg</td>
<td>-</td>
<td>7.0 mg</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Eudragit S100 7.0 mg</td>
<td>-</td>
<td>-</td>
<td>120 mg</td>
<td>-</td>
<td>60 mg</td>
<td>60 mg</td>
<td>7.0 mg</td>
</tr>
<tr>
<td>5</td>
<td>Di basic calcium phosphate 150 mg</td>
<td>150 mg</td>
<td>150 mg</td>
<td>150 mg</td>
<td>150 mg</td>
<td>150 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Talc 15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
</tr>
<tr>
<td>7</td>
<td>Magnesium stearate 15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>15 mg</td>
</tr>
</tbody>
</table>

Total weight of the tablet – 500mg/Tab

Table No.2: Precompression studies of powders

<table>
<thead>
<tr>
<th>S.No</th>
<th>Formulations</th>
<th>Bulk Density(gm/cm³)</th>
<th>Tapped Density(gm/cm³)</th>
<th>Angle of Repose (θ)</th>
<th>Carr's Index (%)</th>
<th>Hausner's Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FOT-1</td>
<td>0.585</td>
<td>0.606</td>
<td>28.05</td>
<td>3.46</td>
<td>1.035</td>
</tr>
<tr>
<td>2</td>
<td>FOT-2</td>
<td>0.587</td>
<td>0.610</td>
<td>29.46</td>
<td>3.77</td>
<td>1.039</td>
</tr>
<tr>
<td>3</td>
<td>FOT-3</td>
<td>0.572</td>
<td>0.594</td>
<td>28.12</td>
<td>3.70</td>
<td>1.038</td>
</tr>
<tr>
<td>4</td>
<td>FOT-4</td>
<td>0.585</td>
<td>0.613</td>
<td>29.25</td>
<td>4.56</td>
<td>1.047</td>
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<tr>
<td>5</td>
<td>FOT-5</td>
<td>0.590</td>
<td>0.617</td>
<td>29.08</td>
<td>4.37</td>
<td>1.045</td>
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<tr>
<td>6</td>
<td>FOT-6</td>
<td>0.595</td>
<td>0.616</td>
<td>27.94</td>
<td>3.40</td>
<td>1.035</td>
</tr>
<tr>
<td>7</td>
<td>FOT-7</td>
<td>0.581</td>
<td>0.609</td>
<td>28.36</td>
<td>4.59</td>
<td>1.048</td>
</tr>
</tbody>
</table>

Table No.3: Post compression studies of Ornidazole colon targeted tablets

<table>
<thead>
<tr>
<th>S.No</th>
<th>Formulations</th>
<th>Hardness Test (kg/cm)</th>
<th>Thickness Test (cm)</th>
<th>Friability Test (%)</th>
<th>% of Weight variation test</th>
<th>Estimation of Drug Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FOT-1</td>
<td>8.45</td>
<td>0.48</td>
<td>0.6</td>
<td>99.6</td>
<td>99.5</td>
</tr>
<tr>
<td>2</td>
<td>FOT-2</td>
<td>8.62</td>
<td>0.48</td>
<td>0.6</td>
<td>99.6</td>
<td>99.5</td>
</tr>
<tr>
<td>3</td>
<td>FOT-3</td>
<td>8.94</td>
<td>0.48</td>
<td>0.5</td>
<td>99.8</td>
<td>99.8</td>
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<tr>
<td>4</td>
<td>FOT-4</td>
<td>8.58</td>
<td>0.48</td>
<td>0.6</td>
<td>99.5</td>
<td>99.2</td>
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<td>0.48</td>
<td>0.6</td>
<td>99.5</td>
<td>99.2</td>
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<td>FOT-6</td>
<td>8.62</td>
<td>0.48</td>
<td>0.6</td>
<td>99.6</td>
<td>99.4</td>
</tr>
<tr>
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<td>FOT-7</td>
<td>8.72</td>
<td>0.48</td>
<td>0.5</td>
<td>99.6</td>
<td>99.4</td>
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Table No.4: Comparative dissolution study of different formulations with various ratios of polymers

<table>
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<tr>
<th>S.No</th>
<th>Time  (hrs)</th>
<th>% of drug release (FOT-1)</th>
<th>% of drug release (FOT-2)</th>
<th>% of drug release (FOT-3)</th>
<th>% of drug release (FOT-4)</th>
<th>% of drug release (FOT-5)</th>
<th>% of drug release (FOT-6)</th>
<th>% of drug release (FOT-7)</th>
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<tr>
<td>1</td>
<td>0</td>
<td>0.00</td>
<td>0.00</td>
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<td>0.00</td>
<td>0.00</td>
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<td>1</td>
<td>2.54</td>
<td>2.23</td>
<td>2.05</td>
<td>2.36</td>
<td>2.16</td>
<td>2.52</td>
<td>0.12</td>
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<tr>
<td>3</td>
<td>2</td>
<td>8.42</td>
<td>6.56</td>
<td>5.82</td>
<td>7.84</td>
<td>6.12</td>
<td>7.25</td>
<td>0.04</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>20.83</td>
<td>16.26</td>
<td>12.74</td>
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<td>14.52</td>
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<td>14.67</td>
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<tr>
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<td>36.27</td>
<td>28.18</td>
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<td>33.53</td>
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<td>46.62</td>
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<td>12</td>
<td>71.26</td>
<td>62.18</td>
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<td>53.78</td>
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<td>51.92</td>
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<td>15</td>
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<td>76.32</td>
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<td>77.68</td>
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<tr>
<td>9</td>
<td>18</td>
<td>102.3</td>
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<td>93.64</td>
<td>82.13</td>
<td>91.02</td>
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<td>-</td>
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<td>87.12</td>
<td>107.05</td>
<td>94.18</td>
<td>104.7</td>
<td>90.24</td>
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<td>11</td>
<td>24</td>
<td>-</td>
<td>-</td>
<td>99.34</td>
<td>-</td>
<td>106.4</td>
<td>-</td>
<td>103.1</td>
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Table No.5: Stability studies of Ornidazole colon targeted tablets (FOT-3)

<table>
<thead>
<tr>
<th>S.No</th>
<th>Time  (hrs)</th>
<th>After 30 days</th>
<th>After 60 days</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>30±2°C /65±5% RH</td>
<td>40±2°C /75±5% RH</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0.00</td>
<td>0.00</td>
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<tr>
<td>11</td>
<td>24</td>
<td>99.34</td>
<td>99.34</td>
</tr>
</tbody>
</table>
CONCLUSION
The present investigation was concerned with the development of the colon targeted tablets, which after oral administration were designed to prevent the drug release in stomach and small intestine. It improves the bioavailability of the drug as well as its half life. The tablets possessed the required physicochemical parameters such as hardness, friability, weight variation, drug content. The in vitro drug release showed best formulation is FOT3 compared all. The most satisfactory formulation (FOT-3) had showed no significant change in physicochemical properties, drug content, in vitro dissolution pattern after storage at 30 ± 2 °C / 65 ± 5 % RH and at 40 ± 2 °C /75 ± 5 % RH during stability studies for two months. Therefore, it was concluded that the most satisfactory formulation (FOT-3).

ACKNOWLEDGEMENT
We are thankful to Seven Hills College of Pharmacy, India for providing facility to carry out the research work.

CONFLICT OF INTEREST
We declare that we have no conflict of interest.

REFERENCES