7. PREFORMULATION

Preformulation is defined as application of biopharmaceutical principles to the physicochemical properties of the drug to make effective dosage form.

PREFORMULATION STUDIES:

ANALYSIS OF LANSOPRAZOLE:

UV Spectroscopy:
30 mg of sample was dissolved in 50 ml of methanol, filtered and then 1ml diluted to 50 ml. 2ml of the above solution was diluted to 50ml with methanol.\textsuperscript{122} This solution was scanned between 200nm to 400nm. The UV curve obtained was given in results and discussion section as Fig 7.1.

IR Spectroscopy:
An IR spectrum of lansoprazole was obtained by a Perkin-Elmer Fourier transform infrared spectrophotometer using KBr pellets.\textsuperscript{122} KBr pellets were prepared by gently mixing the lansoprazole with KBr (1:100). The scanning range used was 4000 to 400cm\textsuperscript{-1}. The obtained graph was compared with the reference standard. The IR graph was given in results and discussion part Fig 7.2.

Melting point:
MP was measured by capillary tube method.\textsuperscript{123} The readings were given in table 7.1

Loss on drying:
One gram of lansoprazole was heated to a temperature of 105°C in hot air oven until it attained constant weight.\textsuperscript{124} The formula to calculate LOD was
The results were recorded and given in the table 7.1.

**Angle of repose:**

It was measured by fixed funnel technique.\(^{125}\) In this technique a funnel containing lansoprazole was kept at a fixed height, and it was allowed to flow to the ground surface which contains graph paper. The height (h) and radius (r) of the heap formed was measured and from this value angle of repose (\(\theta\)) was determined by the formula

\[
\theta = \tan^{-1}(h/r)
\]

The results were recorded and given in table 7.1.

**Bulk density & Tapped density:**

Weighed amount of lansoprazole was placed in a measurable cylinder, the volume (untapped) was noted and then the measurable cylinder was tapped until the volume remains constant. Bulk and Tapped densities were calculated by the following formulas\(^{125}\)

\[
\text{Bulk Density} = \frac{\text{Mass of Powder}}{\text{Volume of Powder (Untapped)}}
\]

\[
\text{Tapped Density} = \frac{\text{Mass of Powder}}{\text{Volume of Powder (Tapped)}}
\]

The results were recorded and presented in results and discussion section, table 7.1.

**Compressibility Index:**

CI of the powder was determined from the bulk and tap density as follows\(^{126}\)

\[
\text{Percentage Compressibility Index} = 100 \times \frac{(\text{Tapped Density} - \text{Bulk Density})}{\text{Tapped Density}}
\]
The results were recorded and presented in results and discussion section, table 7.1.

**Hausner’s ratio:**

It was calculated as

\[
\text{Hausner ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}
\]

The results were recorded and presented in results and discussion section, table 7.1.

**Drug-Excipient Compatibility Studies**

*IR Spectroscopy*

IR spectra of pure lansoprazole, additives and combination of lansoprazole with additives were obtained by using Perkin-Elmer Fourier transform infrared spectrophotometer using KBr pellets.\(^6\) KBr pellets were prepared by gently mixing the sample with KBr. The scanning range used was 4000 to 400 cm\(^{-1}\). IR spectra for the samples were given in results and discussion section from Fig. 7.2 to Fig. 7.6.

*DSC technique*

For DSC studies lansoprazole, additives and combination of lansoprazole with additives were sealed in aluminum pans and the DSC thermograms were recorded at a heating rate of 10°/min.\(^{127}\) DSC thermograms were given in results and discussion section from Fig. 7.7 to Fig. 7.13.

**Preparation of Standard Curve of Lansoprazole:**

Standard curve of the drug was prepared using standard lansoprazole in methanol 5 to 25 µg. The absorbance was measured at 285 nm. Linear relationship was observed with
absorption to concentration of drug. The values of absorbance related to concentration were given in table 7.2 and graphs were given in fig 7.14.

RESULTS AND DISCUSSION:
The UV, IR and melting point studies helped to identify the lansoprazole. The obtained UV and IR spectra of the sample were similar to that of standard. The spectra were represented in Fig 7.1 & 7.2.

Fig. 7.1. UV Spectra of Lansoprazole
Physical Characteristics:

Physical characteristics indicated that lansoprazole possess poor flow.

The results were given below:

**Table 7.1. Physical characteristics of lansoprazole**

<table>
<thead>
<tr>
<th>S.No</th>
<th>Particulars</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Melting point</td>
<td>179°C</td>
</tr>
<tr>
<td>2.</td>
<td>LOD</td>
<td>≤1.0%</td>
</tr>
<tr>
<td>3</td>
<td>Angle of repose (°)</td>
<td>40.11 ±0.72</td>
</tr>
<tr>
<td>4</td>
<td>Bulk density (g/ml)</td>
<td>0.38±0.04</td>
</tr>
<tr>
<td>5</td>
<td>Tapped density (g/ml)</td>
<td>0.47±0.13</td>
</tr>
<tr>
<td>6</td>
<td>Compressibility Index</td>
<td>19.41±1.72</td>
</tr>
<tr>
<td>7</td>
<td>Hausner’s ratio</td>
<td>1.23±0.12</td>
</tr>
</tbody>
</table>

Drug-Excipient Compatibility Studies

**IR and DSC analysis:**

The characteristic absorption peaks of Lansoprazole appeared at 3231, 2984 & 2930, 1580, 1282, 1118 denoting stretching vibration of –NH₂, - CH₂, aromatic ring, C-O and ether bond, respectively. These characteristic bands were observed in all of the recorded IR spectra. The DSC thermogram revealed that the additives showed superimposition on thermogram, however mild preshift was observed. The FTIR and DSC results revealed that there was no interaction between the drug and additives used in the formulation. The IR and DSC were shown from Fig. 7.2 to Fig. 7.13.
Fig 7.2 IR spectra of lansoprazole
Fig. 7.3 IR spectra of Chitosan
Fig. 7.4 IR spectra of PLGA
Fig. 7.5 IR spectra of lansoprazole + chitosan
Fig. 7.6 IR spectra of lansoprazole + PLGA
Fig. 7.7 DSC spectra of lansoprazole
DSC of CHITOSAN

File Name: Chitosan.tac
Detector: DSC-60
Sample Name: Chitosan
Sample Weight: 5.000 [mg]
Cell: Aluminum Seal
Atmosphere: Nitrogen
Flow Rate: 30 [ml/min]
Annotation: interaction study

Fig. 7.8 DSC spectra of Chitosan
DSC of PLGA

- File Name: PLGA.tad
- Detector: DSC-60
- Sample Name: PLGA
- Cell: Aluminum Seal
- Atmosphere: Nitrogen
- Flow Rate: 30 [ml/min]
- Annotation: drug-excipient compatibility study

DSC spectra of PLGA

Fig. 7.9 DSC spectra of PLGA
Fig.7.10 DSC spectra of lansoprazole + chitosan
Fig. 7.11 DSC spectra of lansoprazole + PLGA
DSC OF LANSOPRAZOLE-CHITOSAN NANOPARTICLES

Fig. 7.12 DSC of lansoprazole-chitosan nanoparticles

File Name: Lansoprazole + Chitosan.tad
Detector: DSC-60
Sample Name: Nanoparticle-PLGA
Atmosphere: Nitrogen
Flow Rate: 10 ml/min
Operator: Nagaraj
Annotation: Drug-Excipients compatibility study

Peak
Onset: 178.47°C
Endset: 180.16°C
Heat: -172.41°C
DSC OF LANSOPRASOLE-PLGA NANO PARTICLES

File Name: lanso- PLGA.tad
Detector: DSC-60
Sample Name: Lansoprazole-PLGA
Atmosphere: Nitrogen
Flow Rate: 10[ml/min]
Operator: Nagaraj
Annotation: Drug- Excipients compatibility study

Peak 174.77
Onset 171.50
Endset 179.82
Heat 73.18

Fig.7.13 DSC of Lansoprazole PLGA nanoparticles
STANDARD CURVE OF LANSOPRAZOLE:

Table 7.2 Concentration and absorbance of lansoprazole in methanol

<table>
<thead>
<tr>
<th>S.No</th>
<th>Conc (µg/ml)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>0.426</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>0.803</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>1.229</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>1.496</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>1.801</td>
</tr>
</tbody>
</table>

Fig. 7.14 Standard curve of lansoprazole in Methanol