FORMULATION AND EVALUATION OF FLOATING MATRIX TABLET OF Captopril BY USING NATURAL AND SYNTHETIC POLYMER

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ABSTRACT
The present study involves preparation and evaluation of floating matrix tablet of Captopril as model drug for prolongation of gastric residence time. The tablets were prepared by direct compression method using polymers HPMC (K4M), HPMC (K4M), Xantham gum and Guar gum. The tablet were evaluated for angle of repose, bulk density, tapped density, Carr’s index, hausner’s ratio. The prepared tablets were characterized by hardness, thickness, friability, weight variation and drug content respectively. In-vitro drug release studies were performed by using an USP dissolution test apparatus (Basket type II) at 37±0.5°C and 50 rpm speed. To study the release behavior, kinetic analyses were performed on the optimized formulation. The dissolution data were fitted to zero order, first order, matrix, Hixson-Crowell, Peppas model. The prepared tablet exhibited prolonged drug release (~ 12 h) and remained buoyant for > 12 h. The optimized formulations F13 were kept for short term stability study. The conditions for stability study were 40ºC and relative humidity of 75% from the study; it was observed that there is no significant change in stability and drug release rate.

Keywords: Floating matrix tablet, Captopril, In-vitro release.

INTRODUCTION
The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper Site in the body to achieve promptly and then maintain the desired drug concentration. The Most convenient and commonly employed route of drug delivery has historically been by oral ingestion. Oral sustained drug delivery system is complicated by limited gastric residence times (grts). Rapid GI transit can prevent complete drug release in the absorption zone and reduce the efficacy of the administered dose since the majority of drugs are absorbed in Stomach or the upper part of small intestine. To overcome these limitations, various approaches have been proposed to increase gastric residence of drug delivery systems in the Upper part of the gastrointestinal tract includes floating drug dosage systems (FDDS) Swelling or expanding systems, mucoadhesive systems, modified-shape systems, High-density system and other delayed gastric emptying devices. [1]
Captopril is an angiotensin converting enzyme inhibitor; it inhibits the conversion angiotensin I to angiotensin II. As angiotensin II is a vasoconstrictor and a negative feedback mediator for renin activity, lower angiotensin II levels results in a decrease in blood pressure. It has been widely used for the treatment of hypertension and congestive heart failure. Captopril acts orally and the dosage used for the treatment of congestive heart failure ranges from 50 to 150 mg daily. After oral ingestion of a single dose the maximum hemodynamic effect is observed after 45–90 min. The drug is freely water-soluble and it has elimination half-life after an oral dose is 2-3 h. It is stable at pH 1.2, and as the pH increase, the drug becomes unstable and undergoes a degradation reaction. Captopril has been a drug of choice in hypertension management. However, after single oral dosing of the drug, the antihypertensive action is only effective for 6–8 h.\[2\]

**MATERIAL AND METHODS**

Captopril was obtained as a gift sample from Inventia Healthcare Ltd., Mumbai, India. Hydroxypropylmethylcellulose, K4M, K15M, Xantham gum and Guar gum from Rajesh Chemicals, Mumbai, India. Lactose, sodium bicarbonate, citric acid, manitol, magnesium stearate, and talc were obtained from SD Fine Chemicals, Mumbai, India.

**Characterization of Captopril[^3[^4]**

**Melting point determination**

The melting point of Captopril was determined using Thiel’s tube method.

**Determination of λ max**

Stock solution of Captopril was prepared by dissolving 10 mg of drug in 100 ml of solvent pH 1.2 after proper dilutions analyze spectrophotometrically to determine the λ max.

**Preparation of Calibration Curve in 0.1 N HCl (pH 1.2)**

Accurately weighed amount of Captopril 10 mg was dissolved in 100 ml 0.1 N HCl. A series of standard solution containing 5-25 µg/ml of Captopril was prepared and analyzed using UV-visible spectrophotometer at 210.2 nm.

**Drug-polymer compatibility study**

To determine possible incompatibilities between pure drug and polymers the sample of pure drug, HPMC K4M, HPMC K15M, Xantham gum, Guar gum and its physical mixture were...
subjected to FTIR studies and the spectrum was recorded in the stretching frequency range of 400-4000 cm\(^{-1}\). The samples were prepared by KBr press pellet technique.

**Characterization of tablet blend\(^{[5,6,7]}\)**

**Angle of Repose**

The angle of repose of each powder blend was determined by glass funnel method. Powders were weighed accurately and passed freely through the funnel so as to form a heap. The height of funnel was so adjusted that the tip of funnel just touched the apex of the heap. The diameter of the powder cone so formed was measured and the angle of repose was calculated by using the following equation,

\[
\tan \theta = \frac{h}{r}
\]

Where,

\[
h = \text{height of cone}\\
\]

\[
r = \text{radius of powder cone}
\]

**Bulk Density**

Bulk density of the powder blend was determined by pouring gently 2 gm of sample through a glass funnel into a 10 ml graduated cylinder. The volume occupied by the sample was recorded. The bulk density was calculated by the following formula,

\[
\text{Bulk Density} = \frac{\text{Weight of sample in grams}}{\text{Volume occupied by the sample}}
\]

**Tapped Density**

About 2 gram of powder blend was poured gently through a glass funnel into a 10 ml graduated cylinder. The cylinder was tapped from height of 2 inches until a constant volume was obtained. Volume occupied by the sample after 100 tapping were recorded and tapped density was calculated by the following formula,

\[
\text{Tapped Density} = \frac{\text{Weight of sample in grams}}{\text{Volume occupied by the sample}}
\]

**Carr’s Index**

One of the important measures that can be obtained from bulk and tapped density determinations is the percent compressibility or the Carr’s index \(I\), which is determined by the following equation,

\[
I = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100
\]
Compressibility Index = \[
\frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100
\]

**Hausner ratio**

Hausner ratio is related to interparticle friction and as such used to predict powder flow properties.

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

**Formulation design**

In order to investigate the drug release profile, the formulations (F1-F12) were prepared in the ratio of Drug: Polymer in 1:1, 1:1.5, and 1:2. and (F13) 1:1.5 with combination of HPMC K4M and HPMC K15M. and (F14) with combination of Xantham gum and Guar gum respectively. The dose of the Captopril which is 50 mg was kept constant.

**Preparation of floating matrix tablet**

Different tablets formulations F1-F14 were prepared by the direct compression technique. All the powders were passed through 18 mesh sieve. The required quantity of drug, matrix polymer and low-density powder were mixed thoroughly. Magnesium stearate was added as a lubricant. The blend was compressed (10 mm diameter, concave punches) using a rotary tablet compression machine. Each tablet contained 50 mg Captopril and other excipients as listed in Table:1

**TABLE 1: COMPOSITION OF TABLETS**

<table>
<thead>
<tr>
<th>Formulation (mg/tablet)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
<th>F10</th>
<th>F11</th>
<th>F12</th>
<th>F13</th>
<th>F14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
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<td>50</td>
<td>50</td>
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<tr>
<td>HPMC K4M</td>
<td>50</td>
<td>75</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>35.5</td>
</tr>
<tr>
<td>HPMC K15M</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>50</td>
<td>75</td>
<td>100</td>
<td>-</td>
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<td>-</td>
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<td>35.5</td>
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<tr>
<td>Xantham gum</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>50</td>
<td>75</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>35.5</td>
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<tr>
<td>Guar gum</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
<td>50</td>
<td>75</td>
<td>100</td>
<td>-</td>
<td>35.5</td>
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<td>Sodium bicarbonate</td>
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<td>Citric acid</td>
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<td>5</td>
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<td>5</td>
</tr>
<tr>
<td>Mg. stearate</td>
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<td>1</td>
<td>1</td>
<td>1</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
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</tr>
<tr>
<td>Talc</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
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<td>2</td>
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<tr>
<td>Manitol</td>
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<td>20</td>
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<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Lactose</td>
<td>60</td>
<td>35</td>
<td>10</td>
<td>60</td>
<td>35</td>
<td>10</td>
<td>60</td>
<td>35</td>
<td>10</td>
<td>60</td>
<td>35</td>
<td>10</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Total Weight (mg)</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
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<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
</tbody>
</table>
Evaluation of tablet\textsuperscript{[8,9,10]}

**Hardness**

The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet was measured by Monsanto hardness tester (Nevtex). The hardness was measured in terms of kg/cm\textsuperscript{2}.

**Thickness**

Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter were measured using Vernier caliper.

**Friability**

Friability is the measure of tablet strength. Roche friabilator was used for testing the friability using the following procedure. Ten tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 minutes, the tablets were weighed and the percentage loss in tablet weight was determined.

\[
\text{\% Loss} = \frac{\text{Initial weight of tablets} - \text{Final weight of tablets}}{\text{Initial weight of tablets}} \times 100
\]

**Weight variation**

Weigh 20 tablets at random and calculate the average weight. Not more than two of the individual weights deviate from the average weight by more than the percentage shown and none deviates by more than twice that percentage.

**Determination of Drug Content**

For drug content, accurately weighed tablets was selected and ground to fine powder. An amount equivalent to 50 mg drug was dissolved in 0.1N HCl and filtered through filter paper. The filtered solutions of appropriate dilutions were analyzed at 210.2 nm using UV spectrophotometer. The amount of Captopril was determined by measuring the absorbance at 210.2 nm.

**Swelling index**
The swelling index of tablets was determined in 0.1 N HCl (pH 1.2) at room temperature. The swollen weight of the tablets was determined at predefined time intervals. The swelling index was calculated by the following equation:

\[
\text{Swelling index } WU = \frac{(W_t - W_0) \times 100}{W_0}
\]

Where, \(W_t\) = Weight of tablet at time \(t\).

\(W_0\) = Initial weight of tablet

**Buoyancy Lag Time**

The in vitro buoyancy was determined by floating lag time method described as The tablets were placed in 250 ml beaker containing 0.1 N HCl. The time required for the tablets to rise to the surface and float was determined as floating lag time. The time between introduction of dosage form and its buoyancy in 0.1 N HCl and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).

**In-vitro Dissolution Studies**

The release of Captopril for different formulations of floating tablets was determined using USP dissolution test apparatus (type II). The dissolution medium was 900 ml in 0.1N HCl at 37±0.2 °C with a stirring speed of 50 rpm. Aliquots of 10 ml were withdrawn at predetermined intervals of 1 hr, filtered and replaced by equivalent volume of fresh dissolution media. The test sample was filtered through membrane filter, (0.45 μm) and the concentration of drug release was determined by using UV- Visible Spectrophotometer at \(\lambda_{max}\) 210.2 nm.

**Stability Studies**

The optimized formulation was kept for short term stability study. The conditions for stability study were 40°C and relative humidity of 75%. All tablets were suitably packed in group of 10 in aluminum foil. The stability study condition was maintained at 75% RH using saturated solution of sodium chloride. At the end of one month the sealed tablets
were opened and evaluated for hardness, thickness, friability, uniformity of weight, determination of drug content and dissolution studies.

RESULT AND DISCUSSION
Characterization of Captopril
A. Melting point determination
Melting point of Captopril was found in the range of 106-108ºC which is in the reported range that is 104ºC to 108ºC which indicates purity of drug sample.

B. Determination of $\lambda_{\text{max}}$
Wavelength of maximum absorbance ($\lambda_{\text{max}}$) of stock solution of Captopril prepared in 0.1N HCl were found to 210.2 nm, which was reported in the literature. The spectrum is shown in Figure:1

![Figure 1: UV Spectrum of Captopril](image)

Calibration curve for Captopril in pH 1.2 (0.1N HCl)
The calibration curve for captopril in pH 1.2 was prepared in the range of 5-25 µg/ml and the results are shown in Table 2 and Figure 2

<table>
<thead>
<tr>
<th>Concentration (µg/ml)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>0.134</td>
</tr>
<tr>
<td>10</td>
<td>0.266</td>
</tr>
<tr>
<td>15</td>
<td>0.419</td>
</tr>
<tr>
<td>20</td>
<td>0.550</td>
</tr>
<tr>
<td>25</td>
<td>0.683</td>
</tr>
</tbody>
</table>
The prepared calibration obeyed Beer Lambert’s law in the concentration range of 5-25 µg/ml. The value of regression coefficient (0.9996) shows the linearity relationship between concentration and absorbance.

Drug and polymer compatibility study

FTIR Spectroscopy

The FTIR spectrum of Captopril, HPMC K4M, HPMC K15M, Xantham gum, Guar gum and its physical mixture are shown in figure:3-11 and Table:3
Figure: 4 FTIR spectra of HPMC (K4M)

Figure: 5 FTIR spectra of HPMC K4M+Captopril
Figure 6: FTIR spectra of HPMC (K15M)

Figure 7: FTIR spectra of HPMC K15M+Captopril
Figure: 8 FTIR spectra of xanthan gum

Figure: 9 FTIR spectra of xanthan gum + Captopril
Figure: 10 FTIR spectra of guar gum

Figure: 11 FTIR spectra of guar gum + captopril
TABLE 3: RESULTS OF FTIR STUDY

<table>
<thead>
<tr>
<th>Material</th>
<th>Peaks (cm(^{-1}))</th>
<th>Characteristic Functional Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>2981, 2949, 2877, 2567, 1747, 1469, 1228</td>
<td>CH(_3) and CH(_2) Asymmetric Stretching, CH(_3) Symmetric Stretching, SH Stretching, C=O Stretching, CH(_3) Bending, CN Stretching</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPMC (K4M)</td>
<td>2929.97, 1064.81, 1462.09</td>
<td>C-H Stretching, C-O Stretching, C-OH Stretching</td>
</tr>
<tr>
<td>HPMC (K15M)</td>
<td>3450.77, 1458.23, 1375.29</td>
<td>O-H Stretching, C-H Bending, C-O Stretching</td>
</tr>
<tr>
<td>Xantham gum</td>
<td>1346.67, 1008.77</td>
<td>C-H Bending, C-O Stretching</td>
</tr>
<tr>
<td>Guar gum</td>
<td>1336.67, 1105.21</td>
<td>C-H Bending, C-O Stretching</td>
</tr>
</tbody>
</table>

From the figure:3-11 and Table:3 the Captopril showed 2981, 2949 cm\(^{-1}\) for CH\(_3\) and CH\(_2\) asymmetric stretching, 2877 cm\(^{-1}\) for symmetric CH\(_3\) stretching mode, 2567 cm\(^{-1}\) for SH stretching vibration, 1747 cm\(^{-1}\) for C=O stretching vibration of carboxylic acid, 1469 cm\(^{-1}\) for CH\(_3\) bending vibration, 1228 cm\(^{-1}\) for C-N stretching vibration. In IR spectra HPMC (K4M) showed 2929.97 cm–1 for C-H Stretching, 1064.81cm–1 for C-O Stretching, 1462.09 cm–1 for C-OH stretching. In IR spectra of HPMC (K15M) the peak showed 3450.77 cm-1 for O-H Stretch, 1458.23 cm-1 for C-H Bending, 1375 cm-1 for C-O Stretching. Xantham gum C-O stretching occurs at 1008.77 and C-H bending occurs at 1359.82. Guar gum C-O stretching occurs at 1105.21 and C-H bending occurs at 1336.67. From the results there is no significant changes were observed, when physical mixture was subjected to FTIR studies.

Evaluation of tablet

Characterization of tablet blend

All the formulation powder mixtures were evaluated for pre-compression parameters such as Angle of the repose, Loose Bulk Density, Tapped Bulk Density, Carr’s Index and Hausner’s Ratio and results obtained are shown in the table 4.
**TABLE: 4 RESULTS OF TABLET BLEND**

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Angle of Repose (°)</th>
<th>Bulk Density (gms/cm³)</th>
<th>Tapped Density (gms/cm³)</th>
<th>Carr’s Index (%)</th>
<th>Hausner’s Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>28.90±1.29</td>
<td>0.59±0.03</td>
<td>0.69±0.04</td>
<td>13.81±2.36</td>
<td>1.16±0.03</td>
</tr>
<tr>
<td>F2</td>
<td>28.07±1.18</td>
<td>0.60±0.03</td>
<td>0.70±0.03</td>
<td>14.50±1.00</td>
<td>1.17±0.01</td>
</tr>
<tr>
<td>F3</td>
<td>28.61±1.58</td>
<td>0.57±0.02</td>
<td>0.67±0.02</td>
<td>14.16±2.21</td>
<td>1.17±0.03</td>
</tr>
<tr>
<td>F4</td>
<td>28.85±0.35</td>
<td>0.58±0.01</td>
<td>0.68±0.01</td>
<td>15.68±1.88</td>
<td>1.19±0.03</td>
</tr>
<tr>
<td>F5</td>
<td>29.28±1.06</td>
<td>0.61±0.02</td>
<td>0.71±0.00</td>
<td>14.68±2.67</td>
<td>1.17±0.04</td>
</tr>
<tr>
<td>F6</td>
<td>29.25±0.60</td>
<td>0.61±0.01</td>
<td>0.70±0.02</td>
<td>13.48±2.41</td>
<td>1.16±0.03</td>
</tr>
<tr>
<td>F7</td>
<td>28.27±1.85</td>
<td>0.58±0.04</td>
<td>0.67±0.02</td>
<td>13.12±3.44</td>
<td>1.15±0.04</td>
</tr>
<tr>
<td>F8</td>
<td>29.28±1.26</td>
<td>0.59±0.02</td>
<td>0.68±0.03</td>
<td>12.08±1.40</td>
<td>1.14±0.02</td>
</tr>
<tr>
<td>F9</td>
<td>27.27±0.32</td>
<td>0.60±0.01</td>
<td>0.68±0.03</td>
<td>12.89±2.14</td>
<td>1.15±0.03</td>
</tr>
<tr>
<td>F10</td>
<td>28.23±0.93</td>
<td>0.58±0.01</td>
<td>0.68±0.02</td>
<td>14.71±0.99</td>
<td>1.17±0.01</td>
</tr>
<tr>
<td>F11</td>
<td>29.67±0.34</td>
<td>0.59±0.02</td>
<td>0.70±0.02</td>
<td>15.14±0.20</td>
<td>1.18±0.00</td>
</tr>
<tr>
<td>F12</td>
<td>30.04±0.70</td>
<td>0.62±0.02</td>
<td>0.71±0.02</td>
<td>12.44±0.83</td>
<td>1.14±0.01</td>
</tr>
<tr>
<td>F13</td>
<td>28.43±1.46</td>
<td>0.61±0.02</td>
<td>0.70±0.03</td>
<td>13.14±1.15</td>
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<tr>
<td>F14</td>
<td>27.68±1.80</td>
<td>0.60±0.01</td>
<td>0.72±0.01</td>
<td>16.50±2.35</td>
<td>1.20±0.03</td>
</tr>
</tbody>
</table>

*All values are expressed as mean± S.D, n=3*

From the result, the angle of repose, bulk density, tapped density, Carr’s index and Hausner’s ratio were found to be within the limits. The compressibility index was the lowest for all the formulations which had good flow properties. Also, lower values for Hausner ratio indicate excellent flow properties of the formulations.

**Characterization of formulation**

The hardness, thickness, friability, weight variation and drug content of all the formulations were determined and the results obtained are mentioned in the Table 5. The tablets evaluated for the weight variation showed within limit and thus passed the test. The friability of the tablets was found to be less than 1% which was considered within the limit.

The drug content of the optimized formulation was found to be within the limits (98 – 102%).
TABLE 5 RESULTS OF CHARACTERIZATION OF FLOATING MATRIX TABLETS:

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Weight variation (mg)</th>
<th>Thickness (mm)</th>
<th>Hardness (kg/cm²)</th>
<th>Friability (%)</th>
<th>Drug content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>201.85±0.22</td>
<td>3.17±0.06</td>
<td>6.67±0.29</td>
<td>0.77±0.19</td>
<td>96.53±0.12</td>
</tr>
<tr>
<td>F2</td>
<td>201.68±0.18</td>
<td>3.20±0.09</td>
<td>6.40±0.53</td>
<td>0.67±0.20</td>
<td>97.54±0.29</td>
</tr>
<tr>
<td>F3</td>
<td>201.22±0.19</td>
<td>3.08±0.11</td>
<td>6.57±0.40</td>
<td>0.90±0.14</td>
<td>96.80±0.29</td>
</tr>
<tr>
<td>F4</td>
<td>201.00±0.41</td>
<td>3.25±0.09</td>
<td>6.83±0.35</td>
<td>0.59±0.21</td>
<td>95.93±0.22</td>
</tr>
<tr>
<td>F5</td>
<td>200.72±0.48</td>
<td>3.20±0.06</td>
<td>6.83±0.29</td>
<td>0.58±0.20</td>
<td>97.57±0.16</td>
</tr>
<tr>
<td>F6</td>
<td>202.55±0.51</td>
<td>3.03±0.23</td>
<td>6.40±0.53</td>
<td>0.45±0.19</td>
<td>97.37±0.29</td>
</tr>
<tr>
<td>F7</td>
<td>201.00±0.41</td>
<td>3.21±0.13</td>
<td>6.50±0.62</td>
<td>0.66±0.28</td>
<td>95.63±0.29</td>
</tr>
<tr>
<td>F8</td>
<td>200.72±0.48</td>
<td>3.09±0.14</td>
<td>6.73±0.64</td>
<td>0.38±0.03</td>
<td>96.50±0.45</td>
</tr>
<tr>
<td>F9</td>
<td>202.55±0.51</td>
<td>3.18±0.15</td>
<td>6.57±0.40</td>
<td>0.63±0.20</td>
<td>97.57±0.33</td>
</tr>
<tr>
<td>F10</td>
<td>200.58±0.57</td>
<td>3.04±0.15</td>
<td>6.30±0.17</td>
<td>0.61±0.31</td>
<td>95.36±0.29</td>
</tr>
<tr>
<td>F11</td>
<td>200.88±0.19</td>
<td>3.08±0.13</td>
<td>6.47±0.31</td>
<td>0.75±0.12</td>
<td>95.99±0.34</td>
</tr>
<tr>
<td>F12</td>
<td>200.60±0.35</td>
<td>3.22±0.10</td>
<td>6.77±0.25</td>
<td>0.80±0.26</td>
<td>97.59±0.25</td>
</tr>
<tr>
<td>F13</td>
<td>200.65±1.04</td>
<td>3.08±0.18</td>
<td>6.60±0.17</td>
<td>0.69±0.22</td>
<td>99.36±0.16</td>
</tr>
<tr>
<td>F14</td>
<td>200.45±0.15</td>
<td>3.21±0.13</td>
<td>6.93±0.51</td>
<td>0.72±0.27</td>
<td>97.70±0.21</td>
</tr>
</tbody>
</table>

*All values expressed as mean± are S.D., n=3

Swelling Index

The swelling of the polymers used could be determined by 0.1N HCl uptake of the microspheres. The complete swelling was achieved by the end of 6 hours, so percent swelling was determined at the end of 6 hours for all the developed formulation. The values of swelling index of various batches were evaluated as shown in figure:12 to 16 and table:6 to 10 There was a significant increase in the percent swelling of the microspheres with increase in concentration of polymers. After 6 hours swelling index was observed between 70.76±2.74 to 86.99±1.22 %.

![Swelling Index](image)

**Figure:12 Results of swelling index of formulation F1 to F3**
TABLE: 6 RESULTS OF SWELLING INDEX OF FORMULATIONS F1 TO F3

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28.69±0.65</td>
<td>29.31±1.14</td>
<td>32.58±1.92</td>
</tr>
<tr>
<td>2</td>
<td>42.39±2.76</td>
<td>41.02±3.67</td>
<td>44.73±2.92</td>
</tr>
<tr>
<td>3</td>
<td>52.42±1.68</td>
<td>52.42±1.68</td>
<td>54.90±2.95</td>
</tr>
<tr>
<td>4</td>
<td>67.17±1.24</td>
<td>67.17±1.24</td>
<td>68.99±2.22</td>
</tr>
<tr>
<td>5</td>
<td>72.50±0.99</td>
<td>73.68±2.91</td>
<td>71.52±2.57</td>
</tr>
<tr>
<td>6</td>
<td>70.76±2.74</td>
<td>75.88±6.65</td>
<td>78.01±2.93</td>
</tr>
</tbody>
</table>

Mean ± S.D., n=3

Figure: 13 Results of swelling index of formulation F4 to F6

TABLE: 7 RESULTS OF SWELLING INDEX OF FORMULATIONS F4 TO F6

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28.95±1.64</td>
<td>30.40±1.27</td>
<td>31.60±2.18</td>
</tr>
<tr>
<td>2</td>
<td>38.62±2.10</td>
<td>44.92±3.71</td>
<td>46.46±0.77</td>
</tr>
<tr>
<td>3</td>
<td>52.85±1.07</td>
<td>53.51±1.84</td>
<td>51.74±1.79</td>
</tr>
<tr>
<td>4</td>
<td>65.54±1.24</td>
<td>68.84±0.39</td>
<td>66.47±1.83</td>
</tr>
<tr>
<td>5</td>
<td>71.76±1.74</td>
<td>71.75±1.33</td>
<td>71.75±1.33</td>
</tr>
<tr>
<td>6</td>
<td>73.07±1.84</td>
<td>78.73±2.34</td>
<td>82.33±2.83</td>
</tr>
</tbody>
</table>

Mean ± S.D., n=3
TABLE 8: RESULTS OF SWELLING INDEX OF FORMULATIONS F7 TO F9

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37.02±0.77</td>
<td>40.88±1.77</td>
<td>29.27±0.25</td>
</tr>
<tr>
<td>2</td>
<td>45.71±0.83</td>
<td>49.29±3.05</td>
<td>42.51±3.18</td>
</tr>
<tr>
<td>3</td>
<td>54.84±2.58</td>
<td>58.06±1.23</td>
<td>53.72±0.27</td>
</tr>
<tr>
<td>4</td>
<td>72.55±2.73</td>
<td>75.72±0.86</td>
<td>67.31±2.69</td>
</tr>
<tr>
<td>5</td>
<td>77.42±2.59</td>
<td>82.58±0.85</td>
<td>73.80±1.14</td>
</tr>
<tr>
<td>6</td>
<td>81.12±0.61</td>
<td>84.17±2.10</td>
<td>86.99±1.22</td>
</tr>
</tbody>
</table>

Mean ± S.D., n=3

Figure: 14 Results of swelling index of formulation F7 to F9

Figure: 15 Results of swelling index of formulation F10 to F12
TABLE:9 RESULTS OF SWELLING INDEX OF FORMULATIONS F10 TO F12

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>F10</th>
<th>F11</th>
<th>F12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34.49±2.37</td>
<td>34.63±1.16</td>
<td>37.62±2.32</td>
</tr>
<tr>
<td>2</td>
<td>48.29±4.07</td>
<td>44.60±1.63</td>
<td>46.03±2.77</td>
</tr>
<tr>
<td>3</td>
<td>56.93±1.09</td>
<td>54.51±0.82</td>
<td>54.76±3.35</td>
</tr>
<tr>
<td>4</td>
<td>69.22±1.53</td>
<td>70.59±2.67</td>
<td>72.47±3.02</td>
</tr>
<tr>
<td>5</td>
<td>76.41±2.12</td>
<td>75.77±1.99</td>
<td>77.97±3.92</td>
</tr>
<tr>
<td>6</td>
<td>80.85±1.20</td>
<td>83.41±4.00</td>
<td>84.17±2.97</td>
</tr>
</tbody>
</table>

Mean ± S.D., n=3

The swelling index was calculated with respect to time. As time increases, the swelling index was increased, because weight gain by tablet was increased proportionally with rate of hydration. It was observed that the swelling indices were increased with increase in polymer concentration. The direct relationship was observed between swelling index and...
polymer concentration. It has been observed that the cumulative percent drug release decreases with increasing concentration of polymer and swelling index. The reason attributed to this fact is slow erosion of the gelled layer from the tablets containing higher amount of polymer. For floating the tablets, there should be appropriate balance between swelling and water uptake. It was observed that HPMC grade also affect the swelling. No effect of effervescence on the swelling index was observed. Swelling index values starts decreasing when polymer erosion starts in medium.

**Buoyancy Lag Time**

Buoyancy of the tablet were influenced by both the swelling of the hydrocolloid particle on surface when it contacts the gastric fluid which in turn results in an increase in the bulk volume and porosity buoyancy lag time will increases when the hardness increases, at high compressed, reduces of porosity of tablets occurs, the compacted hydrocolloid particles on the surface of the tablet cannot hydrate rapidly when the tablet reaches the gastric fluid and as a result, the capability of the tablet to float is significantly reduced. The results are shown in Table:11

**TABLE:11 RESULTS OF LAG TIME AND FLOATING TIME**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Buoyancy time in seconds</th>
<th>Floating Time (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>30</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F2</td>
<td>18</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F3</td>
<td>25-30</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F4</td>
<td>15-25</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F5</td>
<td>30</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F6</td>
<td>15-18</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F7</td>
<td>25-30</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F8</td>
<td>20</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F9</td>
<td>30</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F10</td>
<td>15-18</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F11</td>
<td>25-30</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F12</td>
<td>20-25</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F13</td>
<td>15-20</td>
<td>&gt;12</td>
</tr>
<tr>
<td>F14</td>
<td>35</td>
<td>&gt;12</td>
</tr>
</tbody>
</table>

**In-vitro Drug Release Studies**

**Effect of HPMC (K4M)**
In order to investigate the release rate with HPMC (K4M) this is prepared in the ratio of 1:1, 1:1.5 and 1:2. The formulations F1-F3 were subjected to dissolution studies as shown in Figure:17 and Table:12

![Figure:17 Results of \textit{in-vitro} Drug Release Rate Profile of F1- F3](image)

<table>
<thead>
<tr>
<th>Hours</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19.77±0.46</td>
<td>17.17±0.68</td>
<td>14.81±1.46</td>
</tr>
<tr>
<td>2</td>
<td>33.49±0.26</td>
<td>29.45±0.27</td>
<td>24.30±2.77</td>
</tr>
<tr>
<td>3</td>
<td>45.71±0.26</td>
<td>40.86±0.27</td>
<td>33.49±2.77</td>
</tr>
<tr>
<td>4</td>
<td>57.20±0.64</td>
<td>52.51±0.67</td>
<td>46.32±0.95</td>
</tr>
<tr>
<td>5</td>
<td>72.67±0.62</td>
<td>63.59±0.52</td>
<td>58.62±0.67</td>
</tr>
<tr>
<td>6</td>
<td>89.01±1.64</td>
<td>74.74±3.27</td>
<td>67.09±4.54</td>
</tr>
<tr>
<td>7</td>
<td>97.87±0.34</td>
<td>93.42±0.69</td>
<td>76.14±5.94</td>
</tr>
<tr>
<td>8</td>
<td>97.98±0.11</td>
<td>91.06±6.05</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>97.78±1.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean, ± S.D., n=3

From the Figure and Table, the formulation F1 showed drug release rate 97.87 % in 7 hr, F2 showed 97.98 % drug release rate in 8 hr and F3 showed 97.78 % drug release rate in 9 hrs. It was concluded that the drug release rate decreases as the concentration of polymer increases.
Effect of HPMC (K15M)

In order to investigate the release rate with HPMC (K15M), which prepared in the ratio 1:1, 1:1.5 and 1:2. The formulations F4-F6 were subjected to dissolution studies as shown in Figure:18 and Table:13

![Graph showing drug release profile of F4-F6](image)

**Figure:18 Results of *in-vitro* Drug Release Rate Profile of F4- F6**

**TABLE:13 RESULTS OF % DRUG RELEASE RATE OF F4-F6**

<table>
<thead>
<tr>
<th>Hours</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.42±0.58</td>
<td>13.31±0.39</td>
<td>13.64±0.51</td>
</tr>
<tr>
<td>2</td>
<td>27.75±0.57</td>
<td>20.97±0.92</td>
<td>19.02±0.23</td>
</tr>
<tr>
<td>3</td>
<td>35.04±0.57</td>
<td>28.78±0.92</td>
<td>26.14±0.23</td>
</tr>
<tr>
<td>4</td>
<td>48.00±0.79</td>
<td>39.34±1.62</td>
<td>34.64±0.21</td>
</tr>
<tr>
<td>5</td>
<td>59.84±1.04</td>
<td>50.22±0.83</td>
<td>46.14±0.13</td>
</tr>
<tr>
<td>6</td>
<td>73.83±2.16</td>
<td>64.07±1.41</td>
<td>58.66±0.04</td>
</tr>
<tr>
<td>7</td>
<td>91.54±2.77</td>
<td>71.62±1.19</td>
<td>65.78±0.00</td>
</tr>
<tr>
<td>8</td>
<td>97.32±0.54</td>
<td>86.46±1.52</td>
<td>79.26±0.57</td>
</tr>
<tr>
<td>9</td>
<td>96.93±0.80</td>
<td>89.34±0.23</td>
<td>98.02±0.04</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean, ± S.D., n=3

From the Figure 10 and Table 11, the formulation F4 showed drug release rate 97.32 % in 8 hr, F5 showed 96.93 % drug release rate in 9 hr and F6 showed 98.02 % drug release rate in 10 hrs. It was concluded that the drug release rate decreases as the concentration of polymer increases.

**Effect of Xantham gum**
In order to investigate the release rate with Xanthan gum this is prepared in the ratio of 1:1, 1:1.5 and 1:2. The formulations F7-F9 were subjected to dissolution studies as shown in Figure:19 and Table:14

### Figure:19 Results of in-vitro Drug Release Rate Profile of F7- F9

<table>
<thead>
<tr>
<th>Hours</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21.31±0.85</td>
<td>18.37±0.33</td>
<td>17.10±0.08</td>
</tr>
<tr>
<td>2</td>
<td>33.75±1.04</td>
<td>29.10±1.19</td>
<td>25.35±1.84</td>
</tr>
<tr>
<td>3</td>
<td>50.79±1.04</td>
<td>44.48±1.19</td>
<td>37.90±1.84</td>
</tr>
<tr>
<td>4</td>
<td>64.88±0.49</td>
<td>57.29±0.27</td>
<td>48.72±0.69</td>
</tr>
<tr>
<td>5</td>
<td>73.41±1.01</td>
<td>65.10±0.10</td>
<td>58.03±0.85</td>
</tr>
<tr>
<td>6</td>
<td>94.14±1.18</td>
<td>90.30±2.32</td>
<td>72.28±0.15</td>
</tr>
<tr>
<td>7</td>
<td>98.35±1.10</td>
<td>96.01±0.40</td>
<td>89.25±1.09</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td>97.28±0.15</td>
</tr>
</tbody>
</table>

Mean, ± S.D., n=3

From the Figure and Table, the formulation F7 showed drug release rate 98.35 % in 7 hr, F8 showed 96.01 % drug release rate in 7 hr and F9 showed 97.28 % drug release rate in 8 hrs. It was concluded that the drug release rate decreases as the concentration of polymer increases.

**Effect of Guar gum**

In order to investigate the release rate with HPMC (K4M) this is prepared in the ratio of 1:1, 1:1.5 and 1:2. The formulations F10-F12 were subjected to dissolution studies as shown in Figure:20 and Table:15
From the Figure 9 and Table 10, the formulation F1 showed drug release rate 98.26 % in 6 hr, F2 showed 97.85 % drug release rate in 7 hr and F3 showed 96.47 % drug release rate in 8 hrs. It was concluded that the drug release rate decreases as the concentration of polymer increases.

**Effect of combination**

In order to investigate the release rate with HPMC (K4M): HPMC (K15M) and Xantham gum: Guar gum this is prepared in the ratio of 1:1.5. The formulations F13-F14 were subjected to dissolution studies as shown in Figure:21 and Table:16

---

**TABLE:15 RESULTS OF % DRUG RELEASE RATE OF F10-F12**

<table>
<thead>
<tr>
<th>Hours</th>
<th>F10</th>
<th>F11</th>
<th>F12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23.76±0.79</td>
<td>19.57±0.24</td>
<td>17.39±0.16</td>
</tr>
<tr>
<td>2</td>
<td>39.53±0.64</td>
<td>31.61±0.26</td>
<td>26.53±0.26</td>
</tr>
<tr>
<td>3</td>
<td>59.43±0.64</td>
<td>45.84±0.26</td>
<td>35.91±0.26</td>
</tr>
<tr>
<td>4</td>
<td>72.74±0.04</td>
<td>63.22±0.52</td>
<td>50.77±0.48</td>
</tr>
<tr>
<td>5</td>
<td>92.68±0.41</td>
<td>73.85±0.42</td>
<td>58.64±0.52</td>
</tr>
<tr>
<td>6</td>
<td>98.26±0.53</td>
<td>93.77±0.69</td>
<td>73.02±0.30</td>
</tr>
<tr>
<td>7</td>
<td>97.85±0.45</td>
<td>93.53±0.56</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>96.47±0.90</td>
<td></td>
</tr>
</tbody>
</table>

Mean, ± S.D., n=3
From the Figure and Table, the formulation F13 showed drug release rate 98.70% in 12 hr, F14 showed 97.50% drug release rate in 10 hrs. It was concluded that the drug release rate decreases as the concentration of polymer increases.

**Drug Release Kinetics**

Dissolution data of the all formulations was fitted to various mathematical models (Zero-order, First order, matrix, Peppas and Hix. Crowell) in order to describe the kinetics of drug release rate. Higher the value of regression coefficient ($R^2$) was chosen as criteria for selecting the most appropriate model. The dissolution data of was found to fit well into zero order release kinetics as shown in Table.
Release Kinetics:

**TABLE:17 KINETIC DATA OF CAPTOPRIL FLOATING TABLETS**

<table>
<thead>
<tr>
<th>Batch code</th>
<th>Zero Order (R)</th>
<th>First Order (R)</th>
<th>Higuchi Model (R)</th>
<th>Hixson-Crowell (R)</th>
<th>Korsmeyer Peppas (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.995</td>
<td>0.816</td>
<td>0.977</td>
<td>0.925</td>
<td>0.995</td>
</tr>
<tr>
<td>F2</td>
<td>0.994</td>
<td>0.827</td>
<td>0.974</td>
<td>0.926</td>
<td>0.996</td>
</tr>
<tr>
<td>F3</td>
<td>0.997</td>
<td>0.808</td>
<td>0.976</td>
<td>0.921</td>
<td>0.994</td>
</tr>
<tr>
<td>F4</td>
<td>0.994</td>
<td>0.817</td>
<td>0.960</td>
<td>0.936</td>
<td>0.989</td>
</tr>
<tr>
<td>F5</td>
<td>0.976</td>
<td>0.785</td>
<td>0.955</td>
<td>0.929</td>
<td>0.985</td>
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<tr>
<td>F6</td>
<td>0.994</td>
<td>0.777</td>
<td>0.951</td>
<td>0.921</td>
<td>0.973</td>
</tr>
<tr>
<td>F7</td>
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<td>0.839</td>
<td>0.981</td>
<td>0.922</td>
<td>0.993</td>
</tr>
<tr>
<td>F8</td>
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<td>0.844</td>
<td>0.961</td>
<td>0.946</td>
<td>0.988</td>
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<tr>
<td>F9</td>
<td>0.995</td>
<td>0.803</td>
<td>0.96</td>
<td>0.932</td>
<td>0.985</td>
</tr>
<tr>
<td>F10</td>
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<td>0.868</td>
<td>0.987</td>
<td>0.926</td>
<td>0.995</td>
</tr>
<tr>
<td>F11</td>
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<td>0.987</td>
<td>0.931</td>
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</tr>
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<td>F12</td>
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<td>0.953</td>
<td>0.945</td>
<td>0.982</td>
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<tr>
<td>F13</td>
<td>0.997</td>
<td>0.740</td>
<td>0.964</td>
<td>0.909</td>
<td>0.994</td>
</tr>
<tr>
<td>F14</td>
<td>0.993</td>
<td>0.862</td>
<td>0.987</td>
<td>0.924</td>
<td>0.997</td>
</tr>
</tbody>
</table>

**Stability Studies**\(^{[13]}\)

The optimized formulation was kept at room temperature and 75% relative humidity for 30 days. Then tablets were evaluated for physical properties and dissolution studies, the results are shown in Table.

**TABLE:18 RESULTS OF STABILITY STUDY**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness (kg/cm(^2))</td>
<td>6.38±0.13</td>
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<tr>
<td>Thickness (mm)</td>
<td>3.08±0.16</td>
</tr>
<tr>
<td>% Friability (%w/w)</td>
<td>0.69±0.48</td>
</tr>
<tr>
<td>Weight variation (mg)</td>
<td>200.01±0.3</td>
</tr>
<tr>
<td>Drug Content (%w/w)</td>
<td>99.36±0.05</td>
</tr>
</tbody>
</table>

The stability study of formulation F13 showed no significant changes in the hardness, % friability, weight variation, content uniformity of the formulation.
REFERENCES


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