**Effect of Sodium alginate in Combination With HPMC K 100 M in Extending the Release of Metoprolol Succinate from its Gastro-Retentive Floating Tablets**

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**ABSTRACT**

**Aim of work:** The aim of present study was to convert Metoprolol Succinate (MS) into Gastro Retentive Floating Tablet (GRFT) and simultaneously to determine the effect of Sodium alginate (SA) in combination with HPMC K 100M in extending the release of MS.

**Method:** The drug-excipients compatibility studies of MS and the polymers were carried by FTIR studies. The effervescent GRFT of MS was prepared by non-aqueous wet granulation. All Formulations were evaluated for pre-compression, post-compression, *in vitro* buoyancy and accelerated stability studies: for the best formulation for 3 months. **Results:** The drug-excipients compatibility studies reveals that MS and the polymers used are compatible. Evaluation parameters were within the acceptable limits for all formulations. *in vitro* dissolution studies, showed the formulation F4 having the combination of 20% HPMC K100M and 10% SA is exhibiting better extended release up to 12 h, with a Floating Lag Time (FLT) of 20 s, Total Floating Time (TFT) and Matrix Integrity (MI) maintained up to 12 h than other formulations. Regression Coefficients of Zero order and Higuchi equations suggested the drug release follows Zero order and is predominantly by diffusion respectively. The Diffusion exponent (n) of Korsmeyer-Peppas model suggested the release mechanism is by non-Fickian transport. DSC studies further confirmed the drug is in the same state even in the optimized formulation F4 with out interacting with the polymers and excipients in the formulation. Accelerated stability studies indicate no significant differences in the optimized formulation F4. **Conclusion:** In conclusion, by optimizing the right ratios of the release-retarding gel-forming polymers HPMC K100M and SA, GRFT of MS with a better extended release up to 12 h was formulated.

**Key words:** Gastro retentive floating tablets (GRFT), HPMC K100M, *In vitro* buoyancy studies, Metoprolol Succinate (MS), Sodium alginate.

**INTRODUCTION**

Oral route is one of the most extensively utilized routes for administration of dosage forms. Drugs that have an absorption window in stomach or upper small intestine, have low solubility and stability at alkaline pH were suitable to convert as Gastro Retentive Dosage Forms (GRDFs). GRDFs significantly extend the period of time over which the drugs may be released, they not only decrease dosing interval, but also increase patient’s compliance.1,2 Various approaches for GRDFs include: Floating Drug Delivery System (FDDS), bio adhesive systems, swelling and expanding systems, high density systems.3-4 FDDS has
a bulk density lower than gastric fluids and thus remain buoyant in the stomach for a prolonged period of time, without affected by gastric emptying rate.\textsuperscript{5-7} When the system is floating on the gastric contents, the drug is released slowly at a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach. This, results in an increase in the GRT and a better control on the fluctuations in the plasma drug concentration.\textsuperscript{8-10} Based on the mechanism of buoyancy, two different technologies for FDDS were Effervescent Systems and Non-effervescent Systems.\textsuperscript{11-14} Effervescent Systems contain carbonates (sodium bicarbonate) and organic acids (citric acid and tartaric acid) in their formulation to produce carbon dioxide (CO\textsubscript{2}) gas, which reduces the density of the system and making it to float.\textsuperscript{15} The Non-effervescent FDDS is based on mechanism of swelling of polymer or bio-adhesion to mucosal layer in GI tract.\textsuperscript{16} Metoprolol Succinate (MS) is a $\beta$1-selective adrenergic blocking agent.\textsuperscript{17} Since the half-life is $\sim$3 to 4 h,\textsuperscript{18} multiple doses are needed to maintain a constant plasma conc. for a good therapeutic response. MS is highly soluble throughout physiological pH and its solubility was 157mg ml$^{-1}$ in water (pH=5.5) and 183 mg ml$^{-1}$ in 0.1 N HCl (pH=1.0). It has also been reported that MS absorption mainly takes place in the duodenum and jejunum and is directly proportional to the dose available.\textsuperscript{19} Gastro retension is particularly useful for drugs that are having better solubility in acidic pH and primarily absorbed in the duodenum or upper jejunum segments.\textsuperscript{20} Hence it is a suitable candidate for GRFT.\textsuperscript{21} The present study was also interested in deter-

\begin{table}[h]
\centering
\begin{tabular}{|c|c|}
\hline
Concentration (µg/ml) & Absorbance at 274 nm \\
\hline
0 & 0.000 \\
10 & 0.047 \\
20 & 0.096 \\
30 & 0.138 \\
40 & 0.191 \\
50 & 0.23 \\
60 & 0.28 \\
80 & 0.373 \\
100 & 0.456 \\
\hline
\end{tabular}
\caption{Standard calibration plot of Metoprolol Succinate in 0.1N HCl at 274 nm}
\end{table}
Ashok Thulluru et al., Metoprolol Succinate Gastro-Retentive Floating Tablets

mining the effect of Sodium alginate (SA) in combination with HPMC K 100M in extending the release of MS from its GRFT for the better treatment of hypertension.

MATERIALS AND METHODS

MATERIALS

MS was received as a gift sample from Dr. Reddy’s Labs, Hyderabad. SA was purchased from Anshul Agencies and HPMC K100 M, Micro crystalline cellulose (Avicel PH 101), Sodium Bicarbonate, Citric acid, Magnesium Stearate, and Talc were purchased from S.D. Fine-Chem Ltd., India.

ANALYTICAL METHOD

Calibration curve of MS was determined in 0.1 N HCl at 274 nm using a UV-Visible spectrophotometer (Labindia UV-VIS 3000+, Labindia Analytical Instruments Pvt Ltd, India). This calibration curve was used for dissolution studies and drug content determination. (Figure 1 and Table 1).

EXCIPIENT COMPATIBILITY STUDIES

In order to evaluate the integrity and compatibility of the drug with polymers in polymer-drug matrix, FTIR spectra of drug and drug-polymer (1:1) mixture were recorded by the Potassium Bromide pellet method.
PREPARATION OF MS GRFT TABLETS

All the formulations were prepared by non-aqueous wet granulation using Isopropyl Alcohol, by keeping the amount of MS constant at 50 mg per tablet. The compositions of other excipients are varied as mentioned in formulation table (Table 2). MS and all the intra-granular excipients were co-sifted through Sieve No. # 40 (ASTM), blended uniformly in a poly bag for 10 min and granulated with Isopropyl Alcohol. The wet mass was sieved through Sieve No. # 20 (ASTM) and granules were dried to 40°C for 30 min. The dried granules were sieved through Sieve No. # 30 (ASTM) and lubricated with Sieve No. # 60 (ASTM) passed Magnesium Stearate and Talc and mixed for additional 2–3 min. Tablets were compressed on a Tabletting machine (Minipress by Clit, 10 stations, Chamunda Pharma Machinery Pvt. Ltd., India) fitted with a 10.4 mm circular shaped standard concave punch with an average hardness of 6.0 kg/cm².

EVALUATION OF TABLETS

The formulated tablets were evaluated for pre-compression, post-compression, in vitro buoyancy and in vitro dissolution studies.

Pre Compression studies

Angle of Repose (θ): was determined by funnel method, the granules were poured through the walls of a funnel, which was fixed at a position such that its lower tip was at a height of exactly 2 cm above hard surface. The granules were poured till the time when upper tip of the pile surface touched the lower tip of the funnel. The θ calculated by the equation.

\[ \theta = \tan^{-1} \frac{h}{r} \]

Where, \( \theta \) = angle of repose, \( h \) = height of heap, \( r \) = radius of base of heap circle.

Density

a) Bulk density (BD): A quantity of 2 g of granules from each formulation, previously lightly shaken to break any agglomerates formed, was introduced into a 10 ml measuring cylinder and the volume is noted as bulk volume. The BD was calculated by the equation.

\[ \text{Bulk density} = \frac{\text{weight of powder}}{\text{Bulk volume}} \]

b) Tapped density (TD): After the determination of BD, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Angle of repose (°)</th>
<th>Bulk density (g/cc)</th>
<th>Tapped density (g/cc)</th>
<th>Carr’s Index (%)</th>
<th>Hausner’s Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>22.17±0.15</td>
<td>0.515±0.015</td>
<td>0.522±0.008</td>
<td>13.15±1.04</td>
<td>1.10±0.07</td>
</tr>
<tr>
<td>F2</td>
<td>31.11±0.14</td>
<td>0.471±0.011</td>
<td>0.476±0.012</td>
<td>16.23±0.23</td>
<td>1.21±0.11</td>
</tr>
<tr>
<td>F3</td>
<td>25.71±0.13</td>
<td>0.505±0.005</td>
<td>0.527±0.015</td>
<td>14.26±0.65</td>
<td>1.15±0.31</td>
</tr>
<tr>
<td>F4</td>
<td>23.31±0.13</td>
<td>0.522±0.023</td>
<td>0.519±0.022</td>
<td>12.36±0.26</td>
<td>1.09±0.23</td>
</tr>
<tr>
<td>F5</td>
<td>28.27±0.15</td>
<td>0.496±0.065</td>
<td>0.499±0.053</td>
<td>17.42±0.96</td>
<td>1.12±0.08</td>
</tr>
<tr>
<td>F6</td>
<td>24.67±0.12</td>
<td>0.481±0.022</td>
<td>0.511±0.024</td>
<td>18.09±0.52</td>
<td>1.07±0.13</td>
</tr>
</tbody>
</table>

* i.e. 10 tablets were taken for a single test.
The flow ability of powder may be evaluated by comparing BD and TD of powder and the rate at which it packs down. The percentage of compressibility index was calculated by the equation.

\[
\text{Carr's Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100
\]

Hausner’s Ratio is a number that is correlated to the flow ability of a powder. It was calculated by the equation.

\[
\text{Hausner’s Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}
\]

The determination of micromeritics of all the formulations were carried out in triplicate, the consolidated results (mean ± SD) were tabulated in Table 3.

**Post compression studies**

- **Shape of tablet** and general **appearance**: were checked by magnifying lens after compression.\(^{26}\)
- **Thickness of tablet**: thickness of 3 tablets of each formulation was determined using a Vernier caliperse (Mitutoyo Corporation, Japan).\(^ {27}\)
- **Density**: If the density of the tablet is less than the density of gastric fluid (1.004 gm/cc) then only the tablets will float. Density of 3 tablets of each formulation were calculated by the equations\(^ {28}\)

\[
d = \frac{m}{v}
\]
\[
v = \pi r^2 h
\]

- \(d = \text{density}; v = \text{volume of the cylinder}; r = \text{radius of tablet}; h = \text{thickness of tablet}; m = \text{mass of tablet}\)
- **Tablet Weight Uniformity**: An electronic balance (Mettler Toledo, 3-MS-S/MS-L, Switzerland) was used to accurately weigh 10 tablets of each formulation which were randomly selected and the results (mean ± SD) are mentioned\(^ {29,30}\).
- **Hardness test**: To evaluate tablet hardness, 3 tablets of each formulation were tested for diametrical crushing strength using a hardness tester (Monsanto...
type hardness tester, MHT-20, Campbell Electronics, India.\(^\text{29,30}\)

- **Friability test:** The friability of the 10 tablets \((n=1)\) was tested by a friabilator (ERWEKA, TAR 120, Germany), at a speed of 25 rpm for 4 minutes. The percentage friability was calculated by the equation.\(^\text{29,30}\)

\[
\% \text{Friability} = \frac{\text{initial wt.} - \text{wt. after friability}}{\text{initial wt.}} \times 100
\]

- **Drug content:** To evaluate the drug content through a uniformity test, 10 tablets of each formulation were crushed; the quantity of tablet powder equivalent to 100 mg of MS was suspended in 0.1 N HCl to extract the MS from the blend. After 24 hours, media were filtrated, suitably diluted and measured by a UV-Visible spectrophotometer.\(^\text{29,30}\)

**In vitro Buoyancy studies**

- The *in vitro* buoyancy of 3 tablets of each formulation was determined as per the method described.\(^\text{31}\)
- **Floating Lag Time (FLT):** is the time taken for a tablet to rise on medium surface. A tablet was placed in a beaker with 100 ml of 0.1 N HCl, and the time required for the tablet to rise on the surface was determined.
- **Total Floating Time (TFT):** is the floating duration that a tablet remained on medium surface. A tablet was placed in a beaker with 100 ml of 0.1 N HCl, and the duration of tablet that remained on the surface was determined.
- **Matrix integrity (MI):** During the period of TFT the swelled matrix tablets were observed for their integrity. If not disintegrated upto 12 h, indicated as ‘+’, and if disintegrated with in 12 h indicated as ‘-’. The consolidated results of post compression and *in vitro* buoyancy studies are tabulated in Table 4.

**In vitro Dissolution Study**

A dissolution test was performed for 12 h using the dissolution apparatus (Labindia Disso 2000, Labindia Analytical Instruments Pvt Ltd, India) according to United States Pharmacopoeia.\(^\text{32}\) Each vessel contained 900 ml of 0.1N HCl; the paddle apparatus with 50 rpm speed was used, while the temperature was kept stable at 37°C ± 0.5°C. At every time interval, 5 ml of media was withdrawn and measured by UV-VIS spectrophotometer at 274 nm. Furthermore, 5 ml of 0.1N HCl was replaced to keep the volume stable. The dissolution test was repeated 6 times for each formulation and all the results were analyzed using Graph Pad Prism 5.0. (Figure 3 and Table 5).

**Release Kinetics**

The analysis of drug release mechanism from a pharmaceutical dosage form is important but complicated process and is practically evident in the case of matrix systems. The order of drug release from FDDS was described by using zero order kinetics or first order kinetics. The mechanism of drug release from FDDS was studied by using Higuchi equation and the Peppa’s-Korsmeyer equation.

**Zero Order Release Kinetics**

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the zero order equation.\(^\text{33}\)

\[
Q_0 - Q_t = K_0 t
\]

Rearrangement of above equation yields

\[
Q_t = Q_0 + K_0 t
\]

Where \(Q_t\) is the amount of drug dissolved in time \(t\), \(Q_0\) is the initial amount of drug in the solution (most times, \(Q_0=0\)) and \(K_0\) is the zero order release constant expressed

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>(r^2) values (Regression coefficient)</th>
<th>Korsmeyer-Peppas n value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zero order</td>
<td>First order</td>
</tr>
<tr>
<td>F1</td>
<td>0.733</td>
<td>0.968</td>
</tr>
<tr>
<td>F2</td>
<td>0.809</td>
<td>0.952</td>
</tr>
<tr>
<td>F3</td>
<td>0.850</td>
<td>0.971</td>
</tr>
<tr>
<td>F4</td>
<td>0.958</td>
<td>0.858</td>
</tr>
<tr>
<td>F5</td>
<td>0.955</td>
<td>0.991</td>
</tr>
<tr>
<td>F6</td>
<td>0.967</td>
<td>0.993</td>
</tr>
</tbody>
</table>
in units of conc. / time. The data obtained were plotted as cumulative amount of drug released vs time.

**First Order Release Kinetics**
The equation that describes first order kinetics is\(^{34}\)

\[
\log C = \log c_0 - Kt / 2.303
\]

Where \(C\) is the conc. of drug remaining at time ‘\(t\)’, \(c_0\) is the initial conc. of drug and \(K\) is the first order rate constant expressed in units of time\(^{-1}\). The data obtained were plotted as log cumulative percentage of drug remaining vs time, which would yield a straight line with a slope of \(-K/2.303\).

**Higuchi equation**
The first example of a mathematical model aimed to describe drug release from a matrix system was proposed\(^{35}\). Initially conceived for planar systems, it was then extended to different geometries and porous systems.\(^{36}\)
Simplify form of the Higuchi model can be represented by the equation:

\[ Q = K_H t^{1/2} \]

Where, \( Q \) is the amount of drug released in time \( t \) per unit area and \( K_H \) is the Higuchi dissolution constant. The data obtained were plotted as cumulative percentage drug release versus square root of time.

**Korsmeyer-Peppas equation**

Korsmeyer et al. (1983) derived a simple relationship which described drug release from a polymeric system.\(^{37}\) To find out the mechanism of drug release, first 60% drug release data were fitted in Korsmeyer-Peppas model equation.

\[ \frac{M_t}{M_\infty} = K_a t^n \]

Where, \( M_t / M_\infty \) are a fraction of drug released at time \( t \), \( k \) is the release rate constant and \( n \) is the release exponent. The \( n \) value is used to characterize different release mechanisms for different shaped matrices. In this model, the value of \( n \) characterizes the release mechanism of drug by cylindrical shape (Table 6). Data obtained were plotted as log cumulative percentage drug release vs log time.

The consolidated release kinetics of MS GRFTs was tabulated in (Table 7).

**Differential Scanning Calorimetry (DSC) Studies**

DSC scans of MS and the optimized formulation (F4) containing the same amount of drug were performed; using an automatic Thermal Analyser (DSC 60, Shimadzu, Japan). Sealed and perforated Aluminium pans were used in the experiments. Temperature calibrations were performed using Indium as standard. An empty pan sealed in the same way as the sample was used as a reference. The entire samples were run at a scanning rate of 10°C/min from 50-300°C. The DSC-Thermo grams of MS and optimized formulation (F4) were shown in (Figure 4 and 5) respectively.

**Accelerated Stability Studies**

Accelerated Stability Studies for 3 months were carried out according to International Conference on Harmonization (ICH) guidelines,\(^{38}\) to study the quality of the finished optimized formulation F4 under a variety of conditions (time, humidity, and temperature). Tablets were sealed in aluminum packaging having a polyethylene coating on the inside and kept in a humidity chamber (NSW-175, Narang Scientific work, India) maintained at 45°C and 75% RH. At the end of every month the, samples were withdrawn and evaluated for hardness, drug content, floating characteristics (FLT, TFT and MI) and % CDD at 12th. The consolidated Accelerated Stability Studies data for optimized formulation, F4 are tabulated in (Table 8).

**RESULTS & DISCUSSION**

**Analytical Method**

A spectrophotometric method for estimation of MS, based on the measurement of absorbance at 274 nm in 0.1N HCl, gives a straight line with an equation: \( y=0.0046 \) \( X + 0.0038 \) and \( r^2=0.999 \) (Figure 1 and Table 1).

**Drug-Excipients Compatibility Study**

The FTIR spectra of drug-polymer (1:1) blends were compared with that of the MS (Figure 2). FTIR spectrum of MS is characterized by the absorption of COOH group at 1612.5 cm\(^{-1}\), OH stretching absorption at 3061.0 cm\(^{-1}\) and NH deformation at 1375.5 cm\(^{-1}\). FTIR spectra of drug-polymer (1:1) blends, show same absorption patterns and bands as that of pure drug. Thus, indicates no significant chemical interaction occurred between the drug and polymers used.

**Evaluation of tablets**

**Pre Compression studies**

Pre compression studies on lubricated granules of all formulations (Table 2) reveals that the angle of repose was found between 22.17° to 31.11°, bulk density between 0.471 to 0.522 gm/cm\(^3\), tap density between 0.476 to 0.527 gm/cm\(^3\), Carr’s index between 12.36 to 18.09% and Hausner’s Ratio between 1.07 to 1.21. The micromeritic studies indicate better flow and compression characteristics of all formulations (Table 3).

**Post Compression studies**

The avg. wt. of tablet of all the formulations was found to be 300.9 ± 0.3 mg. Tablet thicknesses were found to be 5.91 ± 0.23 mm. The density of the cylindrical shape tablets in all cases was found to be 0.897 ± 0.032 Kg/cm\(^3\), indicating satisfactory buoyancy. The hardness of the formulation was 6.3 ± 0.13 Kg/cm\(^2\), indicating satisfactory mechanical strength. Percentage wt. loss in the friability test between 0.59 to 0.68% in all cases, which indicates good mechanical resistance of the tablets. Tablets of all the prepared batches containing MS were found to be within 100.65 ± 0.18% of the labeled content, indicating content uniformity of the prepared formulations.

**In vitro buoyancy studies**

The results of in vitro buoyancy studies showed quick floating of the tablet within 2 min after placing the tablet in dissolution medium. FLT varied between 20 s to
80 s and expect for formulation F1 remaining all formulations maintained TFT up to 12 h. Buoyancy mainly depends upon the ratio of effervescent mixture (Sodium Bicarbonate: Citric Acid). In all the formulations, the ratio was maintained as 5:1 respectively. The consolidated results of post compression and in vitro buoyancy studies of formulations are tabulated in (Table 4).

In vitro dissolution studies

It indicates, the release was extended with the increase in HPMC percentage in tablets due to the increased percentage of swelling and the decreased percentage of erosion.\(^9\) The more the concentration of HPMC, thicker the gel layer offers more resistance to the drug diffusion and gel erosion,\(^9\) which results in the incomplete release. SA matrix had the ability to provide a sustained release for highly water-soluble drug even in the presence of water-soluble excipients like HPMC\(^41\) the pH independent release profile for basic drugs like MS can be attained by combining HPMC with SA. The combined matrix when exposed to an acidic environment, the HPMC hydrates to form a gel layer at the surface of the tablet while the SA remains insoluble, acting as a barrier to diffusion of the drug.\(^42\) Their proportion had significant effect on the release profiles.\(^43\) Formulation F4 (20% HPMCK 100M and 10% SA) released 100 % of MS in 12 h, with a FLT of 20 s, TFT and a better MI up to 12 h, when compared to other formulations with HPMC only. Hence, formulation F4 was considered the best formulation with desirable floating parameters and in vitro drug release profile (Figure 3 and Table 5).

Release Kinetics

The drug release kinetics of optimized formulation F4 fitted best to the Zero-order (\(R^2=0.958\)). The (\(R^2=0.978\)) value in case of Higuchi release was found to be higher than Zero order and First order, suggesting that the drug release process is predominantly by diffusion. The (n=0.654) value for the case of cylindrical shape in Korsmeyer-Peppas model, suggested the release mechanism of the drug is non-Fickian transport (0.45<n<0.89) (Table 6 and 7).

DSC Studies

DSC Thermo grams in Figure 4 and 5 is pure drug and optimized formulation F4 respectively, reveals that the melting point of MS is 140.12°C and that of MS in the formulation F4 is 140.15°C. As there is no much difference in the melting points, it indicates that the drug is in same state even in the optimized formulation F4 without interacting with the polymers and excipients.

Accelerated stability studies

Results of accelerated stability studies of optimized formulation F4 indicate it is stable at 40°C / 75% RH up to 3Months. As there were no significant differences in hardness, drug content, floating characteristics (FLT, TFT & Matrix integrity) and % CDD at 12th h (Table 8).

CONCLUSION

In the above view of findings the formulation F4 (20% HPMCK 100M and 10% SA) is better suited for GRFT of MS than other formulations with HPMC K100M alone. It was concluded that the optimization of HPMCK 100M and SA, had significant effect on extending the release profiles of MS. A matrix design of this kind can serve as an alternative strategy to targeted drug delivery by GRFT. This work can be extended to alkaline- BCS class I drugs and their salts, which are having half-life less than 5 h.

CONFLICT OF INTEREST

Authors have no conflict of interest to declare.

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SUMMARY

- Drug-Excipient compatibility studies, Pre & post compression evaluation studies and in vitro buoyancy studies of all the formulations are within the acceptable limits.
- In vitro dissolution studies:
  - Indicates, the release was extended with the increase in HPMC Conc. due to the increased % of swelling and the decreased percentage of erosion.
  - The pH independent release profile for basic drugs like MS can be attained by combining HPMC with SA.
  - In acidic medium SA remains insoluble, acting as a barrier to diffusion of the drug. The HPMC K100M: SA ratio had significant effect on the release profiles.
  - Formulation F4 (with HPMC K100M:SA::2:1 ratio respectively) released 100% of MS in 12 h, with a FLT of 20 s, TFT and a better MI up to 12 h, when compared to other formulations with only HPMC.
  - Release Kinetics: The drug release kinetics of optimized formulation F4 fitted best to the Zero-order ($R^2 = 0.958$). The ($R^2 = 0.978$) value in case of Higuchi release was found to be higher than Zero order and First order, suggesting that the drug release process is predominantly by diffusion. The ($n = 0.654$) value for the case of cylindrical shape in Korsmeyer-Peppas model, suggested the release mechanism of the drug is non-Fickian transport ($0.45 < n < 0.89$).
  - Short Term Accelerated stability studies: of optimized formulation F4 indicates it is stable at conditions of 40°C / 75% RH up to 3 Months in Alu-Alu blister packing.

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Ashok Thulluru is an Associate Professor at the Department of Pharmaceutics, Aditya Institute of Pharmaceutical Sciences and Research (AIPSR), SURAMPALEM. His is having 8.5 yrs of teaching experience. His research interest is in the area of oral Extended Release- Floating, Mucoadhesive and herbal formulations. Currently perusing part time Ph.D. from JNTU, Hyderabad, under the guidance of Dr.M. Mohan Varma, Professor & HOD- Pharmaceutics, Shri Vishnu College of Pharmacy, BHIMAVARAM and Dr. C. M. Setty , Professor & HOD-Pharmaceutics, Vishnu Institute of Pharmaceutical Education & Research, NARSAPUR, on topic: Formulation & evaluation of Gastro retentive Floating Tablets.

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