Formulation and Evaluation of Floating Tablets of Tofacitinib Citrate

Department of Pharmaceutics, Saraswati Institute of Pharmaceutical Sciences, Dhanap. Gandinagar-382355, Gujarat, India.
*Corresponding author’s E-mail: rathi.sanjesh@gmail.com

Received: 15-04-2021; Revised: 19-06-2021; Accepted: 26-06-2021; Published on: 15-07-2021.

ABSTRACT

The present research work done with an objective of preparation and evaluation of floating tablets of Tofacitinib Citrate drug with Hydroxy propylene methyl cellulose (HPMC), Polyox N-60K, Carbopol 934 P and Guar gum polymers. Floating tablets were based on effervescent approach using sodium bicarbonate as a gas releasing agent. Direct compression method was used in present study for preparation of tablets. Effect of polymers was evaluated by studying drug release and floating time. In-vitro drug release profile indicates that sustained nature increased by increasing the concentration of polymer. The formulation containing Polyox N-60K and Carbopol 934 P in combination was optimized as it showed drug release up to 12hrs. Optimized formulation F18 was found stable during stability condition up to 1 month.

Keywords: Tofacitinib Citrate, Floating Tablets, Carbopol 934 P.

INTRODUCTION

Oral route of administration is the most important and convenient route for drug delivery. Due to differential absorption from various regions of GIT, the benefits of long-term delivery technology have not been fully realized for dosage forms designed for oral administration. Only few drug delivery systems have been designed to target drugs to differential regions of GIT. These include gastro retentive systems, delayed release systems and colon targeting.1 The real issue in the development of oral controlled release dosage form is not just to prolong the delivery of drugs for more than 12 h but also to prolong the presence of dosage forms in the stomach or somewhere in the upper small intestine. Dosage forms with prolonged gastric residence time (GRT), i.e. gastro remaining or gastro retentive dosage form (GRDF), will bring about new and important therapeutic options.1

Approaches for Gastric Retention 2

Floating System (Low Density Approach)

These systems are also known as hydro dynamically balanced systems. (HBS/FDDS) They have a bulk density lower than gastric fluid (i.e. <1.004 gm/ml)

The specific gravity of gastric fluid is approximately 1.004-1.010 g/cm³ according to the “Documenta Geigy” and thus the FDDS remains buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.

It is an oral dosage form (capsule or tablet) that is designed to prolong the residence time of the dosage form within the GI tract.

Design and Fabrication of FDDS3,4

Non effervescent FDDS

Colloidal gel barrier systems

Hydro dynamically balanced system (HBS™) of this type contains drug with gel forming or swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers. These systems incorporate high levels (20 to 75 % w/w) of one or more gel forming highly swellable cellulose type hydrocolloids for e.g. hydroxy ethyl cellulose (HEC), hydroxy propyl cellulose (HPC), hydroxy propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (NaCMC), polysaccharides and matrix forming polymers such as poly-carpophill, poly-acrylates and polystyrene incorporated either in tablets or capsules. When such a system comes in contact with the gastric fluid, the hydrochloride in the system hydrates and forms a colloidal gel barrier around its surface. This gel barrier controls the rate of the fluid penetration into the device and consequent release of drug from it.

Micro porous compartment system5,6,7

This technology is comprised of encapsulation of a drug reservoir inside a micro porous compartment with pores along its top and bottom surfaces. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of gastric mucosal surface with un-dissolved drug.
In stomach, the floatation chamber containing entrapped air causes the delivery system to float over the gastric contents. Gastric fluid enters through the pores, dissolves the drug and carries the dissolved drug for continuous transport across the intestine for absorption.

**Alginate beads**

Multiple unit floating dosage forms have been developed from freeze-dried calcium alginate. Spherical beads of approximately 2.5 mm in diameter were prepared by dropping a sodium alginate solution into aqueous solution of calcium chloride, causing a precipitation of calcium alginate. These beads were then separated; snap frozen in liquid nitrogen and freeze dried at – 40 °C for 24 h, leading to formation of porous system that maintained floating force for over 12 h.

**Hollow microspheres**

Hollow microspheres (micro balloons), loaded with ibuprofen in their outer polymer shells were prepared by novel emulsion solvent diffusion method. The ethanol: dichloromethane solution of the drug and an enteric acrylic polymer were poured into an agitated aqueous solution of PVA that was thermally controlled at 40 °C. The gas phase was generated in dispersed polymer droplet by evaporation of dichloromethane and formed an internal cavity in microspheres of polymer with drug.

**Effervescent systems**

A drug delivery system can be made to float in the stomach by incorporating a floating chamber, which may be filled with vacuum, air or inert gas. The gas in floating chamber can be introduced either by volatilization of an organic solvent or by effervescent reaction between organic acids and bicarbonate salts.

**Volatile liquid containing systems**

The GRT of a drug delivery system can be sustained by incorporating an inflatable chamber which contains a liquid e.g. Ether or Cyclo-pentane that gasifies at body temperature to cause the inflation of the chamber in the stomach. These devices are osmotically controlled floating systems containing a hollow deformable unit that can be converted from a collapsed to an expanded position and returned to collapse position after an extended period.

**Gas generating systems**

These buoyant delivery systems utilize effervescent reaction between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO₂ which gets entrapped in the jellified hydrochloride layer of the system, thus decreasing its specific gravity and making it float over chyme.

**MATERIALS**

Tofacitinib Citrate received as gift sample from Zydus Research Centre, Ahmedabad. Lactose, HPMC K4M, HPMC K15M, HPMC K100M, Carbopol 934, Sodium bicarbonate Citric Acid, Sodium bicarbonate Citric Acid, PVP K30, Talc, Magnesium Stearate and Polyox N-604 purchase from the ACS Chemicals, Ahmedabad. Polyox N-604 received as gift sample from Colorcon Asia Pvt. Limited.

**METHODS**

**Pre-Formulation Studies**

**Characterization of API**

**Organoleptic Characteristics**

Colour, odour & Appearance of Tofacitinib were characterized and recorded using descriptive terminology.

**Flow Properties**

**Bulk density and tapped density**

An accurately weighed quantity of the Drug (W), was carefully poured into the 10 ml graduated cylinder and the volume (V₀) was measured. Then the graduated cylinder was tap for 100 times and after that the volume (V₁) was measured which was tapped volume. The bulk density and tapped density were calculated by using the following formulas.

\[
\text{Bulk density} = \frac{W}{V_0} \quad \text{Tapped density} = \frac{W}{V_1}
\]

**Compressibility index (CI) / Carr’s index**

It was obtained from bulk and tapped densities. It was calculated by using the following formula.

\[
\% \text{ Carr’s index} = \left( \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \right) \times 100
\]

**Hausner’s ratio**

Hausner’s ratio is a number that is correlated to the flow ability of a powder. It is measured by ratio of tapped density to bulk density.

\[
\text{Hausner’s ratio} = \left( \frac{\text{Tapped density}}{\text{Bulk density}} \right)
\]

**Angle of repose**

Angle of repose of powder was determined by the funnel method. Accurately weight powder blend was taken in the funnel. Height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. Powder blend was allowed to flow through the funnel freely on to the surface. Diameter of the powder cone was measured and angle of repose was calculated using the following equation.

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

**Preparation of Floating Tablets of Tofacitinib Citrate**

**Dose Calculation for Sustained Release dosage form**

The total dose of Tofacitinib Citrate for a sustained release formulation was calculated by following four equations.
using available pharmacokinetic data from a design of one compartment model with simultaneous release of loading dose and a zero order release maintenance dose, as described by Robison and Eriksen.

\[ k_0 = \text{Dike} \]  
\[ D_m = k_0 T \]  
\[ D_i = \text{Di} - k_0 T_p \]  
\[ D_t = D_i + D_m \]  

Where, \( k_0 \) = zero order drug release.  
\( k_e = 0.693/t_{1/2} \)  
\( D_i = \text{initial dose/ conventional dose.} \)  
\( D_l = \text{loading dose} \)  
\( D_m = \text{maintenance dose} \)  
\( T = \text{time for sustained action} \)  
\( T_p = \text{time to reach peak plasma concentration} \)  
\( D_t = \text{total dose of drug.} \)

\[ W_0 = \text{weight before swelling} \]  
\[ W_t = \text{weight after swelling} \]  
\[ \text{Swelling index} = \frac{W_t - W_0}{W_0} \times 100 \]

**Drug content**

Ten tablets were weighed individually, and the drug was extracted in 0.1 N HCl, filter through 0.45μm membrane. The absorbance was measured at 287 nm after suitable dilution using a Shimadzu UV-1700 UV/Vis double beam spectrophotometer.

**In vitro buoyancy studies**

The in vitro buoyancy was determined by using dissolution testing apparatus USP type-II. The tablets were placed in 900 ml 0.1 N HCL at 100 rpm basket rotation at 37±0.5°C. The time required for tablets to ascend to the surface of dissolution medium and time taken by tablet to buoyant on surface of medium was recorded as floating lag time and total floating time.

**Swelling index**

The swelling index of tablets was in 0.1 N HCL. Tablets were weighed individually named as Wo and then it is placed in separately in glass beaker containing 200 ml 0.1N HCL at 37±0.5°C. At periodical time interval tablets were removed from beaker and extra amount of surface water discarded by blotting paper and then tablets were weighed and it is referred as Wt and swelling index was calculated using following formula:

\[ \text{Swelling index} = \frac{W_t - W_0}{W_0} \]

Where,  
\( W_t = \text{weight after swelling} \)  
\( W_0 = \text{weight before swelling} \)

Where, \( W_0 \) is the initial weight of tablet, and \( W_t \) is the weight of the tablet at time t.

**In Vitro Dissolution Studies**

USP apparatus II was used to test the dissolution profile using 900 ml of 0.1N HCl as dissolution medium at 50 rpm and 37°C ± 0.5°C. Six tablets from each batch were placed into respective basket containing HCl. 5 ml of the sample was withdrawn hourly for 12 hrs. The sample was filtered and from filtrate 3ml was withdrawn. The volume was adjusted to 100ml with 0.1N HCl. Absorbance of the solution was measured using UV spectrophotometer at 287 nm.

**Drug Release Kinetic Study**

Data obtained form in vitro drug release studies were fitted to Disso calculation software. The kinetic models
The dissolution data fitted to the Higuchi's equation:

Where, k2 is the diffusion rate constant.

The dissolution data was also fitted to the Korsmeyer-Peppas equation, which is often used to describe the drug release behavior from polymeric systems:

Where, k1 is the release rate constant. The dissolution data was fitted to the Higuchi’s equation:

Where, k2 is the diffusion rate constant.

The dissolution data was also fitted to the Korsmeyer-Peppas equation, which is often used to describe the drug release behavior from polymeric systems:

Where, k0 is the release rate constant.

The dissolution data was fitted to the first order equation:

Where, Q is the amount of drug released at time t, M∞ is the amount of drug release after infinite time, K is a release rate constant incorporating structural and geometric characteristics of the tablet, n is the diffusion exponent indicative of the mechanism of drug release.

**Stability Study**

Optimized Batch of prepared floating tablet subjected to accelerated stability studies at 40 °C and 75% RH for 1 month in a humidity chamber. The tablets of best batch were packed in aluminum foil pouch and analyzed for Assay, floating behavior and in-vitro drug release study.

**RESULTS & DISCUSSION**

**Pre-formulation Studies**

Based on results, it concluded that the API has a poor flow in nature. Hence, it is required to use directly compression grade material which has granular material itself. For this purpose, lactose DCL 11 grade was selected. The proposed formulation was gastro retentive dosage form targeted for 12 hrs so the solubility of API in 0.1 N HCl checked. The API was found soluble in the acidic medium. Hence, solubility enhancement not required.

**Evaluation of Formulation F1-F19 of Tofacitinib Citrate Floating Tablets**

**Pre-Compression Parameters Evaluation**

Powder blend of formulation F1-F19 checked for pre compression parameters like:

<table>
<thead>
<tr>
<th>Bulk density (g/ml) (n=3)</th>
<th>Tapped density (g/ml) (n=3)</th>
<th>Carr’s index (%) (n=3)</th>
<th>Hausner’s ratio (n=3)</th>
<th>Angle of repose (θ°) (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.54 ± 0.02</td>
<td>0.61 ± 0.03</td>
<td>11.48 ± 0.01</td>
<td>1.13 ± 0.02</td>
</tr>
<tr>
<td>F2</td>
<td>0.48 ± 0.03</td>
<td>0.52 ± 0.05</td>
<td>7.69 ± 0.02</td>
<td>1.08 ± 0.01</td>
</tr>
<tr>
<td>F3</td>
<td>0.47 ± 0.05</td>
<td>0.55 ± 0.03</td>
<td>14.55 ± 0.04</td>
<td>1.17 ± 0.02</td>
</tr>
<tr>
<td>F4</td>
<td>0.57 ± 0.07</td>
<td>0.60 ± 0.04</td>
<td>5.00 ± 0.07</td>
<td>1.05 ± 0.01</td>
</tr>
<tr>
<td>F5</td>
<td>0.47 ± 0.04</td>
<td>0.54 ± 0.04</td>
<td>12.96 ± 0.05</td>
<td>1.15 ± 0.02</td>
</tr>
<tr>
<td>F6</td>
<td>0.42 ± 0.05</td>
<td>0.54 ± 0.02</td>
<td>16.00 ± 0.06</td>
<td>1.19 ± 0.02</td>
</tr>
<tr>
<td>F7</td>
<td>0.51 ± 0.08</td>
<td>0.56 ± 0.05</td>
<td>8.93 ± 0.04</td>
<td>1.10 ± 0.01</td>
</tr>
<tr>
<td>F8</td>
<td>0.52 ± 0.02</td>
<td>0.58 ± 0.04</td>
<td>10.24 ± 0.05</td>
<td>1.12 ± 0.01</td>
</tr>
<tr>
<td>F9</td>
<td>0.47 ± 0.04</td>
<td>0.54 ± 0.02</td>
<td>12.96 ± 0.05</td>
<td>1.15 ± 0.01</td>
</tr>
<tr>
<td>F10</td>
<td>0.58 ± 0.03</td>
<td>0.65 ± 0.03</td>
<td>10.77 ± 0.02</td>
<td>1.12 ± 0.01</td>
</tr>
<tr>
<td>F11</td>
<td>0.49 ± 0.04</td>
<td>0.58 ± 0.08</td>
<td>15.52 ± 0.03</td>
<td>1.18 ± 0.02</td>
</tr>
<tr>
<td>F12</td>
<td>0.47 ± 0.05</td>
<td>0.54 ± 0.08</td>
<td>12.96 ± 0.04</td>
<td>1.15 ± 0.02</td>
</tr>
<tr>
<td>F13</td>
<td>0.48 ± 0.06</td>
<td>0.59 ± 0.07</td>
<td>18.64 ± 0.02</td>
<td>1.23 ± 0.01</td>
</tr>
<tr>
<td>F14</td>
<td>0.58 ± 0.05</td>
<td>0.64 ± 0.05</td>
<td>9.38 ± 0.03</td>
<td>1.10 ± 0.01</td>
</tr>
<tr>
<td>F15</td>
<td>0.48 ± 0.04</td>
<td>0.53 ± 0.06</td>
<td>9.43 ± 0.05</td>
<td>1.10 ± 0.02</td>
</tr>
<tr>
<td>F16</td>
<td>0.43 ± 0.03</td>
<td>0.49 ± 0.04</td>
<td>12.24 ± 0.06</td>
<td>1.14 ± 0.01</td>
</tr>
<tr>
<td>F17</td>
<td>0.46 ± 0.07</td>
<td>0.52 ± 0.07</td>
<td>11.54 ± 0.02</td>
<td>1.13 ± 0.01</td>
</tr>
<tr>
<td>F18</td>
<td>0.51 ± 0.03</td>
<td>0.57 ± 0.05</td>
<td>10.53 ± 0.04</td>
<td>1.12 ± 0.02</td>
</tr>
<tr>
<td>F19</td>
<td>0.50 ± 0.02</td>
<td>0.59 ± 0.07</td>
<td>15.25 ± 0.08</td>
<td>1.18 ± 0.01</td>
</tr>
</tbody>
</table>
Post Compression Parameters Evaluation

- **Weight variation**
  Weight variation results of Formulations F1-F19 showed in table 2. So, it was predicted that all the formulation exhibited uniform weight with low standard deviation values within the acceptable variation as per IP.

- **Thickness**
  Thickness of Formulations F1-F19 showed in table 2. No any major difference observed in formulation batches

- **Hardness**
  It was observed that all the formulation has a good hardness and increase in polymer amount will increase the hardness of tablet. All Formulations have good strength to withstand the mechanical shocks.

- **Friability**
  All formulation has a friability value less than 1 %, so this shows the durability of the prepared tablets.

- **Drug Content**
  Formulations F1-F19 results of Drug Content found within the limit. No any deviation observed.

- **Swelling Index**
  Water Intake ratio or swelling index of Formulations F1-F19 results are given in table 3 shows that all formulations has a good swelling capacity so it’s good for a floating

- **Floating Lag time and Total floating time**
  All the formulations have floating time within 1 min. so it is as per our requirement for floating tablet. Also, the total floating time is up to 12 hr. for all formulations.

In Vitro Drug Release Study

In vitro drug release study results are given in table 4. Results shows that low amount of polymer in tablet does not release drug up to 12 hr at starting. As we can see that in F1-F5, amount of polymer in tablet was just 25 mg. due to this F1-F5 does not give release up to 12 hr and release observed up to 8 hr only. After increasing the amount of polymer in formulation F6-F10 give the sustained effect up to 10 hr. so again amount of polymer increased to achieve desired release up to 12 hr and finally F11-F19 gives release up to 12 hrs. But here objective not achieved because in 12-hour maximum drug should be release. Results shown that after increasing polymer amount up to 75 mg in single polymer more than 95 % drug release not achieved in 12 hr. also the floating lag time was observed more than 1 min in F1-F20 formulation. Further trials taken with a combination of two polymers.

### Table 2: Post Compression Parameters of Formulation F1-F19

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Weight variation (mg) (n=10)</th>
<th>Thickness(mm) (n=3)</th>
<th>Hardness (Kg/cm²) (n=3)</th>
<th>Friability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>301±1.5</td>
<td>5.51±0.09</td>
<td>5.13±0.15</td>
<td>0.48</td>
</tr>
<tr>
<td>F2</td>
<td>300±1.4</td>
<td>5.59±0.11</td>
<td>4.72±0.07</td>
<td>0.70</td>
</tr>
<tr>
<td>F3</td>
<td>302±1.5</td>
<td>5.50±0.12</td>
<td>5.26±0.22</td>
<td>0.36</td>
</tr>
<tr>
<td>F4</td>
<td>299±1.6</td>
<td>5.52±0.11</td>
<td>5.13±0.15</td>
<td>0.49</td>
</tr>
<tr>
<td>F5</td>
<td>298±1.7</td>
<td>5.51±0.11</td>
<td>5.15±0.15</td>
<td>0.50</td>
</tr>
<tr>
<td>F6</td>
<td>300±1.8</td>
<td>5.48±0.13</td>
<td>4.76±0.17</td>
<td>0.68</td>
</tr>
<tr>
<td>F7</td>
<td>301±1.5</td>
<td>5.52±0.14</td>
<td>5.16±0.13</td>
<td>0.57</td>
</tr>
<tr>
<td>F8</td>
<td>298±1.4</td>
<td>5.51±0.12</td>
<td>5.19±0.11</td>
<td>0.52</td>
</tr>
<tr>
<td>F9</td>
<td>299±1.4</td>
<td>5.51±0.10</td>
<td>5.15±0.06</td>
<td>0.59</td>
</tr>
<tr>
<td>F10</td>
<td>301±1.5</td>
<td>5.50±0.13</td>
<td>5.29±0.13</td>
<td>0.50</td>
</tr>
<tr>
<td>F11</td>
<td>300±1.6</td>
<td>5.49±0.14</td>
<td>4.76±0.11</td>
<td>0.41</td>
</tr>
<tr>
<td>F12</td>
<td>301±1.7</td>
<td>5.47±0.08</td>
<td>5.08±0.11</td>
<td>0.59</td>
</tr>
<tr>
<td>F13</td>
<td>302±1.8</td>
<td>5.51±0.09</td>
<td>5.23±0.12</td>
<td>0.54</td>
</tr>
<tr>
<td>F14</td>
<td>298±1.7</td>
<td>5.48±0.11</td>
<td>4.86±0.15</td>
<td>0.49</td>
</tr>
<tr>
<td>F15</td>
<td>299±1.8</td>
<td>5.47±0.06</td>
<td>5.06±0.17</td>
<td>0.60</td>
</tr>
<tr>
<td>F16</td>
<td>302±1.6</td>
<td>5.49±0.11</td>
<td>4.75±0.14</td>
<td>0.81</td>
</tr>
<tr>
<td>F17</td>
<td>303±1.7</td>
<td>5.52±0.14</td>
<td>5.41±0.10</td>
<td>0.42</td>
</tr>
<tr>
<td>F18</td>
<td>301±1.8</td>
<td>5.50±0.15</td>
<td>5.13±0.09</td>
<td>0.45</td>
</tr>
<tr>
<td>F19</td>
<td>302±1.4</td>
<td>5.54±0.11</td>
<td>4.06±0.12</td>
<td>0.69</td>
</tr>
</tbody>
</table>
In combination batches F16-F19, batch F18 gives maximum % drug release 99.7 % in 12 hr. also the floating lag time observed 32 seconds which was lowest in all formulations. Also, total floating time was 12 hr so main floating parameters of floating tablets fulfill by combination of Carbopol 934 and Polyox N-60K. So the best combination of polymer based on % drug release, floating time and total floating was F18 which contains Carbopol 934 and Polyox N-60K both 50 mg. Initially trials were taken with single polymer. In single polymer trials, Carbopol 934 and Polyox N-60K gives good, sustained effect up to 12 hr so based on that, combination of polymer tried and both polymers in combination give max % drug release of 99.7 %. So F18 formulation finalized as optimized formulation.

Table 3: Post Compression Parameters of Formulation F1-F19

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Drug Content (%) (n=3)</th>
<th>Swelling Index (%) (n=3)</th>
<th>Floating Lag Time (sec) (n=3)</th>
<th>Total Floating Time (hr.) (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>99.2 ± 0.3</td>
<td>58.2 ± 4.4</td>
<td>70 ± 3</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>F2</td>
<td>99.8 ± 0.4</td>
<td>62.5 ± 2.2</td>
<td>95 ± 5</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>F3</td>
<td>98.5 ± 0.5</td>
<td>54.6 ± 5.3</td>
<td>63 ± 2</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>F4</td>
<td>97.8 ± 0.7</td>
<td>51.6 ± 6.2</td>
<td>45 ± 3</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>F5</td>
<td>99.5 ± 0.5</td>
<td>62.4 ± 4.3</td>
<td>64 ± 4</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>F6</td>
<td>99.4 ± 0.4</td>
<td>68.5 ± 5.2</td>
<td>72 ± 4</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>F7</td>
<td>99.5 ± 0.5</td>
<td>72.1 ± 1.6</td>
<td>83 ± 9</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>F8</td>
<td>99.7 ± 0.6</td>
<td>68.6 ± 3.2</td>
<td>64 ± 2</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>F9</td>
<td>98.4 ± 0.4</td>
<td>69.4 ± 2.5</td>
<td>56 ± 4</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>F10</td>
<td>100.5 ± 0.5</td>
<td>68.5 ± 3.2</td>
<td>62 ± 8</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>F11</td>
<td>100.8 ± 0.4</td>
<td>67.4 ± 3.6</td>
<td>186 ± 4</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>F12</td>
<td>98.7 ± 0.2</td>
<td>66.5 ± 5.6</td>
<td>165 ± 3</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>F13</td>
<td>99.5 ± 0.3</td>
<td>69.7 ± 3.9</td>
<td>170 ± 5</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>F14</td>
<td>98.6 ± 0.4</td>
<td>78.5 ± 5.9</td>
<td>120 ± 3</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>F15</td>
<td>99.7 ± 0.5</td>
<td>71.5 ± 3.4</td>
<td>144 ± 4</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>F16</td>
<td>99.4 ± 0.7</td>
<td>75.2 ± 2.5</td>
<td>136 ± 3</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>F17</td>
<td>98.7 ± 0.4</td>
<td>74.1 ± 4.5</td>
<td>178 ± 2</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>F18</td>
<td>99.8 ± 0.5</td>
<td>85.6 ± 5.6</td>
<td>32 ± 8</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>F19</td>
<td>99.4 ± 0.2</td>
<td>76.2 ± 4.1</td>
<td>140 ± 8</td>
<td>12 ± 1</td>
</tr>
</tbody>
</table>

Table 4: % Drug release study of Formulation F1-F19

<table>
<thead>
<tr>
<th>Code</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>26.8±0.1</td>
<td>45.7±0.2</td>
<td>68.9±1.0</td>
<td>84.4±0.5</td>
<td>89.4±0.3</td>
<td>98.6±0.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>F2</td>
<td>36.2±0.3</td>
<td>48.4±0.5</td>
<td>59.7±0.5</td>
<td>80.5±0.4</td>
<td>91.7±0.6</td>
<td>99.5±0.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>F3</td>
<td>45.8±0.5</td>
<td>59.7±0.4</td>
<td>69.7±0.4</td>
<td>89.4±0.5</td>
<td>95.4±0.4</td>
<td>99.8±0.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>F4</td>
<td>52.4±0.7</td>
<td>74.5±0.5</td>
<td>81.6±0.7</td>
<td>94.5±0.7</td>
<td>97.8±0.3</td>
<td>98.9±0.2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>F5</td>
<td>39.8±0.8</td>
<td>48.7±0.6</td>
<td>66.4±0.8</td>
<td>79.3±0.8</td>
<td>89.4±0.2</td>
<td>99.1±0.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>F6</td>
<td>25.5±0.7</td>
<td>39.4±0.4</td>
<td>49.7±0.3</td>
<td>75.4±0.9</td>
<td>81.5±0.7</td>
<td>88.7±0.8</td>
<td>99.5±0.2</td>
<td>-</td>
</tr>
<tr>
<td>F7</td>
<td>30.4±0.7</td>
<td>45.8±0.7</td>
<td>65.4±0.4</td>
<td>79.4±0.4</td>
<td>81.4±0.6</td>
<td>94.5±0.6</td>
<td>98.7±0.1</td>
<td>-</td>
</tr>
<tr>
<td>F8</td>
<td>32.1±0.5</td>
<td>46.1±0.2</td>
<td>65.4±0.5</td>
<td>74.8±0.5</td>
<td>87.4±0.5</td>
<td>95.6±0.5</td>
<td>99.4±0.2</td>
<td>-</td>
</tr>
<tr>
<td>F9</td>
<td>45.6±0.3</td>
<td>68.4±0.5</td>
<td>74.8±0.8</td>
<td>81.4±0.3</td>
<td>84.5±0.3</td>
<td>91.9±0.3</td>
<td>98.7±0.2</td>
<td>-</td>
</tr>
<tr>
<td>F10</td>
<td>29.4±0.4</td>
<td>41.2±0.2</td>
<td>59.4±0.7</td>
<td>72.1±0.1</td>
<td>84.5±0.2</td>
<td>89.1±0.7</td>
<td>99.8±0.7</td>
<td>-</td>
</tr>
<tr>
<td>F11</td>
<td>30.5±0.2</td>
<td>35.6±0.6</td>
<td>40.5±0.9</td>
<td>58.9±0.2</td>
<td>75.1±0.5</td>
<td>80.7±0.2</td>
<td>84.9±0.8</td>
<td>91.6±0.6</td>
</tr>
<tr>
<td>F12</td>
<td>27.5±0.6</td>
<td>30.5±0.5</td>
<td>32.8±0.2</td>
<td>49.7±0.4</td>
<td>56.7±0.4</td>
<td>59.7±0.5</td>
<td>74.8±0.5</td>
<td>88.4±0.4</td>
</tr>
<tr>
<td>F13</td>
<td>8.4±0.4</td>
<td>18.6±0.7</td>
<td>20.8±0.7</td>
<td>36.7±0.5</td>
<td>48.9±0.3</td>
<td>74.4±0.4</td>
<td>79.4±0.3</td>
<td>81.2±0.5</td>
</tr>
<tr>
<td>F14</td>
<td>11.8±0.8</td>
<td>17.8±0.8</td>
<td>22.7±0.8</td>
<td>29.9±0.6</td>
<td>38.4±0.5</td>
<td>49.4±0.6</td>
<td>69.7±0.1</td>
<td>78.4±0.8</td>
</tr>
<tr>
<td>F15</td>
<td>20.4±0.2</td>
<td>39.7±0.2</td>
<td>64.7±0.3</td>
<td>78.0±0.2</td>
<td>87.9±0.2</td>
<td>89.4±0.2</td>
<td>91.7±0.7</td>
<td>92.4±0.7</td>
</tr>
<tr>
<td>F16</td>
<td>18.9±0.6</td>
<td>27.6±0.5</td>
<td>38.7±0.6</td>
<td>52.4±0.3</td>
<td>69.8±0.8</td>
<td>81.7±0.3</td>
<td>84.7±0.8</td>
<td>88.9±0.2</td>
</tr>
<tr>
<td>F17</td>
<td>24.1±0.0</td>
<td>32.5±0.4</td>
<td>39.4±0.5</td>
<td>45.7±0.5</td>
<td>74.7±0.7</td>
<td>79.8±0.8</td>
<td>85.2±0.6</td>
<td>90.2±0.5</td>
</tr>
<tr>
<td>F18</td>
<td>33.5±0.3</td>
<td>39.2±0.8</td>
<td>45.5±0.3</td>
<td>48.7±0.5</td>
<td>64.7±0.2</td>
<td>75.4±0.6</td>
<td>88.9±0.5</td>
<td>99.7±0.2</td>
</tr>
<tr>
<td>F19</td>
<td>29.4±0.6</td>
<td>60.1±0.7</td>
<td>65.8±0.2</td>
<td>69.4±0.8</td>
<td>75.4±0.4</td>
<td>78.9±0.6</td>
<td>80.5±0.5</td>
<td>82.7±0.5</td>
</tr>
</tbody>
</table>
Drug release kinetic study

The drug release data of the final batch F18 was fitted in to different kinetic models. Among all, the best fitted model explained by Higuchi model because R² value of Higuchi model has 0.984 shown in table 5.

Table 5: Kinetic modeling data of batch F18

<table>
<thead>
<tr>
<th>Kinetic Model</th>
<th>Parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero Order</td>
<td>R²</td>
<td>0.932</td>
</tr>
<tr>
<td>First Order</td>
<td>R²</td>
<td>0.730</td>
</tr>
<tr>
<td>Higuchi</td>
<td>R²</td>
<td>0.984</td>
</tr>
<tr>
<td>Korsmeyer-Peppas</td>
<td>R²</td>
<td>0.527</td>
</tr>
<tr>
<td>Hixon Crowell</td>
<td>R²</td>
<td>0.910</td>
</tr>
</tbody>
</table>

Higuchi model was found to best describe the R² (coefficient of determination). Korsmeyer-Peppas equation also best suits the dissolution data where the values of “n” were 0.45-0.89 indicating anomalous, non-Fickian, or nearly zero-order release mechanism. Drug release mechanism from prepared floating tablets of F18 batch was elucidated by fitting the in vitro dissolution data in Korsmeyer-Peppas equation. The value of “n” for the optimized formulation was greater than 0.45 indicating non-Fickian case II transport mechanism.

Stability Study

Stability study of optimized batch F18 performed for 1 month at 40 °C/75 % RH and evaluated for various parameters from the stability study data, it revealed that the formulation F18 stable at 40 °C/75 % RH condition. Results are well within acceptable limits.

CONCLUSION

Review of literature reveals that floating drug delivery systems are easiest approach for technical and logical point of view among gastro retentive drug delivery system, so for present study, floating drug delivery system was chosen to increase the gastric residence time of dosage form which led to increased bioavailability of various drug substances. Tofacitinib Citrate is the drug of choice for the treatment of moderate to severe rheumatoid arthritis. So, in present investigation, an attempt was made to deliver Tofacitinib Citrate via floating drug delivery system to the vicinity of absorption site by prolonging the gastric residence time of the dosage form. Tablets were subjected to various evaluation parameters such as hardness, friability, thickness, weight variation, drug content, floating property study, swelling study, in vitro drug release study. It was revealed that tablets of all batches had acceptable physical parameters. The effervescent-based gastro retentive drug delivery is a promising
approach to achieve in vitro buoyancy by using gel-forming polymer HPMC K4M, HPMC K15M, HPMC K100M, Carbopol 934 P and Polyox N-60 K and gas generating agent sodium bicarbonate. Fourier transform Infrared spectroscopy confirmed the absence of any drug/polymers/excipients interactions. The drug content of all the formulations was found to be in the range of 96.22% to 99.45%, which indicates the uniform drug content. In vitro floatability studies revealed that most of the tablets still floated for more than 12 hours because of their low densities. In vitro drug release studies were performed for all the prepared formulations. All the prepared floating tablets exhibited good drug release. Amount of polymer in floating tablet plays an important role in drug release. Low amount of polymer in formulation doesn’t make a tablet to release a drug up to 12 hr. Hence F18 formulation in combination of Polyox N-60K and Carbopol 934 P makes tablet float and release a drug up to 12hr. The drug release data of formulation F18 fitted to different kinetic models and the best fitted model was Higuchi model. Stability study of formulation F18 was found satisfactory. Hence, F18 batch was optimized batch.

Acknowledgment: The Author and co-author, thanks to Saraswati Institute of Pharmaceutical Sciences, for providing the necessary facility to accomplish the work we also humble gratitude to our colleague and non-teaching staff for their support during the work.

REFERENCES


