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# Formulation and Evaluation of Floating Tablets of Ticagrelor

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**ABSTRACT**:
The present study focused on the development of sustained-release floating tablets of Ticagrelor. Various rate-controlling polymers were screened, including Natrosol 250 HHX, Natrosol 250 M, and Natrosol 250 G. Among these, Natrosol 250 HHX demonstrated the best control over the drug release, making it the chosen polymer for further development. Preformulation studies confirmed the compatibility of the drug with the selected excipients. Batches T1-T9 were prepared, and both physical and chemical analyses were conducted for all formulations. Batch T9 exhibited satisfactory results, prompting further optimization using factorial design. A 32- factorial design was applied to screen the formulation, with Natrosol 250 HHX and Sodium Bicarbonate as independent variables. Evaluation of the F1-F9 factorial batches revealed that weight variation, friability, hardness, and thickness were all within acceptable limits. Additionally, the drug content ranged from 97% to 99% across all batches.Natrosol 250 HHX significantly influenced the drug release at 1 hour, while Sodium Bicarbonate significantly affected the floating time. Results showed that increasing the concentration of Natrosol 250 HHX led to a decrease in drug release, while higher levels of Sodium Bicarbonate resulted in shorter floating times. The formulation F6 demonstrated stability during a one-month stability study and was selected as the optimized formulation.

**KEYWORDS:** Ticagrelor, Floating tablets, Natrosol.

## I. INTRODUCTION

**Introduction of Floating Drug Delivery System**

**Gastroretentive drug delivery system**

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.

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.

**A. Approaches for Gastric Retention** [2]

**A.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/cm$^3$ 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 FDDS** [3]

**A. Non effervescent FDDS**

**Colloidal gel barrier systems**

Hydro dynamically balanced system (HBS$^{TM}$) 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. hydroxylethyl cellulose (HEC), hydroxyl propyl cellulose (HPC), hydroxyl propyl methyl cellulose (HPMC), sodium carboxy methyl cellulose (NaCMC), polysaccharides and matrix forming polymers such as poly-carbophill, 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

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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 system**

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 $^{o}$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.

**B. 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

**1.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.

**2.Gas generating systems**

It basically contains polymers that gasify at body temperature effervescent compounds such as sodium bicarbonate, citric acid, tartaric acid, swellable polymers like methocel, and polysaccharides like chitosan. Resin beads loaded with bicarbonate and coated with ethylcellulose is the most common approach for preparation of these systems. The ethycellulose coating is insoluble but permeable to water which release carbon dioxide due to which it float.

**C Raft forming systems**:

Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft.

The raft floats. because of the buoyancy created by the formation of CO2 and act as a barrier to prevent the reflux of gastric Contents like HCl and enzymes into the esophagus. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluid

**Advantages of floating drug delivery system**

1.Simple and conventional technique for formulation.
2. Site-specific drug delivery.
3. Controlled delivery of drugs.
4. Delivery of drugs for residual action at a specific site in the stomach.
5. Improved drug absorption with increased GRT and excess duration of contact of dosage regimen at its target site.
6. In treating gastroesophageal reflux disorders (GERD)

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7. Ease of administration with higher patient compliance.

**Disadvantages of floating drug delivery system**

1. The major disadvantage of a floating system is due to the necessity of a sufficient level of gastric fluids to float without a sink. However, this limitation can be overcome by coating the dosage form with bio adhesive polymers that easily adhere to gastric mucosa.
2. The drugs those get significantly absorbed throughout gastrointestinal tract, with significant first-pass metabolism, are desirable candidate predominantly.
3. Certain drugs present in the floating system may causes irritation to gastric mucosal linings.
4. Gastric emptying of floating systems may occur at random and highly dependent on its dimensions. Therefore patients should not have dosage prior going to bed.

**Methods of preparation**

1.Direct compression
2.Wet granulation
3.Dry granulation

**Materials**

Ticagrelor was obtained from Zydus research centre,Ahmedabad .Lactose was obtained from ACS Chemicals. Natrosol 250HNX, Natrosol 250M, Natrosol 250G were obstructed from ACS Chemicals. Sodium bicarbonate and citric acid were obtained from ACS Chemicals. Binders and Lubricants were also obtained from ACS Chemicals

**Method of Preparation of Ticagrelor Floating Tablet**

Formula of preliminary trials for polymer selection.

Tablets containing different matrix forming agent were prepared by direct compression technique.

All the blends were passed from 40# sieve.

Required quantity of drug and various ingredients like matrix forming agent, gas generating agent and diluents were mixed thoroughly.

Talc and magnesium stearate were finally added as glidant and lubricant respectively.

The blend was compressed using tablet press machine.

**Drug Excipient Compatibility Study**

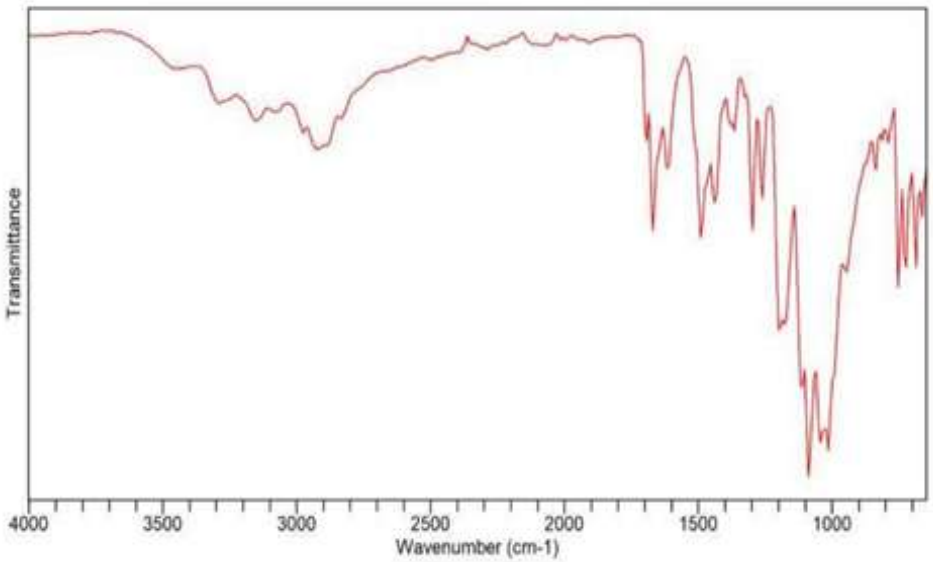


**Table 2. FTIR Spectra of Pure Drug Ticagrelor**

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**Table1. Priliminary batch trials**

| Ingredients (mg) | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 | T9 |
|---|---|---|---|---|---|---|---|---|---|
| Ticagrelor | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |
| Natrosol 250 M | 25 | - | - | 125 | - | - | - | - | - |
| Natrosol 250 HHX | - | 25 | - | - | 125 | - | 75 | 75 | 75 |
| Natrosol 250 G | - | - | 25 | - | | 125 | - | - | - |
| Sod. Bicarbonate | 35 | 35 | 35 | 35 | 35 | 35 | 35 | 15 | 55 |
| Citric Acid | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| DCP | 109 | 109 | 109 | 09 | 09 | 09 | 59 | 74 | 39 |
| Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Mg. stearate | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| **Total weight** | **250** | **250** | **250** | **250** | **250** | **250** | **250** | **250** | **250** |

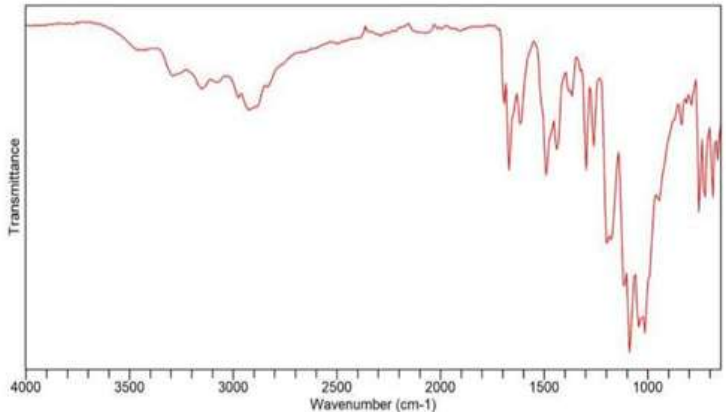


**Table 3. FTIR Spectra of Physical Mixture**

**Evaluation**

**Pre-compression study**

**Table 4. Pre-Compression Parameters of Formulation T1-T9**

| Batch | Bulk density (g/ml) (n=3) | Tapped density (g/ml) (n=3) | Carr's index (%) (n=3) | Hausner's ratio (n=3) | Angle of repose (θ°) (n=3) |
|---|---|---|---|---|---|
| **T1** | 0.54 ± 0.02 | 0.61 ± 0.03 | 11.48 ± 0.01 | 1.13 ± 0.02 | 32.25 ± 0.05 |
| **T2** | 0.48 ± 0.03 | 0.52 ± 0.05 | 7.69 ± 0.02 | 1.08 ± 0.01 | 35.22 ± 0.08 |
| **T3** | 0.47 ± 0.05 | 0.55 ± 0.03 | 14.55 ± 0.04 | 1.17 ± 0.02 | 31.12 ± 0.07 |
| **T4** | 0.57 ± 0.07 | 0.60 ± 0.04 | 5.00 ± 0.07 | 1.05 ± 0.01 | 34.26 ± 0.08 |
| **T5** | 0.47 ± 0.04 | 0.54 ± 0.04 | 12.96 ± 0.05 | 1.15 ± 0.02 | 34.15 ± 0.07 |
| **T6** | 0.42 ± 0.05 | 0.54 ± 0.02 | 16.00 ± 0.06 | 1.19 ± 0.02 | 31.19 ± 0.05 |
| **T7** | 0.51 ± 0.08 | 0.56 ± 0.05 | 8.93 ± 0.04 | 1.10 ± 0.01 | 34.56 ± 0.04 |
| **T8** | 0.52 ± 0.02 | 0.58 ± 0.04 | 10.34 ± 0.05 | 1.12 ± 0.01 | 33.75 ± 0.03 |
| **T9** | 0.47 ± 0.04 | 0.54 ± 0.02 | 12.96 ± 0.05 | 1.15 ± 0.01 | 32.84 ± 0.03 |

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**Table 5. Post Compression Parameters of Formulation T1-T9**

| Batch | Weight variation test (mg) (n=20) | Thickness (mm) (n=3) | Hardness ($kg/cm^2$) (n=3) | Friability (%) (n=3) |
|---|---|---|---|---|
| **T1** | 250 ± 2.3 | 4.52 ± 0.13 | 5.0 ± 0.5 | 0.61 ± 0.22 |
| **T2** | 255 ± 2.1 | 4.51 ± 0.11 | 5.0 ± 0.3 | 0.63 ± 0.19 |
| **T3** | 250 ± 2.6 | 4.48 ± 0.15 | 5.5 ± 0.4 | 0.47 ± 0.13 |
| **T4** | 255 ± 2.2 | 4.51 ± 0.08 | 4.9 ± 0.6 | 0.84 ± 0.17 |
| **T5** | 250 ± 2.7 | 4.49 ± 0.10 | 5.5 ± 0.2 | 0.50 ± 0.26 |
| **T6** | 250 ± 1.8 | 4.50 ± 0.12 | 4.9 ± 0.3 | 0.81 ± 0.11 |
| **T7** | 250 ± 2.5 | 4.52 ± 0.11 | 5.0 ± 0.7 | 0.62 ± 0.16 |
| **T8** | 255 ± 2.5 | 4.51 ± 0.16 | 5.1 ± 0.3 | 0.64 ± 0.12 |
| **T9** | 250 ± 2.0 | 4.51 ± 0.13 | 5.0 ± 0.6 | 0.66 ± 0.23 |

**Table 6.Post Compression Parameters of Formulation T1-T9**

| Batch | Drug Content (%) (n=3) | Swelling Index (%) (n=3) | Floating Lag Time (sec) (n=3) | Total Floating Time (hr.) (n=3) |
|---|---|---|---|---|
| **T1** | 97.9 ± 2.1 | 51.6 ± 6.1 | 45 ± 7 | 4 ± 0.5 |
| **T2** | 99.1 ± 1.5 | 62.4 ± 4.4 | 30 ± 4 | 5 ± 0.3 |
| **T3** | 99.5 ± 2.4 | 68.5 ± 5.3 | 105 ± 12 | 4 ± 0.6 |
| **T4** | 99.0 ± 2.6 | 58.2 ± 4.5 | 84 ± 9 | 12 ± 0.2 |
| **T5** | 98.8 ± 1.4 | 62.5 ± 2.8 | 110 ± 16 | >12 ± 0.5 |
| **T6** | 98.7 ± 2.9 | 54.6 ± 5.4 | 90 ± 5 | 12 ± 0.5 |
| **T7** | 99.4 ± 2.5 | 72.1 ± 1.9 | 35 ± 8 | 12 ± 0.7 |
| **T8** | 99.6 ± 2.8 | 68.6 ± 3.1 | 290 ± 11 | 12 ± 0.4 |
| **T9** | 98.2 ± 2.1 | 69.4 ± 2.6 | 18 ± 3 | 12 ± 0.2 |

- **In Vitro Drug Release Study**

Tablets containing different matrixing agents were prepared as per the composition given in Table 4. For preliminary trial, three different matrixing agents were used, at different concentration level as indicated in formulation table. The polymers were taken Natrosol 250 M(T1), Natrosol 250 HHX (T2) and Natrosol 250 G(T3) as matrixing agent and sodium bicarbonate as gas generating agent. In all among these batches, when 10 % concentration of polymer was used then drug release from matrix was much sustained. All three polymers at 10% concentration gives fast drug release within 6 hrs. Than 50% concentration was taken. Drug release after 12 hours in Natrosol 250 M, Natrosol 250 HHX and Natrosol 250 G are88%, 65% and 99% respectively. Therefore, it was required to decrease the concentration of each of the polymers. Decreasing concentration of each matrixing agent, drug release was evaluated.

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Batches T7 – T9 were prepared and dissolution was taken in 0.1N HCl in Type II dissolution apparatus in 50 RPM at 37.5°C. From these batches, Natrosol 250 HHX matrix shows best release profile which is more similar to the calculated theoretical profile as compare to other polymers. Effect of different matrixing agent on floating lag time also determined. T9 batch which has matrixing agent Natrosol 250 HHX gives floating lag time of only 18 sec., which is lower as compared to other and desirable for best formulation. So, from the preliminary study, we selected Natrosol 250 HHX as a matrixing agent for our formulation

- **In vitro buoyancy studies**

Floating lag time was found to be less than 2 minutes in all formulations.

All T1-T9 batches compared for their drug release profile and floating properties to identify the best suitable batch. Table 7 given below for results summary.

**Table 7. Drug release of batch T1-T9**

| Time in hr. | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 | T9 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 37.9 | 35.8 | 40.3 | 22.9 | 20.8 | 25.1 | 26.7 | 20.9 | 32.5 |
| 2 | 51.8 | 48.8 | 59.7 | 31.8 | 31.5 | 35.9 | 37.8 | 30.9 | 40.5 |
| 3 | 66.0 | 60.5 | 79.8 | 39.5 | 37.9 | 43.8 | 43.5 | 35.9 | 48.9 |
| 4 | 84.2 | 79.8 | 99.0 | 45.5 | 42.5 | 50.8 | 50.7 | 43.7 | 56.8 |
| 5 | 99.2 | 87.3 | - | 50.3 | 45.9 | 56.3 | 58.6 | 51.9 | 64.8 |
| 6 | - | 99.9 | - | 55.6 | 48.7 | 60.4 | 65.2 | 58.4 | 71.8 |
| 7 | - | - | - | 62.8 | 52.4 | 68.2 | 73.4 | 66.1 | 76.4 |
| 8 | - | - | - | 70.4 | 56.8 | 76.9 | 79.9 | 71.3 | 80.9 |
| 9 | - | - | - | 75.9 | 60.2 | 82.8 | 84.5 | 77.2 | 84.5 |
| 10 | - | - | - | 81.8 | 62.5 | 88.6 | 88.6 | 81.3 | 88.6 |
| 11 | - | - | - | 85.3 | 64.9 | 92.9 | 93.7 | 85.6 | 93.7 |
| 12 | - | - | - | 88.1 | 65.4 | 99.8 | 96.4 | 93.5 | 99.8 |

**Table 8 Drug release of batch T1-T9**

**Evaluation of factorial batches**

Powder blend of factorial batches F1-F9 checked for pre-compression parameters. Observed results are mentioned in following table 9. From the below table it concluded that the all batches have a good flow properties.

**Table 9.Pre-compression Parameters of factorial batches F1-F9**

| Batch | Bulk density (g/ml) (n=3) | Tapped density (g/ml) (n=3) | Carr's index (%) (n=3) | Hausner's ratio (n=3) | Angle of repose (θ°) (n=3) |
|---|---|---|---|---|---|
| **F1** | 0.49 ± 0.04 | 0.58 ± 0.08 | 15.52 ± 0.03 | 1.18 ± 0.02 | 32.14 ± 0.08 |
| **F2** | 0.47 ± 0.05 | 0.54 ± 0.08 | 12.96 ± 0.04 | 1.15 ± 0.02 | 31.04 ± 0.07 |
| **F3** | 0.48 ± 0.06 | 0.59 ± 0.07 | 18.64 ± 0.02 | 1.23 ± 0.01 | 33.56 ± 0.05 |
| **F4** | 0.58 ± 0.05 | 0.64 ± 0.05 | 9.38 ± 0.03 | 1.10 ± 0.01 | 31.45 ± 0.06 |
| **F5** | 0.48 ± 0.04 | 0.53 ± 0.06 | 9.43 ± 0.05 | 1.10 ± 0.02 | 34.84 ± 0.04 |
| **F6** | 0.43 ± 0.03 | 0.49 ± 0.04 | 12.24 ± 0.06 | 1.14 ± 0.01 | 32.84 ± 0.06 |

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| | | | | | |
|---|---|---|---|---|---|
| **F7** | 0.46 ± 0.07 | 0.52 ± 0.07 | 11.54 ± 0.02 | 1.13 ± 0.01 | 31.54 ± 0.04 |
| **F8** | 0.51 ± 0.03 | 0.57 ± 0.05 | 10.53 ± 0.04 | 1.12 ± 0.02 | 33.45 ± 0.05 |
| **F9** | 0.52 ± 0.02 | 0.59 ± 0.07 | 15.25 ± 0.08 | 1.18 ± 0.01 | 31.15 ± 0.02 |

**Table 10. Post Compression Parameters of factorial batches F1-F9**

| Batch | Weight variation test (mg) (n=20) | Thickness (mm) (n=3) | Hardness ($kg/cm^2$) (n=3) | Friability (%) (n=3) |
|---|---|---|---|---|
| **F1** | 252 ± 2.2 | 4.53 ± 0.10 | 4.9 ± 0.3 | 0.82 ± 0.12 |
| **F2** | 251 ± 2.8 | 4.53 ± 0.14 | 5.0 ± 0.2 | 0.65 ± 0.08 |
| **F3** | 250 ± 2.9 | 4.52 ± 0.19 | 4.8 ± 0.4 | 0.87 ± 0.13 |
| **F4** | 253 ± 2.8 | 4.51 ± 0.09 | 5.1 ± 0.2 | 0.67 ± 0.11 |
| **F5** | 251 ± 2.5 | 4.50 ± 0.12 | 5.2 ± 0.5 | 0.60 ± 0.18 |
| **F6** | 250 ± 3.1 | 4.48 ± 0.18 | 5.2 ± 0.2 | 0.62 ± 0.17 |
| **F7** | 252 ± 2.8 | 4.47 ± 0.17 | 5.4 ± 0.3 | 0.52 ± 0.12 |
| **F8** | 254 ± 1.9 | 4.45 ± 0.12 | 5.6 ± 0.1 | 0.47 ± 0.15 |
| **F9** | 252 ± 2.4 | 4.46 ± 0.16 | 5.4 ± 0.4 | 0.51 ± 0.14 |

**Table 11 Post Compression Parameters of factorial batches F1-F9**

| Batch | Drug Content (%) (n=3) | Swelling Index (%) (n=3) | Floating Lag Time (sec) (n=3) | Total Floating Time (hr.) |
|---|---|---|---|---|
| **F1** | 96.8 ± 3.1 | 62.5 ± 1.9 | 153 ± 14 | 9 |
| **F2** | 98.7 ± 2.9 | 63.7 ± 2.5 | 38 ± 3 | 9 |
| **F3** | 98.6 ± 2.7 | 64.1 ± 2.1 | 25 ±2 | 9 |
| **F4** | 99.8 ± 2.2 | 67.6 ± 2.6 | 165 ± 17 | 12 |
| **F5** | 97.5 ± 1.8 | 68.9 ± 2.1 | 48 ± 6 | 12 |
| **F6** | 99.1 ± 2.7 | 68.2 ± 2.9 | 40 ± 3 | 12 |
| **F7** | 98.3 ± 2.9 | 70.3 ± 3.4 | 178 ± 15 | >12 |
| **F8** | 99.4 ± 1.4 | 72.5 ± 2.7 | 60 ± 7 | >12 |
| **F9** | 98.6 ± 1.8 | 71.8 ± 3.2 | 48 ± 4 | >12 |

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**Table 12 Drug release of factorial batches F1-F9**

| Time in hr. | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 27.9 | 30.8 | 34.5 | 24.9 | 28.5 | 29.9 | 19.2 | 22.9 | 24.8 |
| 2 | 40.3 | 43.2 | 46.3 | 35.8 | 39.5 | 41.5 | 27.9 | 29.5 | 32.8 |
| 3 | 52.3 | 55.9 | 58.9 | 42.8 | 44.1 | 47.3 | 35.8 | 37.1 | 38.9 |
| 4 | 61.9 | 64.4 | 69.2 | 49.6 | 51.5 | 53.9 | 43.2 | 45.9 | 47.2 |
| 5 | 71.6 | 74.9 | 78.5 | 57.1 | 59.4 | 61.4 | 50.1 | 52.2 | 54.9 |
| 6 | 80.9 | 82.5 | 85.1 | 63.5 | 65.7 | 67.9 | 57.3 | 59.7 | 61.7 |
| 7 | 88.7 | 90.9 | 92.5 | 70.8 | 73.9 | 75.3 | 64.2 | 66.3 | 68.9 |
| 8 | 95.8 | 97.3 | 98.6 | 77.9 | 80.5 | 83.1 | 69.8 | 71.2 | 73.2 |
| 9 | 99.9 | 99.2 | 99.7 | 82.6 | 84.8 | 86.9 | 75.9 | 77.9 | 78.6 |
| 10 | - | - | - | 88.7 | 90.5 | 93.4 | 79.6 | 82.2 | 83.9 |
| 11 | - | - | - | 95.6 | 96.7 | 97.9 | 83.1 | 84.9 | 86.5 |
| 12 | - | - | - | 98.2 | 99.3 | 99.5 | 86.3 | 87.3 | 89.2 |

Drug release of factorial batches was performed to check the impact of the amount of polymer and efferent agent. Based on results it found that the amount of polymer change the release profile of the tablets. The actual impact was checked by using factorial design. The comparative plot was shown in below figure 6.5.

**Stability Study**

F6 batch which shows good results as compared to other batches was selected for stability study. Stability study was performed for 1 month at $40^{o}$ C temperature and 75 % RH in stability chamber. Sample withdraws after 1 month. It showed no change in in-vitro drug release at 12 hrs. Results of the stability study shows no remarkable change in the release profile of the Tablet after the stability. Also % drug content found within range. No any change in outer appearance of tablets.

**Table 13.Results of stability study of batch F6**

| Batch | Time Period | Appearance | Drug Content (%) (n=3) | Floating Lag Time (sec) (n=3) | In-vitro drug release at 12 hrs. (n=3) |
|---|---|---|---|---|---|
| F6 | Initial | White tablet | 99.1 ± 2.7 | 40 ± 3 | 99.8 ± 1.8 |
| | After 30 days | White tablet | 99.0 ± 2.3 | 42 ± 1 | 99.5 ± 2.1 |

## II. CONCLUSION

The present study focused on the development of sustained-release floating tablets of Ticagrelor. The formulation process began with the direct compression method for ease of production. Various rate-controlling polymers were screened, including Natrosol 250 HHX, Natrosol 250 M, and Natrosol 250 G. Among these, Natrosol 250 HHX demonstrated the best control over the drug release, making it the chosen polymer for further development. Preformulation studies confirmed the compatibility of the drug with the selected excipients. Batches T1-T9 were prepared, and both physical and chemical analyses were conducted for all formulations. Batch T9 exhibited satisfactory

results, prompting further optimization using factorial design. A 32-factorial design was applied to screen the formulation, with Natrosol 250 HHX and Sodium Bicarbonate as independent variables. The impact of these variables on drug release at 1 hour and floating time was assessed. Evaluation of the F1-F9 factorial batches revealed that weight variation, friability, hardness, and thickness were all within acceptable limits. Additionally, the drug content ranged from 97% to 99% across all batches. Natrosol 250 HHX significantly influenced the drug release at 1 hour, while Sodium Bicarbonate significantly affected the floating time. Results showed that increasing the concentration of Natrosol 250 HHX led to a decrease in drug release, while higher levels of Sodium Bicarbonate resulted in shorter floating times. The formulation F6 demonstrated stability during a one-month stability study and was selected as the optimized formulation.

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