

**FORMULATION AND CHARACTERIZATION OF SUSTAIN RELEASE TABLETS OF RIVAROXABAN USING NATURAL POLYMERS****Mukesh Chaudhari\*, Reena Shende, Satkar Prasad, Sailesh Kumar Ghatuary****RKDF School of Pharmaceutical Sciences, Bhopal (M.P.)**\*Corresponding Author's E mail: [chaudharimukesh9919@gmail.com](mailto:chaudharimukesh9919@gmail.com)

Received 08Aug. 2025; Revised 16Aug. 2025; Accepted 20Aug. 2025, Available online 15 Oct. 2025



Cite this article as: Chaudhari M, Shende R, Prasad S and Ghatuary SK. Formulation and Characterization of Sustain Release Tablets of Rivaroxaban Using Natural Polymers. Asian Journal of Pharmaceutical Education and Research. 2025; 13(4):22-31.

<https://dx.doi.org/10.38164/AJPER/14.4.2025.22-31>

**ABSTRACT**

Present study aimed to formulate and evaluate sustained release floating tablets of rivaroxaban using natural polymers for improved gastric retention and controlled drug delivery. Pre-compression studies of the powder blend indicated acceptable flow properties suitable for direct compression. Post-compression parameters such as thickness, hardness, friability, weight variation, and drug content were within pharmacopeial limits, ensuring good mechanical strength and uniformity of dosage units. All formulations exhibited buoyancy for more than 12 hours, with formulation F7 showing the shortest floating lag time ( $32 \pm 5$  sec). The in-vitro drug release profile of F7 demonstrated sustained release, with 28.85% drug release at 0.5 h and 99.08% at 12 h. Kinetic modeling revealed that drug release followed first-order kinetics ( $R^2 = 0.9819$ ) and Korsmeyer-Peppas model ( $R^2 = 0.9644$ ), indicating a non-Fickian diffusion mechanism. These findings suggest that natural polymers such as xanthan gum and Carbopol are effective in developing floating sustained release tablets of rivaroxaban, which may enhance therapeutic efficacy and patient compliance by reducing dosing frequency.

**Keywords:** Rivaroxaban, sustained release tablets, floating drug delivery, natural polymers, xanthan gum, Carbopol, drug release kinetics.

**INTRODUCTION**

Rivaroxaban is an oral, direct factor Xa inhibitor widely prescribed for the prevention and treatment of thromboembolic disorders, including venous thromboembolism (VTE), stroke prevention in non-valvular atrial fibrillation, and thromboprophylaxis after orthopedic surgery<sup>1</sup>. Its predictable anticoagulant effect, oral administration, and lack of routine monitoring requirements make it a preferable alternative to vitamin K antagonists. However, rivaroxaban has a relatively short elimination half-life (5–13 hours depending on age and renal function), which may necessitate frequent dosing to sustain therapeutic plasma levels in indications requiring prolonged exposure<sup>2</sup>.

Controlled or sustained-release (SR) oral formulations offer the potential to maintain consistent plasma concentrations, enhance patient adherence, and reduce peak-to-trough fluctuations that could be associated with bleeding risks or diminished efficacy<sup>3</sup>. Among SR approaches, matrix tablets remain widely used owing to their ease of manufacture, cost-effectiveness, and predictable performance, releasing the drug through diffusion, erosion, or combined mechanisms<sup>4</sup>.

Natural polymers such as xanthan gum, guar gum, locust bean gum, sodium alginate, chitosan, and starch derivatives have gained significant interest as matrix formers because of their biocompatibility, biodegradability, wide availability, and regulatory acceptance<sup>5</sup>. These polysaccharides can be used alone or in blends to modify drug release by altering swelling, viscosity, gel strength, and erosion kinetics. Furthermore, natural polymers align with the growing preference for “green” excipients and economical large-scale manufacturing<sup>6</sup>.

Rivaroxaban’s formulation challenges arise from its moderate lipophilicity, pH-dependent solubility (higher in acidic conditions), and absorption localized in the proximal small intestine. Therefore, an optimized SR matrix should (i) ensure controlled release throughout the dosing period, (ii) maintain adequate dissolution in upper GI conditions to support absorption, and (iii) prevent dose dumping<sup>7</sup>.

Critical evaluation parameters for rivaroxaban SR tablets include pre- and post-compression properties (flow, density, hardness, friability), in-vitro dissolution studies under biorelevant media, and kinetic modeling using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. Additionally, FTIR and DSC compatibility assessments, drug content uniformity, and stability testing are essential to confirm the robustness of natural polymer-based matrices<sup>8</sup>.

This investigation aims to formulate and characterize sustained-release matrix tablets of rivaroxaban using natural polymers such as xanthan gum, guar gum, sodium alginate, and chitosan, individually and in binary blends. The goal is to achieve predictable, consistent release while ensuring acceptable physicomachanical quality and stability, thereby offering a viable, patient-friendly alternative to conventional immediate-release therapy.

## **MATERIAL AND METHODS**

### **Material**

The sustained-release tablets of rivaroxaban were developed using natural polymers and standard excipients. Rivaroxaban served as the active drug, while xanthan gum and Carbopol 940 P were employed as matrix-forming agents. Magnesium stearate and talc acted as lubricants and glidants, with lactose as a filler and citric acid as a pH modifier. Methanol, ethanol, and chloroform were used as processing solvents, whereas hydrochloric acid, sodium hydroxide, and potassium dihydrogen phosphate were utilized for buffer preparation

in dissolution studies. All chemicals were of analytical grade, ensuring suitability for pharmaceutical applications.

## Methods

### Method for preparation of sustained release tablets of Rivaroxaban

Floating sustained release tablets of Rivaroxaban were prepared by direct compression method. All ingredients (drug, polymers, and excipients) were accurately weighed as per the formulation design and passed through sieve no. 40, while magnesium stearate was sieved through no. 60. Rivaroxaban was mixed with selected natural polymers (Xanthan gum, Carbopol 940P, and Chitosan) followed by addition of gas-generating agents (citric acid and sodium bicarbonate) and diluent (lactose). Finally, talc and magnesium stearate were incorporated as glidant and lubricant, respectively. The uniform powder blend was then compressed into tablets of 300 mg using a single-punch tablet compression machine and stored in airtight containers for further evaluation.

**Table 1: Preparation of sustained release tablets of Rivaroxaban using natural polymers**

| Excipients (mg)                                                  | F1  | F2  | F3  | F4  | F5  | F6  | F7  | F8  | F9  |
|------------------------------------------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| <b>Rivaroxaban</b>                                               | 10  | 10  | 10  | 10  | 10  | 10  | 10  | 10  | 10  |
| <b>Xanthan gum</b>                                               | 100 | 120 | 140 | -   | -   | -   | 50  | 60  | 70  |
| <b>Carbopol 940 P</b>                                            | -   | -   | -   | 100 | 120 | 140 | 50  | 60  | 70  |
| <b>Chitosan</b>                                                  | 30  | 30  | 30  | 30  | 30  | 30  | 30  | 30  | 30  |
| <b>Citric acid</b>                                               | 5   | 5   | 5   | 5   | 5   | 5   | 5   | 5   | 5   |
| <b>NaHCO<sub>3</sub></b>                                         | 20  | 20  | 20  | 20  | 20  | 20  | 20  | 20  | 20  |
| <b>Mg(C<sub>18</sub>H<sub>35</sub>O<sub>2</sub>)<sub>2</sub></b> | 10  | 10  | 10  | 10  | 10  | 10  | 10  | 10  | 10  |
| <b>Talc</b>                                                      | 5   | 5   | 5   | 5   | 5   | 5   | 5   | 5   | 5   |
| <b>Lactose</b>                                                   | 120 | 100 | 80  | 120 | 100 | 80  | 120 | 100 | 80  |
| <b>Total Weight</b>                                              | 300 | 300 | 300 | 300 | 300 | 300 | 300 | 300 | 300 |

### Evaluation of precompression parameter

**Bulk density:** Both loose bulk density (LBD) and tapped bulk density (TBD) were determined<sup>9</sup>. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formulas:

$$\text{LBD (Loose Bulk Density)} = \frac{\text{Mass of powder}}{\text{Volume of Packing}}$$

$$\text{TBD (Tapped Bulk Density)} = \frac{\text{Mass of powder}}{\text{Tapped Volume of Packing}}$$

**Carr's Compressibility index:** Percent compressibility of powder mix was determined by Carr's compressibility index, calculated by using following formula:-

$$\text{Carr's Index} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \times 100$$

**Hausners ratio:** It is determined by comparing tapped density to the bulk density by using following equation <sup>10</sup>:-

$$\text{Housner's ratio} = \frac{\text{Tapped bulk density}}{\text{Loose Bulk density}}$$

Hausner's ratio value <1.25 shows better flow properties

### Evaluation of tablets

All the tablets were evaluated for following various parameters which includes;

#### General Appearance

Five tablets from various batches were randomly selected and organoleptic properties such as color, odor, shape, were evaluated. Appearance was judged visually. Very good (+++), good (++), fair (+) poor (-), very poor (- -) <sup>11</sup>.

#### Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated <sup>12</sup>.

#### Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 10mg of drug was transferred to 10ml standard flask. The powder was dissolved in 5 ml of 0.1 N HCl and made up to volume with of 0.1 N HCl. The sample was mixed thoroughly and filtered through a 0.45μ membrane filter. The filtered solution was diluted suitably and for drug content by UV spectrophotometer at λ<sub>max</sub> of 270 nm using of 0.1 N HCl as blank <sup>13</sup>.

#### Hardness

For each formulation, the hardness of five tablets was resolved utilizing the Monsanto hardness tester <sup>14</sup>.

#### Friability

The friability of a sample of 10 tablets was estimated utilizing a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes<sup>15</sup>. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated.

### **Uniformity of weight**

Twenty tablets were randomly selected from each batch individually weighed; the average weight and standard deviation of 20 tablets was calculated<sup>16</sup>.

### ***In vitro* buoyancy studies:**

*In vitro* buoyancy was determined by floating lag time as per the method described by Rosa *et al.* (1994)<sup>17</sup>. The tablets were separately in a 100 ml glass beaker containing simulated gastric fluid, pH 1.2 as per USP. The time necessary for the tablet to increase to the outside and float was determined as floating lag time.

### **Dissolution rate studies**

*In vitro* drug release of the sample was done using USP-type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml 0.1N HCl was set into the dissolution flask maintaining the temperature of  $37 \pm 0.5^\circ\text{C}$  and rpm of 75. One prepared Rivaroxaban tablet was set in every container of dissolution apparatus. The mechanical assembly was permitted to keep running for 10 hours. Sample measuring 5 ml were pulled back after each 1 hour up to 10 hours using 10 ml pipette. The new disintegration medium ( $37^\circ\text{C}$ ) was supplanted each time with a similar amount of the sample and takes the absorbance at 270 nm using UV/Visible spectroscopy.

## **RESULTS AND DISCUSSION**

The pre-compression evaluation of all nine formulations (Table 2) showed bulk density values ranging from 0.332 to 0.352 g/ml and tapped density from 0.442 to 0.468 g/ml, indicating uniform packing behavior of the powder blend. The calculated compressibility index (23.79–25.85%) and Hausner ratio (1.312–1.349) suggested fair to passable flow properties, which were suitable for direct compression.

The post-compression parameters (Table 3) confirmed that all formulations had acceptable quality attributes. Tablet thickness (3.11–3.16 mm) and hardness (6.3–6.7 kg/cm<sup>2</sup>) were consistent, showing uniformity in mechanical strength. Weight variation and friability ( $\leq 0.745\%$ ) were within pharmacopeial limits, ensuring good durability during handling. Drug content ranged between 96.65% and 99.45%, demonstrating uniform drug distribution. The total floating duration of all batches exceeded 12 hours, confirming the effectiveness of the polymers in maintaining buoyancy.

The buoyancy test (Table 4) revealed that floating lag time varied across formulations, with F7 showing the shortest lag time of  $32 \pm 5$  sec, indicating faster initiation of floating compared to other batches. This can be attributed to the optimized polymer and effervescent agent concentration.

The in-vitro drug release study of optimized formulation F7 (Table 5) demonstrated a controlled release profile with 28.85% release at 0.5 h, gradually increasing to 99.08% at 12 h, reflecting sustained drug delivery over the study period. The drug release followed first-order kinetics ( $R^2 = 0.9819$ ) with a high correlation to the Korsmeyer-Peppas model ( $R^2 = 0.9644$ ), indicating a non-Fickian diffusion mechanism involving both drug diffusion and matrix erosion. Higuchi kinetics ( $R^2 = 0.9259$ ) further supported diffusion-based release.

The results suggest that natural polymers such as xanthan gum and Carbopol, when used in optimized concentrations, successfully provided floating ability and sustained release characteristics to rivaroxaban tablets. Formulation F7 was identified as the most effective batch, exhibiting rapid buoyancy, prolonged gastric retention, and desirable sustained release behavior suitable for improving therapeutic efficacy and patient compliance.

**Table 2: Result of pre-compression properties of Rivaroxaban**

| Formulation<br>Code | Bulk<br>density(gm/ml) | Tapped<br>density(gm/ml) | Compressibility<br>index | Hausner ratio |
|---------------------|------------------------|--------------------------|--------------------------|---------------|
| F1                  | 0.345                  | 0.458                    | 24.6725                  | 1.328         |
| F2                  | 0.332                  | 0.442                    | 24.8869                  | 1.331         |
| F3                  | 0.352                  | 0.465                    | 24.3011                  | 1.321         |
| F4                  | 0.349                  | 0.458                    | 23.7991                  | 1.312         |
| F5                  | 0.347                  | 0.468                    | 25.8547                  | 1.349         |
| F6                  | 0.352                  | 0.463                    | 23.9741                  | 1.315         |
| F7                  | 0.337                  | 0.445                    | 24.2697                  | 1.320         |
| F8                  | 0.349                  | 0.459                    | 23.9651                  | 1.315         |
| F9                  | 0.352                  | 0.463                    | 23.9741                  | 1.315         |

**Table 3: Results of post compression properties of sustain release tablets**

| Formulation code | Thickness (mm) | Hardness (kg/cm <sup>2</sup> )<br>n=3 | Weight variation (mg)<br>n=3 | Friability (%)<br>n=3 | Drug content (%)<br>n=3 | Total floating duration (h) |
|------------------|----------------|---------------------------------------|------------------------------|-----------------------|-------------------------|-----------------------------|
| F1               | 3.11±0.05      | 6.5±0.2                               | 295±6                        | 0.665±0.012           | 96.65±0.45              | >12                         |
| F2               | 3.15±0.03      | 6.3±0.3                               | 298±3                        | 0.745±0.015           | 97.12±0.63              | >12                         |
| F3               | 3.12±0.07      | 6.4±0.5                               | 305±4                        | 0.712±0.019           | 98.66±0.25              | >12                         |
| F4               | 3.14±0.05      | 6.5±0.6                               | 306±5                        | 0.665±0.022           | 98.74±0.45              | >12                         |
| F5               | 3.15±0.04      | 6.7±0.4                               | 302±5                        | 0.678±0.032           | 96.65±0.65              | >12                         |
| F6               | 3.12±0.03      | 6.5±0.2                               | 304±3                        | 0.665±0.025           | 97.74±0.32              | >12                         |
| F7               | 3.16±0.05      | 6.5±0.3                               | 298±2                        | 0.685±0.017           | 99.45±0.48              | >12                         |
| F8               | 3.11±0.04      | 6.6±0.7                               | 294±3                        | 0.674±0.011           | 98.62±0.36              | >12                         |
| F9               | 3.16±0.03      | 6.5±0.2                               | 298±4                        | 0.658±0.019           | 97.74±0.25              | >12                         |

**Table 4: Results of *in-vitro* buoyancy study of sustain release floating lag time**

| S. No. | Formulation Code | Floating lag times (sec) |
|--------|------------------|--------------------------|
| 1.     | F1               | 66±6                     |
| 2.     | F2               | 55±5                     |
| 3.     | F3               | 48±4                     |
| 4.     | F4               | 78±7                     |
| 5.     | F5               | 69±8                     |
| 6.     | F6               | 55±6                     |
| 7.     | F7               | 32±5                     |
| 8.     | F8               | 48±3                     |
| 9.     | F9               | 55±4                     |

**Table 5: *In-vitro* drug release data for optimized formulation F7**

| Time (h) | Square Root of Time(h) <sup>1/2</sup> | Log Time | Cumulative* % Drug Release | Log Cumulative % Drug Release | Cumulative % Drug Remaining | Log Cumulative % Drug Remaining |
|----------|---------------------------------------|----------|----------------------------|-------------------------------|-----------------------------|---------------------------------|
| 0.5      | 0.707                                 | -0.301   | 28.85                      | 1.460                         | 71.15                       | 1.852                           |
| 1        | 1.000                                 | 0        | 39.95                      | 1.602                         | 60.05                       | 1.779                           |
| 1.5      | 1.225                                 | 0.176    | 46.65                      | 1.669                         | 53.35                       | 1.727                           |
| 2        | 1.414                                 | 0.301    | 59.85                      | 1.777                         | 40.15                       | 1.604                           |
| 3        | 1.732                                 | 0.477    | 68.85                      | 1.838                         | 31.15                       | 1.493                           |
| 4        | 2.000                                 | 0.602    | 79.95                      | 1.903                         | 20.05                       | 1.302                           |
| 6        | 2.449                                 | 0.778    | 88.58                      | 1.947                         | 11.42                       | 1.058                           |
| 8        | 2.828                                 | 0.903    | 92.28                      | 1.965                         | 7.72                        | 0.888                           |
| 12       | 3.464                                 | 1.079    | 99.08                      | 1.996                         | 0.92                        | -0.036                          |

**Table 6: Regression analysis data of sustain release Tablets**

| Batch | Zero Order<br>R <sup>2</sup> | First Order<br>R <sup>2</sup> | Higuchi<br>R <sup>2</sup> | Peppas<br>R <sup>2</sup> |
|-------|------------------------------|-------------------------------|---------------------------|--------------------------|
| F7    | 0.8006                       | 0.9819                        | 0.9259                    | 0.9644                   |

## CONCLUSION

The sustained-release tablets of rivaroxaban prepared using natural polymers such as xanthan gum and Carbopol 940 P demonstrated satisfactory pre-compression and post-compression characteristics, along with excellent buoyancy and prolonged drug release. The optimized formulation (F7) showed more than 12 hours of floating ability and sustained release following first-order kinetics with a non-Fickian diffusion mechanism. These findings indicate that natural polymers can be effectively utilized for the development of gastroretentive sustained-release formulations of rivaroxaban, offering improved therapeutic efficacy and patient compliance.

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