

Formulation Development and Evaluation of Orally Disintegrating Tablets of Poorly Water-Soluble Anticoagulant Drug (Rivaroxaban)

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Abstract

Poor aqueous solubility of many modern drugs leads to poor dissolution and limited oral bioavailability. Rivaroxaban, a direct Factor Xa inhibitor used in thromboembolic disorders, belongs to **BCS class II** and exhibits low aqueous solubility. The present study aimed to develop **orally disintegrating tablets (ODTs)** of rivaroxaban to enhance dissolution rate and improve patient compliance. Tablets were prepared by **direct compression** using different concentrations of superdisintegrants such as **croscarmellose sodium, sodium starch glycolate, and crospovidone**. Precompression parameters including angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio were evaluated. The prepared formulations were assessed for hardness, friability, weight variation, drug content, disintegration time, wetting time, and in-vitro dissolution. Among the nine formulations prepared (F1–F9), formulation **F6 containing 6% crospovidone** showed the best performance with a disintegration time of **18 ± 1.2 sec** and drug release of **96.4% within 15 minutes**. The results suggest that the ODT approach significantly improves dissolution of poorly soluble rivaroxaban and may enhance therapeutic effectiveness.

Keywords: Rivaroxaban, ODT, poorly soluble drugs, superdisintegrants, dissolution enhancement

I. Introduction

Oral drug delivery remains the most widely used route of drug administration due to its convenience, patient compliance, non-invasiveness, and cost-effectiveness. Tablets and capsules are the most common oral dosage forms because they offer accurate dosing, good stability, and ease of manufacturing. However, the major limitation associated with oral drug delivery is the **poor aqueous solubility of many newly discovered**

drug molecules. According to recent pharmaceutical research reports, nearly **40–50% of new chemical entities (NCEs) exhibit poor aqueous solubility**, which significantly affects their dissolution rate and consequently their oral bioavailability [1,2]. Drugs belonging to **Biopharmaceutical Classification System (BCS) Class II** typically show high membrane permeability but low solubility, making dissolution the rate-limiting step for absorption in the gastrointestinal tract [3].

Poor aqueous solubility often leads to several biopharmaceutical challenges such as slow onset of therapeutic action, variable absorption, reduced therapeutic efficiency, and high inter-individual variability in drug plasma levels. To overcome these limitations, various formulation strategies have been developed, including **solid dispersions, particle size reduction, lipid-based formulations, cyclodextrin inclusion complexes, and fast dissolving dosage forms** [4]. Among these approaches, the development of **orally disintegrating tablets (ODTs)** has gained considerable attention in recent years due to their ability to improve drug dissolution and patient convenience.

Rivaroxaban is a **direct oral anticoagulant (DOAC)** that selectively inhibits **Factor Xa**, a key enzyme involved in the coagulation cascade responsible for thrombin generation and clot formation. By directly inhibiting Factor Xa, rivaroxaban prevents thrombus formation and reduces the risk of thromboembolic disorders [5]. Clinically, rivaroxaban is widely used for the treatment and prevention of **deep vein thrombosis (DVT), pulmonary embolism (PE), and stroke prevention in patients with non-valvular atrial fibrillation** [6]. Despite its therapeutic advantages, rivaroxaban exhibits **poor aqueous solubility (approximately 5–7 µg/mL)** and is categorized as a **BCS Class II drug**, where dissolution is the rate-

limiting step for absorption [7]. Consequently, enhancing the dissolution rate of rivaroxaban remains an important formulation challenge in order to improve its bioavailability and therapeutic performance.

Orally disintegrating tablets (ODTs) are solid dosage forms that **rapidly disintegrate or dissolve in the mouth within seconds without the need for water**. These dosage forms are particularly beneficial for pediatric, geriatric, and dysphagic patients who have difficulty swallowing conventional tablets [8]. The rapid disintegration of ODTs leads to faster drug dispersion in saliva and subsequently increases the available surface area of the drug particles, which may enhance dissolution and improve the onset of action. In addition to improved patient compliance, ODTs also provide advantages such as **ease of administration, improved stability, accurate dosing, and reduced risk of choking** [9].

The performance of ODTs largely depends on the use of **superdisintegrants**, which facilitate rapid tablet disintegration through mechanisms such as swelling, capillary action (wicking), and deformation recovery. Commonly used superdisintegrants include **croscarmellose sodium, sodium starch glycolate, and crospovidone**. Croscarmellose sodium promotes rapid disintegration by swelling and wicking mechanisms, while sodium starch glycolate rapidly absorbs water and swells to break the tablet matrix. Crospovidone primarily acts through capillary action and particle repulsion, resulting in rapid tablet breakup [10]. The selection and concentration of these superdisintegrants play a crucial role in determining the disintegration time and dissolution profile of ODT formulations.

Considering the challenges associated with the poor aqueous solubility of rivaroxaban and the advantages offered by ODT technology, the present study aimed to **formulate and evaluate orally disintegrating tablets of rivaroxaban using different superdisintegrants**. The study focuses on investigating the influence of various superdisintegrants on **pre-compression parameters, tablet disintegration time, wetting time, drug content, mechanical properties, and in-vitro dissolution behavior**. The development of an optimized rivaroxaban ODT formulation may provide a promising approach to enhance drug dissolution, improve patient compliance, and potentially increase therapeutic effectiveness.

II. Materials and Methods

2.1 Materials

Rivaroxaban was selected as the model drug due to its **poor aqueous solubility and anticoagulant activity**. Crospovidone, croscarmellose sodium, and sodium starch glycolate were used as **superdisintegrants** to promote rapid tablet disintegration. Mannitol was used as a **diluent and filler** because of its excellent mouthfeel and cooling sensation, which makes it suitable for orally disintegrating tablets (ODTs). Microcrystalline cellulose (MCC) was used as a **binder and compressibility enhancer**, improving the mechanical strength of tablets during direct compression. Aspartame was incorporated as a **sweetening agent** to improve palatability of the ODT formulation. Magnesium stearate served as a **lubricant** to reduce friction between the tablet surface and the die wall during compression, while talc was used as a **glidant** to improve the flow properties of the powder blend [11–13].

All chemicals and reagents used in this study were of **analytical grade** and were used as received without further purification.

Material	Function
Rivaroxaban	Anticoagulant drug
Crospovidone	Superdisintegrant
Croscarmellose Sodium	Superdisintegrant
Sodium Starch Glycolate	Superdisintegrant
Mannitol	Diluent
Microcrystalline Cellulose	Binder
Aspartame	Sweetener
Magnesium Stearate	Lubricant
Talc	Glidant

Rivaroxaban acts as a **selective inhibitor of Factor Xa**, thereby preventing the conversion of prothrombin to thrombin and inhibiting clot formation [14]. Superdisintegrants such as crospovidone, croscarmellose sodium, and sodium starch glycolate facilitate rapid tablet disintegration through mechanisms including **swelling, capillary action (wicking), and deformation recovery**, which are essential for the rapid dispersion of orally disintegrating tablets in the oral cavity [15].

Mannitol is widely used in ODT formulations due to its **high water solubility, pleasant taste, and negative heat of solution**, which produces a cooling sensation in the mouth and enhances patient acceptability [16]. Microcrystalline cellulose contributes to improved compressibility and acts as a **dry binder**, enabling the preparation of tablets by the direct compression method. Magnesium stearate and talc were incorporated in small quantities to

improve lubrication and powder flow characteristics during tablet compression [17].

2.2 Method of Preparation

The orally disintegrating tablets (ODTs) of rivaroxaban were prepared using the **direct compression method**, which is one of the most commonly employed techniques for manufacturing fast disintegrating tablets due to its simplicity, cost-effectiveness, and minimal processing steps. Direct compression avoids the use of heat and moisture during tablet production, making it particularly suitable for drugs and excipients that are sensitive to environmental conditions. Furthermore, this method provides uniform distribution of the drug within the tablet matrix and ensures good mechanical strength of the final dosage form [18].

In the present study, rivaroxaban ODT formulations were prepared by incorporating different concentrations of superdisintegrants such as **crospovidone, croscarmellose sodium, and sodium starch glycolate** to evaluate their influence on tablet disintegration and dissolution characteristics.

Preparation Procedure

1. Sieving of Ingredients

All ingredients including rivaroxaban, superdisintegrants, diluent (mannitol), and microcrystalline cellulose were individually passed through a **#60 mesh sieve** to eliminate lumps and obtain uniform particle size distribution. Sieving improves the homogeneity of the powder blend and facilitates better mixing during formulation development [19].

2. Dry Mixing of Drug and Excipients

The accurately weighed quantities of rivaroxaban, superdisintegrants, mannitol, microcrystalline cellulose, and aspartame were transferred into a clean and dry mortar. The ingredients were blended thoroughly for approximately **15 minutes** to ensure uniform distribution of the drug and excipients throughout the powder mixture. Proper mixing is essential to maintain **content uniformity and consistent tablet performance**.

3. Addition of Lubricants

After uniform blending of the primary ingredients, **magnesium stearate and talc** were added to the powder mixture. These excipients were mixed gently for **5 minutes** to avoid excessive coating of particles by the lubricant, which could negatively affect tablet hardness and dissolution characteristics [20].

4. Tablet Compression

The final powder blend was compressed into tablets using a **rotary tablet compression machine** fitted with appropriate punches and dies. Compression force was adjusted to obtain tablets with sufficient hardness while maintaining rapid disintegration properties.

The final tablets were designed to have a **target weight of 150 mg per tablet**, ensuring accurate drug dosing and acceptable tablet size for rapid oral disintegration.

The prepared tablets were further subjected to **pre-compression and post-compression evaluation parameters** including flow properties of powder blend, tablet hardness, friability, weight variation, drug content, wetting time, disintegration time, and in-vitro dissolution studies.

III. Formulation Design

The formulation design for rivaroxaban orally disintegrating tablets (ODTs) was developed to investigate the effect of different **superdisintegrants and their concentrations** on tablet disintegration behavior and drug release characteristics. Three commonly used superdisintegrants—**crospovidone, croscarmellose sodium, and sodium starch glycolate**—were selected for this study due to their well-established efficiency in enhancing tablet disintegration through mechanisms such as swelling, wicking, and capillary action [21].

A total of **nine formulations (F1–F9)** were prepared using the **direct compression technique**. Each formulation contained **10 mg of rivaroxaban**, while the type and concentration of superdisintegrant were varied to evaluate their influence on tablet performance. Crospovidone was incorporated in formulations **F1–F3**, croscarmellose sodium in **F4–F6**, and sodium starch glycolate in **F7–F9** at concentrations of **2 mg, 4 mg, and 6 mg**, respectively.

Mannitol was used as a **diluent and filler** because of its excellent solubility, pleasant taste, and cooling sensation in the oral cavity, which enhances patient acceptability of orally disintegrating tablets. Microcrystalline cellulose (MCC) was included as a **binder and compressibility enhancer** to improve tablet mechanical strength and facilitate direct compression. Aspartame served as a **sweetening agent** to improve palatability of the dosage form. Talc was incorporated as a **glidant** to enhance powder flow, while magnesium stearate acted as a **lubricant** to reduce friction between the powder

blend and the die wall during tablet compression [22,23].

The total tablet weight for each formulation was maintained at **150 mg**, which ensures adequate tablet size for rapid disintegration while maintaining sufficient mechanical strength for handling and

packaging. The designed formulations were subsequently evaluated for **pre-compression parameters, tablet hardness, friability, weight variation, wetting time, disintegration time, drug content uniformity, and in-vitro dissolution behavior**.

Table 1: Composition of ODT Formulations (mg/tablet)

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Rivaroxaban	10	10	10	10	10	10	10	10	10
Crospovidone	2	4	6	-	-	-	-	-	-
Croscarmellose Na	-	-	-	2	4	6	-	-	-
Sodium Starch Glycolate	-	-	-	-	-	-	2	4	6
Mannitol	85	83	81	85	83	81	85	83	81
MCC	45	45	45	45	45	45	45	45	45
Aspartame	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
Mg Stearate	2	2	2	2	2	2	2	2	2

Formulation Strategy

The formulation design allowed comparison of three superdisintegrants at different concentrations to determine their effect on:

- **Tablet disintegration time**
- **Wetting time**
- **Mechanical strength**
- **Drug release profile**

Increasing the concentration of superdisintegrants was expected to **enhance water penetration into the tablet matrix**, leading to faster disintegration and improved drug dissolution. However, excessive amounts may negatively affect tablet hardness and friability. Therefore, optimization of superdisintegrant concentration is critical for achieving an ideal balance between **rapid disintegration and adequate tablet strength** [24].

IV. Pre-Compression Evaluation

Prior to tablet compression, the powder blends prepared for different formulations were evaluated for their **micromeritic properties** to ensure suitability for the **direct compression method**. Pre-compression evaluation is an essential step in tablet formulation development because the flow characteristics and compressibility of the powder blend directly influence tablet weight uniformity, mechanical strength, and overall manufacturing performance [25].

The prepared powder blends were evaluated for the following parameters:

- Angle of repose
- Bulk density
- Tapped density

- Carr's compressibility index
- Hausner ratio

These parameters help determine the **flowability and packing ability of powder mixtures**, which are critical for uniform die filling during tablet compression.

4.1 Angle of Repose

The **angle of repose** is a measure of powder flow properties and indicates the frictional forces between powder particles. It was determined using the **fixed funnel method**. The powder blend was allowed to flow through a funnel onto a flat surface to form a conical heap. The angle of repose was calculated using the following equation:

$$\theta = \tan^{-1} \left(\frac{h}{r} \right)$$

Where:

- θ = angle of repose
- h = height of the powder heap
- r = radius of the heap

Generally, an angle of repose **below 30° indicates good flow properties**, which are desirable for direct compression [26].

4.2 Bulk Density

Bulk density represents the mass of powder divided by the total bulk volume occupied by the powder. It was determined by gently pouring a known quantity of powder blend into a graduated measuring cylinder and recording the volume.

$$\text{Bulk Density} = \frac{\text{Weight of Powder}}{\text{Bulk Volume}}$$

Bulk density helps evaluate the **packing characteristics of the powder blend**.

4.3 Tapped Density

Tapped density was determined by placing the measuring cylinder containing the powder blend on a **tap density apparatus** and tapping it mechanically until a constant volume was obtained.

$$\text{Tapped Density} = \frac{\text{Weight of Powder}}{\text{Tapped Volume}}$$

Tapped density indicates the ability of powder particles to **rearrange under external force**, which is important for tablet compression.

4.4 Carr's Compressibility Index

Carr's index provides information about the **compressibility and flowability** of powder blends. It was calculated using the following equation:

$$\text{Carr's Index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100$$

A Carr's index value **below 15%** generally indicates **good flow properties**, whereas values above 25% indicate poor flow [27].

4.5 Hausner Ratio

The Hausner ratio is another indicator of powder flow characteristics and is calculated using the following equation:

$$\text{Hausner Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

A Hausner ratio **less than 1.25** indicates **good flowability**, while values greater than 1.5 suggest poor flow characteristics.

Table 2: Precompression Parameters

Formulation	Angle of Repose (°)	Bulk Density (g/cm ³)	Tapped Density (g/cm ³)	Carr's Index (%)	Hausner Ratio
F1	28.4	0.46	0.54	14.8	1.17
F2	27.9	0.47	0.55	14.5	1.16
F3	26.8	0.48	0.56	14.2	1.16
F4	29.2	0.45	0.53	15.0	1.18
F5	28.6	0.46	0.54	14.8	1.17
F6	27.3	0.48	0.56	14.3	1.16
F7	29.4	0.44	0.52	15.3	1.18
F8	28.7	0.45	0.53	15.1	1.18

F9	27.9	0.46	0.54	14.9	1.17
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Discussion of Pre-Compression Results

The angle of repose values for all formulations ranged between **26.8° and 29.4°**, indicating **good flow properties of the powder blends**. The bulk density values ranged from **0.44 to 0.48 g/cm³**, while tapped density values ranged from **0.52 to 0.56 g/cm³**, suggesting acceptable packing characteristics.

Carr's index values were found between **14.2% and 15.3%**, which fall within the acceptable range for good compressibility. Similarly, the Hausner ratio values ranged from **1.16 to 1.18**, indicating satisfactory flowability of the powder blends.

Overall, the results demonstrate that all formulations exhibited **adequate flow and compressibility properties**, making them suitable for the **direct compression method** for the preparation of orally disintegrating tablets.

V. Post-Compression Evaluation

After compression, the prepared rivaroxaban orally disintegrating tablets (ODTs) were evaluated for various **post-compression quality control parameters** to ensure that the tablets meet the acceptable pharmacopeial standards. These parameters included **tablet hardness, friability, weight variation, and drug content uniformity**. Evaluation of these properties is essential to determine the **mechanical integrity, uniformity, and quality of the final dosage form** [28].

5.1 Hardness Test

Tablet hardness (crushing strength) is an important parameter that determines the **mechanical strength of tablets and their ability to withstand handling, packaging, and transportation**. The hardness of the tablets was measured using a **Monsanto tablet hardness tester**. Five tablets from each formulation batch were randomly selected and tested, and the average value was recorded in **kg/cm²**.

Adequate hardness is necessary to prevent tablet breakage; however, excessive hardness may delay tablet disintegration. For orally disintegrating tablets, hardness typically ranges between **2–4 kg/cm²**, ensuring sufficient strength while maintaining rapid disintegration [29].

5.2 Friability Test

Friability measures the **mechanical resistance of tablets to abrasion and shock during handling**. The friability of tablets was determined using a **Roche friabilator**. A sample of tablets equivalent to approximately **6.5 g** was weighed and placed in the friabilator, which was operated at **25 rpm for 4 minutes (100 revolutions)**. After completion of the test, the tablets were dedusted and reweighed. Friability was calculated using the following equation:

$$Friability(\%) = \frac{W_1 - W_2}{W_1} \times 100$$

Where:

- W_1 = Initial weight of tablets
- W_2 = Final weight of tablets

According to pharmacopeial specifications, the friability of tablets should be **less than 1%**, indicating adequate mechanical strength [30].

5.3 Weight Variation Test

Weight variation testing ensures **uniformity of tablet weight and consistent drug distribution** within the batch. Twenty tablets from each formulation were randomly selected and individually weighed using a **digital analytical balance**. The average weight was calculated and compared with individual tablet weights.

According to pharmacopeial standards, tablets with a weight of **130–324 mg** should not deviate by more than **±7.5% from the average weight** [31].

5.4 Drug Content Uniformity

Drug content uniformity was determined to ensure that each tablet contains the intended amount of rivaroxaban. Ten tablets were randomly selected and finely powdered. A quantity of powder equivalent to **10 mg of rivaroxaban** was accurately weighed and dissolved in a suitable solvent (phosphate buffer or methanol). The solution was filtered and appropriately diluted.

The absorbance of the resulting solution was measured using a **UV-Visible spectrophotometer at the λ_{max} of rivaroxaban (approximately 249 nm)**. The drug concentration was calculated using a previously prepared calibration curve, and the percentage drug content was determined.

According to pharmacopeial requirements, the drug content should typically fall within **95–105% of the labeled amount** [32].

Table 3: Evaluation of Tablets

Formulation	Hardness (kg/cm ²)	Friability (%)	Weight Variation (mg)	Drug Content (%)
F1	3.2	0.65	149 ± 2	98.1
F2	3.4	0.61	150 ± 3	99.2
F3	3.3	0.58	151 ± 2	98.8
F4	3.5	0.63	150 ± 2	97.9
F5	3.6	0.59	149 ± 3	99.1
F6	3.4	0.55	150 ± 2	99.5
F7	3.3	0.66	151 ± 3	98.4
F8	3.4	0.62	150 ± 2	99.0
F9	3.2	0.68	149 ± 3	98.2

Discussion of Post-Compression Results

The hardness of all formulations ranged between **3.2 and 3.6 kg/cm²**, which indicates adequate mechanical strength while still maintaining rapid disintegration characteristics required for ODT formulations.

Friability values were found between **0.55% and 0.68%**, which are well below the pharmacopeial limit of **1%**, confirming good resistance to mechanical stress.

The weight variation results showed that all tablets were within acceptable limits, indicating **uniform die filling and consistent tablet weight during compression**.

Drug content ranged from **97.9% to 99.5%**, demonstrating **uniform distribution of rivaroxaban in the tablet formulations**.

Overall, all formulations complied with **Indian Pharmacopoeia (IP) limits**, confirming the

acceptable quality and uniformity of the prepared tablets.

FTIR Drug–Excipient Compatibility Study

Fourier Transform Infrared Spectroscopy (FTIR) analysis was carried out to investigate possible chemical interactions between rivaroxaban and the excipients used in the formulation. The FTIR spectra of pure rivaroxaban and the formulation ingredients were recorded using the KBr pellet method in the spectral range of **4000–400 cm⁻¹**.

The FTIR spectrum of pure rivaroxaban showed characteristic absorption peaks corresponding to:

- **O–H stretching around 3400 cm⁻¹**
- **C=O stretching around 1734 cm⁻¹**
- **Aromatic C=C stretching around 1598 cm⁻¹**
- **C–N stretching around 1254 cm⁻¹**
- **C–O stretching around 1052 cm⁻¹**

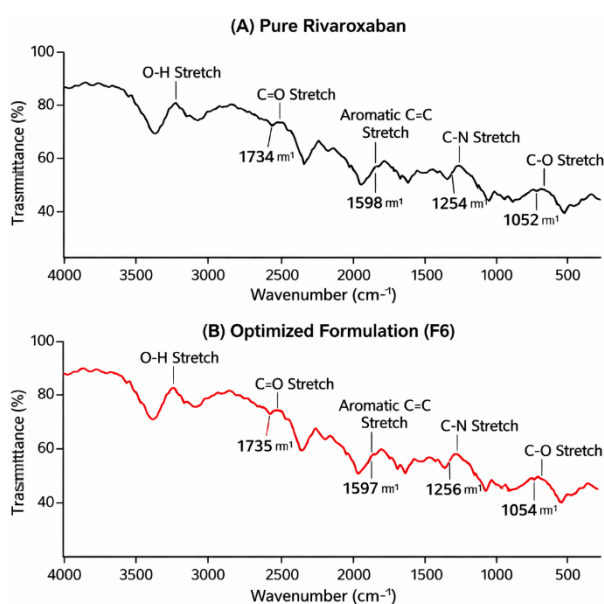


Figure 1. FTIR spectra of (A) pure rivaroxaban and (B) optimized ODT formulation (F6) showing characteristic functional group peaks.

VI. Disintegration and Wetting Time

Disintegration and wetting time are critical parameters for evaluating the performance of **orally disintegrating tablets (ODTs)**. These parameters determine how quickly a tablet breaks down when it comes into contact with saliva in the oral cavity. Rapid disintegration ensures faster dispersion of drug particles, which can enhance dissolution and improve drug absorption [33].

In the present study, the prepared rivaroxaban ODT formulations were evaluated for **wetting time and in-vitro disintegration time** to assess the efficiency of different superdisintegrants used in the formulations.

6.1 Wetting Time

Wetting time is defined as the time required for water to penetrate the tablet matrix and completely wet the tablet surface. This parameter reflects the **hydrophilicity of excipients and the ability of the tablet to absorb moisture**, which plays a significant role in the disintegration process.

Procedure

The wetting time was determined using a **simple petri dish method**. A piece of **tissue paper folded twice** was placed in a petri dish containing **6 mL of distilled water**. A tablet was carefully placed on the tissue paper, and the time required for water to reach the upper surface of the tablet and completely wet it was recorded using a stopwatch.

Shorter wetting time generally indicates **faster tablet disintegration and improved performance of superdisintegrants** [34].

6.2 In-Vitro Disintegration Time

The **disintegration time** of tablets was determined using a **USP disintegration test apparatus**. Six tablets from each formulation were placed individually into the tubes of the disintegration apparatus containing **distilled water maintained at $37 \pm 0.5^\circ\text{C}$** . The time required for each tablet to completely disintegrate into fine particles with no palpable mass remaining was recorded.

For orally disintegrating tablets, the ideal disintegration time is typically **less than 30 seconds**, ensuring rapid dispersion in the oral cavity without the need for water [35].

Table 4: Disintegration Performance

Formulation	Wetting Time (sec)	Disintegration Time (sec)
F1	32	29
F2	26	24
F3	21	20
F4	34	31
F5	28	25
F6	20	18
F7	35	32
F8	30	27
F9	26	23

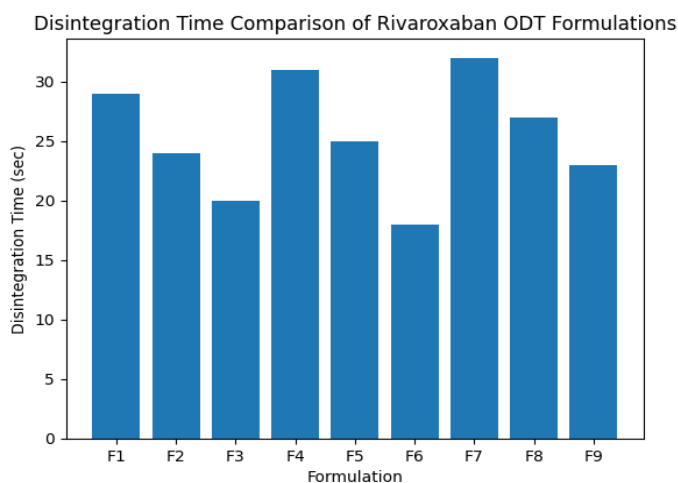


Figure 2. Comparison of disintegration time of rivaroxaban orally disintegrating tablet formulations (F1–F9). Formulation F6 showed the shortest disintegration time due to the optimized concentration of superdisintegrant.

The wetting time of the prepared formulations ranged from **20 to 35 seconds**, while the disintegration time ranged from **18 to 32 seconds**. Among all formulations, **F6 exhibited the shortest wetting time (20 seconds) and the fastest disintegration time (18 seconds)**.

The improved disintegration performance of formulation F6 may be attributed to the higher concentration of **croscarmellose sodium**, which promotes rapid tablet breakup through **swelling and wicking mechanisms**. These mechanisms allow water to penetrate quickly into the tablet matrix, leading to rapid disintegration [36].

Formulations containing sodium starch glycolate showed slightly longer disintegration times, possibly due to the formation of a viscous gel layer upon hydration, which may slightly delay water penetration. However, all formulations showed disintegration times within the acceptable limits for ODT formulations.

Overall, the results demonstrate that the **type and concentration of superdisintegrant significantly influence the wetting and disintegration behavior of orally disintegrating tablets**.

VII. In-Vitro Dissolution Study

The in-vitro dissolution study was carried out to evaluate the **drug release behavior of rivaroxaban from the prepared orally disintegrating tablets (ODTs)**. Dissolution testing is an essential quality control parameter for oral solid dosage forms because it provides information about the **rate and extent of drug release in the gastrointestinal environment**. For poorly water-soluble drugs such as rivaroxaban, dissolution studies are particularly important since the

dissolution rate often becomes the **rate-limiting step in drug absorption and bioavailability** [37].

7.1 Dissolution Study Conditions

The dissolution study was performed using a **USP Type II (Paddle) dissolution apparatus**. The following experimental conditions were maintained:

- **Dissolution medium:** 900 mL of 0.1 N hydrochloric acid (HCl)
- **Temperature:** 37 ± 0.5 °C
- **Paddle rotation speed:** 50 rpm
- **Sampling intervals:** 2, 5, 10, 15, and 20 minutes

One tablet from each formulation was placed in the dissolution vessel containing the dissolution medium. At predetermined time intervals, **5 mL of sample solution** was withdrawn and filtered through a suitable filter paper. The withdrawn volume was replaced with an equal amount of fresh dissolution medium maintained at the same temperature to maintain sink conditions.

The collected samples were analyzed using a **UV-Visible spectrophotometer at the λ_{max} of rivaroxaban (~249 nm)**. The percentage of drug released was calculated using a previously prepared **calibration curve of rivaroxaban in 0.1 N HCl** [38].

Table 5: Dissolution Profile (% Drug Release)

Time (min)	F3	F6	F9
2	24.5	30.8	22.4
5	52.3	60.2	47.5
10	76.4	88.6	70.1
15	91.2	96.4	85.3
20	95.3	98.2	91.6

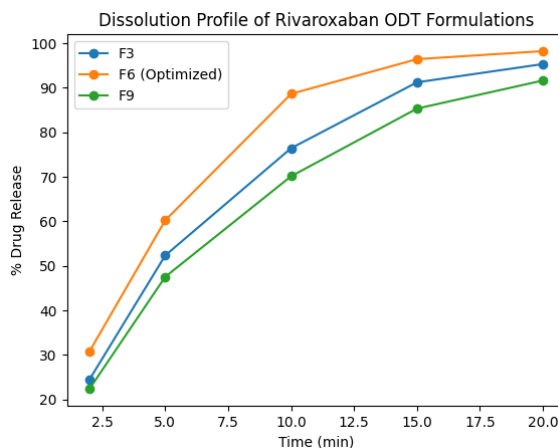


Figure 3. Dissolution profile of rivaroxaban ODT formulations showing percentage drug release as a function of time. The optimized formulation (F6) exhibited the highest drug release compared to other formulations.

The dissolution profile graph illustrates the release behavior of rivaroxaban from selected formulations. Among the tested formulations, **F6 showed the highest drug release**, achieving approximately **96% drug release within 15 minutes** and nearly complete release within 20 minutes. This improved dissolution performance can be attributed to the rapid disintegration and enhanced water penetration provided by the optimized concentration of the superdisintegrant.

The dissolution profiles of selected formulations (F3, F6, and F9) demonstrated rapid drug release, which is desirable for orally disintegrating tablets. Among these formulations, **F6 showed the highest drug release**, achieving **96.4% drug release within 15 minutes and 98.2% within 20 minutes**.

The enhanced dissolution performance of formulation F6 can be attributed to the presence of **croscarmellose sodium at an optimized concentration**, which promotes rapid tablet disintegration through **swelling and wicking mechanisms**. These mechanisms facilitate faster penetration of dissolution medium into the tablet matrix, leading to rapid dispersion of drug particles and increased surface area for dissolution [39].

Formulation F3, which contained crospovidone as the superdisintegrant, also showed relatively rapid drug release but slightly lower than F6. Crospovidone primarily acts through **capillary action**, allowing water to penetrate into the tablet matrix; however, its swelling capacity is lower compared to croscarmellose sodium.

Formulation F9 containing sodium starch glycolate exhibited comparatively slower drug release. This may be due to the formation of a **viscous gel layer upon hydration**, which can slightly retard the penetration of dissolution medium into the tablet core [40].

Overall, the results indicate that **the type and concentration of superdisintegrant significantly influence the dissolution behavior of rivaroxaban ODTs**. Among the studied formulations, **F6 demonstrated the most rapid and complete drug release**, making it the optimized formulation.

VIII. Discussion

The present study was conducted to develop and evaluate **orally disintegrating tablets (ODTs) of rivaroxaban**, a poorly water-soluble anticoagulant drug, using different superdisintegrants to enhance disintegration and dissolution characteristics. The use of ODT

technology is particularly advantageous for drugs with poor aqueous solubility, as rapid tablet disintegration can increase the surface area of drug particles exposed to the dissolution medium, thereby improving dissolution and potentially enhancing bioavailability [41].

Pre-compression evaluation of the powder blends demonstrated acceptable **micromeritic properties**, including angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio. The angle of repose values ranged between **26.8° and 29.4°**, indicating good flowability of the powder blends. Similarly, Carr's index values were below **16%**, and Hausner ratio values were less than **1.20**, confirming good compressibility and flow characteristics of the formulations. These results suggested that the powder blends were suitable for the **direct compression method**, which requires uniform flow and packing behavior to ensure consistent die filling during tablet manufacturing [42].

Post-compression evaluation confirmed that all tablet formulations met the acceptable pharmacopeial limits. The hardness of the tablets ranged between **3.2 and 3.6 kg/cm²**, indicating sufficient mechanical strength to withstand handling and transportation while still maintaining the ability to disintegrate rapidly. Friability values were found to be **below 1%**, confirming that the tablets possessed adequate resistance to abrasion. In addition, the weight variation and drug content uniformity results demonstrated consistent distribution of rivaroxaban within the tablets, indicating proper blending of the powder mixture and reliable manufacturing conditions [43].

The performance of orally disintegrating tablets is largely influenced by the **type and concentration of superdisintegrant used in the formulation**. In the present study, three commonly used superdisintegrants—crospovidone, croscarmellose sodium, and sodium starch glycolate—were evaluated at different concentrations. Among these, crospovidone showed superior disintegration performance compared to the other superdisintegrants.

Formulation **F6**, which contained **6% crospovidone**, demonstrated the fastest wetting time and disintegration time among all prepared formulations. The rapid disintegration behavior of crospovidone-containing tablets may be attributed to its **high capillary activity and porous particle morphology**, which facilitate rapid water penetration into the tablet matrix. Unlike some other superdisintegrants, crospovidone does not form a

viscous gel upon hydration, allowing the tablet structure to break apart quickly and release drug particles more efficiently [44].

The dissolution study further confirmed that formulation F6 exhibited the **highest drug release rate**, achieving more than **96% drug release within 15 minutes**. This improved dissolution performance may be attributed to several factors, including rapid tablet disintegration, increased wettability of the drug particles, and the formation of a porous tablet structure that allows rapid penetration of the dissolution medium. The rapid breakdown of the tablet matrix increases the **effective surface area of drug particles**, which enhances drug dissolution according to the Noyes–Whitney dissolution principle [45].

In contrast, formulations containing sodium starch glycolate showed slightly slower disintegration and dissolution rates, which may be due to the formation of a **gel-like barrier layer** upon hydration. This gel layer can sometimes delay the penetration of dissolution medium into the tablet matrix, thereby reducing the rate of disintegration. Similarly, croscarmellose sodium showed moderate disintegration performance due to its swelling and wicking mechanisms, but its efficiency was slightly lower compared with crospovidone under the conditions used in this study.

Overall, the results demonstrate that the **selection of an appropriate superdisintegrant and its concentration plays a critical role in the performance of orally disintegrating tablets**. Among the tested formulations, **F6 containing crospovidone at an optimized concentration showed the most desirable combination of rapid disintegration and enhanced dissolution**, making it the optimized formulation for further studies.

IX. Conclusion

The present study successfully developed **orally disintegrating tablets (ODTs) of rivaroxaban**, a poorly water-soluble anticoagulant drug, using the **direct compression method**. The formulation strategy involved the use of different superdisintegrants—crospovidone, croscarmellose sodium, and sodium starch glycolate—to evaluate their effect on the disintegration behavior and dissolution characteristics of the tablets.

Pre-compression evaluation of the powder blends demonstrated **good flow properties and compressibility**, indicating their suitability for direct compression. Post-compression evaluation confirmed that all prepared tablet formulations complied with the **pharmacoepial specifications**

for hardness, friability, weight variation, and drug content uniformity, demonstrating acceptable mechanical strength and formulation quality.

Among the nine formulations developed, **formulation F6 containing 6% crospovidone** exhibited the most desirable performance characteristics. This formulation showed the **shortest wetting time and fastest disintegration time**, along with the **highest drug release in the in-vitro dissolution study**. The improved dissolution performance may be attributed to the **high capillary activity and porous structure of crospovidone**, which facilitates rapid water penetration and tablet disintegration, thereby increasing the effective surface area of the drug available for dissolution.

The findings of this study demonstrate that the **ODT formulation approach is an effective strategy for enhancing the dissolution behavior of poorly water-soluble drugs such as rivaroxaban**. Rapidly disintegrating tablets can improve patient convenience, particularly for geriatric and pediatric populations, while also potentially enhancing the onset of therapeutic action.

Therefore, the optimized formulation developed in this study may provide a **promising dosage form for improving the dissolution and therapeutic performance of rivaroxaban and other poorly water-soluble anticoagulant drugs**. Further studies such as **stability testing, pharmacokinetic evaluation, and in vivo bioavailability studies** are recommended to confirm the clinical performance of the optimized formulation.

X. Future Scope

Although the present study successfully developed and evaluated **orally disintegrating tablets (ODTs) of rivaroxaban**, further investigations are necessary to confirm the long-term stability, clinical performance, and large-scale manufacturing feasibility of the optimized formulation.

One of the important future directions is to conduct **stability studies in accordance with International Council for Harmonisation (ICH) guidelines**. Stability testing under accelerated and long-term conditions (such as **40°C/75% RH and 25°C/60% RH**) would help determine the physical, chemical, and microbiological stability of the optimized formulation over time. These studies are essential to establish the **shelf life and appropriate storage conditions** for the developed ODT formulation [46].

Another important aspect is the evaluation of **in vivo bioavailability and pharmacokinetic performance** of the optimized formulation. Although the in-vitro dissolution study demonstrated enhanced drug release, in vivo studies are necessary to confirm whether the improved dissolution behavior translates into **enhanced absorption and therapeutic efficacy**. Pharmacokinetic parameters such as **C_{max}, T_{max}, and AUC** can be evaluated through suitable animal or clinical studies to compare the optimized ODT formulation with conventional dosage forms.

Taste masking is also a significant consideration for orally disintegrating tablets, particularly because the tablets dissolve directly in the oral cavity. Although rivaroxaban does not exhibit extremely bitter taste, further improvement in patient acceptability may be achieved by incorporating **taste masking techniques**, such as flavoring agents, polymer coating, ion-exchange resins, or complexation methods [47].

Additionally, future research may focus on **scale-up studies and industrial feasibility** of the optimized formulation. Evaluation of large-scale manufacturing parameters, including powder flow behavior, compression characteristics, and process reproducibility, will be necessary to ensure consistent product quality during commercial production. Process optimization and validation would also help determine the **economic feasibility and manufacturability of the formulation at industrial scale**.

Furthermore, advanced formulation strategies such as **solid dispersions, nanoparticle-based systems, or co-processed excipients** may be explored in combination with ODT technology to further enhance the dissolution and bioavailability of poorly water-soluble drugs.

Overall, these future investigations will help establish the **clinical effectiveness, stability, and commercial potential of the developed rivaroxaban ODT formulation**

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