

# Pioneering Prolonged Release: A Novel Pellet-Based Approach to Anti-Anginal Therapy of Ranolazine

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## ABSTRACT

**Aim:** Angina is a clinical syndrome with symptoms attributed to myocardial ischaemia. There are many class of drugs which are used to manage it, among such is ranolazine which acts by inhibiting late Na<sup>+</sup> current. Ranolazine is used for the treatment of recurrent angina. So, the aim of the present work was to develop prolonged release pellets incorporated into capsules. **Materials and Methods:** In the present study, pellets were prepared by the Extruder and Sphero-dizer equipment using polymer Eudragit L 100, Eudragit S 100, HPMC K15M and red iron oxide using (120, 125, 130 mg) for Eudragit L100, likewise for the other polymers. The concentration of polymers was varied in all the preparations. **Results and Conclusion:** The effect of polymers was tested to check the prolonged effect by the help of *in vitro* studies. The FT-IR results indicated that Ranolazine and the other excipients were compatible. The pellets were subjected to different pharmacopoeial tests like tap density, bulk density, rate of flow, angle of repose, microscopic particle, weight variation, drug content and *in vitro* release studies. The *in vitro* release studies were carried out using USP type- I dissolution apparatus, i.e. basket type. Which showed that formulation F1 (Drug, Eudragit L100, Mannitol, MCC) showed the best sustained release for a period of 11 hrs. Hence, we conclude the main aim of the envisaged research work is achieved, i.e. sustaining the release of ranolazine without dose dumping.

**Keywords:** Ranolazine, Sustained Release Pellets, Extrusion and Spheronization, Pelletization.

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## INTRODUCTION

Anemia, irregular heart rhythms, heart failure, the process of atherosclerosis which affects the arteries that support heart, and obstruction or spasm of the coronary arteries can all contribute to angina pectoris, which is characterized by a feeling of pressure, squeezing, or pain in the chest. The phrase, which means "An feeling of rigidity in the chest," is derived from the Latin words angere, which means "to strangle," and pectus, which means "chest."<sup>1</sup>

Over A million instances of angina occur annually, with death rate nearly 40%. According to statistics, angina affects around 7 million Americans, and in some situations, people are unaware that the condition could develop in their bodies under any circumstances. It occurs generally at the age of 55 years. In addition to the statistics, there is a rapid increase in the death rate, in which individuals die suddenly who have no symptoms prior to the attack.<sup>2</sup>

The hallmark of angina pectoris is retrosternal chest pain, which can radiate to the epigastrium, back, neck, chin, or shoulders and is frequently characterized as pressure, heaviness, or squeezing. It usually lasts about 15 min and is alleviated by rest. It can be brought on by physical activity, food, exposure to cold, or stress. Position or breathing had no effect on the pain. Additionally, symptoms could include nausea, perspiration, dyspnea, and elevated blood pressure and pulse. Myocardial ischemia, in which the heart muscle does not receive adequate oxygen because of constricted or blocked coronary arteries, is the cause of angina. Some individuals may experience autonomic symptoms like nausea, vomiting, and pallor during an angina episode.<sup>3</sup> Angina is primarily treated with nitroglycerin, a vasodilator that reduces the heart's oxygen demand. ACE inhibitors, beta blockers, and calcium channel blockers are further therapies that lessen the burden on the heart. Because nitroglycerin can cause severe hypotension, it should not be taken with erectile dysfunction medications like sildenafil. Improved blood flow can be achieved with less intrusive procedures like balloon angioplasty and coronary bypass surgery. It has been demonstrated that beta blockers (such carvedilol and propranolol) and calcium channel blockers (like nifedipine) can lessen symptoms and increase survival. An inhibitor called ivabradine lowers heart rate to prevent ischemia. Statins help manage cholesterol, and low-dose aspirin may reduce heart attack risk, though it's no longer recommended for those without existing cardiovascular disease.



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Lifestyle changes like exercise, weight management, and smoking cessation, along with controlling risk factors (e.g., cholesterol, diabetes, hypertension), are crucial for long-term management.<sup>3,4</sup>

In January 2006, the FDA authorized Ranolazine as a second-line treatment for persistent angina, to be used in conjunction with other drugs. Ranolazine is now a first-line therapy choice, either by itself or in conjunction with other medications, according to a 2007 FDA label change.<sup>5</sup> When first-line medications are unable to address symptoms of chronic stable angina, the European Union authorized Ranolazine sustained-release tablets in April 2008 as an adjunctive therapy. Numerous clinical trials have demonstrated the effectiveness of Ranolazine for patients with chronic angina who have not responded to previous therapies. It helps with chronic angina and other cardiometabolic illnesses by regulating myocardial ischemia through intracellular metabolic alterations.<sup>6</sup>

A new anti-anginal medication called Ranolazine acts by blocking the myocardium's late sodium (Na<sup>+</sup>) current, which obliquely makes it easier for calcium (Ca<sup>2+</sup>) to enter through the Na<sup>+</sup>/Ca<sup>2+</sup> exchanger. This has a cardioprotective effect by lowering myocardial contractility and reducing calcium overload after ischemia. Ranolazine has been demonstrated to increase exercise duration in angina patients while having no effect on blood pressure or heart rate 0.5-1 g BD as SR tab 12 is the dosage.

Because of its ease of use, patient compliance, and potential for sustained release, oral drug delivery is the most popular route, making for 50-60% of all medication formulations. Understanding several fields, such as Gastrointestinal (GI) physiology, pharmacokinetics, pharmacodynamics, and formulation design, is necessary to create efficient oral dose forms. Three essential components are necessary for effective oral drug delivery systems: (1) the physicochemical, pharmacokinetic, and pharmacodynamic properties of the medication; (2) the gastrointestinal tract's anatomy and physiology; and (3) the dosage form's physicochemical qualities and mode of delivery. Reduced dosage frequency, improved drug efficacy, or more reliable drug administration are the objectives of controlled or sustained release systems.<sup>7</sup>

Pellets are small, spherical or cylindrical aggregates of particles, commonly used in various industries, including pharmaceuticals, to form uniform, free-flowing granules with a size range of 500-1500 µm. Pelletization is the process used in the pharmaceutical industry to transform finely ground powders or granules of excipients and active chemicals into tiny, frictionless beads that are usually placed within hard gelatin tablets or capsules. This technique, developed in the 1950s to extend drug release, has evolved through research to improve its performance, cost-effectiveness, and quality. Pellets can be designed for immediate drug release or to sustain release over

time and can also be coated for targeted delivery to specific sites in the gastrointestinal tract.<sup>8</sup>

## MATERIALS AND METHODS

### Chemicals and Reagents

RS Technical Services, 301-816-8129 Rockville, MD 20852 1790 US Ltd., was the supplier of Ranolazine. Microcrystalline cellulose was procured from Remedy Labs and Crospovidone were procured from Marq Chemicals. Eudragit L 100 and Eudragit S 100 were procured from Yogi Tablet Coating Pvt. Ltd., Red Iron Oxide was procured from SMS Industries, HPMC K15M from Destiny Chemicals and Mannitol was procured from Akhil Healthcare Pvt. Ltd.,

### Ranolazine Sustained Release Pellets' Formation

Long-term release Pellets of Ranolazine were created by employing the extrusion-spheronization process. To achieve sustained release qualities, excipients such as the polymers HPMC K15M and Eudragit L-100 were employed. Trials were conducted to determine the volume of the granulation liquid, which was a blend of water and isopropyl alcohol that generated the most cohesive mass for extrusion. The ideal granulating fluid was the one that produced the highest roundness of the pellets and the proper particle size. Mannitol and MCC were used to select the binder; MCC was selected due to its capacity to create spherical pellets. Using a 1.2% PVP K30 aqueous solution, the dry mixture of Ranolazine, Eudragit L-100, Eudragit S-100, HPMC K15M, MCC was granulated. To create spherical or semi-spherical pellets, the moist material was forced through a 1.0 mm die at 80 RPM. The extrudate was then taken for spheronization at 1150 rpm for 15 to 20 min. After that, the pellets were dried for 24 hr at 40°C in an oven. The sustained release formulation was optimized by testing several drug-to-polymer ratios. The procedure made that the pellets were consistent and had the appropriate releasing properties (Table 1).

### Studies on Preformulation

Preformulation studies were conducted to assess potential interactions between the medicine and its excipients and to look into the key physicochemical characteristics of the therapeutic molecule. The melting point and solubility was examined. For the pure medicine and excipients, additional Fourier Transform Infra-Red (FTIR) spectral analyses were performed.

### Determination of Melting Point

Since the sample's melting point is a primary indicator of its purity, it was ascertained. A tiny quantity of the medication was put in a capillary tube that was placed in a melting point apparatus with one end closed to find the drug's melting point. The drug's melting point was recorded, and the average of three readings was obtained.

## Solubility Characteristics of Pure Drug

The drug's solubility in various solvents, including water, methanol, dichloromethane, and pH buffers, was assessed. 25 mL of a chosen solvent were mixed with 20 mL of the medication in various screw-capped solubility bottles. After placing the bottles in the holder, they were shaken in a water bath shaker at room temperature for a whole day. Whatmann filter paper No. 1 used to filter the samples. A UV spectrophotometer set to 272 nm was used to analyze the filtrate after it had been appropriately diluted.

## Partition Coefficient

The n-octanol saline pH 6.8 buffer's partition coefficient was found. 10 mL of n-octanol and equal amounts of phosphate buffer were placed in a separating funnel and shaken for 1 hr. 10 mL of the medication were added to the separating funnel, and it was shaken for 2 hr. The octanol and aqueous layers were separated. A UV spectrophotometer was used to measure absorbance at 272 nm following the pipetting of 0.1 mL of the aqueous layer solution and its dilution to 10 mL. The residue was measured using a UV spectrophotometric technique at 272 nm after being dissolved in the proper solvents.

## FTIR Analysis

Ranolazine and various excipient combinations were subjected to infrared spectroscopy. 100 mg of potassium bromide was ground into a mixture with pure drug or drug-excipient, and pellets were created using a hydraulic press. Pellets made in this way were employed in infrared research. To determine the changes in the functional group peaks of Ranolazine, the IR graphs were compared to the IR graph of Ranolazine.

This design allowed for a systematic analysis of how changes in drug-to-polymer ratio, solvent volume, and carrier preparation method affect the responses, providing a comprehensive approach to optimizing the formulation for improved aqueous solubility and drug content.

## Pre-Compression Parameter Evaluation

**Bulk Density:** It is the proportion of the powder's bulk volume to its overall mass. Volume was recorded when the weighed powder was poured into a measuring cylinder.

**Tapped Density:** It is the proportion of the powder's tapped volume to its overall mass. The powder was tapped to a consistent volume in order to measure the tapped volume.

**Angle of Repose ( $\Theta$ ):** angle of repose,  $\theta$ , can be used to quantify the frictional forces in a loose powder. It is the greatest angle that can exist between a powder pile's freely sliding surface and the horizontal plane.

**Hausner's Ratio:** An indirect measure of powder flow easiness is Hausner's ratio.

**Carr's Index:** A material's ease of inducing flow is shown by this.

## Assessments of Pellets

### Content of drugs

U.V. spectrophotometry was used to evaluate the drug concentration of the pellets. After dissolving 20 mg of the drug equivalent in 100 mL of 0.1 M NaOH for 10 min, the pellets were filtered using Whatmann filter paper. A UV spectrophotometer was used to evaluate the filtrate at 272 nm following the proper dilution.

## Research on Scanning Electron Microscopy (SEM)

SEM was employed for evaluating the sample's surface morphology. A small quantity of pellets was manually applied to a carbon tab, which is double-adhesive carbon-coated tape that is fastened to aluminum stubs. The POLARON-E 3000 sputter coater was then used to apply a thin layer of gold on these sample stubs. Using a scanning electron microscope, the samples were inspected. They were then photographed at different magnifications, and the photos were directly sent to a computer.

## Drug release investigations of pellet formulations *in vitro*

Using USP equipment of the basket type, the drug release profile of pellets was ascertained at  $37 \pm 0.50^\circ\text{C}$  and 75 rpm of spin. For the first 2 hr, 5 mL of the dissolution medium was taken out every 30 min in 900 mL of pH 1.2. The medium was then filtered through Whatmann filter paper. After transferring the pellets that had been held on filter paper to a dissolution flask, 900 mL of pH 6.8 were added, and the dissolution process was run at 75 rpm. 5 mL of the dissolving media were taken out every hour and replaced with 5 mL of the same medium every 7 hr. In a Shimadzu U.V. spectrophotometer, the withdrawn samples were spectrophotometrically examined at 272 nm against a blank, and absorbance was noted.

## Preparation of Drug Loaded Capsules

Formulation 1 was chosen as the optimal formulation for sustained release pellets based on the drug content, solubility, and characterisation investigations. The capsule's body was packed with pellets. The entire dosage of the medication in the capsule was 350 mg. Both were then sealed after the cap was reinserted into the body. These capsules were filled in bulk and rubbed with a cloth. This process removed the resistive material and produced a respectable volume fill. It also gives the capsules a glossy appearance.

## Assessment of capsules

### Average weight of a capsule that is filled

The formula below was used to get the average weight of the 20 capsules after they were weighed. The weight of 20 capsules in grams divided by 20 is the average weight in grams.

### Dosage unit uniformity (by weight variation)

Either weight variation or content uniformity can be used to show how uniform the dose units are. 10 capsules were precisely weighed one at a time while maintaining each capsule's identification. Each capsule's contents were extracted using the appropriate technique. Each empty shell was precisely weighed separately. The net weight of each capsule's contents was calculated by subtracting the shell's weight from the equivalent gross weight. Each capsule's drug content, expressed as a percentage of the label claim, was determined using the assay's outcome and the net weight of each individual capsule. Ranolazine pellet content as a percentage =  $\frac{\text{Weight of capsules in milligrams} \times \text{assay in \%}}{\text{Average weight of a capsule (mg)}}$

## RESULTS AND DISCUSSION

### Determination of Melting Point

Using the capillary tube method, the melting point of Ranolazine was determined to be 162°C, which is the same value reported in the literature. As a result, it was determined that the medication employed satisfied British Pharmacopoeia specifications, with a value of 162°C. This value was then utilized for the research.

### Solubility Characteristics of Pure Drug

It was discovered that Ranolazine is highly soluble in methanol, mildly soluble in water, moderately soluble in pH 6.8 phosphate buffer, and sparingly soluble in phosphate buffer pH 7.4 (Figure 1, Table 2).

### Partition Coefficient

Ranolazine's partition coefficient in a pH 6.8 phosphate buffer system including n-Octanol and saline. Ranolazine's partition coefficient was determined to be 1.53. This suggests that the medication has a hydrophilic and somewhat lipophilic character. It involved placing 10 mL of n-octanol and equal amounts of phosphate buffer in a separating funnel and shaking for an hour. The literature review revealed that the values were in agreement with one another.

### Compatibility studies

#### FTIR Analysis

FTIR spectroscopy was used to verify Ranolazine's compatibility with various excipients prior to formulation development. Since their spectra did not significantly differ, it was determined that the medication was still intact in the presence of the polymer.

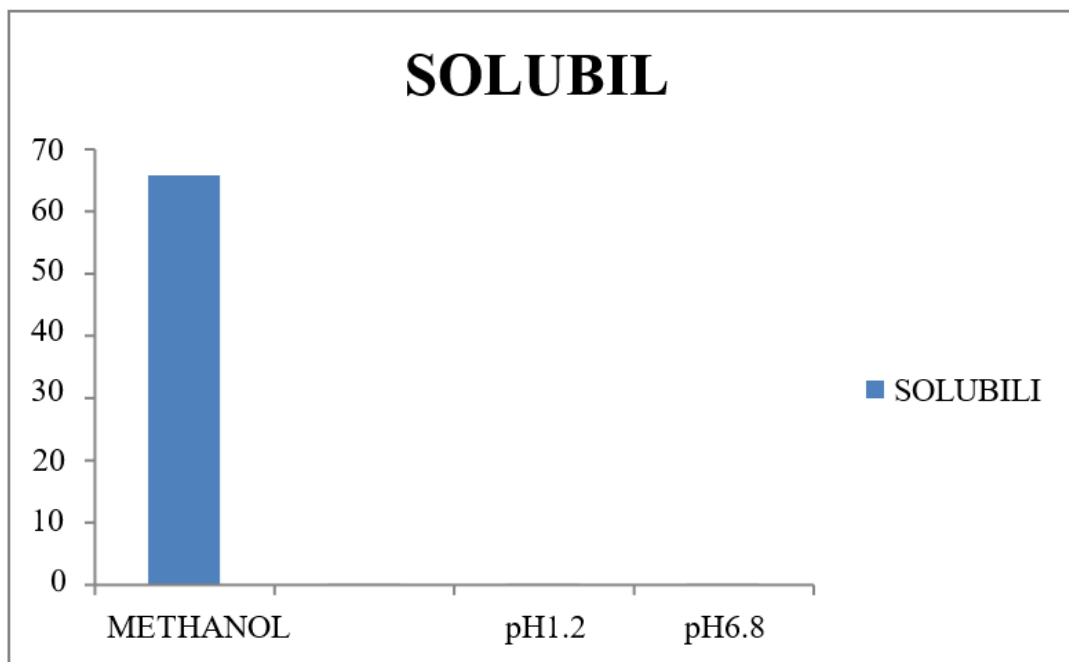


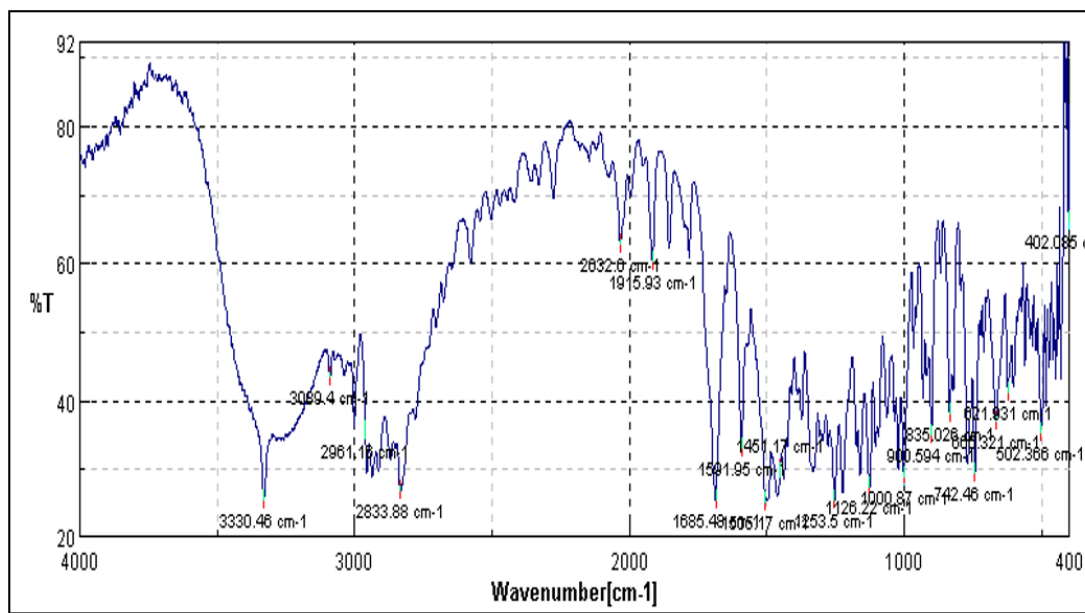
Figure 1: Solubility Bar graph Of Pure Drug.

Table 1: Solubility Characteristics of Pure Drug.

Sl. No.	Media	Solubility(mg/mL)	Result
1.	Methanol	65.90	Highly Soluble
2.	Water	0.064	Slightly Soluble
3.	pH 1.2	0.069	Slightly Soluble
4.	pH 7.4	0.066	Sparingly Soluble

**Table 2: FTIR Interpretation Table.**

Sl. No.	Functional Group	Peak Value	Sample-1 cm <sup>-1</sup>	Sample-2 cm <sup>-1</sup>	Sample-3 cm <sup>-1</sup>
1	-OH	3650- 3600(m)	3330.48	3333.36	3330.46
	-NH	3500- 3100(m)			
2	-Ar.CH	3150-3050	3089.4	Merged with -OH peak	3084.58
3	-Ar.CH	3000-2800 cm <sup>-1</sup>	2833.88	2997.80	2999.93
4	C=O	1850-1630 cm <sup>-1</sup>	1685.48	1716.34	1666.44
5	C-O	1000-1200 cm <sup>-1</sup>	1253.5	1262.18	1253.5
6	C=C	1600 and 1475 (mw)	1581.95	1591.95	1591.95
7	CH <sub>2</sub>	1465 cm <sup>-1</sup>	1451.17	1493.6	1448.28

**Figure 2:** FTIR Spectra of Drug-Ranolazine.

Figures 2-4 show the IR spectra of pure Ranolazine and Ranolazine with various polymers. IR analyses showed that there was no interaction between the drug and other excipients since the characteristic peaks of Ranolazine were not disturbed in the IR graph of Ranolazine with the excipients (Table 3).

### Evaluation of Pre-Formulation Parameters of Powdered Blend

Pre-formulation and post-formulation parameters were applied to each formulation. For the enlisted formulations, bulk density-the ratio of the powder's total mass to bulk volume-was

measured. The volume was recorded when the weighed powder was poured into the measuring cylinder. The bulk density values were determined to be within the range, and formulation F1 produced the best result, 0.249. For the enlisted formulations, tapped density-the ratio of the powder's total mass to its tapped volume-was measured. The powder was tapped to a consistent volume in order to measure the tapped volume. The unit of measurement is gm/mL. Formulation F1 was found to have the highest value within the range of 0.3031. The enlisted formulations were subjected to the angle of repose, which is the greatest angle that can exist between the horizontal plane and

the freely sliding surface of a powder pile. With formulation F1, angle of repose also demonstrated good results, ranging from 25°19" to 27°21". The ease with which a material can be made to flow is indicated by Carr's index. The Carr's index value fell between 10.82 and 16.27. The ratio of Hausner's 1.12 to 1.19. The pre-formulation studies indicated that the formulation had good flow characteristics (Table 4).

## Assessment of Pellets

### Content of drugs

A drug content analysis was conducted on the sustained release pellets that contained Ranolazine. Using the UV technique, the percentage drug concentration of Ranolazine pellets was found to be between 93.52±0.4043% and 99.73±0.153%. When the drug content of the produced formulations was examined, the results fell between 96.52 and 99.7%. The optimal Ranolazine formulation, F1, was determined to be 99.73±0.153 out of all the formulations. The findings show that the medication was evenly dispersed throughout each formulation (Table 5).

## SEM

The particle diameter was found to be 773.2 µm. The morphology of the particle was found to be spherical in nature. Following SEM analysis, the samples' surface morphology was observed, and the formulation with Eudragit L100 polymer was determined to be the best one, exhibiting a homogenous and spherical structure. A carbon tape (double-adhesive carbon-coated tape) attached to aluminum stubs was manually covered with a modest quantity of pellets. The POLARON-E 3000 sputter coater was then used to apply a thin layer of gold on these sample stubs. When SEM images were examined at different magnifications and resolutions, they were discovered to be spherical. These results were then compared to sieve analysis values, which showed similarities. The morphology of all the generated formulations is spherical in shape and quite homogeneous, with no surface hinderance in the flow property, as the SEM photos clearly demonstrate.

## Dissolution Studies *in vitro*

The USP type 1 equipment was employed to conduct the dissolving studies. When compared to other formulations, the drug release

**Table 3: Formulation Table.**

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Ranolazine	350	350	350	350	350	350	350	350
MCC	110	100	110	100	110	100	110	100
Eudragit L100	120	-	130	-	-	-	-	-
Eudragit S100	-	125	-	-	130	-	-	-
HPMC K15M	-	-	-	120	-	-	-	-
Eudragit L100+S100	-	-	-	-	-	60:60 (1:1)	30:90 (1:2)	-
Eudragit L100+HPMC K15M	-	-	-	-	-	-	-	60:60 (1:1)
Mannitol	70	65	70	70	70	70	70	70

**Table 4: Evaluation of Pre-Formulation Parameters of Powdered Blend.**

Formulation Code	Bulk Volume (mL)	Tapped Volume (mL)	Bulk density (g/cmt)	Tapped density (g/cmt)	Carr's Index	Hausner's ratio	Angle of repose (θ)
F1	23.12	21.08	0.249	0.3031	16.27	1.194	27°45"
F2	21.50	18.00	0.2325	0.2777	13.84	1.191	27°21"
F3	21.66	18.66	0.2308	0.2679	13.27	1.192	26°57"
F4	18.50	16.50	0.2702	0.3030	10.825	1.121	25°19"
F5	22.12	20.12	0.2701	0.270	10.821	1.13	25°05"
F6	20.52	18.20	0.231	0.2700	13.2	1.18	26°50"
F7	22.66	20.06	0.232	0.274	14.5	1.17	26°56"
F8	21.72	19.08	0.231	0.297	15.4	1.15	26°35"

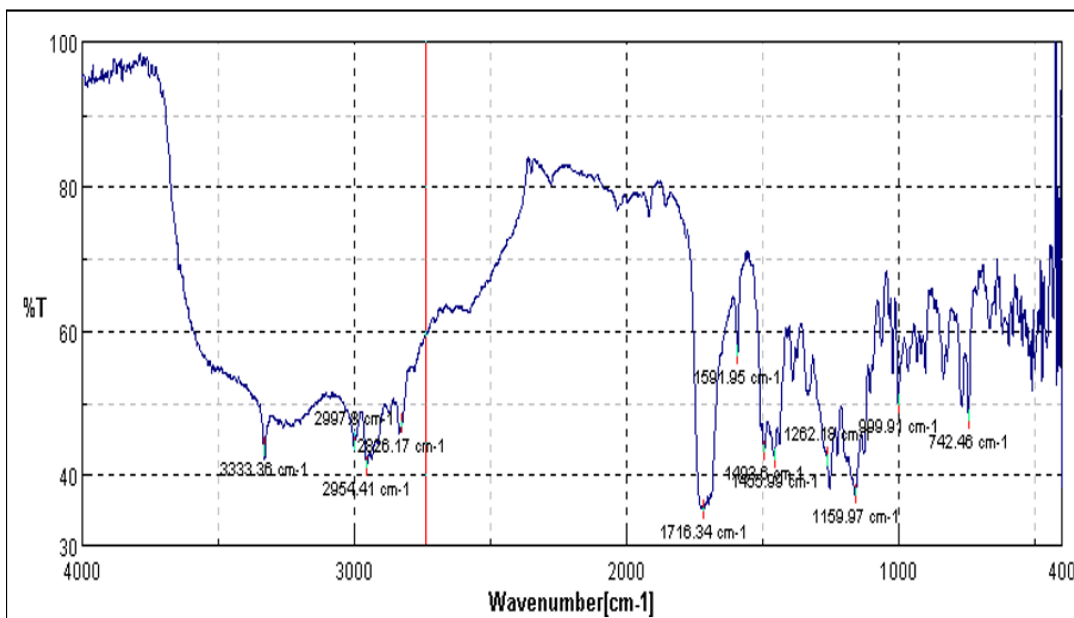


Figure 3: FTIR of Drug+Eudragit L100.

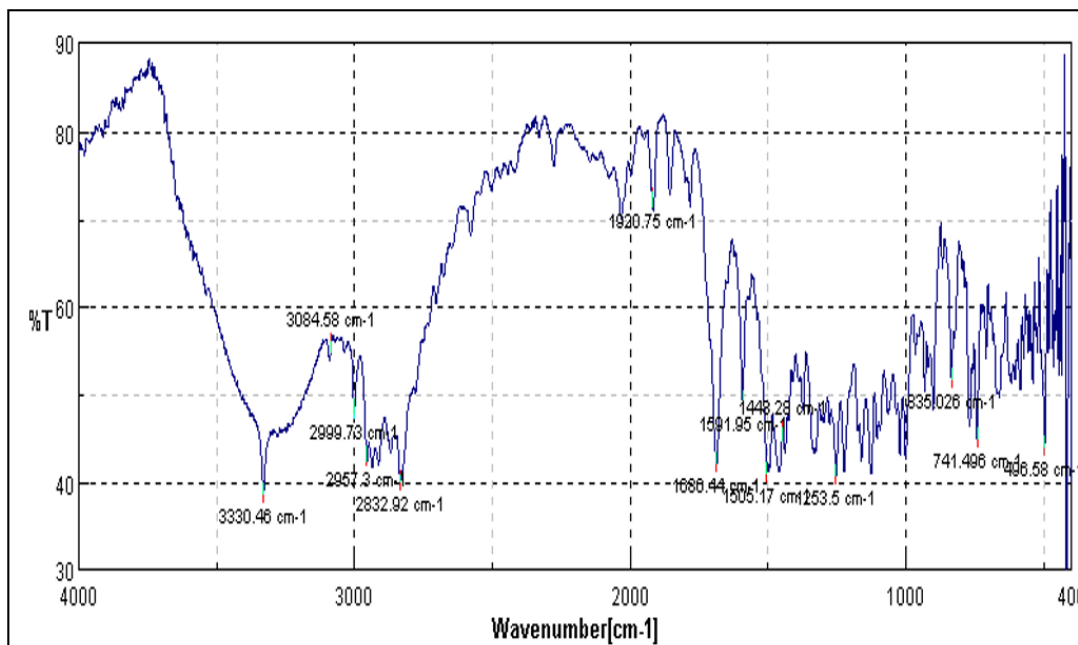


Figure 4: FTIR of Drug+HPMC K15M.

Table 5: Percentage drug content of SR pellets.

Sl. No.	Formulation Code	%Drug Content
1	F1	99.73±0.153
2	F2	98.12±0.307
3	F3	95.44±0.221
4	F4	96.52±0.403
5	F5	96.40±0.257
6	F6	97.44±0.196
7	F7	96.34±0.182
8	F8	97.14±0.147

**Table 6: *In vitro* Dissolution Formulation-1.**

Time	Absorbance	Conc/mL	Conc/5 mL	Cumm.loss	Conc/900	Total conc	%CDR
0	0	0	0	0	0	0	0
30	0.006	0.0014	0.0070	0	1.2558	1.2558	0.3588
60	0.0123	0.0029	0.0143	0.0070	2.5744	2.5814	0.7375
90	0.04	0.0093	0.0465	0.0213	8.3721	8.3934	2.3981
120	0.087	0.0202	0.1012	0.0608	18.2093	18.2701	5.2200
150	0.287	0.0667	0.3337	0.1477	60.0698	60.2174	17.2050
180	0.5	0.1163	0.5814	0.4349	104.6512	105.0860	30.0246
240	0.518	0.1205	0.6023	0.9151	108.4186	109.3337	31.2382
300	0.55	0.1279	0.6395	1.1837	115.1163	116.3000	33.2286
420	0.635	0.1477	0.7384	1.2419	132.9070	134.1488	38.3282
540	0.71	0.1651	0.8256	1.3779	148.6047	149.9826	42.8522
600	0.74	0.1721	0.8605	1.5640	154.8837	156.4477	44.6993
660	0.823	0.1914	0.9570	1.6860	172.2558	173.9419	49.6977

rate from formulation F1, which comprised ranolazine (350 mg), MCC (110 mg), Eudragit L100 (120 mg), and mannitol (70 mg), was slow, steady, and sustained as intended. It is shown by the drug release percentage that formulations exhibiting sustained release release 50% of the drug by the end of 12 hr and 100% of the drug by the end of 24 hr. Formulation F1 released 49.697% of the drug in 11 hr, which will subsequently release 98-99% of the drug by the end of 24 hr (Table 6).

## CONCLUSION

The goal of the study was to create and assess Ranolazine-loaded pellets in capsule form for longer-lasting medication release and better patient adherence. Compatibility investigations revealed no interactions between the medication and excipients. Extrusion-spheronization, a popular pelletization method, was utilized to create the pellets utilizing a variety of excipients (MCC, Eudragit L100, Eudragit S100, HPMC K15M, Mannitol, and Red Iron Oxide). Evaluations of bulk density, medication content, and weight fluctuation were carried out both before and after compression. Formulation F1 demonstrated the best sustained release, according to *in vitro* drug release tests conducted in simulated intestinal and stomach fluids. With a high release value of 99.73%. The findings showed that Ranolazine may be effectively made into sustained-release pellets, which will improve patient adherence and provide an efficient treatment for angina pectoris.

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insightful feedback and encouragement during the research and writing process.

## ABBREVIATIONS

**Na<sup>+</sup>**: Sodium; **FT-IR**: Fourier-transform infrared; **MCC**: Microcrystalline cellulose; **FDA**: Food and Drug Administration; **Ca<sup>2+</sup>**: Calcium; **BD**: Twice a day; **SR**: Sustained release; **µm**: Micrometer; **mL**: Milli Liter; **Rpm**: Revolutions per minute; **°C**: Degree Centigrade; **nm**: Nanometer; **IR**: Infrared; **SEM**: Scanning Electron Microscope; **mg**: Miligram.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## SUMMARY

The intent of the study was to develop and assess ranolazine sustained-release pellets with a view to increase patient compliance. The  $\lambda_{\max}$  of ranolazine in phosphate buffer was determined using a UV spectrophotometric method, and FTIR compatibility tests confirmed no interactions between the drug and excipients. Using the extrusion-spheronization process, the pellets were created with excipients such as MCC, Eudragit L100, Eudragit S100, HPMC K15M, mannitol, and red iron oxide. The pellets were assessed for post-compression tests (drug content and weight change) and preformulation characteristics (bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose). Studies on *in vitro* drug release in intestinal fluid (pH 6.8) and simulated gastric fluid (pH 1.2) demonstrated prolonged drug release. Formulation F1, which offers the intended sustained release effect, was found to be the optimal formulation. The study came to findings that ranolazine pellets in capsule form can enhance patient adherence and offer a successful long-term remedy for angina pectoris.

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