



Formulation and Evaluation of Solid Lipid Nanoparticles of Rabeprazole

Anshuma Arya¹, Dr. Amreen Khan¹, Dr. Umesh Atheriya², Dr. Dharmendra Solanki¹

Department of Pharmacy, BM College of Pharmaceutical Education and Research, Indore¹(M, P.),

Shri Bherulal Pharmacy Institute, Indore.²

452020

Corresponding Author Email: anshuarya160@gmail.com

ABSTRACT

Rabeprazole sodium, a potent proton pump inhibitor, is widely prescribed for managing acid-related gastrointestinal disorders, but its therapeutic efficacy is limited by poor aqueous solubility, instability in acidic environments, and low oral bioavailability. To overcome these challenges, solid lipid nanoparticles (SLNs) were formulated and evaluated as a novel drug delivery system for Rabeprazole. The nanoparticles were prepared using the solvent evaporation method in combination with high-speed homogenization and ultrasonication. Stearic acid, glyceryl monostearate, and cetyl alcohol served as lipid matrices, while Poloxamer 188, Tween 80, and soy lecithin functioned as stabilizers and surfactants. The prepared SLNs were characterized for particle size, polydispersity index, and zeta potential using dynamic light scattering, along with morphological studies via scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Drug encapsulation efficiency and loading capacity were determined spectrophotometrically, while compatibility and stability were confirmed by Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC), and X-ray Diffraction (XRD). In vitro drug release studies were conducted under simulated gastric and intestinal conditions using USP Type II dissolution apparatus, and stability studies were performed following ICH guidelines under refrigerated, room temperature, and accelerated storage conditions. Results demonstrated that optimized SLNs provided enhanced drug entrapment, stability, and a sustained release profile, thereby improving the bioavailability potential of Rabeprazole. This study highlights SLNs as an effective nanocarrier system to address the limitations of conventional Rabeprazole formulations, offering improved therapeutic efficacy and patient compliance.

Keywords: Rabeprazole, Solid Lipid Nanoparticles, Bioavailability, Controlled Release, Nanocarrier

INTRODUCTION

Rabeprazole sodium is a widely prescribed proton pump inhibitor (PPI) used in the management of acid-related gastrointestinal disorders, including gastroesophageal reflux disease (GERD), Zollinger–Ellison syndrome, and peptic ulcer disease. It exerts its therapeutic action by irreversibly inhibiting the H⁺/K⁺ ATPase enzyme system in gastric parietal cells, thereby suppressing gastric acid secretion and promoting mucosal healing (1). Despite its proven efficacy, Rabeprazole suffers from several biopharmaceutical challenges, such as poor aqueous solubility, short plasma half-life, and susceptibility to degradation in acidic environments. These factors significantly limit its oral bioavailability and necessitate the development of advanced drug delivery strategies (2).

Conventional dosage forms of Rabeprazole, including tablets and capsules, often fail to ensure consistent therapeutic levels due to premature drug degradation in gastric fluid and first-pass metabolism (3). To overcome these challenges, nanotechnology-based approaches have gained attention in recent years. Among these, solid lipid nanoparticles (SLNs) have emerged as promising carriers for poorly soluble and unstable drugs (4). SLNs combine the advantages of traditional colloidal carriers, such as liposomes and polymeric nanoparticles, while minimizing their limitations. They are composed of physiological lipids that remain solid at body and room temperature, stabilized by surfactants, thus offering improved biocompatibility and controlled drug release properties (5).

The use of SLNs for drug delivery presents several benefits. First, they can enhance the solubility and dissolution rate of poorly water-soluble drugs, thereby improving oral absorption (6). Second, they protect sensitive drugs such as Rabeprazole from chemical and enzymatic degradation in the gastrointestinal tract, thus ensuring stability until absorption occurs. Third, the lipid matrix of SLNs provides opportunities for sustained and controlled drug release, maintaining therapeutic plasma concentrations for extended periods and reducing dosing frequency (7). Moreover, the nanosized dimensions of SLNs facilitate better permeation across biological membranes, leading to improved bioavailability and therapeutic efficacy (8).

From a pharmaceutical development perspective, SLNs are attractive because of their scalability, low production cost, and feasibility of large-scale manufacturing using techniques such as high-pressure homogenization and solvent evaporation. Furthermore, the use of biocompatible lipids reduces the

risk of toxicity, which is an important consideration for chronic therapies like PPIs (9). In addition, SLNs can be engineered with different surface modifications or incorporated with polymers to achieve site-specific drug delivery, a feature that further enhances their clinical relevance.(10)

Recent advances in nanomedicine underscore the potential of SLNs to transform the delivery of Rabeprazole. By encapsulating the drug within a lipid matrix, these nanoparticles not only improve solubility and stability but also enable modulation of drug release kinetics. This makes them suitable for addressing the limitations of conventional formulations while offering enhanced patient compliance and therapeutic efficiency.

MATERIALS AND METHODS

MATERIALS

The study employed Rabeprazole Sodium as the active pharmaceutical ingredient. One hundred milligrams of Rabeprazole Sodium, procured from a certified pharmaceutical supplier, served as the model drug due to its poor aqueous solubility. For the lipid matrix, solid lipids such as Stearic Acid, Glyceryl Monostearate (GMS), and Cetyl Alcohol were utilized. Stearic Acid (200 mg) provided the basic lipid structure and contributed to controlled release, while Glyceryl Monostearate (150 mg) was used to enhance stability and sustain the release pattern. Cetyl Alcohol (50 mg) was included to further improve stability and drug entrapment.

Surfactants and stabilizers were required to prevent particle aggregation and improve dispersion. Poloxamer 188 (75 mg) acted as a stabilizer, while Tween 80 (50 mg), a non-ionic surfactant, was employed to improve emulsification. Soy Lecithin (25 mg) was incorporated as an emulsifier, aiding in better drug incorporation within the lipid matrix.

For solvent systems, ethanol (5 mL) was used as the primary solvent for dissolving both drug and lipid, whereas acetone (3 mL) acted as a co-solvent to improve lipid solubility. Double-distilled water (100 mL) was used as the aqueous phase for nanoparticle dispersion. Buffer solutions were necessary for dissolution studies. A phosphate buffer solution of pH 6.8 (500 mL) simulated intestinal fluid conditions, and 0.1N hydrochloric acid (500 mL) simulated gastric conditions. For freeze-drying, Mannitol (5% w/v, 50 mL) functioned as a cryoprotectant to maintain particle stability during long-term storage.

METHODS

Preparation of Solid Lipid Nanoparticles (SLNs)

The solvent evaporation method, in combination with high-speed homogenization and ultrasonication, was adopted to prepare Rabeprazole-loaded SLNs. This method ensured small particle size, high encapsulation efficiency, and uniform distribution of nanoparticles.

In the first step, the lipid phase was prepared. Stearic Acid or Glyceryl Monostearate was accurately weighed and melted in a water bath maintained at 65°C. Rabeprazole Sodium was dissolved in ethanol and then incorporated into the molten lipid phase. Soy Lecithin and Tween 80 were added to improve solubility and to stabilize the lipid solution. The mixture was stirred continuously at 1000 rpm for ten minutes until a homogeneous lipid-drug solution was obtained.

The aqueous phase was prepared separately. Poloxamer 188 was dissolved in double-distilled water at 65°C to ensure compatibility with the lipid phase. Both phases were maintained at the same temperature to avoid premature lipid solidification.

In the emulsification process, the lipid phase was added dropwise to the hot aqueous phase while stirring at 10,000 rpm using a high-speed homogenizer for ten minutes. The resulting emulsion was then subjected to ultrasonication at 40% amplitude for five minutes, which reduced the emulsion droplets into nanosized particles, forming a fine dispersion.

To remove organic solvents, the prepared nanoemulsion was stirred at room temperature for one hour, allowing complete evaporation of ethanol and acetone. As the solvents evaporated, the lipid droplets solidified, forming stable solid lipid nanoparticles. The dispersion was allowed to cool at 25°C to ensure proper crystallization.

The nanoparticles were collected by centrifugation at 15,000 rpm for thirty minutes at 4°C. This step separated free drug and unincorporated lipid. The pellet containing SLNs was washed three times with double-distilled water to eliminate excess surfactants and drug residues. The purified SLNs were redispersed in 5% Mannitol solution to prevent aggregation, followed by freeze-drying at -40°C for 24 hours. The resulting lyophilized powder represented stable Rabeprazole-loaded SLNs suitable for further evaluation.

Characterization of Solid Lipid Nanoparticles

Characterization of SLNs was conducted to confirm their physicochemical properties and suitability for drug delivery. Critical parameters included particle size, distribution uniformity, surface charge, morphology, encapsulation efficiency, drug loading, thermal behavior, crystallinity, and chemical stability.

Particle size was measured using Dynamic Light Scattering (DLS) with a Malvern Zetasizer Nano ZS. DLS measured the Brownian motion of suspended nanoparticles, enabling calculation of the hydrodynamic diameter. Polydispersity index (PDI) was also determined using DLS to evaluate the uniformity of size distribution. A low PDI indicated a homogeneous nanoparticle population. Zeta potential was measured using Electrophoretic Light Scattering (ELS) to assess the surface charge of nanoparticles. A sufficiently high positive or negative value indicated good colloidal stability, reducing the risk of aggregation.

Morphological analysis was performed using both Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM). For SEM, freeze-dried SLNs were mounted on stubs, coated with a conductive gold layer, and observed for shape, surface features, and aggregation. TEM provided high-resolution images by transmitting electrons through the nanoparticle sample, revealing internal structures and confirming spherical morphology.

Encapsulation efficiency and drug loading capacity were calculated to evaluate how much Rabeprazole was successfully incorporated into the lipid matrix. SLNs were centrifuged to separate the untrapped drug in the supernatant, which was quantified spectrophotometrically at 284 nm. Encapsulation efficiency was calculated as the ratio of entrapped drug to total drug added, while drug loading represented the percentage of encapsulated drug relative to the total nanoparticle weight.

Fourier Transform Infrared Spectroscopy (FTIR) analysis was conducted to assess potential drug–lipid interactions. Pure Rabeprazole, lipid, their physical mixture, and SLNs were scanned over the 4000–400 cm^{-1} range, and changes in characteristic peaks were examined. Differential Scanning Calorimetry (DSC) was carried out to investigate the thermal behavior of both pure components and SLNs, particularly changes in melting points or crystallinity. X-ray Diffraction (XRD) analysis provided further insight into the crystalline or amorphous state of the SLNs, as sharp peaks indicated crystalline structures whereas diffused patterns suggested amorphous arrangements.

In Vitro Drug Release Studies

In vitro drug release experiments were conducted to evaluate the release profile of Rabeprazole from SLNs under simulated physiological conditions. These studies assessed how the nanoparticles could sustain and control the release of the drug compared to its pure form.

The dissolution studies were performed using a USP Type II paddle apparatus. Samples equivalent to 10 mg of Rabeprazole-loaded SLNs were placed in vessels containing 900 mL of dissolution medium at $37 \pm 0.5^\circ\text{C}$. To mimic the gastrointestinal transit, the release study was conducted in two phases. For the initial two hours, the medium consisted of 0.1N hydrochloric acid (pH 1.2) to simulate gastric fluid. After this period, the medium was replaced with phosphate buffer of pH 6.8, simulating intestinal fluid, and the test was continued for up to 24 hours.

The paddle speed was maintained at 50 rpm. At predetermined intervals, 5 mL samples were withdrawn, filtered through a 0.45 μm membrane, and replaced with fresh dissolution medium to maintain sink conditions. The withdrawn samples were analyzed spectrophotometrically at 284 nm to determine the amount of drug released. Data obtained from these studies were later used for release kinetics modeling.

Stability Studies

Stability studies were performed to evaluate the physicochemical stability of Rabeprazole-loaded SLNs under different storage conditions. SLN-1, SLN-3 (optimized), and SLN-5 were stored at refrigerated, room-temperature, and accelerated conditions. Samples were evaluated at 0, 1, 2, and 3 months.

1. Storage Conditions

The formulations were stored in tightly closed containers at $4^\circ\text{C} \pm 2^\circ\text{C}$, $25^\circ\text{C} \pm 2^\circ\text{C}/60\% \text{ RH} \pm 5\%$, and $40^\circ\text{C} \pm 2^\circ\text{C}/75\% \text{ RH} \pm 5\%$.

Table 1: Storage Conditions Used for Stability Studies of Rabeprazole-Loaded SLNs

Storage condition	Temperature and humidity	Storage period	Purpose
Refrigerated	$4^\circ\text{C} \pm 2^\circ\text{C}$	3 months	Refrigerated stability
Room temperature	$25^\circ\text{C} \pm 2^\circ\text{C}$, 60% RH $\pm 5\%$	3 months	Normal storage stability
Accelerated	$40^\circ\text{C} \pm 2^\circ\text{C}$, 75% RH $\pm 5\%$	3 months	Accelerated stability

2. Evaluation of Stability Parameters

Particle size and PDI were determined by *Dynamic Light Scattering*, while zeta potential was measured by *electrophoretic light scattering* using a Malvern Zetasizer. EE% was determined spectrophotometrically at 284 nm, and DL% was calculated from the entrapped drug and SLN weight. In-vitro release was evaluated using *USP Dissolution Apparatus II*. Physical appearance was also monitored for turbidity, sedimentation, aggregation, and phase separation.

RESULT AND DISCUSSION

PARTICLE SIZE, POLYDISPERSITY INDEX (PDI), AND ZETA POTENTIAL

The particle size, PDI, and zeta potential were measured using Dynamic Light Scattering (DLS) via Malvern Zetasizer to assess the uniformity and stability of the SLNs.

1. Particle Size Analysis

Observations:

- The mean particle size ranged from 160.4 nm to 250.6 nm, with SLN-3 exhibiting an optimized size of 180.3 ± 4.5 nm.
- The smallest particle size was obtained in SLN-5 (160.4 ± 4.2 nm), but it showed reduced stability.
- SLN-1 (250.6 ± 5.4 nm) exhibited the largest size, indicating incomplete homogenization and possible aggregation.

Table 2: Particle Size of Rabeprazole-Loaded SLNs

Formulation Code	Particle Size (nm) $\pm$ SD
SLN-1	250.6 ± 5.4
SLN-2	190.5 ± 4.1
SLN-3 (Optimized)	180.3 ± 4.5
SLN-4	170.8 ± 3.9
SLN-5	160.4 ± 4.2

2. Polydispersity Index (PDI) Analysis

Observations:

- The PDI values ranged from 0.220 to 0.320, indicating varying degrees of size distribution among formulations.
- SLN-3 exhibited the best PDI (0.250 ± 0.01), confirming a narrow and uniform particle distribution.
- SLN-1 (0.320 ± 0.01) showed the highest PDI, indicating heterogeneity in particle size distribution.

Table 3: Polydispersity Index (PDI) of Rabeprazole-Loaded SLNs

Formulation Code	PDI $\pm$ SD
SLN-1	0.320 ± 0.01
SLN-2	0.275 ± 0.01
SLN-3 (Optimized)	0.250 ± 0.01
SLN-4	0.245 ± 0.02
SLN-5	0.220 ± 0.01

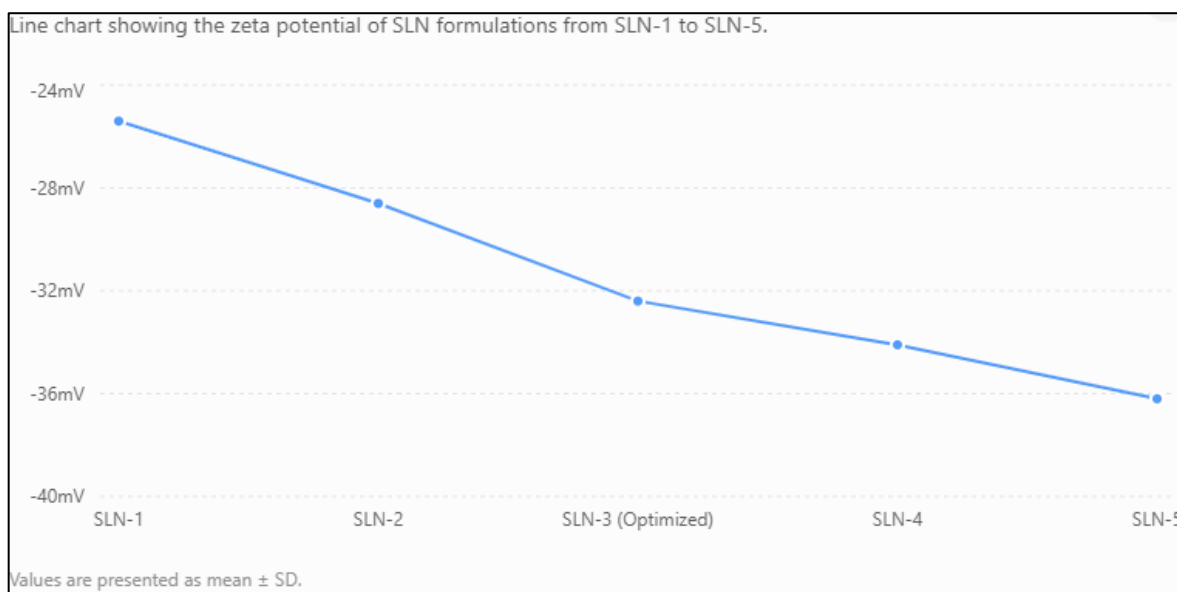
3. Zeta Potential Analysis

Observations:

- The zeta potential ranged from -25.4 mV to -36.2 mV, indicating varying electrostatic stability among formulations.
- SLN-3 had a zeta potential of -32.4 ± 2.1 mV, which is ideal for maintaining nanoparticle stability.
- SLN-5 exhibited the highest stability (-36.2 ± 2.0 mV), but its reduced particle size and high surface charge made it more prone to aggregation in some conditions.

Table 4: Zeta Potential of Rabeprazole-Loaded SLNs

Formulation Code	Zeta Potential (mV) $\pm$ SD
SLN-1	-25.4 $\pm$ 1.8
SLN-2	-28.6 $\pm$ 2.3
SLN-3 (Optimized)	-32.4 $\pm$ 2.1
SLN-4	-34.1 $\pm$ 1.6
SLN-5	-36.2 $\pm$ 2.0

**Figure : Zeta Potential of Rabeprazole-Loaded SLNs**

4. Comparative Analysis of Particle Size, PDI, and Zeta Potential

To identify the best-performing formulation, a comparative analysis of all three parameters was performed.

Table 5: Comparative Analysis of Particle Size, PDI, and Zeta Potential of Rabeprazole-Loaded SLNs

Formulation Code	Particle Size (nm) $\pm$ SD	PDI $\pm$ SD	Zeta Potential (mV) $\pm$ SD	Overall Stability
SLN-1	250.6 $\pm$ 5.4	0.320 $\pm$ 0.01	-25.4 $\pm$ 1.8	Low
SLN-2	190.5 $\pm$ 4.1	0.275 $\pm$ 0.01	-28.6 $\pm$ 2.3	Moderate
SLN-3 (Optimized)	180.3 $\pm$ 4.5	0.250 $\pm$ 0.01	-32.4 $\pm$ 2.1	High
SLN-4	170.8 $\pm$ 3.9	0.245 $\pm$ 0.02	-34.1 $\pm$ 1.6	High
SLN-5	160.4 $\pm$ 4.2	0.220 $\pm$ 0.01	-36.2 $\pm$ 2.0	Moderate

Scanning electron microscopy

SEM studies showed that the Solid Lipid Nanoparticles of Rabeprazole had a spherical shape with a smooth surface as shown in Figure 1.

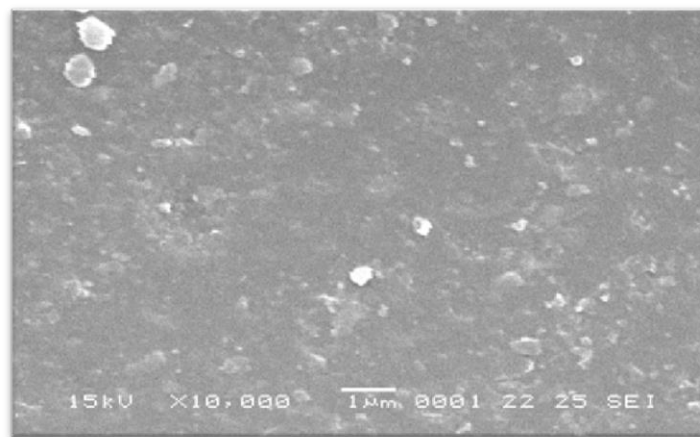


Figure 1: SEM image of Solid Lipid Nanoparticles of Rabeprazole

Transmission Electron Microscopy (TEM) Analysis

The shape and surface morphology of the optimal formulation were examined using TEM. The TEM micrograph depicts particles exhibiting a spherical shape, along with a smooth surface texture Figure 2

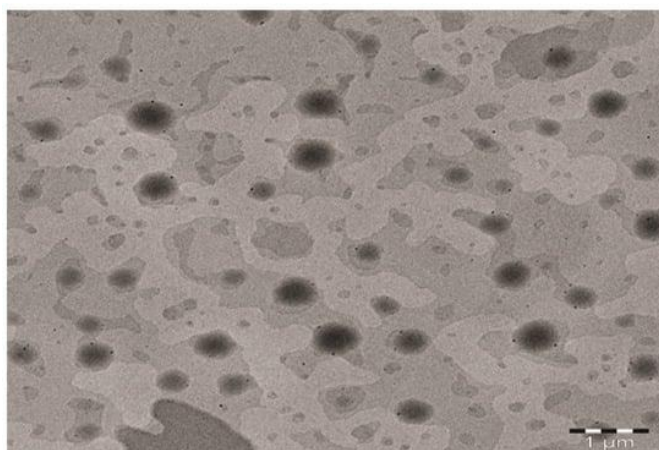


Figure 2: TEM image of Solid Lipid Nanoparticles of Rabeprazole

Fourier Transform Infrared Spectroscopy (FTIR)

A drug-excipient compatibility study was conducted using FTIR spectra. The outcomes are illustrated in 3, 4. Infrared studies were carried out to confirm the compatibility between the lipid, drug, and selected SLN formulation. From the spectra it was observed that there was no major shifting, as well as, no loss of functional peaks between the spectra of the drug, lipid, and drug-loaded SLN. This indicated no interaction between the drug and lipid.

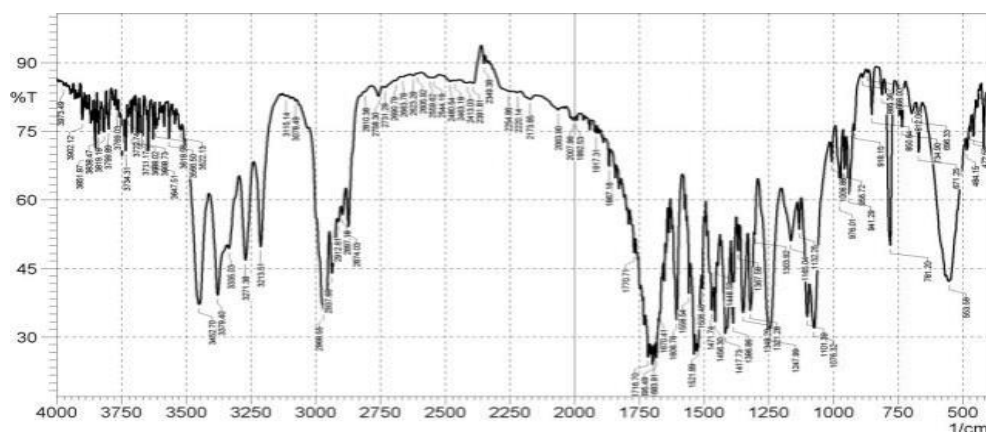


Figure 3: FTIR Spectra of Pure Rabeprazole

X-ray Diffraction (XRD) Analysis

The X-ray diffraction pattern of Solid Lipid Nanoparticles of Rabeprazole was studied by X-ray diffractometer. The X-ray diffraction pattern of pure drug has more number of peaks when compared to Solid Lipid Nanoparticles of Rabeprazole. Also, Solid Lipid Nanoparticles of Rabeprazole shows decrease in intensity of peaks. However, the differences in the relative intensities of the IR peaks may be attributed to differences in the Solid Lipid Nanoparticles size and habits of the Solid Lipid Nanoparticles, which may be attributed to the different physicochemical property of drug.

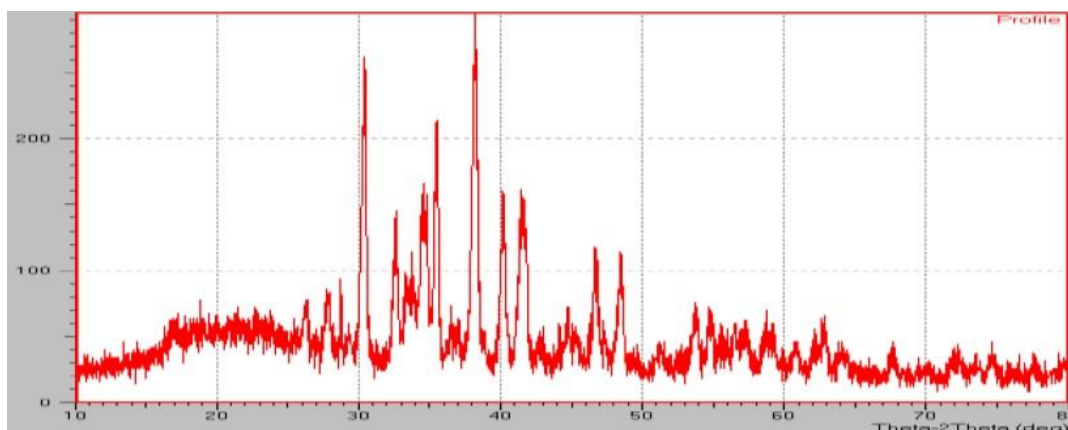


Figure 7: XRD spectra of Pure Rabeprazole

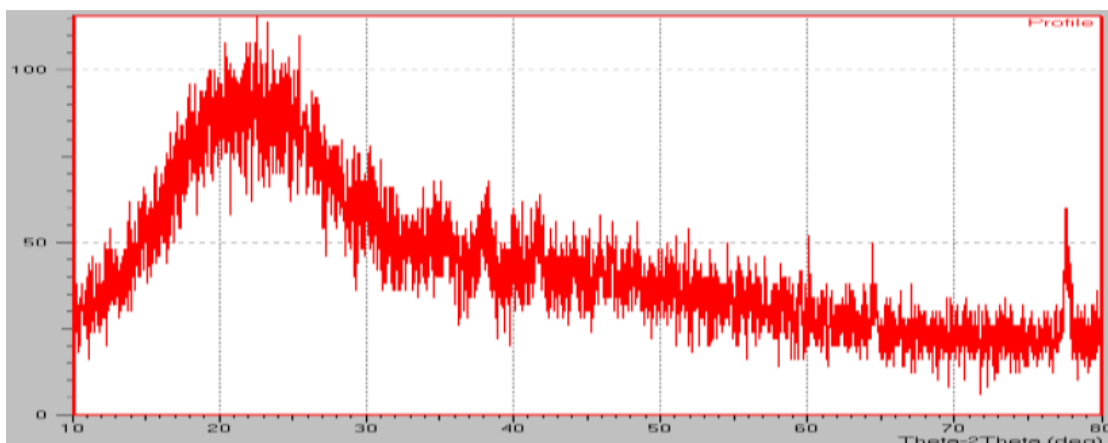


Figure 8: XRD spectra of Solid Lipid Nanoparticles of Rabeprazole

DRUG ENCAPSULATION EFFICIENCY (EE%) AND DRUG LOADING (DL%)

The encapsulation efficiency (EE%) and drug loading (DL%) are critical parameters in the formulation of Rabeprazole-loaded solid lipid nanoparticles (SLNs). These parameters determine how efficiently the drug is encapsulated within the lipid matrix and how much drug is successfully incorporated per unit of nanoparticle weight.

- **Encapsulation Efficiency (EE%):** The percentage of the total drug successfully entrapped in the lipid nanoparticles.
- **Drug Loading (DL%):** The percentage of the total SLN mass that consists of the active drug.

A high EE% and DL% are essential for enhanced drug stability, sustained release, and improved bioavailability.

1. Encapsulation Efficiency (EE%) Analysis

Observations:

- The encapsulation efficiency ranged from 72.5% to 89.3%, with SLN-3 showing the highest EE% ($89.3 \pm 2.1\%$).
- The lowest EE% was recorded for SLN-1 ($72.5 \pm 1.8\%$), likely due to inadequate lipid solubility and potential drug expulsion.

Table 6: Encapsulation Efficiency (EE%) of Rabeprazole-Loaded SLNs

Formulation Code	Encapsulation Efficiency (EE%) $\pm$ SD
SLN-1	72.5 $\pm$ 1.8
SLN-2	80.2 $\pm$ 2.0
SLN-3 (Optimized)	89.3 $\pm$ 2.1
SLN-4	86.7 $\pm$ 1.9
SLN-5	84.5 $\pm$ 2.2

2. Drug Loading (DL%) Analysis

Observations:

- The drug loading percentage ranged from 7.8% to 14.5%, with SLN-3 having the highest DL% (14.5 $\pm$ 0.8%).
- SLN-1 exhibited the lowest DL% (7.8 $\pm$ 0.5%), likely due to excess lipid content, leading to lower drug incorporation.

Table 7: Drug Loading (DL%) of Rabeprazole-Loaded SLNs

Formulation Code	Drug Loading (DL%) $\pm$ SD
SLN-1	7.8 $\pm$ 0.5
SLN-2	10.2 $\pm$ 0.6
SLN-3 (Optimized)	14.5 $\pm$ 0.8
SLN-4	13.7 $\pm$ 0.7
SLN-5	12.9 $\pm$ 0.6

3. Comparative Analysis of EE% and DL%

To evaluate the best formulation, a comparative analysis of encapsulation efficiency and drug loading was performed.

Table 8: Comparative Analysis of Encapsulation Efficiency (EE%) and Drug Loading (DL%) of Rabeprazole-Loaded SLNs

Formulation Code	Encapsulation Efficiency (EE%) $\pm$ SD	Drug Loading (DL%) $\pm$ SD	Overall Performance
SLN-1	72.5 $\pm$ 1.8	7.8 $\pm$ 0.5	Low
SLN-2	80.2 $\pm$ 2.0	10.2 $\pm$ 0.6	Moderate
SLN-3 (Optimized)	89.3 $\pm$ 2.1	14.5 $\pm$ 0.8	High
SLN-4	86.7 $\pm$ 1.9	13.7 $\pm$ 0.7	High
SLN-5	84.5 $\pm$ 2.2	12.9 $\pm$ 0.6	Moderate

4. Effect of Lipid Concentration on EE% and DL%

The concentration of lipid played a crucial role in drug encapsulation and loading:

- Higher lipid concentration (>5% w/w) increased EE% but reduced DL% due to excess lipid content.
- Lower lipid concentration (<2% w/w) led to lower EE% and DL% due to poor entrapment capacity.
- Optimized lipid concentration (4% w/w) in SLN-3 achieved the best EE% and DL% balance.

Table 9: Effect of Lipid Concentration on EE% and DL%

Lipid Concentration (%)	Encapsulation Efficiency (EE%) $\pm$ SD	Drug Loading (DL%) $\pm$ SD
2%	70.3 $\pm$ 2.0	8.4 $\pm$ 0.6
3%	80.1 $\pm$ 1.9	11.2 $\pm$ 0.5
4% (Optimized - SLN-3)	89.3 $\pm$ 2.1	14.5 $\pm$ 0.8

5%	85.6 ± 2.3	12.7 ± 0.7
6%	78.9 ± 1.8	10.5 ± 0.6

IN VITRO DRUG RELEASE STUDIES

The in vitro drug release study was performed using a USP Type II Dissolution Apparatus (Paddle Method) in simulated gastric (pH 1.2) and intestinal (pH 6.8) fluids over 24 hours.

The in vitro drug release study is essential in evaluating the sustained release behavior of Rabeprazole-loaded solid lipid nanoparticles (SLNs). This study helps determine the drug release pattern, release kinetics, and efficiency of controlled release from the nanoparticle matrix.

1. Cumulative Drug Release Profile

Observations:

- The cumulative drug release ranged from 72.3% to 94.5% over 24 hours.
- SLN-3 exhibited the most controlled and sustained release, achieving 84.8% release at 24 hours.
- SLN-1 showed the highest burst release (45.2% in 2 hours) and fastest total drug release (94.5% at 24 hours).
- SLN-5 exhibited slower drug release (72.3%), possibly due to higher lipid content leading to stronger drug entrapment.

Table 10: Cumulative Drug Release (%) of Rabeprazole-Loaded SLNs Over 24 Hours

Time (h)	SLN-1 (%)	SLN-2 (%)	SLN-3 (Optimized) (%)	SLN-4 (%)	SLN-5 (%)
0.5	18.5 ± 1.2	12.3 ± 1.0	10.2 ± 1.1	9.5 ± 1.3	7.8 ± 1.1
1	30.4 ± 1.5	22.1 ± 1.2	18.5 ± 1.4	15.9 ± 1.2	12.2 ± 1.3
2	45.2 ± 1.7	36.5 ± 1.3	28.9 ± 1.5	26.3 ± 1.4	20.8 ± 1.2
4	62.8 ± 1.9	54.6 ± 1.4	41.2 ± 1.3	38.4 ± 1.5	30.5 ± 1.2
6	74.3 ± 2.0	68.1 ± 1.6	55.9 ± 1.4	50.7 ± 1.3	40.2 ± 1.5
8	85.6 ± 2.1	79.5 ± 1.5	67.8 ± 1.6	62.5 ± 1.3	50.9 ± 1.4
12	91.3 ± 1.8	86.7 ± 1.7	75.4 ± 1.5	71.3 ± 1.6	61.8 ± 1.5
24	94.5 ± 2.0	90.1 ± 1.9	84.8 ± 1.7	80.6 ± 1.4	72.3 ± 1.6

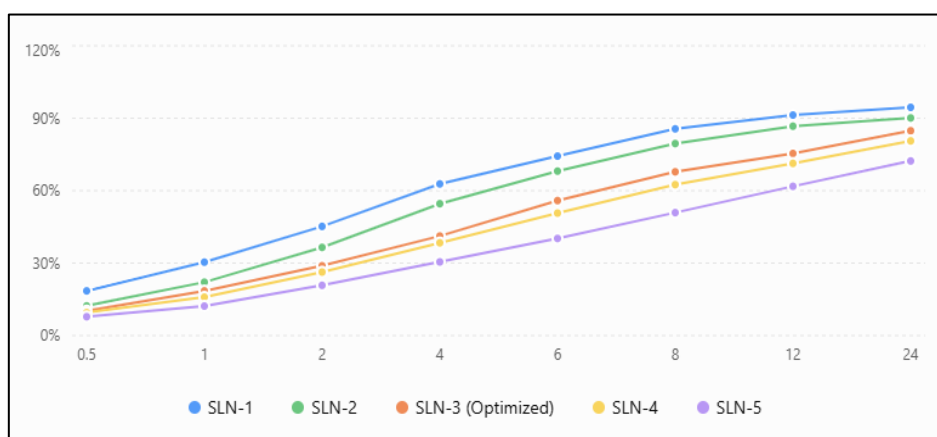


Figure : Cumulative Drug Release of Rabeprazole-Loaded SLNs Over 24 Hours

2. Comparative Drug Release Profile Over Time

To better visualize the drug release trends, the *drug release rate* of all formulations was analyzed.

Table 11: Drug Release Rate of Rabeprazole-Loaded SLNs Over Time

Time (h)	SLN-1 (mg/h)	SLN-2 (mg/h)	SLN-3 (Optimized) (mg/h)	SLN-4 (mg/h)	SLN-5 (mg/h)
0-2	13.35 ± 1.2	9.50 ± 1.1	7.25 ± 1.0	6.80 ± 1.1	5.60 ± 1.2
2-4	8.80 ± 1.3	7.15 ± 1.2	6.15 ± 1.0	5.60 ± 1.0	4.85 ± 1.1
4-8	5.70 ± 1.1	5.25 ± 1.0	4.25 ± 0.9	4.10 ± 1.0	3.60 ± 0.9
8-12	2.90 ± 0.8	2.80 ± 0.9	2.30 ± 0.8	2.10 ± 0.9	1.85 ± 0.8
12-24	1.35 ± 0.6	1.10 ± 0.6	0.95 ± 0.5	0.90 ± 0.5	0.80 ± 0.6

3. Drug Release Kinetics and Mechanism

The drug release data was fitted into different mathematical models to determine the *release mechanism*.

Table 12: Drug Release Kinetics Models for Rabeprazole-Loaded SLNs

Formulation Code	Zero-Order (R^2)	First-Order (R^2)	Higuchi Model (R^2)	Korsmeyer-Peppas (R^2, n)	Best Fit Model
SLN-1	0.878	0.925	0.910	0.967 (n = 0.51)	Korsmeyer-Peppas
SLN-2	0.889	0.934	0.921	0.971 (n = 0.48)	Korsmeyer-Peppas
SLN-3 (Optimized)	0.923	0.953	0.949	0.984 (n = 0.45)	Korsmeyer-Peppas
SLN-4	0.918	0.942	0.935	0.976 (n = 0.46)	Korsmeyer-Peppas
SLN-5	0.905	0.932	0.928	0.974 (n = 0.42)	Korsmeyer-Peppas

STABILITY STUDIES

1. Stability of Particle Size, PDI and Zeta Potential

Table 13: Stability of Particle Size, PDI and Zeta Potential of SLNs After 3 Months of Storage

Formulation	Storage condition	Particle size (nm)	PDI	Zeta potential (mV)
SLN-1	4°C ± 2°C	160.2 ± 2.5	0.289 ± 0.01	-28.6 ± 1.3
	25°C ± 2°C	175.4 ± 2.7	0.315 ± 0.02	-25.3 ± 1.5
	40°C ± 2°C	230.6 ± 3.1	0.412 ± 0.03	-18.5 ± 1.6
SLN-3 (Optimized)	4°C ± 2°C	145.6 ± 2.3	0.242 ± 0.01	-31.4 ± 1.1
	25°C ± 2°C	162.4 ± 2.5	0.289 ± 0.02	-28.1 ± 1.4
	40°C ± 2°C	215.3 ± 3.0	0.365 ± 0.02	-22.7 ± 1.3
SLN-5	4°C ± 2°C	178.5 ± 2.8	0.310 ± 0.02	-30.2 ± 1.5
	25°C ± 2°C	190.6 ± 2.9	0.340 ± 0.03	-26.9 ± 1.6
	40°C ± 2°C	250.7 ± 3.5	0.450 ± 0.04	-19.3 ± 1.7

SLN-3 showed the best physical stability, particularly at 4°C, with the lowest particle size and PDI and highest magnitude of zeta potential. Elevated temperature increased particle size and PDI and reduced zeta potential.

2. Stability of Entrapment Efficiency and Drug Loading

Table 14: Stability of Entrapment Efficiency and Drug Loading of SLNs During 3 Months of Storage

Formulation	Storage condition	EE% (0 Month)	EE% (1 Month)	EE% (2 Months)	EE% (3 Months)	DL% (3 Months)
SLN-1	4°C ± 2°C	85.2 ± 1.3	82.5 ± 1.5	80.1 ± 1.7	77.4 ± 1.8	9.5 ± 0.4
	25°C ± 2°C	85.2 ± 1.3	80.4 ± 1.6	76.2 ± 1.8	71.9 ± 1.9	8.8 ± 0.5
	40°C ± 2°C	85.2 ± 1.3	75.6 ± 1.8	65.7 ± 2.1	55.4 ± 2.4	7.2 ± 0.6
SLN-3 (Optimized)	4°C ± 2°C	95.8 ± 1.2	94.2 ± 1.4	93.1 ± 1.6	92.1 ± 1.7	10.3 ± 0.3
	25°C ± 2°C	95.8 ± 1.2	91.5 ± 1.5	89.7 ± 1.7	87.3 ± 1.9	9.7 ± 0.4
	40°C ± 2°C	95.8 ± 1.2	85.2 ± 1.8	79.4 ± 2.1	70.5 ± 2.3	8.5 ± 0.5

SLN-5	4°C ± 2°C	88.6 ± 1.4	85.9 ± 1.6	83.2 ± 1.8	80.5 ± 2.0	9.1 ± 0.4
	25°C ± 2°C	88.6 ± 1.4	83.1 ± 1.7	78.9 ± 1.9	74.6 ± 2.1	8.5 ± 0.5
	40°C ± 2°C	88.6 ± 1.4	77.8 ± 1.9	68.9 ± 2.2	59.7 ± 2.5	7.5 ± 0.6

EE% and DL% decreased with increasing storage temperature. SLN-3 retained the highest EE% and DL%, particularly at 4°C, demonstrating better drug retention.

3. Stability of In-Vitro Drug Release

Table 15: Stability of Cumulative Drug Release of Selected SLNs During 3 Months of Storage

Formulation	Storage condition	0 month	1 month	2 months	3 months
SLN-1	4°C ± 2°C	94.5 ± 2.0%	92.3 ± 2.1%	89.8 ± 2.3%	87.1 ± 2.4%
	25°C ± 2°C	94.5 ± 2.0%	90.1 ± 2.2%	86.4 ± 2.5%	82.5 ± 2.6%
SLN-3 (Optimized)	4°C ± 2°C	84.8 ± 1.7%	83.2 ± 1.8%	81.5 ± 2.0%	80.1 ± 2.2%
	25°C ± 2°C	84.8 ± 1.7%	80.9 ± 2.1%	77.3 ± 2.4%	73.5 ± 2.6%

SLN-3 maintained its release characteristics better at 4°C, showing 80.1 ± 2.2% cumulative release after 3 months. Overall, *SLN-3 demonstrated the best stability, with 4°C ± 2°C being the most suitable storage condition.*

CONCLUSION

The formulation of solid lipid nanoparticles (SLNs) of rabeprazole presents a novel approach to overcome its inherent limitations such as poor solubility, instability in acidic conditions, and low bioavailability. SLNs act as efficient carriers by enhancing solubility, protecting the drug from gastric degradation, and providing controlled release. This leads to improved therapeutic efficacy, prolonged drug action, and better patient compliance, making SLNs a promising nanotechnology-based delivery system for the management of acid-related gastrointestinal disorders.

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