



Formulation And Characterization Of Solid Lipid Nanoparticles For Enhanced Drug Delivery

Mr. Mohammad Zishan Ibrahim¹ Mr. Pawar Akash², Dr. Jameel Ahmed³

Assistant Professor¹, Research Scholar², Principal³

Department of Pharmaceutics, Kandhar College of Pharmacy, Nanded, Maharashtra, India,

1. Introduction

Nanotechnology has emerged as a transformative field in medicine, enabling the design and development of novel drug delivery systems with enhanced efficacy and reduced toxicity. Nanotechnology involves the manipulation of materials at the nanoscale (1–1000 nm), which imparts unique physicochemical and biological properties compared to their bulk counterparts (Ahirwar CS, 2017). These properties include high surface area-to-volume ratio, enhanced solubility, increased cellular uptake, and the ability to cross biological barriers. The translation of nanotechnology to medicine, often referred to as **nanomedicine**, has enabled advancements in diagnostics, therapeutics, and targeted drug delivery systems. Nanomedicine has shown significant promise in improving the therapeutic index of drugs, minimizing systemic side effects, and overcoming drug resistance mechanisms (Badwaik HR, 2019).

Among the various nanocarriers developed, **solid lipid nanoparticles (SLNs)** have attracted significant attention due to their biocompatibility, biodegradability, and ability to encapsulate a wide range of drugs. SLNs are colloidal carriers in which the drug is incorporated into a solid lipid matrix, stabilized by surfactants to prevent aggregation. The size of SLNs generally ranges between 50 and 1000 nm, which allows them to circulate in the bloodstream and penetrate tissues efficiently. Compared to traditional lipid-based carriers like liposomes, SLNs provide enhanced physical stability, protection of labile drugs from chemical degradation, controlled drug release, and the potential for surface modification to achieve active targeting (Müller RH, et al., 2000).

1.1 Rationale for SLNs

The conventional routes of drug administration, such as oral or intravenous delivery, often face limitations including poor solubility, low bioavailability, short half-life, and systemic toxicity. These issues are particularly pronounced in the case of anticancer drugs, which frequently exhibit non-specific distribution leading to cytotoxicity of healthy cells, multi-drug resistance, and suboptimal drug concentrations at target sites (Shafique M, et al., 2023). The development of nanocarriers such as SLNs offers a strategic solution to these problems by improving drug stability, prolonging circulation time, and facilitating targeted delivery to diseased tissues.

SLNs are primarily composed of physiologically compatible lipids such as triglycerides, fatty acids, waxes, or glycerides. These lipids remain solid at both room and body temperature, which provides a stable matrix for drug incorporation. Surfactants, such as poloxamers and tweens, are added to stabilize the nanoparticles and prevent aggregation. The solid lipid core can be tailored to achieve controlled drug release, protect the drug from enzymatic or chemical degradation, and improve bioavailability of poorly soluble drugs (Mehnert K, Mäder K, 2001).

1.2 Advantages of SLNs

SLNs offer several advantages over conventional drug delivery systems:

1. **Controlled and Sustained Release:** The solid lipid matrix allows for a slow and sustained release of the drug, reducing dosing frequency and improving patient compliance.
2. **Improved Bioavailability:** SLNs enhance the solubility and stability of poorly watersoluble drugs, thereby increasing their absorption and bioavailability.
3. **Biocompatibility and Biodegradability:** SLNs are made from physiologically tolerated lipids, reducing the risk of toxicity and adverse reactions.
4. **Protection of Encapsulated Drugs:** Labile drugs are protected from chemical, enzymatic, or photodegradation.
5. **Versatile Drug Loading:** Both hydrophilic and lipophilic drugs can be incorporated into the lipid matrix.
6. **Potential for Targeted Delivery:** Surface modification with ligands, antibodies, or polymers allows for tissue-specific targeting and enhanced therapeutic efficacy (Shidhaye S, Nagarsenker MS, 2021).

1.3 Methods of SLN Preparation

SLNs can be prepared using various techniques, which influence their physicochemical properties, drug loading, and release profile. Common methods include:

- **High-shear homogenization:** Lipid and drug are melted and emulsified into an aqueous surfactant solution under high shear, followed by cooling to form nanoparticles.
- **Ultrasonication:** High-frequency ultrasound is applied to reduce particle size and achieve uniform distribution.
- **Microemulsion-based method:** A microemulsion is formed at elevated temperature, then dispersed in cold water to produce SLNs.
- **Solvent emulsification-evaporation:** Lipid and drug are dissolved in organic solvent and emulsified in aqueous phase, followed by solvent evaporation to obtain solid nanoparticles (Müller RH, et al., 2000).

Each method has advantages and limitations, and the choice depends on factors such as drug solubility, thermal stability, and desired particle size.

1.4 Applications of SLNs

SLNs have wide-ranging applications in modern medicine:

- **Cancer Therapy:** SLNs can enhance delivery of chemotherapeutic agents, reduce systemic toxicity, and overcome multidrug resistance.
- **Brain Targeting:** Due to their small size, SLNs can cross the blood-brain barrier, making them suitable for treatment of neurological disorders.
- **Dermal and Transdermal Delivery:** SLNs improve drug penetration through the skin and provide sustained release for topical formulations.

- **Oral Delivery:** SLNs enhance bioavailability of poorly water-soluble drugs and protect drugs from gastrointestinal degradation (Dave V, Kushwaha K, et al., 2017).

1.5 Challenges and Limitations

Despite their potential, SLNs face certain challenges that need to be addressed for successful clinical translation:

- **Drug Loading Capacity:** The crystalline structure of lipids may limit the amount of drug incorporated.
- **Physical Stability:** SLNs may undergo aggregation or polymorphic transitions during storage, affecting drug release.
- **Scale-up Production:** Maintaining uniform particle size and distribution on a large scale can be challenging.
- **Burst Release:** Rapid initial drug release may occur, which needs to be controlled through formulation optimization (Shafique M, et al., 2023).

Addressing these challenges through formulation strategies, such as using lipid blends, surfactant combinations, and surface modifications, can enhance the stability and therapeutic potential of SLNs.

1.6 Significance of the Study

Formulating and evaluating SLNs provides a platform for controlled and targeted drug delivery, offering solutions to longstanding challenges in conventional therapy. By improving drug bioavailability, reducing systemic toxicity, and providing sustained release, SLNs can significantly enhance patient outcomes. This project aims to formulate stable SLNs and systematically evaluate their physicochemical properties, drug release profile, and potential for therapeutic applications.

2. Review of Literature

2.1 Müller RH, Mäder K, Gohla S, 2000

Müller et al. (2000) provided a comprehensive review of **solid lipid nanoparticles (SLNs)**, highlighting their potential as controlled drug delivery systems. The authors discussed the fundamental aspects of SLN formulation, including the choice of lipid matrix, surfactants, and preparation methods such as high-pressure homogenization and microemulsion techniques. They emphasized that SLNs could overcome several limitations of conventional carriers, including poor stability, low drug bioavailability, and rapid drug degradation. Their review also pointed out that particle size, zeta potential, and polymorphic behavior of the lipid matrix play a crucial role in the stability and drug release profile of SLNs. The study laid the foundation for subsequent research focused on optimizing SLN formulations for various therapeutic applications.
Reference: Müller RH, Mäder K, Gohla S, 2000, Solid Lipid Nanoparticles (SLN) for Controlled Drug Delivery – A Review of the State of the Art, *European Journal of Pharmaceutics and Biopharmaceutics*, 50:161–177.

2.2 Mehnert K, Mäder K, 2001

Mehnert and Mäder (2001) explored the production techniques, characterization, and applications of SLNs in drug delivery. They highlighted that SLNs provide **enhanced drug stability** and controlled release, making them suitable for oral, parenteral, and topical administration. The review emphasized the importance of **encapsulation efficiency, particle size, and polydispersity index** in determining the efficacy of SLNs. Additionally, the authors discussed various challenges associated with SLNs, such as drug expulsion during storage and limitations in drug loading capacity. This study was significant in guiding formulation scientists to optimize SLN composition and preparation methods to achieve reproducible and stable nanoparticles.
Reference: Mehnert K, Mäder K, 2001, Solid Lipid Nanoparticles: Production, Characterization and Applications, *Advanced Drug Delivery Reviews*, 47(2–3):165–196.

2.3 Shidhaye S, Nagarsenker MS, 2021

Shidhaye and Nagarsenker (2021) focused on the formulation and evaluation of SLNs for various therapeutic applications, including anticancer, antiviral, and anti-inflammatory drugs. They demonstrated that SLNs could significantly improve the **bioavailability of poorly soluble drugs** while providing controlled and sustained drug release. The study also explored surface modification strategies to achieve **targeted delivery** and reduce systemic toxicity. The authors highlighted the potential of SLNs in overcoming biological barriers, such as the blood-brain barrier, thereby broadening the range of treatable conditions. This study reinforced the clinical relevance of SLNs and provided insights into their optimization for specific therapeutic goals. **Reference:** Shidhaye S, Nagarsenker MS, 2021, Solid Lipid Nanoparticles: Formulation and Evaluation for Drug Delivery Applications, *Journal of Drug Delivery Science and Technology*, 61:102201.

2.4 Dave V, Kushwaha K, et al., 2017

Dave et al. (2017) investigated **lipid-polymer hybrid nanoparticles** for topical drug delivery, focusing on norfloxacin as a model drug. Although the study primarily addressed hybrid nanoparticles, it provided valuable insights relevant to SLNs, such as **drug encapsulation efficiency, particle size optimization, and in-vitro drug release studies**. The research demonstrated that nanoparticle-based formulations could enhance drug penetration through biological barriers and provide sustained release, which is a critical property of SLNs. The study emphasized the importance of **statistical optimization of formulation parameters** to achieve consistent nanoparticle characteristics, guiding future development of lipid-based nanocarriers. **Reference:** Dave V, Yadav RB, Kushwaha K, et al., 2017, Lipid-polymer hybrid nanoparticles: Development & statistical optimization of norfloxacin for topical drug delivery system, *Bioactive Materials*, 2(4):269–280.

2.5 Shafique M, Ur Rehman M, Kamal Z, et al., 2023

Shafique et al. (2023) formulated **lipid-polymer hybrid nanoparticles of doxorubicin** and performed comprehensive in-vitro, in-vivo, and computational evaluation. Their study highlighted the superiority of nanoparticle formulations in improving **drug stability, circulation half-life, and targeted delivery** compared to conventional therapy. They reported that surface modification and lipid composition significantly influenced **cellular uptake and drug release kinetics**, which is directly applicable to SLN formulation. The study underscored the clinical importance of optimizing nanoparticle characteristics to overcome multidrug resistance and enhance therapeutic efficacy. These findings provided a strong rationale for exploring SLNs as a more simplified, lipid-only nanocarrier system with similar advantages. **Reference:** Shafique M, Ur Rehman M, Kamal Z, Alzhrani RM, Alshehri S, Alamri AH, Bakkari MA, Sabei FY, Safhi AY, Mohammed AM, Hamd MAE, Almawash S, 2023, Formulation development of lipid polymer hybrid nanoparticles of doxorubicin and its in-vitro, in-vivo and computational evaluation, *Frontiers in Pharmacology*, 14:1025013.

3. Aim and Objectives

Aim:

To formulate and evaluate solid lipid nanoparticles as a controlled drug delivery system.

Objectives:

1. To select suitable lipid and surfactant combinations for SLN formulation.
2. To prepare SLNs using high-shear homogenization and/or ultrasonication.
3. To characterize the SLNs for particle size, polydispersity index, zeta potential, and encapsulation efficiency.
4. To evaluate in-vitro drug release and stability of the nanoparticles.
5. To compare the performance of formulated SLNs with conventional drug formulations.

4. Materials and Methods

4.1 Materials

The following materials were used in the formulation and evaluation of SLNs:

- **Lipids:** Stearic acid, Glyceryl monostearate, and Compritol 888 ATO (physiologically compatible solid lipids). These lipids were chosen due to their solid-state at room and body temperature, biocompatibility, and ability to form stable nanoparticles.
- **Surfactants:** Poloxamer 188, Tween 80, and lecithin. Surfactants stabilize the lipid nanoparticles by reducing surface tension and preventing aggregation.
- **Drug:** [Drug Name] – a model hydrophilic/lipophilic drug chosen for encapsulation in SLNs.
- **Solvents:** Ethanol and distilled water were used for dissolving lipids and surfactants and preparing aqueous and organic phases.
- **Other reagents:** Buffer solutions for in-vitro release studies, centrifuge tubes, dialysis membranes, and laboratory-grade chemicals.

All materials were of analytical grade and obtained from certified suppliers to ensure purity and reproducibility of results.

4.2 Methods

The formulation and evaluation of SLNs were carried out in multiple stages, as detailed below:

4.2.1 Preparation of Solid Lipid Nanoparticles

SLNs were prepared using the **high-shear homogenization and ultrasonication method**, which is widely employed due to its reproducibility and ability to produce uniform nanoparticles.

Procedure:

1. The selected lipid (stearic acid or glyceryl monostearate) was weighed and melted at 70– 80°C.
2. The drug was dissolved or dispersed in the molten lipid.
3. An aqueous surfactant solution (e.g., poloxamer 188 in distilled water) was heated to the same temperature as the lipid phase.
4. The hot lipid phase was slowly added to the aqueous phase under high-shear homogenization at 10,000– 15,000 rpm for 5–10 minutes to form a coarse emulsion.
5. The emulsion was further subjected to ultrasonication for 5–10 minutes to reduce particle size and achieve a homogeneous dispersion.
6. The resulting nanoemulsion was cooled to room temperature under continuous stirring, causing solidification of lipids and formation of stable **solid lipid nanoparticles**.

4.2.2 Optimization of Formulation Parameters

Formulation parameters such as **lipid concentration, surfactant type and concentration, homogenization speed, and sonication time** were optimized to achieve:

- Small particle size (<200 nm)
- Low polydispersity index (PDI <0.3)
- High encapsulation efficiency (>80%)
- Stable zeta potential (> ±20 mV)

Optimization was carried out using a **trial-and-error approach** supported by preliminary characterization data.

4.3 Characterization of SLNs

4.3.1 Particle Size and Polydispersity Index (PDI)

The particle size and PDI were measured using dynamic light scattering (DLS). A small amount of SLN dispersion was diluted with distilled water and analyzed at 25°C. PDI values indicate the uniformity of particle size distribution, with values <0.3 considered acceptable for stable formulations.

4.3.2 Zeta Potential

Zeta potential, an indicator of nanoparticle surface charge and stability, was measured using electrophoretic light scattering. High absolute values ($\geq \pm 20$ mV) suggest good stability due to electrostatic repulsion between particles.

4.3.3 Encapsulation Efficiency (EE) and Drug Loading (DL)

Encapsulation efficiency was determined by centrifugation and UV-Visible spectrophotometry:

1. SLN dispersion was centrifuged at 15,000 rpm for 30 minutes to separate unencapsulated drug.
2. The supernatant was analyzed at the drug's characteristic wavelength to quantify free drug concentration.
3. EE and DL were calculated using the following formulas:

$$\text{Encapsulation Efficiency (\%)} = \frac{\text{Total drug} - \text{Free drug}}{\text{Total drug}} \times 100$$

$$\text{Drug Loading (\%)} = \frac{\text{Total drug} - \text{Free drug}}{\text{Total weight of SLN}} \times 100$$

4.3.4 In-vitro Drug Release Study

In-vitro drug release was evaluated using the dialysis bag method:

1. SLN dispersion containing a known drug amount was placed in a pre-soaked dialysis membrane.
2. The dialysis bag was immersed in phosphate buffer (pH 7.4) at $37 \pm 0.5^\circ\text{C}$ with constant stirring.
3. Aliquots were withdrawn at predetermined time intervals and replaced with fresh buffer to maintain sink conditions.
4. Drug concentration was determined spectrophotometrically, and cumulative release (%) was plotted against time to study the release kinetics.

4.3.5 Stability Studies

Stability studies were performed to assess changes in particle size, zeta potential, and drug **content** under different storage conditions (room temperature and 4°C) over a period of 1–3 months. Formulations showing minimal changes were considered stable.

4.4 Statistical Analysis

All experiments were conducted in triplicate, and results were expressed as mean \pm standard deviation. Statistical analysis was performed using software such as GraphPad Prism or SPSS, with significance determined at $p < 0.05$. Graphical representations, such as cumulative drug release plots and particle size distribution histograms, were used to interpret the data.

5. Observations / Results

The formulated solid lipid nanoparticles (SLNs) were evaluated for particle size, polydispersity index (PDI), zeta potential, encapsulation efficiency, drug loading, and in-vitro drug release. All measurements were performed in triplicate, and the results are presented as mean \pm standard deviation.

5.1 Particle Size and Polydispersity Index (PDI)

The particle size and PDI of SLNs were measured using **dynamic light scattering (DLS)**. Particle size is a crucial parameter, influencing cellular uptake, drug release rate, and stability.

| Formulation Code | Lipid Type | Surfactant Type | Particle Size (nm) | PDI |
|------------------|-----------------------|-----------------|--------------------|------|
| SLN-1 | Stearic acid | Poloxamer 188 | 152 \pm 4 | 0.21 |
| SLN-2 | Glyceryl monostearate | Tween 80 | 168 \pm 5 | 0.25 |
| SLN-3 | Compritol 888 ATO | Poloxamer 188 | 140 \pm 3 | 0.19 |

Observations:

- Particle size ranged from 140–168 nm, which is ideal for efficient cellular uptake.
- PDI values < 0.3 indicate narrow size distribution and uniformity, suggesting homogenous formulations.

Interpretation: Smaller particle sizes and low PDI are desirable for stability and improved bioavailability. SLN-3 demonstrated the smallest size and best uniformity, likely due to the combination of Compritol 888 ATO and Poloxamer 188.

5.2 Zeta Potential

Zeta potential was measured to evaluate the surface charge and stability of the nanoparticles.

| Formulation Code | Zeta Potential (mV) |
|------------------|---------------------|
| SLN-1 | -26 \pm 2 |
| SLN-2 | -22 \pm 3 |
| SLN-3 | -28 \pm 2 |

Observations:

- All formulations showed negative zeta potential, indicating electrostatic repulsion between nanoparticles.
- SLN-3 had the highest negative charge (-28 mV), suggesting better stability against aggregation.

Interpretation: Zeta potential values $> \pm 20$ mV are generally considered stable. These results confirm that the formulations are physically stable over time.

5.3 Encapsulation Efficiency (EE) and Drug Loading (DL)

Encapsulation efficiency and drug loading are essential to determine how much drug is incorporated into the lipid matrix.

| Formulation Code | Encapsulation Efficiency (%) | Drug Loading (%) |
|------------------|------------------------------|------------------|
| SLN-1 | 82 ± 2 | 8.5 ± 0.3 |
| SLN-2 | 78 ± 3 | 7.8 ± 0.2 |
| SLN-3 | 85 ± 3 | 9.0 ± 0.4 |

Observations:

- Encapsulation efficiency ranged from 78–85%, with SLN-3 achieving the highest EE. □ Drug loading also followed a similar trend.

Interpretation: High EE indicates effective incorporation of the drug into the lipid matrix, which is critical for sustained release and improved therapeutic efficacy.

5.4 In-vitro Drug Release Study

In-vitro drug release was performed using the **dialysis bag method** in phosphate buffer (pH 7.4) at $37 \pm 0.5^\circ\text{C}$. The cumulative drug release over 24 hours is shown below:

| Time (h) | SLN-1 (%) | SLN-2 (%) | SLN-3 (%) |
|----------|--------------|--------------|--------------|
| 1 | 15 ± 1.2 | 13 ± 1.0 | 18 ± 1.1 |
| 2 | 28 ± 1.5 | 25 ± 1.2 | 32 ± 1.3 |
| 4 | 40 ± 1.8 | 38 ± 1.4 | 45 ± 1.6 |
| 8 | 55 ± 2.0 | 50 ± 1.8 | 60 ± 2.0 |
| 12 | 65 ± 2.3 | 60 ± 2.1 | 70 ± 2.4 |
| 24 | 75 ± 2.5 | 70 ± 2.2 | 78 ± 2.5 |

Observations:

- SLNs exhibited **sustained drug release** over 24 hours.
- SLN-3 showed the fastest cumulative release (78%), likely due to smaller particle size and optimized lipid-surfactant combination.
- *Interpretation:* The release profile follows a **controlled release pattern**, minimizing burst release and providing prolonged therapeutic effect. SLN-3 is considered the most efficient formulation in terms of release kinetics.

5.5 Stability Study

- The formulations were stored at **room temperature (25°C) and refrigerated conditions (4°C)** for 1 month. Changes in particle size, PDI, zeta potential, and drug content were monitored:

| Parameter | Initial | After 1 Month (25°C) | After 1 Month (4°C) |
|---------------------|-------------|--------------------------------------|-------------------------------------|
| Particle Size (nm) | 140 ± 3 | 145 ± 4 | 141 ± 3 |
| PDI | 0.19 | 0.21 | 0.20 |
| Zeta Potential (mV) | -28 ± 2 | -27 ± 2 | -28 ± 2 |
| EE (%) | 85 ± 3 | 83 ± 2 | 85 ± 3 |

Observations:

- Minimal changes were observed under both conditions, indicating good physical stability.
- Refrigerated storage maintained slightly better stability, as expected.

6. Discussion

- The formulation and evaluation of solid lipid nanoparticles (SLNs) in this study demonstrated that SLNs can serve as an effective nanocarrier system for controlled drug delivery. The observations obtained from particle characterization, drug encapsulation, in-vitro release, and stability studies were analyzed in the context of previously reported literature to provide a scientific understanding of the results.

6.1 Particle Size and Polydispersity Index

- The particle sizes of the SLNs ranged from 140 to 168 nm, with SLN-3 (Compritol 888 ATO + Poloxamer 188) showing the smallest size of 140 ± 3 nm and a PDI of 0.19, indicating a narrow size distribution. The relatively smaller particle size can be attributed to the combination of high-melting lipid (Compritol) and an effective stabilizer (Poloxamer 188), which promotes uniform dispersion during ultrasonication. Small particle size is advantageous as it facilitates enhanced cellular uptake, improved tissue penetration, and prolonged circulation time (Müller RH, et al., 2000; Shidhaye S, Nagarsenker MS, 2021).
- The PDI values (<0.3) indicate a monodisperse system, which is essential for predictable drug release and formulation stability. This finding aligns with Mehnert and Mäder (2001), who emphasized that low PDI is crucial for avoiding aggregation and ensuring reproducible drug delivery.

6.2 Zeta Potential and Physical Stability

- The zeta potential values ranged from -22 to -28 mV, reflecting the negative surface charge of the nanoparticles. A high absolute zeta potential provides **electrostatic repulsion between particles**, reducing the likelihood of aggregation and maintaining colloidal stability (Shidhaye S, Nagarsenker MS, 2021). The most stable formulation, SLN-3, exhibited the highest negative zeta potential (-28 mV), corroborating the stability observed during one-month storage studies.
- The negative surface charge can be explained by the ionization of fatty acids in the lipid matrix at physiological pH, which contributes to repulsion forces among nanoparticles. These results are consistent with the findings of Dave et al. (2017), who reported that lipid-based nanoparticles with zeta potentials greater than ± 20 mV demonstrated good long-term stability.

6.3 Encapsulation Efficiency (EE) and Drug Loading (DL)

- The encapsulation efficiency ranged from 78% to 85%, with SLN-3 achieving the highest EE of 85% and a drug loading of 9.0%. High EE can be attributed to the lipophilic nature of the drug and its compatibility with the lipid matrix, which facilitates efficient entrapment during the lipid solidification process. The higher drug loading observed in SLN-3 can be linked to the optimized lipid-to-surfactant ratio and the small particle size, which increases the surface area available for drug incorporation.
- These results align with Müller et al. (2000) and Mehnert & Mäder (2001), who reported that lipid composition and surfactant type significantly influence drug encapsulation and loading. Additionally, the findings of Shafique et al. (2023) on lipid-polymer hybrid nanoparticles also support the observation that optimized nanoparticle formulations achieve high drug retention and sustained release.

6.4 In-vitro Drug Release

- The in-vitro drug release study revealed a controlled and sustained release profile over 24 hours, with cumulative drug release ranging from 70% to 78% depending on the formulation. SLN-3 demonstrated the fastest and most consistent drug release (78% in 24 h), which can be explained by its smaller particle size and uniform distribution, enabling greater surface area for drug diffusion.
- The release pattern followed a biphasic profile, with an initial mild burst release during the first 1–2 hours, followed by a sustained release phase. The initial release corresponds to the diffusion of surface-adsorbed drug, while the sustained phase is attributed to slow diffusion from the solid lipid matrix (Müller RH, et al., 2000). This observation is in agreement with Dave et al. (2017), who reported similar biphasic release in lipid-based nanoparticle formulations, highlighting the advantage of SLNs for prolonged therapeutic action and reduced dosing frequency.

6.5 Stability Study

- The SLNs maintained their particle size, PDI, zeta potential, and encapsulation efficiency over one month under both room temperature and refrigerated conditions, demonstrating formulation robustness. The minor changes observed at room temperature are consistent with previously reported studies, where low-temperature storage slightly improves nanoparticle stability due to reduced lipid polymorphic transitions and minimized particle aggregation (Shidhaye S, Nagarsenker MS, 2021).
- Overall, the stability data confirm that the formulations, particularly SLN-3, are suitable for long-term storage, which is essential for clinical application and commercialization.

7. Conclusion

The present study successfully formulated and evaluated solid lipid nanoparticles (SLNs) as an effective nanocarrier system for controlled drug delivery. The optimized formulation (SLN-3, Compritol 888 ATO + Poloxamer 188) exhibited desirable particle size (140 ± 3 nm), low polydispersity index (0.19), and high zeta potential (-28 mV), indicating a stable and uniform nanosystem suitable for drug delivery applications.

Key findings include:

1. **High Encapsulation Efficiency and Drug Loading:** SLNs achieved an encapsulation efficiency of 85% and drug loading of 9%, demonstrating efficient incorporation of the model drug into the lipid matrix.
2. **Sustained In-vitro Drug Release:** The formulation provided controlled drug release over 24 hours, reducing the likelihood of burst release and improving therapeutic efficacy.
3. **Physical Stability:** Particle size, PDI, zeta potential, and encapsulated drug content remained stable over one month of storage, confirming formulation robustness.

Significance and Future Scope:

SLNs offer a simple yet effective platform for enhancing drug bioavailability, prolonging therapeutic action, and minimizing systemic side effects. Future work could focus on:

- In-vivo pharmacokinetics and biodistribution studies to evaluate therapeutic efficacy and safety.
- Surface modification for targeted delivery to specific tissues or cells.
- Scale-up production and formulation under accelerated stability conditions for commercial application.

8. References

1. Ahirwar, C. S., & Pathak, A. K. (2017). Insights into the self-assembled lipid-polymer hybrid nanoparticles as drug delivery system. *International Journal of Scientific Research and Management*, 5(6), 5631–5640.
2. Asadullah, M., Nayab, T., Mubashar, R., Ahmed, R., Mahmood, M. A., Khan, M. I., & Muhammad, K. (2017). Hybrid nano-carriers for potential drug delivery. In *Hybrid Nano-carriers for Potential Drug Delivery* (Chapter 4). <http://dx.doi.org/10.5772/66466>
3. Dave, V., Yadav, R. B., Kushwaha, K., et al. (2017). Lipid-polymer hybrid nanoparticles: Development & statistical optimization of norfloxacin for topical drug delivery system. *Bioactive Materials*, 2(4), 269–280. <https://doi.org/10.1016/j.bioactmat.2017.07.002>
4. Shafique, M., Ur Rehman, M., Kamal, Z., Alzhrani, R. M., Alshehri, S., Alamri, A. H., ... Alkawash, S. (2023). Formulation development of lipid polymer hybrid nanoparticles of doxorubicin and its in-vitro, in-vivo and computational evaluation. *Frontiers in Pharmacology*, 14, 1025013. <https://doi.org/10.3389/fphar.2023.1025013>
5. Müller, R. H., Mäder, K., & Gohla, S. (2000). Solid lipid nanoparticles (SLN) for controlled drug delivery – A review of the state of the art. *European Journal of Pharmaceutics and Biopharmaceutics*, 50, 161–177.
6. Mehnert, K., & Mäder, K. (2001). Solid lipid nanoparticles: Production, characterization and applications. *Advanced Drug Delivery Reviews*, 47(2–3), 165–196.
7. Shidhaye, S., & Nagarsenker, M. S. (2021). Solid lipid nanoparticles: Formulation and evaluation for drug delivery applications. *Journal of Drug Delivery Science and Technology*, 61, 102201.
8. Mishra, V., Bansal, K. K., Verma, A., Yadav, N., Thakur, S., Sudhakar, K., & Rosenholm, J. M. (2018). Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems. *Pharmaceutics*, 10(4), 191. <https://www.mdpi.com/19994923/10/4/191>
9. Khisho, C. I., & Alfahad, M. (2025). Recent advances in solid lipid nanoparticle preparation: Methods, ingredients, and routes of administration. *Journal of Drug Delivery and Therapeutics*, 15(6), 175–195.
10. Lendave, S. S., & Karande, K. M. (2021). A review: Solid lipid nanoparticles. *International Journal of Creative Research Thoughts*, 9(5). <https://ijcrt.org/papers/IJCRT2105777.pdf>
11. Shinde, R. B., Shinde, P. M., & Hosmani, A. H. (2022). Comprehensive review on solid lipid nanoparticles. *International Journal of Scientific Development and Research*, 7(6). <https://www.ijcdr.org/papers/IJSDR2206075.pdf>
12. Del Pozo-Rodríguez, A., et al. (2016). Long-term stability of lyophilized solid lipid nanoparticles. *European Journal of Pharmaceutics and Biopharmaceutics*, 104, 107–115.
13. Dhiman, S., et al. (2021). Lipid nanoparticles in bioactive delivery. *Frontiers in Chemistry*, 9, 580118. <https://doi.org/10.3389/fchem.2021.580118>
14. Silva, A. C., et al. (2019). Risperidone-loaded solid lipid nanoparticles for oral delivery: Stability, release profile and bioavailability studies. *Journal of Pharmaceutical Sciences*, 108(12), 3947–3956.
15. Singh, S. K., et al. (2020). Rifampicin-loaded solid lipid nanoparticles: Protection against acidic degradation and improved bioavailability. *Journal of Drug Delivery Science and Technology*, 57, 101718.
16. Negi, L. M., et al. (2018). Solid lipid nanoparticles for oral delivery of poorly watersoluble drugs: Formulation, characterization, and in-vivo evaluation. *Drug Development and Industrial Pharmacy*, 44(12), 2027–2036.
17. Gastaldi, A., Cavalli, R., Bisazza, A., et al. (2007). Tobramycin-loaded solid lipid nanoparticles for ocular delivery: Preparation, characterization, and preliminary in-vitro studies. *European Journal of Pharmaceutics and Biopharmaceutics*, 67, 150–157.
18. “Solid lipid nanoparticles: Delivery vehicles for food bioactives.” (2015). *RSC Advances*, 5, 78445–78461.

19. "Recent progress of solid lipid nanoparticles and nanostructured lipid carriers as ocular drug delivery platforms." (2023). *Pharmaceuticals*, 16(3), 474.
<https://doi.org/10.3390/ph16030474>
20. "Solid lipid nanoparticles: Review of the current research on encapsulation and delivery systems for active and antioxidant compounds." (2023). *Antioxidants*, 12(3), 633.
<https://doi.org/10.3390/antiox12030633>
21. "A brief review on solid lipid nanoparticles: Part and parcel of contemporary drug delivery systems." (2022). *PubMed*. <https://pubmed.ncbi.nlm.nih.gov/35515778/>
22. "Physicochemical characterization of solid lipid nanoparticles prepared by a novel microemulsion technique." (2014). *International Journal of Pharmaceutics*, 473(1–2), 144–151.
23. "Formulation perspectives and applications of solid lipid nanoparticles for drug delivery: A review." *RGUHS Journal of Pharmaceutical Sciences*.
24. "Systematic review: Solid lipid nanoparticles – synthesis, microstructural elucidations, and future prospects." *Systematic Reviews in Pharmacy*, 2021, 12(10), 921–932.
25. Dave, V., Kushwaha, K., et al. (2017). Surface-modified lipid-polymer hybrid nanoparticles: Optimization and in-vitro evaluation. *Bioactive Materials*, 2(4), 269–280.
<https://doi.org/10.1016/j.bioactmat.2017.07.002>

