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Solid Lipid Nanoparticles: A Carrier for Modern Therapeutics

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Abstract: Solid Lipid Nanoparticles (SLNs) are colloidal drug delivery systems consisting of a solid lipid matrix stabilized by surfactants. They are particularly advantageous for poorly soluble drugs (BCS Class II and IV) owing to their biocompatibility, reduced toxicity, and ability to enhance stability, absorption, and controlled release. The solid lipid matrix minimizes drug migration, lowers molecular mobility, and delays lipid digestion, thereby sustaining drug release and protecting chemically sensitive compounds. SLNs can be prepared by several techniques, including high-pressure homogenization, microemulsion, solvent emulsification–diffusion, double emulsion, membrane contactor, precipitation, solvent injection, and film–ultrasound dispersion. Post-processing methods such as lyophilization and spray drying are used to improve long-term stability. Characterization involves particle size and zeta potential determination using Dynamic Light Scattering (DLS), Static Light Scattering (SLS), electron microscopy, acoustic methods, and Nuclear Magnetic Resonance (NMR). Crystallinity is assessed by Differential Scanning Calorimetry (DSC) and Powder X-ray Diffraction (PXRD), while entrapment efficiency and drug loading are quantified by direct extraction or separation followed by analytical methods such as HPLC or UV–Visible spectrophotometry. In vitro release studies commonly employ dialysis tubing and reverse dialysis, whereas ex vivo intestinal models assess permeability and absorption. Despite limitations such as gel formation and reduced drug loading, SLNs remain a promising platform for improving bioavailability and controlled delivery of therapeutic agents.

Keywords: *Solid Lipid Nanoparticles (SLNs); Drug Delivery; Bioavailability; Controlled Release; High-Pressure Homogenization; Lyophilization; Particle Size; in Vitro Drug Release.*

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I. INTRODUCTION

Solid Lipid Nanoparticles (SLNs) are colloidal carrier systems consisting of a solid lipid core- typically a high-melting-point lipid-surrounded by an aqueous surfactant layer. These systems are particularly useful for delivering drugs classified under BCS Class II and IV[1]. The term "lipid" broadly encompasses triglycerides, partial glycerides, fatty acids, hard fats, and waxes. One significant advantage of SLNs is their composition of physiologically compatible lipids, which reduces the risk of both acute and chronic toxicity[2]. Using solid lipids instead of liquid ones offers better control over the drug release profile and enhances the stability of chemically sensitive lipophilic compounds. Several physicochemical properties of solid lipids contribute to these benefits. First, the limited mobility of reactive molecules in a solid matrix slows down chemical degradation. Second, solid lipids help minimize micro-phase separation between the drug and carrier lipid within each particle, reducing the likelihood of drug migration to the particle surface, where it is more vulnerable to degradation. Third, SLNs have been shown to enhance the absorption of poorly bioavailable compounds. Moreover, the solid matrix can slow down lipid digestion, resulting in a more sustained release of the encapsulated drug. Surfactants, another key component of SLNs, act as emulsifying agents to form oil-in-water (o/w) emulsions and stabilize the SLN dispersion. The selection of surfactants largely depends on the intended route of administration. Typically, SLNs consist of a solid, hydrophobic core in which the drug is either dissolved or dispersed[3]. Solid Lipid Nanoparticles (SLNs) are primarily produced using techniques like high-pressure homogenization or micro emulsification. Regardless of the method used, SLNs are initially obtained in a dispersed form.

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However, prolonged storage of these dispersions can lead to instability, mainly due to hydrolytic degradation. To enhance their stability, SLNs can be transformed into dry, reconstitutable powders through lyophilization. An economical and simpler alternative to lyophilization is the spray drying method[4]. Lipid nanoparticles are classified into two main types: Nanostructured Lipid Carriers (NLCs), which are composed of a blend of solid and liquid lipids at room temperature, and Solid Lipid Nanoparticles (SLNs), which are made entirely of solid lipids at temperatures between 20–28°C. Despite their advantages, SLNs present certain limitations such as a tendency to form a gel-like structure, high water diffusion, reduced drug loading capacity, increased mobility of polymers, and structural instability. These issues can result in drug leakage, challenges in formulation optimization, and, in some cases, complex manufacturing processes.[5]

Solid lipid nanoparticles (SLNs) are generally spherical in morphology with a particle size ranging from 10 to 1000 nm. Their solid lipid core provides an efficient medium for the incorporation and solubilization of lipophilic therapeutic agents[6-8]. The choice of lipid matrix depends on the intended route of administration, with injectable formulations being comparatively more restricted. In this context, the term “lipid” is used in a broad sense, encompassing fatty acids (e.g., stearic acid), steroids (e.g., cholesterol), waxes (e.g., acetyl palmitate), triglycerides (e.g., tristearin), diglycerides (e.g., glycerol derivatives), and monoglycerides (e.g., glycerol monostearate). Emulsifiers, also referred to as surface-active agents, play a crucial role in dispersing and stabilizing the lipid phase. Studies indicate that a combination of emulsifiers is more effective in reducing particle aggregation and enhancing colloidal stability. Structurally, SLNs consist of a solid lipid core stabilized by surfactants, and are predominantly composed of fatty acids, acylglycerols, waxes, or suitable combinations thereof.

In addition to the primary lipid components, membrane lipids such as sphingomyelins, phospholipids, bile salts (e.g., sodium taurocholate), and sterols particularly cholesterol contribute to the biological stabilization of SLNs. Natural lipids are generally favoured because of their lower cytotoxicity and solid-state nature, which offers greater resistance to mass transfer and facilitates controlled drug release[9-10].

The choice of preparation technique is influenced by parameters such as particle size, drug loading capacity, release kinetics, and drug stability[11]. SLNs are typically composed of lipids, emulsifiers, and an aqueous or solvent phase, and structurally they represent a phospholipid-coated solid hydrophobic lipid core matrix[12].

A variety of techniques have been developed for SLN production, including[13] which is represented in Figure 1:

- Pressure-Based Homogenization
- Microemulsion Approach
- Membrane-Assisted Technique
- Ultrasonication (Probe or Bath Method)
- Spray-Drying Approach
- Double-Emulsion Technique
- Supercritical Fluid Approach
- Solvent Emulsification and Diffusion Technique

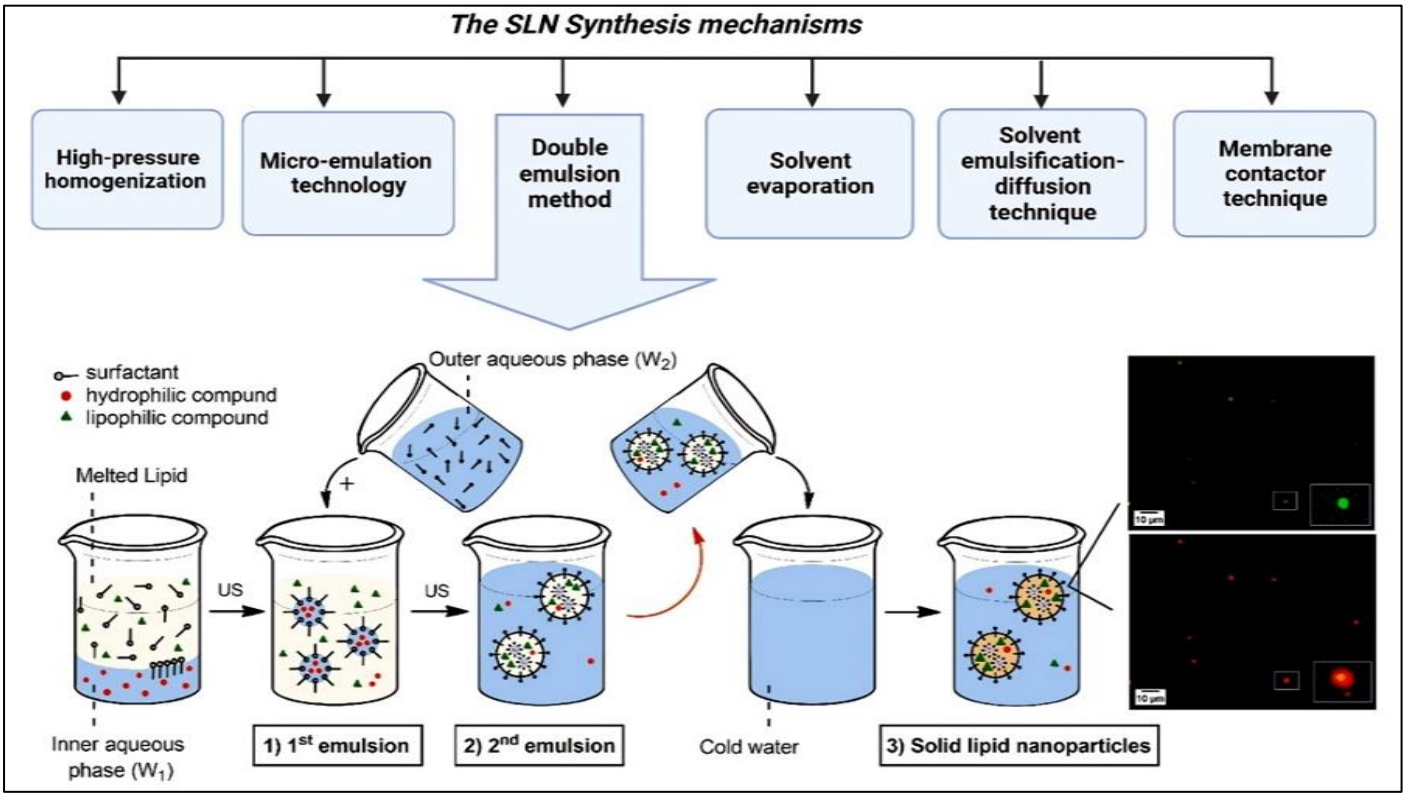

Fig 1 SLN Synthesis Mechanism

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In high-pressure homogenization (100–2000 bar), the formulation is forced through a narrow gap of micrometer dimensions, resulting in rapid acceleration of the fluid to high velocity. In this process, the application of intense shear stress and turbulence helps to break down the particles to the submicron size range, ensuring uniformity in the dispersion. The technique can be carried out in two principal ways: hot homogenization and cold homogenization. In both approaches, the central goal is to effectively incorporate the drug into the molten lipid phase, thereby enhancing drug stability and ensuring controlled release in the final nanoparticle formulation. In both methods, the lipid and drug are initially heated to about 5–10 °C higher than the melting point of the lipid. enabling uniform dispersion of the drug molecules within the molten lipid. This lipid phase is then combined with an aqueous phase containing amphiphilic stabilizers.A hot pre-emulsion is first produced using high-speed stirring, after which it is subjected to three to five cycles through a homogenizer operated at elevated pressures (100–1000 bar).

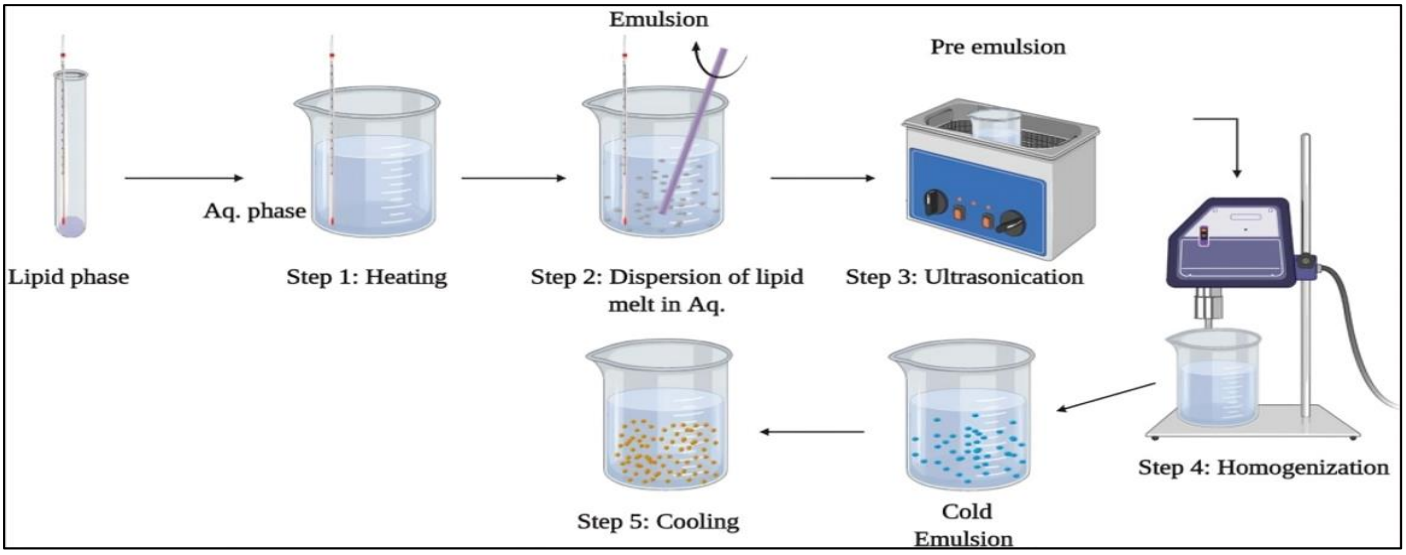

Fig 2 High Pressure Homogenization

The microemulsion dilution technique is based on a biphasic system comprising an inner and outer phase. Typically, a transparent mixture of emulsifier, co-emulsifier, a low-melting fatty acid, and water is homogenized at 65–70 °C. The surfactants are preheated to the lipid's melting point and incorporated into the molten lipid under gentle mixing. The formed microemulsion is slowly introduced into cold water (4 °C) under mechanical stirring, often by dropwise addition from a temperature-controlled reservoir[17-18]. This method requires relatively low mechanical energy and offers high stability; however, it is highly sensitive to changes in formulation parameters and allows only limited particle and drug concentrations.

In another approach using the microemulsion technique, lipophilic compounds are first dissolved in a water-immiscible organic solvent, which is subsequently emulsified in an aqueous phase. This technique produces nanoparticles with an average diameter of around 25 nm, as the lipid solidifies within the aqueous phase. Following emulsification, the organic solvent is evaporated and eliminated[19-20]. Advantages of this method include scalability, technological maturity, continuous processing, and proven commercial feasibility. However, this method also has limitations, including high energy consumption, wide particle size distribution, and the risk of biomolecule degradation.

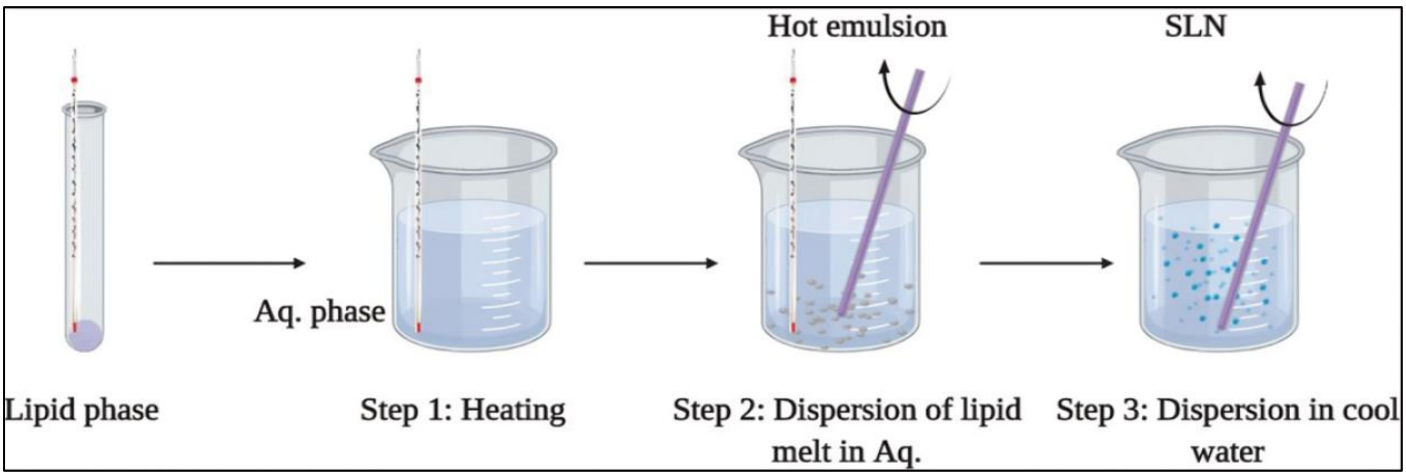

Fig 3 Microemulsion Technique

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The solvent emulsification–diffusion method involves dissolving the lipid in a water-saturated organic solvent under constant stirring, followed by emulsification with an aqueous phase. Subsequent dilution with water facilitates diffusion of the solvent into the continuous phase, leading to the precipitation of lipid nanoparticles. This technique typically produces particles in the range of 30–100 nm[21].

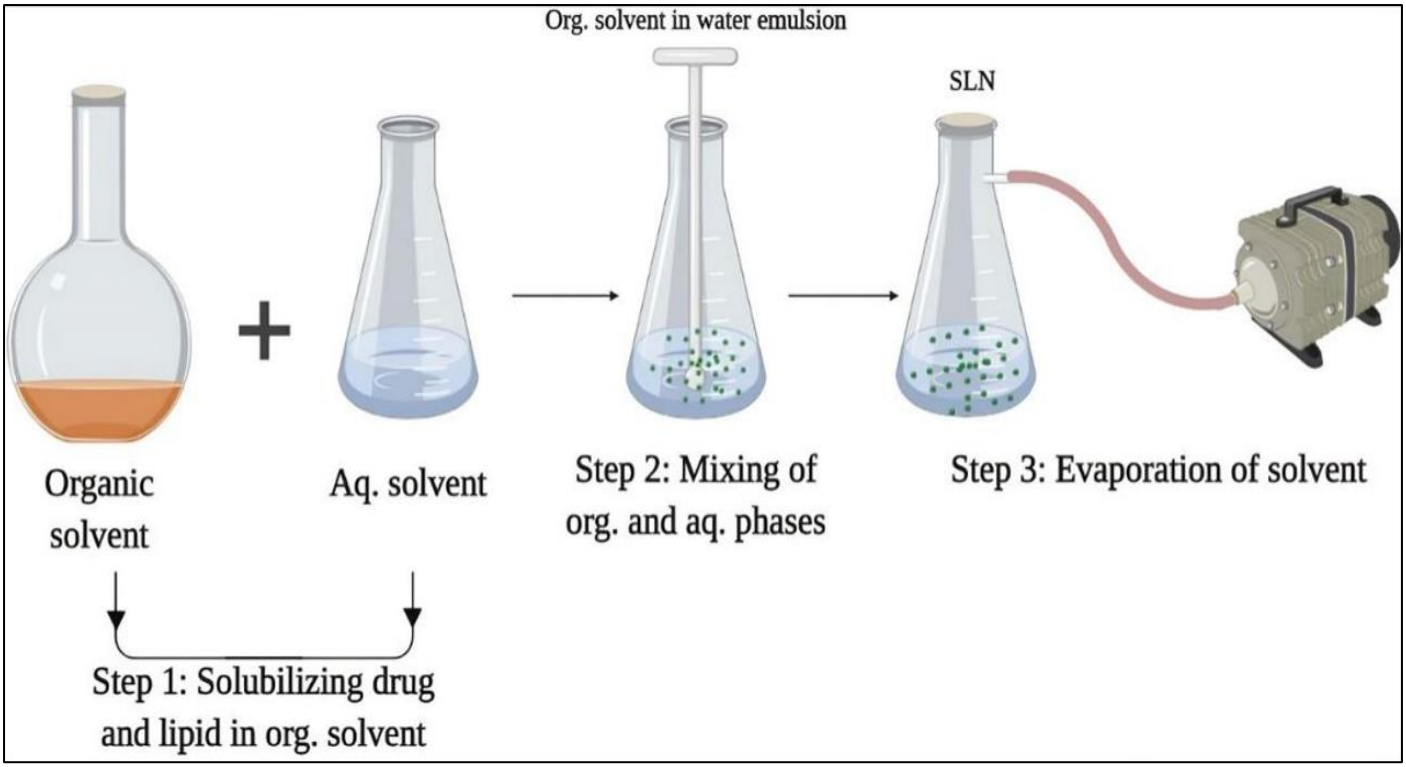

Fig 4 Solvent Emulsification Technique

In the w/o/w double emulsion method, solvent evaporation is employed to encapsulate hydrophilic drugs within a lipid matrix, thereby minimizing drug leakage into the external aqueous phase. This approach is particularly suitable for the entrapment and delivery of hydrophilic therapeutics and biomolecules such as peptides. For instance, in insulin-loaded SLNs, insulin is first dissolved in the innermost aqueous phase (acidic medium), while the lipid is solubilized in an organic phase. Upon dilution with water, SLNs are formed. Critical parameters in this process include the physicochemical properties of the solvent and its interaction with the hydrophilic drug, both of which strongly influence nanoparticle formation[22].

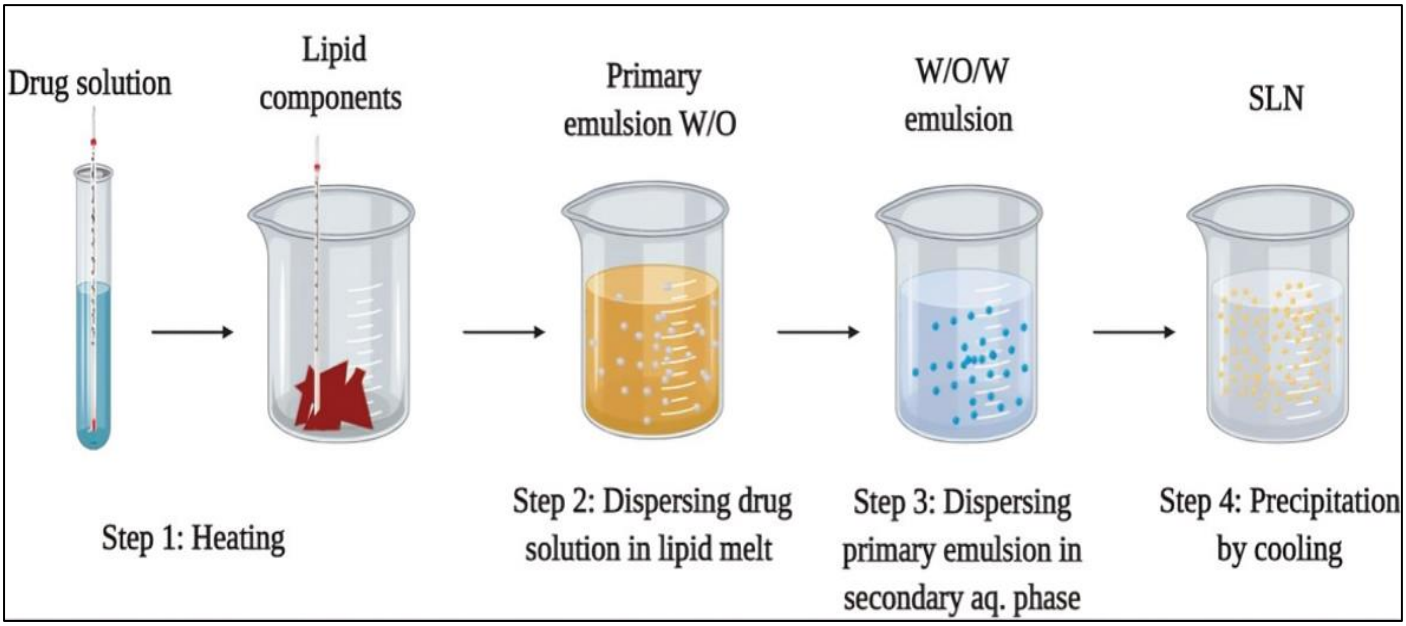

Fig 5 Double Emulsi Fication Technique

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In the membrane contactor method, the aqueous and organic phases are kept apart within a thermostatically controlled water bath. When subjected to elevated pressure and temperature, lipid droplets are formed, which then solidify as the system is cooled to20 °C. Nitrogen is often used to prevent oxidation, and both phases are required to be purified to enhance stability. The method follows three main steps: (i) preparation of a matrix comprising surfactant, co-surfactant, lipids, drug molecules, and polymers at 55–70 °C; (ii) addition of preheated water under continuous stirring to form emulsions; and (iii) gradual cooling to 20 °C with constant agitation to yield SLNs[23-24]

➢ *Precipitation Technique*

Solid lipid nanoparticles (SLNs) may also be prepared using the precipitation technique. which involves the use of organic solvents. In this approach, glycerides are first dissolved in an organic solvent such as chloroform, followed by emulsification into an aqueous phase. Upon evaporation of the solvent, the lipid precipitates, leading to the formation of nanoparticles[25].

➢ *Film-Ultrasound Dispersion Technique*

In this method, the drug and lipid are initially dissolved in a suitable organic solvent. After decompression, rotary evaporation is applied to remove the solvent, leaving behind a thin lipid film. An aqueous solution containing emulsifiers is then added, and ultrasonic probe dispersion is used to achieve uniform particle size distribution, ultimately yielding SLNs with small and homogeneous dimensions[25.]

➢ *Solvent Injection Technique*

The solvent injection method represents a relatively simple and efficient approach for SLN preparation. In comparison with other techniques, this method provides benefits like the use of pharmaceutically safe organic solvents, simple operation, fast processing, and no need for sophisticated equipment. The principle relies on lipid precipitation from an organic solution, where the lipid is first dissolved in a solvent that is miscible with water (e.g., ethanol, acetone, or isopropanol) or a mixture thereof, and the solution is injected through a fine needle into a stirred aqueous phase containing surfactant. The emulsifier present in the aqueous phase reduces interfacial tension, thereby facilitating the formation of lipid droplets at the injection site and stabilizing the SLNs until solvent diffusion is complete. The resulting dispersion is filtered to remove excess lipid, ensuring a stable nanoparticulate system.[25-28]

II. POST-PROCESSING AND STABILIZATION STRATEGIES FOR SOLID LIPID NANOPARTICLES

➢ *Lyophilization*

Lyophilization is widely regarded as a valuable strategy for enhancing the chemical and physical stability of SLNs over prolonged storage periods. It is particularly required when formulating products containing hydrolyzable drugs or when designing dosage forms suitable for oral administration. Converting SLNs into a solid state prevents Ostwald ripening and reduces the likelihood of hydrolytic degradation. However, freeze-drying often results in the formation of larger nanoparticles with broader size distribution due to aggregation among particles. This aggregation is promoted by the removal of water and the specific conditions applied during the lyophilization process. The incorporation of suitable cryoprotectants can minimize aggregation and preserve the nanoparticulate structure during freeze drying[29-33.]

➢ *Spray Drying*

Spray drying offers a cost-effective alternative to lyophilization for improving the stability of SLNs. This method is particularly recommended for lipids with melting points above 70 °C. Optimal results have been reported with formulations containing 1% SLN in aqueous Trehalose or a 20% trehalose solution in ethanol–water mixtures is employed. The addition of carbohydrates along with low lipid concentrations aids in preserving the colloidal particle size throughout the process. Additionally, employing ethanol–water mixtures instead of pure water minimizes lipid melting during drying, as the cooling effect of ethanol promotes the formation of smaller and less heterogeneous crystals, particularly under reduced inlet temperature conditions[25,30].

➢ *Measurement of Particle Size and Zeta Potential of Solid Lipid Nanoparticles (SLNs)*

The determination of particle size and zeta potential is essential for evaluating the stability, dispersion quality, and functional performance of SLNs. Several instrumental techniques are commonly employed, each providing specific insights into nanoparticle characteristics.

- *Photon Correlation Spectroscopy (PCS) / Dynamic Light Scattering (DLS)*

PCS, also known as DLS, measures fluctuations in the intensity of laser light scattered by particles undergoing Brownian motion in a liquid medium. These fluctuations are correlated to obtain the diffusion coefficient, which is further used to calculate the hydrodynamic diameter of nanoparticles using the Stokes–Einstein equation. This method is effective for measuring particles in the range of a few nanometers to around 3 microns and is widely used for nanoparticle size distribution analysis.

- *Static Optical Scattering / Fraunhofer Diffraction Technique*

SLS is a bulk measurement technique that analyzes the intensity of light scattered at various angles by a suspension of particles is recorded. The data is then fitted using Mie theory or Fraunhofer diffraction models to determine particle size distribution. This method is suitable for analyzing systems that contain a broad range of particle sizes, including both nanosized and microsized particles.

- *Acoustic Methods*

Acoustic techniques rely on measuring the attenuation of ultrasonic waves as they pass through a dispersion of nanoparticles. The degree of sound wave attenuation is influenced by particle size, concentration, and compressibility. By applying appropriate theoretical models, the particle size distribution of the system can be derived.

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- *Nuclear Magnetic Resonance (NMR)*

NMR techniques use the magnetic properties of atomic nuclei to provide insights into nanoparticle size and structure. Pulsed-field gradient NMR measures the self-diffusion coefficients of nanoparticles in a suspension. These diffusion values are mathematically correlated with particle size, offering both quantitative and qualitative information about nanoparticle dimensions and characteristics.

- *Electron Microscopy*

✓ Scanning Electron Microscopy (SEM): SEM produces high-resolution images of nanoparticle surfaces by detecting secondary electrons emitted when a focused electron beam scans the particle surface. It provides direct visualization of particle shape, surface morphology, and aggregation state.
✓ Transmission Electron Microscopy (TEM): TEM operates by transmitting an electron beam through an ultrathin sample, producing images at extremely high resolution. It allows direct measurement of particle size and visualization of internal structure, enabling detailed nanoscale characterization.

- *Zeta Potential Measurement*

Zeta potential is determined by measuring the electrophoretic mobility of particles in a dispersion subjected to an external electric field. The obtained mobility values are converted to zeta potential using the Smoluchowski equation. Zeta potential represents the surface charge of nanoparticles, which plays a crucial role in predicting dispersion stability and interactions within the medium.

➢ *Measurement of Crystallinity and Lipid Modifications*

The crystallinity of lipids in solid lipid nanoparticles (SLNs) can be evaluated using Powder X-ray Diffraction (PXRD) and Differential Scanning Calorimetry (DSC), which provide information on crystal structure, melting, and glass transition behavior. Drug incorporation capacity decreases with increasing lipid order, following: *supercooled melt* < *α-form* < *β'-form* < *β-form*. The nanoscale size of SLNs and emulsifier presence often delay lipid crystallization.

Other techniques like infrared (IR) and Raman spectroscopy can probe structural properties, though less explored in SLNs. Furthermore, Nuclear Magnetic Resonance (NMR) and Electron Spin Resonance (ESR) help study dynamic molecular events and nano-compartments. Dilution of SLN dispersions may cause surfactant removal, triggering crystallinity and structural changes.

➢ *Estimation of Drug Incorporation (Loading Capacity and Entrapment Efficiency)*

The quantification of drug encapsulated in solid lipid nanoparticles (SLNs) is an essential step in their characterization, as it determines both the loading efficiency (LE) and entrapment efficiency (EE) of the formulation. These parameters reflect how much of the drug is successfully incorporated into the lipid matrix relative to the total drug used, which directly influences the release profile and therapeutic performance of SLNs[34-35].

➢ *Separation of Free and Entrapped Drug*

Before measurement, it is necessary to separate the free drug (unencapsulated) from the entrapped drug within the lipid core. Different techniques are employed for this separation:

- *Centrifugation and Filtration*

✓ SLN dispersions are subjected to high-speed centrifugation.
✓ Special membranes, such as Ultrafree®-MC (Millipore) or Ultrasart®-10 (Sartorius), are used in combination with centrifugation to retain nanoparticles while allowing the free drug to pass through.
✓ After separation, the supernatant (containing free drug) is analyzed, while the sediment (SLNs) can be dissolved in a suitable organic solvent to release the entrapped drug.

- *Ultracentrifugation*

✓ High centrifugal forces sediment the SLNs, and the concentration of drug in the clear supernatant is determined.
✓ The difference between the total drug added and the amount present in the supernatant corresponds to the entrapped fraction.

- *Gel Permeation Chromatography (GPC)*

✓ A column packed with gels such as Sephadex® or Sepharose® is first calibrated using free drug and SLN dispersions.
✓ SLN formulations are loaded onto the column and then eluted using an appropriate buffer solution.
✓ The free drug elutes separately, while SLN fractions are collected and later dissolved or extracted to determine actual drug content.

➢ *Analytical Methods for Drug Quantification*

Once the separation is complete, different analytical methods are used to measure drug content:

- UV–Visible Spectrophotometry – used for drugs with characteristic absorbance in the UV-Vis range.
- Spectrofluorophotometry – applied for fluorescent drugs or drugs derivatized with fluorescent markers.
- High-Performance Liquid Chromatography (HPLC) – a highly accurate and sensitive technique, especially suitable for complex formulations.
- Liquid Scintillation Counting – used for radiolabeled drugs to quantify entrapment with precision.

➢ *Direct Drug Extraction Method*

Rather than using indirect methods, the drug content may also be measured directly through extraction. The entrapped drug from SLNs using a suitable solvent under optimized conditions. The drug is released from the lipid

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matrix into the solvent, and the aqueous extract is subsequently analyzed by one of the above-mentioned techniques.

➢ *In Vitro and Ex Vivo Methods for Evaluating Drug Release from SLNs*

Solid lipid nanoparticles (SLNs) have been investigated as carriers for a wide range of drugs, including highly hydrophilic compounds. To study their release characteristics, several ***in vitro*** techniques are commonly employed, such as:

- Side-by-side diffusion cells using either artificial or biological membranes.
- Dialysis bag diffusion method.
- Reverse dialysis bag method.
- Agitation followed by ultracentrifugation

➢ *In Vitro and Ex vivo Evaluation of Drug Release from SLNs*

- *Dialysis Tubing Method*

This is one of the most commonly used techniques to study drug release from Solid Lipid Nanoparticles (SLNs). In this method, the nanoparticle dispersion containing the drug is placed inside a dialysis sac (or tubing) that has been pre-washed to remove impurities. The sac is tightly sealed to avoid leakage and then immersed in a suitable dissolution medium (such as phosphate buffer) at controlled room temperature.

✓ The dialysis membrane acts as a barrier, allowing only the released drug molecules (not the nanoparticles) to diffuse into the medium.
✓ At fixed time intervals, samples are withdrawn from the external medium, centrifuged if necessary, and analyzed using analytical techniques such as UV–Visible spectrophotometry, HPLC, or spectrofluorimetry to determine the amount of drug released.
✓ This method gives a controlled simulation of how the drug is released in a biological system.

- *Reverse Dialysis Method*

Unlike the conventional dialysis tubing method, reverse dialysis involves placing multiple small dialysis sacs, each containing a known volume (usually 1 mL) of dissolution medium, into a bulk SLN dispersion.

✓ In this setup, instead of the drug diffusing out from the sac, the drug from the SLN dispersion diffuses into the dialysis sacs.
✓ After specified intervals, the sacs are removed, and the medium inside is analyzed to determine the extent of drug release.
✓ This technique is particularly useful for poorly water-soluble drugs and offers a way to assess drug transfer directly from nanoparticles to a surrounding aqueous environment.

- *Ex Vivo Intestinal Permeability Studies*

Ex vivo methods are designed to simulate drug absorption across the intestinal mucosa and provide a more realistic evaluation of drug transport from SLNs.

✓ In these studies, freshly excised segments of animal intestine (commonly rat or rabbit) are used. For example, Ahlin et al. studied the transport of Enalaprilat-loaded SLNs through the rat jejunum (located 20–30 cm away from the pyloric sphincter).
✓ Similarly, Qing Zhi Lu et al. excised different sections of the rat intestine, including the duodenum, jejunum, ileum, and colon. These segments were immediately cannulated (inserted with tubing for drug flow) and ligated (tied at both ends) to maintain closed sections.
✓ The SLN formulation is introduced into these segments, and the movement of drug molecules across the intestinal wall is monitored over time.
✓ This setup provides direct information about site-specific absorption and the potential for oral delivery of the drug[36].

III. CONCLUSION

Solid Lipid Nanoparticles (SLNs) are advanced nanocarriers that improve the delivery of both lipophilic and hydrophilic drugs by enhancing stability, bioavailability, and controlled release while reducing toxicity. Various preparation and post-processing methods enable optimization of particle size, drug loading, and long-term stability. Characterization techniques ensure reproducibility and therapeutic efficiency, while *in vitro* and ex vivo studies confirm their potential for sustained and site-specific delivery. Although challenges such as low drug loading and formulation complexity remain, ongoing advancements continue to overcome these issues. Overall, SLNs represent a promising platform for future pharmaceutical, nutraceutical, and biomedical applications.

➢ *Conflict of Interest*

The author declares that there is conflict of interest.

- Funding Source: None
- Ethical Statements: None

REFERENCES

[1]. Loxley A. Solid Lipid Nanoparticles for the Delivery of Pharmaceutical Actives. Drug Delivery Technology2009; 9 Suppl 8 :32
[2]. Mandawgade SD, Patravale VB. Development of SLNs from natural lipids: Application to topical delivery of tretinoin. International Journal of Pharmaceutics2008; 363 :132-138.
[3]. Helgason T, Awad TS, Kristbergsson K, McClements DJ, Weiss J. Effect of surfactant surface coverage on formation of solid lipid nanoparticles (SLN). Journal of Colloid and Interface Science2009; 334 :75–81
[4]. Sinha VR, Srivastava S, Goel H, Jindal V. Solid Lipid Nanoparticles (SLN'S) – Trends and Implications in Drug Targeting. International Journal of Advances in Pharmaceutical Sciences2010; 1 :212-238.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25sep096

[5]. Prastiwi N., Lesbatta K. Application of solid lipid nanoparticles preparation in infection caused by antibiotic-resistant bacteria. Indonesian Journal of Pharmacology and Therapy.2(3).
[6]. A. Zielinska, ´ N.R. Ferreira, A. Feliczak-Guzik, I. Nowak, E.B. Souto, Loading, release profile and accelerated stability assessment of monoterpenes-loaded solid lipid nanoparticles (SLN), Pharm. Dev. Technol. 25 (7) (2020) 832–844
[7]. G. Amasya, A.D. Ergin, O.E. Cakirci, A.T. Ozçelikay, Z.S. Bayindir, N. Yuksel, A study to enhance the oral bioavailability of s-adenosyl-l-methionine (SAMe): SLN and SLN nanocomposite particles, Chem. Phys. Lipids 237 (2021) 105086
[8]. S. Scioli Montoto, G. Muraca, M.E. Ruiz, Solid lipid nanoparticles for drug delivery: pharmacological and biopharmaceutical aspects, Front. Mol. Biosci. 7 (2020) 587997.
[9]. M. Muchow, P. Maincent, R.H. Müller, Lipid nanoparticles with a solid matrix (SLN®, NLC®, LDC®) for oral drug delivery, Drug Dev. Ind. Pharm. 34 (12) (2008) 1394–1405.
[10]. S.B. Routray, C.N. Patra, R. Raju, K.C. Panigrahi, G.K. Jena, Lyophilized SLN of Cinnacalcet HCl: BBD enabled optimization, characterization and pharmacokinetic study, Drug Dev. Ind. Pharm. 46 (7) (2020) 1080–1091.
[11]. A. Alsaad, A.A. Hussien, M.M. Gareeb, Solid lipid nanoparticles (SLN) as a novel drug delivery system: a theoretical review, Syst. Rev. Pharm. 11 (5) (2020) 259–273.
[12]. Y. Duan, A. Dhar, C. Patel, M. Khimani, S. Neogi, P. Sharma, et al., A brief review on solid lipid nanoparticles: Part and parcel of contemporary drug delivery systems, RSC Adv. 10 (45) (2020) 26777–26791.
[13]. V.J. Lingayat, N.S. Zarekar, R.S. Shendge, Solid lipid nanoparticles: a review, Nanosci. Nanotechnol. Res. 4 (2) (2017) 67–72
[14]. S. Scioli Montoto, G. Muraca, M.E. Ruiz, Solid lipid nanoparticles for drug delivery: \pharmacological and biopharmaceutical aspects, Front. Mol. Biosci. 7 (2020) 587997
[15]. M. Muchow, P. Maincent, R.H. Müller, Lipid nanoparticles with a solid matrix (SLN®, NLC®, LDC®) for oral drug delivery, Drug Dev. Ind. Pharm. 34 (12) (2008) 1394–1405.
[16]. S.B. Routray, C.N. Patra, R. Raju, K.C. Panigrahi, G.K. Jena, Lyophilized SLN of Cinnacalcet HCl: BBD enabled optimization, characterization and pharmacokinetic study, Drug Dev. Ind. Pharm. 46 (7) (2020) 1080–1091.
[17]. S. Mukherjee, S. Ray, R. Thakur, Solid lipid nanoparticles: a modern formulation approach in drug delivery system, Indian J. Pharm. Sci. 71 (4) (2009) 349.
[18]. N. Jawahar, S. Meyyanathan, G. Reddy, S. Sood, Solid lipid nanoparticles for oral delivery of poorly soluble drugs, J. Pharm. Sci. Res. 4 (7) (2012) 1848.
[19]. V.R. Sinha, S. Srivastava, H. Goel, V. Jindal, Solid lipid nanoparticles (SLN'S)- trends and implications in drug targeting, Int. J. Adv. Pharm. Sci. 1 (3) (2010).
[20]. M. Hanumanaik, S.K. Patel, K.R. Sree, Solid lipid nanoparticles: a review, Int J. Pharm. Sci. Res 4 (3) (2013) 928–940.
[21]. R. Paliwal, S. Rai, B. Vaidya, K. Khatri, A.K. Goyal, N. Mishra, et al., Effect of lipid core material on characteristics of solid lipid nanoparticles designed for oral lymphatic delivery, Nanomed.: Nanotechnol., Biol. Med. 5 (2) (2009) 184–191.
[22]. S.M. Hosseini, R. Abbasalipourkabir, F.A. Jalilian, S.S. Asl, A. Farmany, G. Roshanaei, et al., Doxycycline-encapsulated solid lipid nanoparticles as promising tool against Brucella melitensis enclosed in macrophage: a pharmacodynamics study on J774A. 1 cell line, Antimicrob. Resist. Infect. Control. 8 (1) (2019) 1–12
[23]. N. Jawahar, S. Meyyanathan, G. Reddy, S. Sood, Solid lipid nanoparticles for oral delivery of poorly soluble drugs, J. Pharm. Sci. Res. 4 (7) (2012) 1848
[24]. H. Yuan, L.-F. Huang, Y.-Z. Du, X.-Y. Ying, J. You, F.-Q. Hu, et al., Solid lipid nanoparticles prepared by solvent diffusion method in a nanoreactor system, Colloids Surf. B: Biointerfaces 61 (2) (2008) 132–137
[25]. Ekambaram P, Sathali AH, Priyanka K. Solid Lipid Nanoparticles: A Review. Scientific Reviews and Chemical. Communication2012; 2 Suppl 1 :80-102.
[26]. Cavalli R, Donalisio M, Civra A, Ferruti P, Ranucci E, Trotta F, Lembo D. Enhanced antiviral activity of Acyclovir loaded into β- cyclodextrin-poly (4-acryloylmorpholine) conjugate nanoparticles. Journal of Controlled Release 2009; 137 :116–122.
[27]. Pandita D, Ahuja A, Velpandian T, Lather V, Dutta T, Khar RK. Characterization and in vitro assessment of paclitaxel loaded lipid nanoparticles formulated using modified solvent injection technique. Pharmazie2009; 64 :301–310.
[28]. Shah M, Pathak K. Development and Statistical Optimization of Solid Lipid Nanoparticles of Simvastatin by Using 23 FullFactorial Design. AAPS PharmSciTech2010; 11 Suppl 2 :489-496.
[29]. Sinha VR, Srivastava S, Goel H, Jindal V. Solid Lipid Nanoparticles (SLN'S) – Trends and Implications in Drug Targeting. International Journal of Advances in Pharmaceutical Sciences2010; 1 :212-238.
[30]. Mehnert W, Mader K. Solid lipid nanoparticles-Production, characterization and applications. Advanced Drug Delivery Reviews 2001; 47 :165–196.
[31]. Ohshima H, Miyagishima A, Kurita T, Makino Y, Iwao Y, Sonobe T, Itai S. Freeze-dried nifedipine-lipid nanoparticles with long term nano-dispersion stability after reconstitution. International Journal of Pharmaceutics2009; 377 :180–184.
[32]. Subedi RK, Kang KW, Choi KH. Preparation and characterization of solid lipid nanoparticles loaded with doxorubicin. European Journal of Pharmaceutical Sciences2009; 37 :508–513.
[33]. Dong X, Mattingly CA, Tseng M, Cho M, Adams VR, Mumper RJ. Development of new lipid-based paclitaxel nanoparticles using sequential simplex

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optimization. European Journal of Pharmaceutics and Biopharmaceutics2009; 72 :9–17.
[34]. Ye J, Wang Q, Zhou X, Zhang N. Injectable actarit-loaded solid lipid nanoparticles as passive targeting therapeutic agents for rheumatoid arthritis. International Journal of Pharmaceutics2008; 352 :273–279.
[35]. Huang G, Zhang N, Bi X, Dou M. Solid lipid nanoparticles of temozolomide: Potential reduction of cardial and nephric toxicity. International Journal of Pharmaceutics2008; 255 :314–320.
[36]. Elnaggar YSR, El-Massik MA, Abdallah OY. Fabrication, appraisal, and transdermal permeation of sildenafil citrate loaded nanostructured lipid carriers versus solid lipid nanoparticles. International Journal of Nanomedicine 2011;