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A Comprehensive Review Of Solid Lipid Nanoparticles

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ABSTRACT

Liposomes, polymeric nanoparticles, and emulsions are alternatives to other popular colloidal carriers. Because of its advantages, solid lipid nanoparticles were developed in the early 1990s, including controlled drug release, focused drug delivery, and outstanding durability. The many methods utilized to manufacture solid lipid nanoparticles and excipients, including the membrane contractor technique, are summarised in this article, along with their possible benefits and drawbacks. Solid lipid nanoparticle (SLN) stability relies on maintaining particle size, drug encapsulation, and integrity over time. Excipients like surfactants and lipids influence stability, preventing aggregation and oxidation. Drying techniques, such as spray drying and lyophilization, enhance stability by converting SLNs to solid forms, while lipid composition and drug-lipid compatibility are crucial factors. So, the instrumental techniques employed and the difficulties associated with SLN manufacturing are thoroughly examined. Particular focus is placed on the SLN release pattern and drug integration models in SLN. The main uses of SLNs, including targeted drug delivery, and the analytical approaches used in SLN assessments, are covered in detail. The main objective of this work is a thorough overview of solid lipid nanoparticles, including production methods, characterization, and routes of administration. A discussion of the components of the SLN delivery mechanism and the in vivo destiny of the carriers are also included.

Keywords: Solid lipid nanoparticles, solid lipid, surfactants, colloidal drug carriers, and drug incorporation.

INTRODUCTION

Advancements in fields like biotechnology, biomedical engineering, and nanotechnology have significantly contributed to the rapid growth of novel drug delivery systems. Nanotechnology is used extensively in several of the most modern formulation techniques, which entails the development of API-carrying nanostructures. Nanotechnology, as defined by the National Nanotechnology Initiative (NNI), involves the research and use of structures ranging from 1 to 100 nanometers in size.

Using a regulated and focused medication delivery mechanism, nanotechnology's main objective is to diagnose as precisely and quickly as is practical and treat as efficiently and securely as is practical. Nanoparticles, solid lipid nanoparticles, nanosuspension, nanoemulsion, nanocrystals, and other drug delivery systems are some of the most popular ones created by nanotechnology principles. This essay's main concern is Solid Lipid Nanoparticles (SLNs). Solid lipid nanoparticles (SLNs), first developed in 1991, offer advantages over traditional colloidal carriers like emulsions, liposomes, and polymeric micro- and nanoparticles.(Khatak et al., n.d.2013)

Solid lipid nanoparticles (SLNs) are effective for delivering water-soluble drugs in dynamic therapy. These nanoparticles are colloidal particles, typically ranging from 10 to 1000 nanometers in size. They are constructed of artificial polymers intended to enhance drug delivery while lowering lethality. They have evolved into a versatile replacement for liposomes as a method of medication administration. SLNs are made from synthetic or specialized polymers, making them well-suited for enhancing drug delivery while minimizing toxicity.

SLNs are alluring due to their ability to enhance pharmaceutical execution due to their high drug stacking, big surface area, and stage communication at the interface. Aqueous colloidal dispersions with a solid biodegradable lipid matrix are known as solid lipid nanoparticles (SLN). SLN formulations have been created and are in vogue, completely characterized for various administration routes (parenteral, oral, cutaneous, ocular, pulmonary, and rectal). In Figure 1, a solid lipid nanoparticle has replaced the fluid lipid in the parenteral nutrition method's equivalent oil-in-water emulsion. As a result, one of the few viable colloidal transporter systems that might replace polymers is made up of solid lipid nanoparticles. Solid lipid nanoparticles provide several benefits, including great biocompatibility, less risk, improved lipophilic drug delivery, and a physically strong structure. (Scioli Montoto et al., 2020)

ADVANTAGES OF SLN

Small sizes and controlled distribution make SLNs ideal for targeted drug delivery to specific sites in the body.

- Useful traditional emulsion manufacturing methods
- Detailing powder can be stop-dried.
- Controlled delivery of dynamic medication over a long period is possible.
- Excellent biocompatibility
- Make medications more stable
- High repeatability resulted from the ready methodology's creative use of high-weight homogenization.
- Increased and better drug content. (Ghasemiyeh & Mohammadi-Samani, 2018)

DISADVANTAGES OF SLN

- Insufficient sedate stacking restriction.
- Drug ejection after a polymeric capacity change.
- Variability in the propensity for gelation.
- Stacking hydrophilic medications is difficult due to the effects being allocated during the manufacturing process. (Müller et al., 2000)

METHODS OF PREPARATION OF SOLID LIPID NANOPARTICLES

The dissolvable infusion technique, dissolvable emulsification-dissemination, and dissolvable emulsification/vanishing are all included in the SLN-ready approach: micro emulsion-based SLN planning, supercritical liquid invention, splash drying, and compressive homogenization. Lipid nanoparticles have recently been created using this method. This process relies on the precipitation of lipid broken down during organization. Using this method, lipids accelerate while dissolvable removal happens. Dissolvable expulsion is necessary if not evacuated under specific circumstances and can be accomplished by refining or another method. Following the disappearance of the water-immiscible

natural dissolvable lipid nanoparticles organize. Particle size is influenced by factors such as the infusion volume, lipid composition, temperature, mixing conditions, solvent type, and the choice of emulsifier.

SLNs are composed of lipids, emulsifiers, and water or solvents, created through various methods and classified into different types based on their formulation and preparation techniques. (Lingayat et al., 2017)

High-pressure homogenization

- Hot homogenization
- Cold homogenization

Ultrasonication /high-speed homogenization

- Probe ultrasonication
- Bath ultra-sonication

Solvent emulsification-diffusion method

- Supercritical fluid method
- Micro emulsion-based method
- Double emulsion method
- Solvent Injection Technique
- Film-ultrasound dispersion

Using Membrane Contractor (Garud et al., 2012)

HIGH-PRESSURE HOMOGENIZATION (HPH)

High-pressure homogenization (HPH) is a reliable and effective method for creating SLNs. This technique involves forcing a liquid through a small orifice under high pressure (100–2000 bar), causing the fluid to accelerate to velocities exceeding 1000 km/h. The rapid motion breaks particles via cavitation and shear forces, resulting in submicron-sized particles. While lipid content up to 40% has been explored, typical formulations use 5–10% lipids. HPH can be performed using either cold or hot homogenization. In both cases, the drug is first dissolved or dispersed in the lipid melt before being incorporated into the bulk lipid. (Schultz et al., 2004)

Hot homogenization

Emulsion homogenization might be thought of as hot homogenization, which occurs at temperatures higher than the lipid's melting point. The drug-loaded lipid melt and the aqueous emulsifier phase are mixed vigorously (both at the same temperature) to create a pre-emulsion (Ultra-Turrax). Preferably, you want droplets in the few micrometer range since the pre-emulsion quality significantly impacts the end product's quality. Higher temperatures generally lead to smaller particle sizes in SLN production, as they reduce the viscosity of the inner phase. However, elevated temperatures can also cause degradation of both the carrier and the drug. If needed, the homogenization process can be repeated. It's important to note that during high-pressure homogenization, the sample temperature increases by approximately 10°C for every 500 bar of pressure, which must be carefully controlled to avoid unwanted thermal degradation.

Cold Homogenization

On the other hand, cold homogenization uses solid lipids and thereby grinds a suspension at high pressure. Effective temperature control during homogenization is essential to prevent the lipid from melting. The three main challenges associated with heat homogenization are lipid degradation, drug instability, and carrier breakdown. To overcome these issues, cold homogenization was introduced as an

alternative to maintain lipid integrity and avoid thermal degradation. (*Submicron Emulsions in Drug Targeting and Delivery - Google Books*, n.d.)

1. Tools for drug degradation caused by temperature
2. Drugs are dispersed into the aqueous phase during homogenization.
3. Multiple variations and/or supercooled melt pressure emerge from the Nano emulsion's complicated crystallization stage.

HIGH-SPEED HOMOGENIZATION AND ULTRASONICATION

SLNs can also be created using high-speed homogenization or ultrasonication methods. A combination of both techniques is often required to achieve smaller particle sizes. While this approach reduces shear stress, it has drawbacks, including the risk of metal contamination and potential physical instability, such as particle formation during storage. A probe or bath sonicator is typically used in this process.

SOLVENT EMULSIFICATION DIFFUSION METHOD

This method typically produces particles with diameters ranging from 30 to 100 nm. A key advantage is that no heat is required during the preparation process. Lipids are usually dissolved in the organic phase at 50°C in a water bath. This process can alter the zeta potential and induce coacervation of the SLNs. After centrifugation, lipids are easily separated, and the SLN suspension is quickly formed. The system can then be re-dissolved in distilled water post-centrifugation.

SUPERCRETICAL FLUID METHOD

This comparatively recent technique for making SLN has the benefit of not using solvents. This platform technique for creating powders and nanoparticles has undergone multiple versions. The explosive growth of saturated carbon dioxide solutions can be used to create SLN (RESS). An excellent solvent was carbon dioxide (99.99%). (Mehnert & Mäder, 2012)

MICROEMULSION BASED METHOD

SLN preparation methods were developed by Gasco and colleagues using microemulsion dilution. Stearic acid is a low-melting fatty acid, An optically clear mixture typically consists of water, co-emulsifiers, sodium taurodeoxycholate, polysorbate 20, polysorbate 60, soy phosphatidylcholine, and polysorbate 20. The heated microemulsion is dispersed using cold water (2–3°C). The hot microemulsion to cold water volume ratio is typically in the 1:25-2:50 range while agitated.

The micro-emulsion composition significantly impacts the dilution process. According to the literature, no additional energy is required to produce submicron particle sizes, as the microemulsion already possesses a droplet-like structure. Fessi created polymer particles by diluting polymer solutions with water. The distribution processes' velocities have a significant influence on particle size. Only acetone, which dissolves fast into the water, produces nanoparticles; other solvents, which are more lipophilic, yield larger particle sizes. Just as acetone is used to create lipid nanoparticles, the hydrophilic co-solvents in the microemulsion are utilized to produce polymer nanoparticles. (Shah et al., 2014)

DOUBLE BASED METHOD

Warm double microemulsions without water may be created in two steps. To create a transparent system, an aqueous solution containing the drug is first added to a mixture of melted lipid, surfactant,

and co-surfactant at a temperature slightly above the lipid's melting point.
In the second stage, the w/o microemulsion is mixed with water, surfactant, and co-surfactant to form a clear w/o/w system. Warm micro double emulsions can then be combined with cold water to produce SLNs, followed by ultrafiltration and cleaning with dispersion media. However, multiple emulsions are inherently unstable due to coalescence of internal aqueous droplets within the oil phase, coalescence of oil droplets, and rupture of the internal droplet surface layers. Transparent double microemulsions are made, and then they are quenched in cold aqueous media. SLNs must maintain their stability for as little time as is physically feasible.
Another method for making solid lipid nanoparticles (SLNs) is precipitation, which involves the use of solvents. In this process, glycerides are dissolved in an organic solvent (such as chloroform) and then emulsified into an aqueous phase. The lipid will precipitate and form nanoparticles when the organic solvent has evaporated. (Subroto et al., 2022)

ULTRASOUND DISPERSION IN FILMS

The lipid and drug are first dissolved in the appropriate organic solvents. After the organic solutions undergo decompression, rotation, and evaporation, a lipid film is formed. Finally, small and **homogeneous SLNs are produced by applying ultrasonic treatment using a probe or diffuser.**

SOLVENT INJECTION TECHNIQUE

This innovative technology for producing SLNs offers several advantages over traditional methods, including the use of pharmacologically acceptable organic solvents, ease of handling, and a quick production process that doesn't require complex machinery. The process is based on lipid precipitation from dissolved lipids in solution. A water-miscible solvent (such as ethanol, acetone, or isopropanol) or a mixture of such solvents is used to dissolve the solid lipid. The lipid-solvent mixture is then injected into a stirred aqueous phase, with or without a surfactant, using an injection needle. The resulting dispersion is filtered through filter paper to remove excess lipids. An emulsifier added to the aqueous phase reduces surface tension between water and the solvent, helping to form lipid droplets at the injection site and stabilizing the SLNs until the solvent has fully diffused.(Duong et al., 2020)

MEMBRANE CONTRACTOR METHOD

The current study focuses on exploring a novel SLN preparation method using a membrane contactor for large-scale production. A schematic representation of this process is provided in Fig. 3. In this method, the lipid phase is pushed through the membrane pores at a temperature above the lipid's melting point, forming small droplets. These droplets, created at the pore exits, are carried away by the aqueous phase as it flows through the membrane module. Once the preparation has reached room temperature, SLN is produced. We investigate how process variables affect SLN size and lipid phase flux (Membrane pore size, lipid phase pressure, aqueous phase cross-flow velocity, and aqueous phase temperature). Additionally, SLN, loaded with vitamin E, is synthesized, and its stability is shown. (Qushawy & Nasr, 2020)

APPLICATION OF SOLID LIPID NANOPARTICLES

SLN for Parenteral Application

Since SLNs are composed of physiologically well-tolerated components and have great storage capaci-

ties after being lyophilized and/or sterilized, they are ideal for systemic administration. Small enough to pass through the microvascular system when given intravenously, SLN can inhibit macrophage absorption when coated with a hydrophilic substance.

Respiratory Application of SLN

By minimizing first-pass effects, the lungs provide a large surface area for medicine absorption. Because the alveoli in the deep lung have incredibly thin walls, aerosolized medications (in the 1-3 m size range) quickly enter the bloodstream.

SLN for Nasal Application

Nasal administration was a potential alternative non-invasive method of drug delivery because of the rapid absorption and early start of therapeutic activity. This prevented the breakdown of labile pharmaceuticals (such as peptides and proteins) in the GI tract and insufficient transport through epithelial cell layers.

SLN for Ocular Application

Several recorded instances of SLN administration of eye medications (Friedrich et al. 2005). The biocompatibility and mucoadhesive qualities of SLN promote their interaction with the ocular mucosa and extend the duration of the drug's corneal residence with the goal of ocular drug targeting.

CHARACTERIZATION OF SOLID LIPID NANOPARTICLES

Solid lipid nanoparticle characterization is a real challenge given their small size and intricate structure. Particle size estimation, transport energy (zeta potential), level of lipid polymorphism and crystallinity, the combination of additional colloidal structures (micelles, liposomes, supercooled, softens, sedate nanoparticles), tranquilize, in vitro drug release, and surface morphology are crucial parameters for SLNs.

The following are some criteria that must be considered while characterizing anything.

ZETA POTENTIAL AND PARTICLE SIZE

Several techniques can be used to measure nanoparticle size, including filtered test microscopy, Fraunhofer diffraction, transmission electron microscopy (TEM), scanning electron microscopy (SEM), photon correlation spectroscopy (PCS), and X-ray spectrometry. Among these, PCS and electron microscopy methods are the most commonly used. SEM and TEM are particularly useful for verifying particle size, distribution, and the morphology of lipid nanoparticles. Additionally, atomic force microscopy (AFM) is a sophisticated technique for characterizing nanoparticles at a smaller scale. (AFM).

Atomic force microscopy (AFM) is another technique used to preserve the particles' surface properties and original structure. This method provides spatial resolution of up to 0.01 nm by utilizing a probe that interacts with the surface, allowing detailed examination of the particle surface and its topography. The lipids and emulsifying agents used, as well as the kind and quantity of lattice components, all influence particle estimation. According to calculations, the mean width of the bulk falls as emulsifier concentration rises. The distance across the SLNs is also influenced by the associated drug's size and structure. (Hou et al., 2003)

DETERMINATION OF INCORPORATED DRUGS

After removing free drug and solid lipids from the medium using ultracentrifugation, centrifugation filtr-

ation, or gel permeation chromatography, the amount of drug encapsulated in the SLNs can be calculated. The drug-loaded material can be precisely measured by dissolving the drug in an appropriate solvent under optimal conditions, then analyzing the resulting substance in the SLNs. Several models have been proposed to describe the drug distribution in SLNs. The enhanced shell model suggests that the drug is selectively positioned at the interface, where it competes for space or is incorporated due to rapid lipid solidification. This model may result in a "burst release" effect during drug delivery. The homogeneous framework model proposes that the drug is evenly distributed within the lipid matrix, similar to a solid structure. The advanced core model suggests that the drug is preferentially located at the core of the SLNs, likely due to the drug solidifying faster than the surrounding lipid matrix.

IN- VTRO DRUG RELEASE STUDIES

In-vitro drug release testing is commonly used for quality assurance and to predict the in-vivo performance of the drug. It is possible to lead medication discharge profiles with and without dialysis tubing. Transferring SLNs dispersion into prewashed dialysis tubing is the first step in the dialysis process. The tube is then continually mixed against the disintegration medium while hermetically sealed, dialyzed, and heated to a specific temperature. In 1990, Imose and Benita developed an alternative method based on switch dialysis, which avoids the confined space of the colloidal drug carrier within a dialysis bag.This method is not sensitive enough to determine the speed at which medicines are released from a colloidal transporter. (Zur Mühlen et al., 1998)

STORAGE STABILITY

The physical stability of SLNs during extended storage can be monitored by tracking changes in particle size, drug content, appearance, and viscosity. This should be possible with thin-layer chromatography as well. For example, temperature and light are essential factors in long-term stability. A scattering is normally regarded as physically stable when the zeta potential is greater than - 60 mV. 4°C is the optimal temperature for stockpiling. 20°C- Long-term storage did not cause medication loss or drug stacking. At 50°C, there was a sharp increase in particle size. (Üner & Yener, 2007)

SLNS POLYMORPHIC BEHAVIOR AND CRYSTALLIZATION TENDENCY

Lipid crystallization plays a crucial role in drug encapsulation and release rates, making it essential to carefully consider this phenomenon. The solidity of the particles is vital, as it limits the movement of encapsulated drugs, preventing leakage from the carrier. Techniques such as thermal analysis and X-ray diffraction are key methods for determining the physicochemical state of the particles. Differential warm examination (DTA) and differential filtering caliper are the two most frequently employed in warm inquiry (DSC). (Bunjes et al., 1996)

SOLID LIPID NANOPARTICLES EVALUATION

SOLID LIPID NANOPARTICLES ELECTRON MICROSCOPY

Solid lipid nanoparticles (SLNs) were observed using transmission electron microscopy (TEM). Tests showed that the SLNs were ten times weaker before being placed on the gold plate for examination. The plated plates were dried and inspected without applying dye under a transmission electron microscope. A transmission electron magnifying device, a CCD camera, and a delicate picture framework were employed to observe SLN.

ZETA POTENTIAL OF SOLID LIPID NANOPARTICLES

The zeta potential of the SLN definitions was determined using Zetasizer. The tests were sufficiently weakened with deionized water, resulting in 50 and 200 Kcps. Zeta potential was correctly measured during the tests carried out in the equipment-accessible cubit. (Omwoyo et al., 2014)

POLYDISPERSITY INDEX AND PARTICLE SIZE OF SOLID LIPID NANOPARTICLES

The Zetasizer DTS was employed to measure the average particle size and polydispersity index of the SLNs. Deionized water was used to dilute the SLN samples for scattering analysis. The results of recording polydispersity and normal particle size were obtained using an instrumentally based calculating approach.

ENCAPSULATION EFFICIENCY OF SOLID LIPID NANOPARTICLES

Calculations were used to determine the testosterone productivity represented by solid lipid nanoparticles (EE). Solid lipid nanoparticles kept in a dialysis tube were subjected to dialysis. 30 milliliters of 30% v/v PEG 400 in a phosphate cushion (pH-6) setup used as the dialysis medium. Solid lipid nanoparticles were dialyzed for two hours. Using elite fluid chromatography (HPLC) (Shimadzu, Japan) at 254 nm, 100 milligrams of dialyzed Solid lipid nanoparticles were removed from the dialysis pack and examined for drug content. The samples were suitably attenuated and separated using a Millipore film channel (0.2 m). (Ahmad et al., 2019)

VISCOSITY OF SOLID LIPID NANOPARTICLES

The encapsulation efficiency (EE) of testosterone in solid lipid nanoparticles (SLNs) was calculated. SLNs were placed in a dialysis tube and subjected to dialysis in a phosphate buffer (pH 6), containing 30 milliliters of 30% v/v PEG 400. Dialysis was conducted for two hours. Afterward, 100 milligrams of dialyzed SLNs were removed from the dialysis bag and analyzed for drug content using Shimadzu's Elite Fluid Chromatography (HPLC) at 254 nm. The samples were properly diluted and separated using a Millipore filtration membrane (0.2 µm).

SOLID LIPID NANOPARTICLES IN VITRO RELEASE STUDY

In vitro, the concentration of solid lipid nanoparticles (SLNs) was measured using a custom-built Franz diffusion cell. The operating temperature for the experiment was maintained at 32°C. The receptor compartment of the diffusion cell was continuously stirred at 50 rpm and contained 30 ml of a 30% v/v PEG 400 solution in a phosphate buffer (pH 6). A dialysis membrane (with a molecular weight cutoff of 12 kDa) was used as a diffusion barrier between the donor and receptor compartments, which were pre-washed with purified water and rinsed with the 30% v/v PEG 400 solution. Samples of 5 ml were periodically withdrawn through the sampling port of the diffusion cell at hourly intervals. The collected samples were properly diluted and analyzed using HPLC at 254 nm for drug content analysis (Venkateswarlu & Manjunath, 2004).

****Route of Administration:****

SLNs can be administered according to the specific procedure outlined by the organization.

****Oral Administration:****

SLNs can also be administered orally in the form of water or after being transformed into conventional dosage forms such as tablets, pellets, capsules, or powder sachets. During the granulation process for ta-

blet formation, the SLN dispersion can be used as a substitute for the granulation fluid.
The type of SLN planning covered in an oral course is fluid scatterings. Tablets, pellets, and cases are a few dose forms available in SLNs. The stomach's acidic milieu, which has a high ionic character, encourages particle aggregation. It is rare for nutrition to affect how SLN is carried out significantly.

PARENTERAL ORGANIZATION

Animals frequently get SLNs intravenously. It was shown that SLN conveyances induced more dispersion into the liver and kidneys while having more pharmacological fixations in the lungs, spleen, and brain. SLN showed higher blood levels than a sedate commercial setup after IV treatment. Sterilization of SLN scatterings is required for the parenteral organization. Due to the average particle size in these situations, sterile filtration is not feasible.

TRANSDERMAL APPLICATION

The SLN scatterings with the lowest particle sizes (up to 5%) have minimal lipid contents. The inadequate lipid grouping and thickness of the cutaneous organization are its drawbacks. To develop a formulation tailored for skin applications, SLN dispersions must be incorporated into a therapeutic gel or cream. This allows for controlled delivery and enhances the stability of the solid lipid nanoparticles, ensuring they are effectively utilized for topical treatments.

PULMONARY ADMINISTRATION

The aspiring organization of SLN looks to be a highly fascinating application. Powders containing SLN cannot be controlled to the lung and will instead be exhaled because the particle size is too tiny. Fluid SLN scattering aerosolization is a very straightforward procedure. The SLN should not be total, while aerosolization is the key requirement. The vaporized beads were collected by striking the flying beads with the mass of a measuring glass. Essentially, this shows that SLN are suitable for lung transfer. Following limitation, the medication may be carefully transferred from the lipid particles into the bronchi and alveoli.

RECTAL ORGANIZATION

Standard rectal medication delivery is practiced on young patients as much as is practical due to its simplicity. Sometimes, when quick pharmacological action is required, parenteral or rectal delivery is chosen. In the same assessment, it was discovered that the Drug given parenteral had higher plasma concentrations and therapeutic efficacy than medication delivered orally or intramuscularly. There are a few accounts of how rectal medications are organized using SLN in the literature. They stressed that using a solid lipid network at temperature is not an appropriate foundation for administering diazepam and employed concentrated diazepam and SLN fusion to provide quick action. (Fonseca-Santos et al., 2020)

CONCLUSION

It is not true that solid lipid nanoparticles "combine the benefits of conventional colloidal drug carriers while avoiding their downsides." The products go beyond simple solid-core Nanoemulsions. The advantages of solid lipid nanoparticles (SLNs) include their compatibility with physiological compounds, rapid and efficient production process, avoidance of organic solvents, ability to create

carriers with improved encapsulation efficiency, and scalability in manufacturing. However, SLNs also have some drawbacks, such as low drug loading capacities and the availability of alternative colloidal structures like micelles, liposomes, mixed micelles, and drug nanocrystals. Additionally, the lipid's physical state can be complex, as it can undergo transformations between different modifications, leading to challenges like gelation, particle size increase, and drug expulsion. Supercooled melts may also impact stability during storage or administration. By diluting or removing water from the sample, the equilibrium between colloidal species and the lipid's physical state can be significantly altered. Accurate characterization of complex surfactant/lipid dispersions requires the use of multiple analytical techniques, in addition to particle size measurement. Kinetic factors need to be taken into account. Drug Nano suspensions will be able to cohabit in the sample using NMR, ESR, and synchrotron radiation. Unfortunately, In the SLN literature, the phrase "drug incorporation" can be a little deceptive because these factors are not usually considered. In conclusion, SLN are extraordinarily complex systems that differ from conventional colloidal carriers in their benefits and shortcomings. More research is necessary to understand the molecular dynamics of SLN in vivo and in vitro.

CONFLICTS OF INTEREST

There is no conflict of interest.

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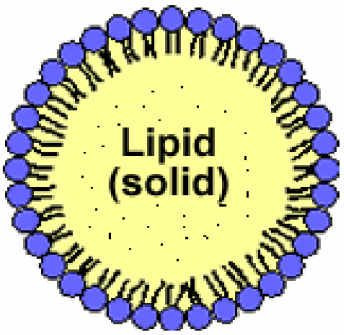

Fig 1 – Solid lipid nanoparticle structure: *Source-research gate*

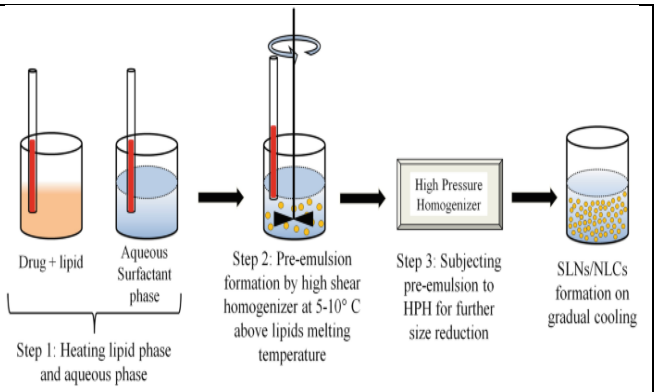

Figure 2 – Steps involved in high-pressure homogenization techniques *Source-springer*

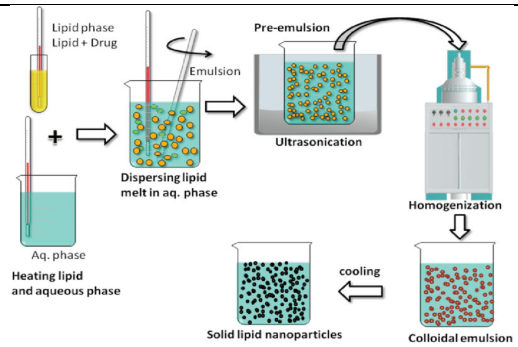

Figure 3 - Schematic representations of the various steps required in producing Solid Lipid nanoparticles utilising the hot homogenization technique are shown. *Source-research gate*

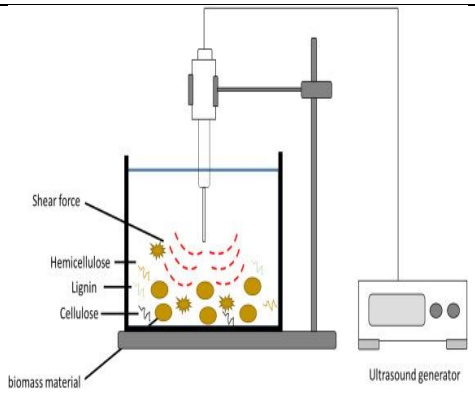

Figure 4 – ultra sonication instrument *Source-hielscher*

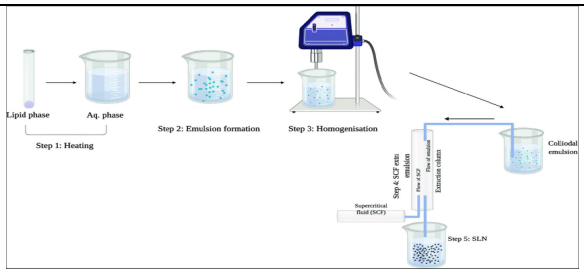

Figure 5 – supercritical fluid technique *Source-research gate*

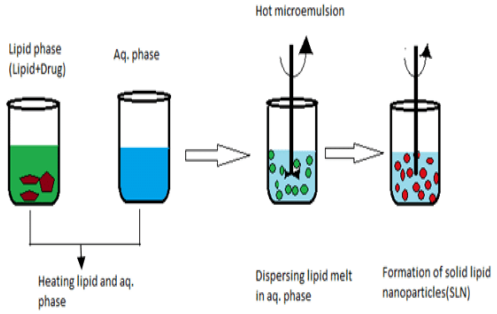

Figure 6 - Micro emulsion-based method. *Source-research gate*

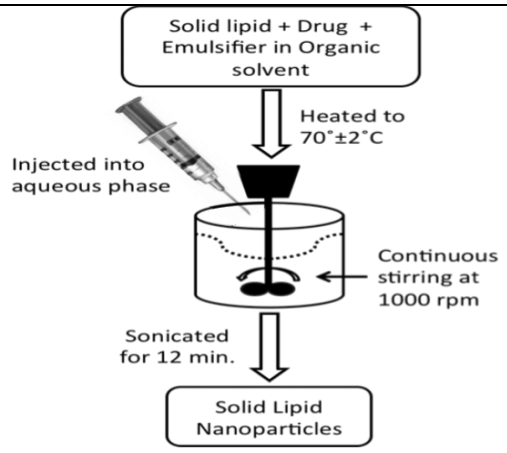

Figure 7– Schematic representation of solvent injection technique *Source-research gate*

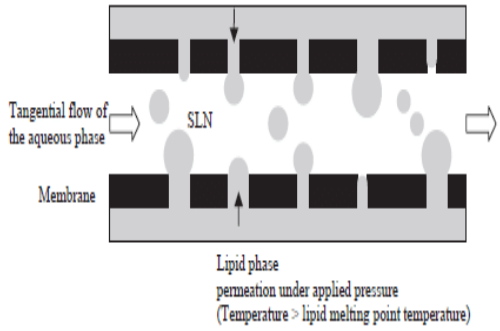

Figure 8 - demonstrates a schematic drawing of a membrane contractor used to prepare SLN *Source-research gate*

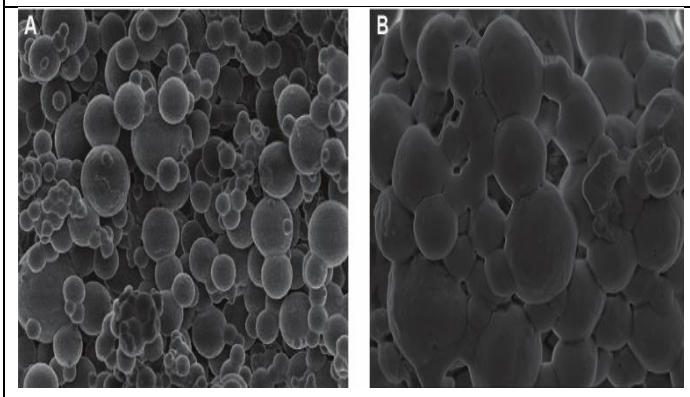

Figure 9 - Scanning electron microscopy images of drug-loaded solid lipid nanoparticles at 20,000 (A) 50,000 (B) magnification. *Source-research gate*

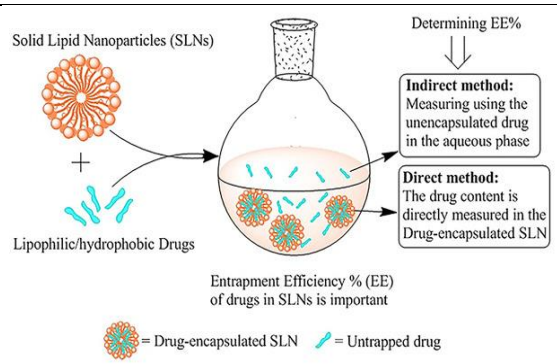

Figure 10 – Efficiency of solid lipid nanoparticle encapsulation is shown in the following schematic *Source-online library Wiley*

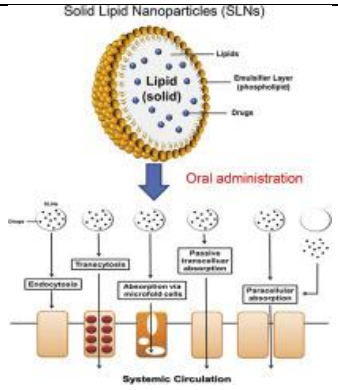

Figure 11 - Recent advances in oral delivery of drugs *Source-science direct*

Table 1 - compares various formulation processes is shown.

Sl.no	Formulation procedure	Advantages	Disadvantages
1.	High pressure homogenization	affordable and doable at laboratory size	Process that uses much energy is poly dispersion distribution.
2.	Ultra-sonication	decreased shear stress and protection against temperature-induced deterioration	chances of particle development and metal contamination during storage
3.	Solvent emulsification evaporation	Continuous, easily scalable procedure	Damage to biomolecules, polydisperse distributions, and energy-intensive processes
4.	Solvent emulsification diffusion	Do not use heat when preparing.	Process that uses a lot of energy and residual organic solvent
5.	Supercritical fluid technology	Dry powder particles are produced under low pressure and temperature conditions.	High cost
6.	Microemulsion	Particles of dry powder are created at low temperatures and pressures.	poor yield and extreme sensitivity to change
7.	Solvent injection	Fast SLN manufacture without the need of highly advanced machinery	Using an organic solvent
8.	Double emulsion	Suitable for hydrophilic drugs; sterically stabilised.	a high proportion of microparticles

Table 2 - Parameters for solid lipid nanoparticle characterization

Sl.no	Parameters	Characterization methods
1.	particle size analysis	Transmission electron microscopy, atomic force microscopy, photo correlation spectroscopy, scanning electron microscopy
2.	Charge calculation	Laser dopler anemometer and zeta potentiometer

3.	Capacity for loading and effectiveness of entrapment	UV-spectrophotometry, spectrofluorophotometry, and high-performance liquid chromatography
4.	Release history	In-vitro release studies
5.	Crystallinity and lipid modification	X-ray diffraction, DSC
6.	Interaction research on drug excipients	DSC
7.	Drug stability	Nanoparticle-based drug extract bioassay, physical, and chemical drug analysis
8.	presence of additional structures	electron spin resonance and nuclear magnetic resonance