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Review Article

Solid Lipid Nanoparticles (SLNs): A Novel Formulation in Drug Delivery System

Shikha Upadhyay*, Dr Govind Soni
Oriental University, Indore, Madhya Pradesh 453555, India.
***Corresponding author's E-mail:** shikhaupadhyay8@gmail.com

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ABSTRACT

Solid lipid nano-particles ((SLNs)) are alternative drug delivery system to colloidal carriers as liposomes, emulsions and polymeric micro- and nanoparticles. SLNs are one of the advanced technologies to improve bioavailability and targeting issues of drug delivery. This review includes all the essential details of SLNs such as production techniques for SLNs, different models of SLNs, drug incorporation, loading capacity and drug release, latest characterization methods, their applications as well as advancements taken place in the field of delivery of biological drugs like gene vector, new adjuvant for vaccines, protein, and peptide with SLNs. Based on the available data, the future success of SLNs is widened because they could be easily fabricated with various functionalities which would display enormous potential for targeting and diagnosing various diseases. This review would help the budding researchers to find out the unexplored areas of SLNs with the present discussion that reframes the potential of SLNs by gathering the various research findings of SLNs in tabular form along with the approved patent technologies of SLNs.

Keywords: Solid lipid nanoparticles (SLNs), Method of preparation, Surfactants, TEM, PCS.

INTRODUCTION

Nanotechnology and Nanoparticles:

Nanotechnology is the science of the nano (very small sized) particles. Nanoscience studies have developed rapidly in last few years in a wide range of product domains. Nanoparticles or Colloidal particles are fine particle which have size ranges between 1-1000nm.[1] They are manufactured from synthetic or natural polymers and ideally suitable to optimize drug delivery and reduce toxicity. Oral administration of a medicine through this system can improve the efficacy, specificity, tolerability, and therapeutic index of corresponding drugs.[2]

Nanoparticles based drug delivery systems have created great impact on every branch of medicine including endocrinology, cardiology, immunology, pulmonology, ophthalmology, oncology and also on highly specialized areas like tumor targeting, gene delivery, brain targeting, oral vaccine formulations and various other areas. Nanoparticle based formulations are an emerging approach that utilizes a broad range of technique and procedures aimed for diagnosis of disease and novel drug delivery.[1,3]

Researcher mainly focused on development of nano-particle-based systems for drugs which have oral bioavailability issues due to the hydrophilic nature of the GIT. For such type of medicine they have tried different chemical structure, proteolytic enzyme inhibitors, using permeation enhancers, decrease in hepatic first-pass metabolism, alteration in GIT transit duration, and designing modern drug delivery methods to enhance absorption and bioavailability of medicine. The pharmacokinetics of drugs via nanoparticles has exhibit that they can enhance circulation time, extend residence time and half-life, decrease clearance, and eliminate pre-systemic metabolism at the site of absorption.[2,3]

The nanoparticles are designed to employ control over shape, size, charge, lipophilicity and also allowing them to pass through the GI membrane in easy way. Nanotechnology includes various nanoparticulate systems, such as microcapsules, **lipid-based drug delivery** systems, liposomes, niosomes, lipoproteins, metal-oxide nanoparticles, micelles, cell ghosts, and different nano-assemblies.[4]

However, nanopartical based drug delivery systems such as quantum dots, dendrimers, etc. are linked to certain limitations like, the requirement of organic solvents for the synthesis process, the residues of which can cause cytotoxicity and the difficulty in scaling up the manufacturing methods with some specific nanoparticles. Lipid-based drug delivery systems indicate as a promising tool to overcome such problems. Simple oil solutions to combinations of oils, surfactants, co-surfactants, and co-solvents are all included in lipid-based delivery systems. To overcome all above mentioned problems, solid lipid nanoparticles (SLNs) for treatment of various disorders were formulated.[1-3]

Advantages of polymeric nanoparticles:

- Increases the intercellular concentration of medicines by increase permeability and retention effect.
- Protection of encapsulated drugs from degradation.
- Reduces the frequency of required medication.
- We can achieve control and sustained release of the drug.

- Enhancement of aqueous solubility of hydrophobic drug.
- Decrease in the systemic toxicity of the drug by encapsulation and targeting the drug to specific site.
- Enhancement of therapeutic effectiveness of the drug.
- Provides an opportunity to incorporate both hydrophilic and hydrophobic drugs in a single polymeric matrix.
- Improvement in the bio-distribution and circulation time of the drug.
- Feasibility of administration through various routes including oral, nasal, parenteral, topical, intraocular etc.
- Nanoparticles shows better stability as compared to liposomes which makes it more important for many modes of targeting.
- A high degree of patient compliance can be achieved.
- The overall pharmacological response per unit dose is increased.
- Toxicity and adverse drug reactions are reduced to a possible extent.
- Nanoparticles formulated as amorphous spheres offer more solubility than crystalline formulations, so improving the poor aqueous solubility and bioavailability of the drug.

Lipid based Nanoparticles drug delivery system:[5,6]

Lipid-based drug delivery systems are promising, as lipids are known for oral drug absorption enhancers and can be prepared with small particle size and shape. This system comprises of a range of products from simple oil solutions to complex mixtures of oils, surfactants, co-surfactants and co-solvents.

Lipid formulations used for oral delivery of drugs usually consist of a drug dissolved in a blend of two or more excipients, such as triglyceride oils, partial glycerides, surfactants or co-surfactants6. In the oral delivery of poorly water soluble, lipophilic drugs, lipid based delivery systems are finding increasing application. Improved oral bioavailability of lipidic dosage forms may be due to several mechanisms.[5,6]

The primary mechanism is typically partial or complete avoidance of the slow dissolution process responsible for limited bioavailability of hydrophobic drugs from solid dosage forms. Preferably the lipidic formulation allows the drug to remain in a dissolved state during its transit through the gastrointestinal tract.

The traditional lipid based systems such as emulsions are ineffective to solve the problems of lipophilic drugs such as poor solubility, low stability and poor patient compliance etc. The need for new carrier systems led to the development of novel lipid based carriers. Amongst the several approaches, lipid and surfactant based formulation approach received attention as it has proved efficient to improve the oral bioavailability of drugs with poor aqueous solubility.

The two types of lipid nanoparticles viz. solid lipid nanoparticles and nanostructured lipid carriers (second generation lipid nanoparticles) distinguish themselves by the composition and structure of the lipid matrix.[7-9]

Table 1: Lipid based formulation and their particle size

Formulation	Particle Size
Solid lipid nanoparticles (SLNs)	1-1000 nm
Nanostructured lipid carriers (NLC)	50-300 nm
Liposomes	50~1,000 nm
Self- micro-emulsifying drug delivery system (SMEDDS)	>50 nm
Self-emulsifying drug delivery system (SEDDS)	100-200 nm
Micro emulsions	10-300 nm
Macro emulsions	1000~10,000 nm
Micelles	5~50 nm

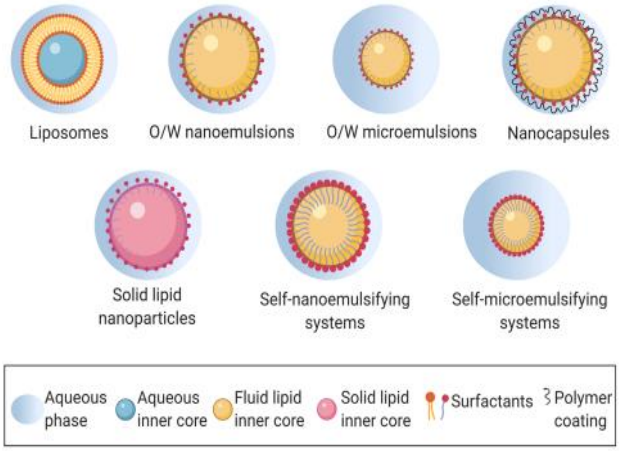

Figure 1: Classification of lipid-based nanoparticle drug delivery systems[10]

In solid lipid nanoparticles, lipid matrix consists of a solid lipid or a mixture of solid lipids which form almost a perfect crystalline structure. In nanostructured lipid carrier, lipid matrix is composed of a blend of a solid lipid and an oil leading to a crystal structure with more imperfections and therefore with more room for drug accommodation. Solid lipid carrier and nanostructured lipid carrier retain the advantages of traditional liposomes and niosomes such as high absorption and biocompatibility, while overcoming issues of stability commonly encountered with liposomes.[1, 8,11]

Table 2: Comparison of various nanotechnology based formulations

Property	SLNs	Liposomes	Polymeric Nano-particles	Nano Emulsions	Nano-Suspensions
Ability to deliver hydrophobic and hydrophilic drugs	Yes	Yes	Yes	Yes	Only hydrophobic drugs
Physical stability	Good	Poor	Good	Moderate	Good
Biological stability	Moderate	Poor	Good	Moderate	Moderate
Biocompatibility	Good	Good	Moderate	Good	Moderate
Drug targeting	Moderate	Moderate	Moderate	Poor	Poor
Drug loading	High	Low to moderate	Moderate	High	High
Ability to deliver biotechnological therapeutics	Moderate	Moderate	Moderate	Poor	No
Oral delivery	Possible	Not possible	Possible	Possible	Possible
Parenteral delivery	Possible	Possible	Possible	Possible	Possible

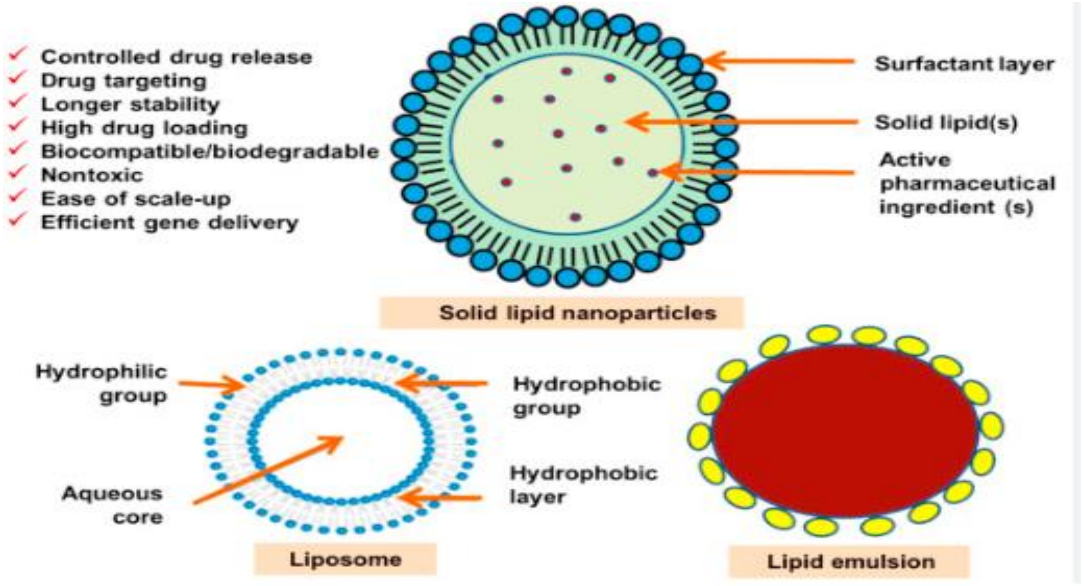

Figure 2: Diagrammatic representations of advantages of SLNs over other nanotechnology Solid lipid Nanoparticles: [12]

Solid lipid nanoparticles (SLN) are significant nano-technological area in drug delivery for the treatment of chronic disorders due to its easy permeability and high drug loading capacity. The SLNs are sub-micron size range of 50-500 nm colloidal carriers which is composed of physiological lipid (triglycerides, fatty acids, or waxes), dispersed in water or in an aqueous surfactant solution. SLNs are considered to be the most effective lipid based colloidal carriers and one of the most popular approaches to improve the oral bioavailability of poorly water soluble drugs. SLNs have a solid hydrophobic lipid core, in which both hydrophilic and lipophilic drugs can be dispersed. As they are formed of a physiological solid lipid emulsion system by maximally avoiding organic solvents, they display better biocompatibility and reduced systemic toxicity in comparison to polymeric nanoparticles. Due to their small size (50–500 nm), bypass the liver and the spleen metabolism and are directly absorbed from the intestines via the lymphatic system. This enhances the bioavailability of the drugs. SLNs, if smaller than 50 nm in diameter, can pass through the blood-brain barrier, and thus have been widely studied for treating brain disorders. SLNs containing drug also show a sustained release feature due to the use of solid lipids, modified drugs, and additive ingredients in a particular ratio, providing a particular physicochemical state with the longest diffusion pathway and controlled drug release.[13,14]

Advantages of solid lipid nanoparticle:

- They prevent drug leakage and provide controlled drug release: Encapsulated drugs are more stable within SLN in comparison to the polymeric nanoparticle, so prolonged release profile even for months to years.
- Improved bioavailability of poor water soluble molecules due to the physiological stability of the lipids

- SLNs escape RES bypassing liver and spleen filtration due to their unique physicochemical properties
- Feasibilities of carrying both lipophilic and hydrophilic drugs.
- SLNs have better long term stability and ease of upgradability by immobilizing within and resulting a stable formulation
- Drug formulations are cost-effective during scale-up processes.
- Use of biodegradable physiological lipids which decreases the danger of acute and chronic toxicity and avoidance of organic solvents in production method.
- Site specific delivery of drugs, enhanced drug penetration into the skin via dermal application
- More affordable (less expensive than polymeric/surfactant based carriers): The lipid raw materials for SLNs are cheaper than the polymers
- They have no reports of any acute or chronic toxicity due to lipid matrix.
- Easy to manufacture than bipolymeric nanoparticles.
- Protection of chemically labile agents from degradation in the gut and sensitive molecules from outer environment.

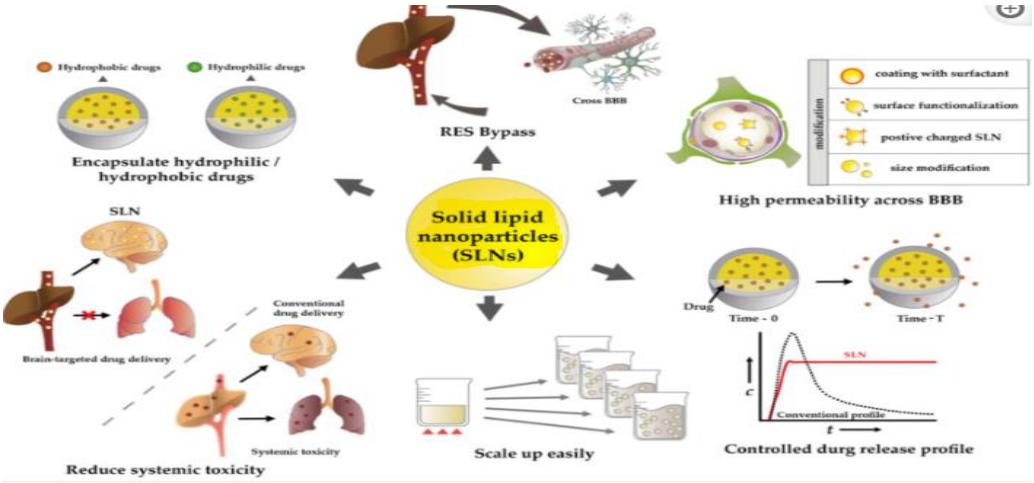

Figure 3: Advantages of solid lipid nanoparticle

Disadvantages of solid lipid nanoparticles[9]

Major drawbacks are particle growth, drug expulsion during long storage caused by high crystallization of lipid matrix, unpredictable gelation tendency and limited drug loading capacity.

- Drug molecule loading capacity is poor.
- Unforeseen motion of polymeric transition
- The low capacity to load water soluble drugs due to partitioning effects during the production process(11)
- Drug expulsion after polymeric transition during storage.
- Eccentric gelation propensity.
- Relatively high water content of the dispersions (70-99.9%).

Excipients used in solid lipid nanoparticles:

Solid lipid nanoparticles are prepared by using the blend of solid lipids and surfactant. Lipid and surfactant/stabilizer are the key components used to fabricate SLNs along with co-surfactant, preservatives, cryoprotectant, and charge modifiers.

Table 3: Ingredients used in SLNs-based formulations[15]

Ingredients	Examples
Lipid component	Stearic acid, Beeswax, triglyceride, Cholesterol, Caprylic/capric, Cetylpalmitate, Glyceryl stearate (-mono, and -tri), Glyceryl trilaurate, Glyceryl trimyristate, Glyceryl, behenate (Compritol), Glyceryl tripalmitate, Hardened fat (Witepsol E85, H5 and W35), Monostearate monocitrate, Solid paraffin, Behenic acid
Surfactant/ Emulsifiers	Phosphatidyl choline, Soy and Egg lecithin, Poloxamer, Poloxamine, Polysorbate 80
Co-surfactant	Sodium dodecyl sulphate, Tyloxopol, Sodium oleate, Taurocholate sodium salt, Sodium glycocholate, Butanol
Preservative	Thiomersal
Cryoprotectant	Gelatin, Glucose, Mannose, Maltose, Lactose, Sorbitol, Mannitol, Glycine, Polyvinyl alcohol, Polyvinyl pyrrolidone
Charge modifiers	Dipalmitoyl phosphatidyl choline, Stearylamine, Dicetylphosphate, Dimyristoyl phophatidyl glycerol

By reducing the interfacial tension between the aqueous environment and the hydrophobic surface of the lipid core,

surfactants help in stabilizing the SLN structure. All classes of emulsifiers (with respect to charge and molecular weight) have been used to stabilize the lipid dispersion. It has been found that the combination of emulsifiers might prevent particle agglomeration more efficiently.[15]

Methods of preparation of SLN:

SLNs can be formulated by various methods. Broadly, there are two common approaches to formulate SLNs. In the first approach, the solid lipid is initially melted and the drug is dispersed in it prior to the formulation of the SLNs. Methods such as high-pressure homogenization, microemulsion, double emulsion, and high- speed homogenization are used for the formulation of the SLNs in this approach. In the second approach, the drug is dissolved in an appropriate solvent along with the solid lipid prior to the formulation of the SLNs. Double emulsion and microemulsion-based methods such as solvent injection, solvent evaporation, thin film, and supercritical fluid extraction are used to formulate the SLNs with the help of a surfactant, followed by evaporation of the solvent.[16,17]

1. High pressure homogenization:
   - Hot homogenization
   - Cold homogenization
2. Ultra-sonication/high speed homogenization
3. Solvent evaporation method
4. Solvent emulsification-diffusion method
5. Microemulsion based method
6. Spray drying method
7. Double emulsion method
8. Precipitation technique

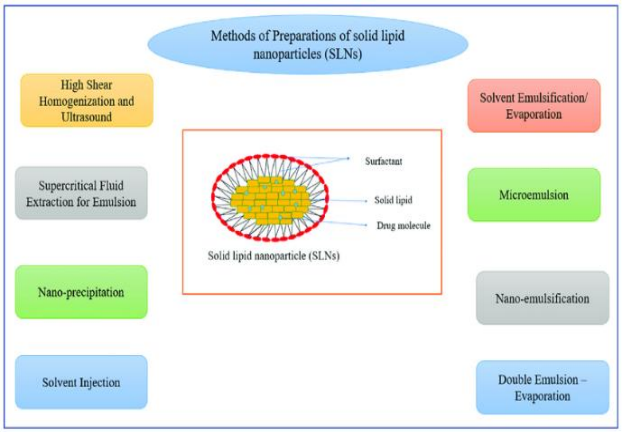

Figure 4: Different methods of preparation of SLNs.[18]

1. High shear pressure homogenization: (HSPH):[20-21]

High pressure homogenizers push a liquid with high pressure (100–2000 bar) through a narrow gap (in the range of a few microns). The fluid accelerates on a very short distance to very high velocity (over 1000 km/h). Very high shear stress and cavitation forces disrupt the particles down to the submicron range. Two general approaches are available to prepare SLNs, the hot and cold homogenization method.

Hot homogenization: Hot homogenization is carried out at temperatures above the melting point of the lipid and is similar to the homogenization of an emulsion. The quality of the pre-emulsion affects the quality of the final product to a great extent and it is desirable to obtain droplets in the size range of a few micrometers. Better products are obtained after several passes through the HSPH, typically 3-5 passes. High pressure processing always increases the temperature of the sample (approximately 10° at 500 bar)

Cold Homogenization: The first preparatory step is the same as in the hot homogenization procedure and includes the solubilization or dispersion of the drug in the lipid melt. The drug is dispersed in the melt of the bulk lipid and then the melt is cooled rapidly. This method developed to overcome the problems of the hot homogenization, such as temp-induced drug degradation, drug distribution into the aqueous phase during homogenization, complexity of the crystallization step of the nanoemulsion leading to various modifications and super cooled melts.

Advantages:

- **Low capital cost.**
- **Demonstrated at lab scale.**

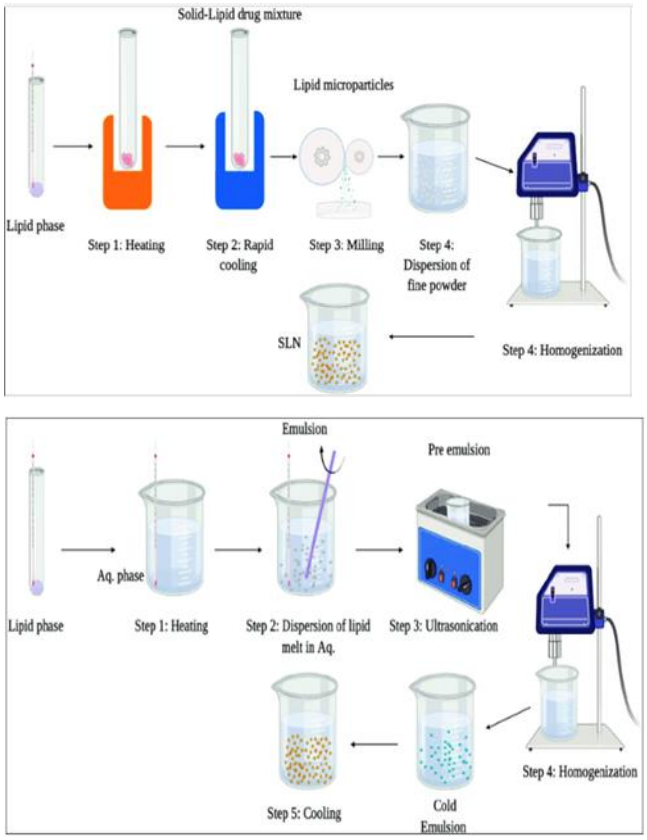

Figure 5: Hot and Cold homogenization techniques for SLNs preparation[19]

2. High speed homogenization followed by ultrasonication:

SLNs are also prepared by ultrasonication or high speed homogenization techniques. For smaller particle size combination of both ultrasonication and high speed homogenization is required. The solid lipid is heated 5–10°C above its melting point, and then added to a mixture of surfactants and water, previously heated at the same temperature. A sonication probe is placed in this pre-emulsion, which lead to droplet breakage by acoustic cavitation, and subsequent formation of nanoparticles.[22]

Advantages: Reduced shear stress.

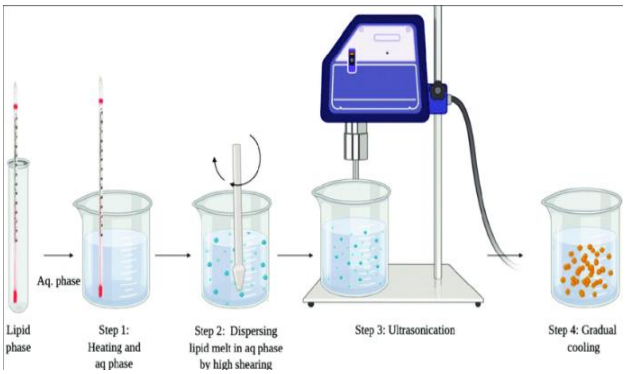

Figure 6: High speed homogenization techniques and ultrasonication

3. Preparation of SLNs by Solvent Emulsification/Evaporation method

Formulation of nanoparticle dispersions by precipitation in o/w emulsions the lipophilic material is dissolved in water-immiscible organic solvent (cyclohexane) that is emulsified in an aqueous phase. On evaporation of the solvent nanoparticle dispersion is prepared by precipitation of the lipid in the aqueous medium.[23] The mean diameter of the obtained particles was 25 nm with cholesterol acetate as model drug and lecithin/sodium glycocholate blend as emulsifier.[24]

Advantages:

- ✓ Scalable
- ✓ Mature technology.
- ✓ Continuous process.
- ✓ Commercially demonstrated.

4. Micro-Emulsion-Based SLN Preparations:

During this process indirect heating is used to prepare the solid lipid melts. This method is based on the dilution of microemulsions.[25]

As micro-emulsions are two-phase systems composed of an inner and outer phase (e.g. o/w microemulsions). The aqueous solution of the solid lipid melts is then prepared using water, surfactant, and a co-surfactant.[26]

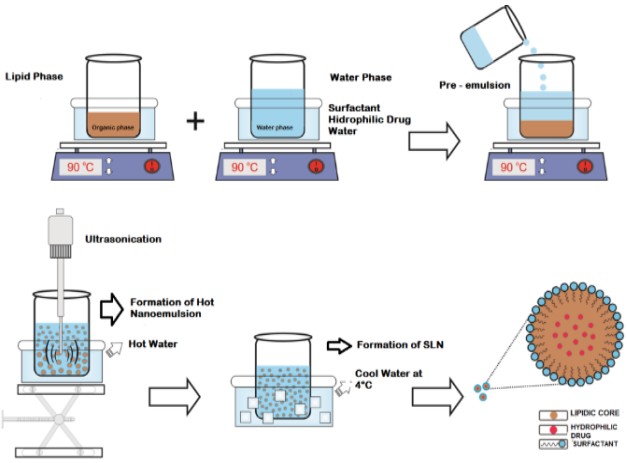

Figure 7: Micro-Emulsion-Based techniques for SLNs preparation[27]

5. SLNs formulation by supercritical fluid:

SLNs can be formulated by the using rapid expansion of supercritical carbon dioxide solutions (RESS) method. Carbon dioxide (99.99%) is the good choice as a solvent for this process.[19,28]

Advantages:

- ✓ Low mechanical energy input
- ✓ Theoretical stability

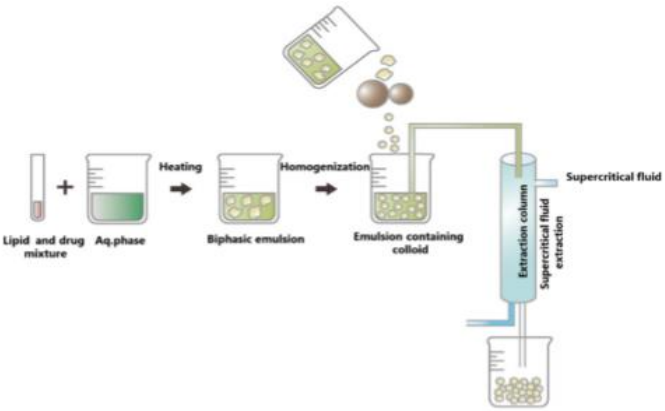

Figure 8: Supercritical Fluid Technique

6. Spray drying method:

This method is rarely used at present. It is an alternative technique to the lyophilization process. This recommends the use of lipid with melting point more than 70o C. The best results were obtained with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol-water mixture.[24, 27]

7. Double emulsion method:

This method mainly used for hydrophilic drugs. Mechanism is similar to solvent emulsification-evaporation. Drug is encapsulated with a stabilizer to prevent the partitioning of drug in to external water phase during solvent evaporation in the external water phase of w/o/w double emulsion.[29]

8. Precipitation method:

In this method lipid dissolved in an organic solvent and the mixure will be emulsified in an aqueous phase. After evaporation of the organic solvent the lipid will be precipitated forming nanoparticles.[30]

Secondary Processing:[31-34]

A. Sterilization: After formulation of SLNs, sterilization by autoclaving is necessary for parenteral administration of drug. Effects of sterilization on particle size have been investigated and it was found to cause a distinct increase in particle size due to particle aggregation.

B. Lyophilisation: Lyophilisation increase chemical and physical stability especially hydrolysable drugs. In case of freeze drying of the preparation, lipid matrices form larger SLNs with a wider size distribution due to presence of aggregates between the nanoparticles. The effect of the freeze drying method and the removal of water promote the aggregation among SLNs. An appropriate amount of cryo-protectant can protect the aggregation of SLNs during the freeze drying process.

C. Spray drying: Spray drying might be an alternative procedure to lyophilization in order to transform an aqueous SLN dispersion into a dry product. This method has been used scarcely for SLN formulation, although spray drying is cheaper as compared to lyophilization.

Characterization of SLNs for Quality and Structure:[35-42]

After formulation, it is necessary to characterize the SLNs for quality control. Adequate and proper characterization of the SLNs is necessary for its quality control. SLNs are characterized using an array of analytical tools to assess the particle size, the zeta potential, the entrapment efficiency, the crystallinity, and the surface morphology.

Physiochemical Characterization of SLN's:[35-37]

1. Particle Size and Shape:

Photon correlation spectroscopy (PCS) and laser diffraction (LD) are the most powerful techniques for determination of particle size. Electron Microscopy used for determination of shape of SLNs.

A. Photon Correlation Spectroscopy (PCS): PCS which also known as dynamic light scattering measures the fluctuation of the intensity of the scattered light which is caused by particle movement. This method is suitable for the measurement of particles in the range of 3 nm to 3 mm. The PCS device consists of laser source, a sample cell (temperature controlled) and a detector. Photomultiplier is used as detector to detect the scattered light. The PCS diameter is based on the intensity of the light scattering from the particles.

B. Electron Microscopy: Scanning Electron Microscopy and Transmission Electron Microscopy utilized to determine the physical characterization such as shape and morphology of nano-particles. It allows to determination of particle size and distributions. SEM uses electrons transmitted from the surface of the sample while TEM uses electrons transmitted through the sample. TEM has a smaller size limit of detection.

Table 4: Methods of particle size measurement of SLN

Sr. No	Method	Principle	Measured size
1	Light scattering	Light Interaction	50 nm-1µm
2	Laser light diffraction	Light Interaction	1-1000 µm
3	Scanning electron microscope	Microscopy	50 nm-100 µm
4	Atomic force microscopy	Microscopy	10 nm-1µm
5	Analytical ultracentrifugation	Centrifugation	20 nm-1µm
6	Capillary electrophoresis	Electrophoresis	20-500 nm

2. Measurement of zeta potential: The measurement of the zeta potential allows for predictions about the storage stability of colloidal dispersion. In general, particle aggregation is less likely to occur for charged particles (high zeta potential) due to electric repulsion. Malvern Zetasizer is most widely used instrument for measurement of Zeta potential. Zeta potential below -25 mV and above + 25mV are required for full electrostatic stabilization of the formulation.[38]

3. Determination of incorporated drug (drug loading and entrapment efficiency):[37,38]

Amount of drug incorporated in nanoparticles affects the release property; hence it is very important to measure the amount of incorporated drug. The amount of drug encapsulated per unit weight of nano-particles is determined after separation of the free drug and solid lipids from the aqueous medium by ultracentrifugation, centrifugation filtration or gel permeation chromatography. The drug can be assayed by standard analytical technique such as spectroscopy and HPLC methods.

Two parameters expressing the efficiency of drug loading are most widely used. Entrapment efficiency is the amount of the drug incorporated in the particles divided by its overall amount in the formulation.

$$EE = \frac{Actual\ amt.\ of\ drug\ in\ formulation - soluble\ unencapsulated\ drug}{Amount\ of\ drug\ added\ during\ formulation} \times 100$$

Drug loading capacity (DL) is another parameter that expresses the amount of drug in the particles divided

by the weight of total carrier system (all ingredients taken together). DL is also expressed in %.

$$L = \frac{Actual\ amount\ \text{of}\ encapsulated\ drug \times 100}{Amount\ \text{of}\ lipid\ used\ to\ prepare\ the\ \text{formulation}}$$

4. Measurement of degree of crystallinity and lipid modification:[37, 39, 40]

The relation between thermodynamic stability and lipid packing density, and drug incorporation and release rates has been investigated for decades and is well established. Methods are mainly based on X-ray diffractometry (XRD) and differential scanning calorimetry (DSC) measurements.

5. In vitro drug release from SLNs[41,42]

Various methods used to study the in vitro release of the drug are:

a) Dialysis bag diffusion technique.

b) Reverse dialysis bag technique.

c) Agitation followed by ultracentrifugation or centrifugal ultra filtration

Applications of SLNs:[43-55]

- **Cancer Chemotherapy by using SLNs:**

Various chemotherapeutic agents have been encapsulated in the form of SLNs and their in-vitro and in-vivo efficacy have been evaluated by different scientist.[43] Different characteristics of SLNs like enhanced drug efficacy, batter pharmacokinetics, improved drug stability, encapsulation of chemotherapeutic agents with diversified physicochemical properties, *in-vitro* less toxicity make them a suitable carrier for delivering chemotherapeutic agents. Problem associated with anticancer compound like normal tissue toxicity, less stability, poor specificity and a high incidence of drug resistant overcome by using SLNs. The rapid removal of colloidal particles by the macrophages of the RES is a major obstacle to targeting tissues elsewhere in the body, such as bone marrow and solid tumors.[44,45]

- ✓ **SLNs in brain tumor and cancer:**

The main problem associated with anti-cancer drugs is difficulty in effective transport of across the BBB, resulting in lower therapeutic efficacy. A broad range of medicine and their modification have been investigated for their ability to treat glioblastoma, such as the SLNs of etoposide and paclitaxel. In vitro studies demonstrated that these had an enhanced inhibitory effect on the proliferation of glioma cell lines, which was performed more efficiently than when using the free drug alone.[43, 46]

- ✓ **SLNs as targeted carrier for anticancer drug to solid tumor:**

SLNs have been to be useful as drug carriers. Tamoxifen is an anticancer drug incorporated in SLN to prolong the release of drug after IV administration in breast cancer. Tumor targeting has been achieved with SLN loaded with drugs like methotrexate and camptothecin.[44]

- ✓ **SLNs in breast cancer and lymph node metastases:[47, 48]**

Mitoxantrone SLN local injections were formulated to reduce the toxicity and improve the safety and bioavailability of the drug in breast and lymph node cancer.

- **SLNs as potential new adjuvant for vaccines:**

To enhance the immune response of vaccine adjuvants are used. New developments in the adjuvant area are the emulsion systems. These are O/W emulsions that degrade rapidly in the body. Being in the solid state, the lipid components of SLNs will be degraded more slowly providing a longer lasting exposure to the immune system.[49]

- **Solid lipid nanoparticles for delivering peptides and proteins:**

Proteins and antigens intended for therapeutic purposes may be incorporated or adsorbed onto SLN. Formulation of protein SLNs confers enhance stability, prevent proteolytic degradation, sustained release can achieved of incorporated molecules. Peptides as cyclosporine A, insulin, calcitonin and somtostatin have been incorporated into solid lipid particles and are currently under investigation. There are several local or systemic therapeutic.[50]

- **SLN for Topical application:**

SLNs and NLCs are very attractive colloidal carrier systems for skin applications due to their various desirable effects on skin besides the characteristics of a colloidal carrier system. During the last few years, SLNs have been studied with active compounds such as Vit E, tocopherol acetate, retinol, clotrimazole, triptolide, and phodphyllotoxin for topical application.[51]

SLNs used for topical preparation for various drugs such as anticancers, imidazole, ketoconazole tropolide, glucocorticoids, vitamin A, isotretinoin, antifungals etc. By using glyceryl derivative vitamine A-loaded SLNs can be prepared.[52]

- **Solid lipid nanoparticles for parasitic diseases:**

SLNs and NLCs are effective alternative to liposomes mainly due to their better stability profile, ease of scalability and commercialization and relative cost efficacy. Both the formulation shows particulate nature and inherent structure which exhibit good potential in the treatment of parasitic infections. Parasitic diseases (malaria, leishmaniasis, tryanosomiasis) can treated by using SLNs.[49, 50]

- **Oral SLNs in anti-tubercular chemotherapy:**

Drugs such as isonizide, rifampicin, pyrazinamide-loaded SLNs systems, were able to reduce the dosing frequency and also improve patient compliance. By using the emulsion solvent diffusion technique these anti-tubercular drugs loaded SLN are prepared.[53] The nebulization in animal by incorporating the above drug in SLN also reported for improving the bioavailability of the drug.

➢ **SLNs as cosmeceuticals:**

The SLNs have been applied in the preparation of sunscreens and as an active carrier agent for molecular sunscreens and UV blockers. The in vivo study showed that skin hydration will be increased by 31% after 4 weeks by addition of 4% SLN to a conventional cream. SLN and NLCs have proved to be controlled release innovative occlusive topicals.[54, 55]

➢ **SLN for potential agriculture application:**

Artemisia arborescens extract when incorporated in SLNs, were able to decrease the rapid evaporation compared with emulsions and the systems have been used in agriculture as a suitable carrier of ecologically safe pesticide.[56]

Conclusion and Future Prospects:

In current scenario SLNs formulations mainly used as drug delivery system for poorly soluble drug. Nanoparticle has low toxicity, can be utilized for target drug delivery, controlled release application and the capacity to include lipophilic or hydrophilic drugs. This review focused on the variety of aspects of SLNs and their applicability in the encapsulation of various drugs. This article covers different technique of preparation of SLNs and evaluation, characterization parameters along with their applications in different fields. SLNs are, therefore, an option for administering poorly-soluble molecules via the oral route since they act as enhancers of intestinal absorption and provide protection for the encapsulated drugs. A combination of lipid or fatty acid with non-ionic emulsifiers has been shown to reduce the lipase-mediated degradation of SLNs after oral administration. According to the main applications reported in the literature, the use of SLNs to target drug delivery to the brain has increased in importance as alternative carriers for polymeric nanoparticles. Because of the SLN potential for facilitating controlled drug delivery to a target tissue and its biocompatibility, there will be much investigation in improvement of quality, efficacy, and safety profile of drugs using them in the future. A front line of research should merely be focused on the development of surface-modified SLNs for future perspectives. If properly explored, a very well-designed, SLNs seems to be a promising carrier that may open a new benchmark in treatment, diagnosis, and as a carrier for biological drugs.

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