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A REVIEW ON SOLID LIPID NANOPARTICLES AND ITS METHODS OF PREPARATIONS

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ABSTRACT

Solid lipid nanoparticles (SLN) are regarded as the forefront of nanotechnology's fast evolving sector, with numerous potential uses in drug delivery and research. SLN has potential characteristics for achieving the goal of regulated and site-specific drug delivery, and has so piqued the interest of many researchers .SLNs have emerged as effective vaccine delivery strategies. SLN-based vaccines promote site specific transfer, antigen presentation, innate immune response, robust T cell response, and safety against infectious illnesses, malignancies, autoimmune diseases, and neuro degeneration .This review discusses the morphology, structural properties, materials utilized in manufacture, production processes, and characterisation utilizing various methods of nano-structured lipid carriers and SLNs.

KEYWORD:- Bioavailability, Nanoparticles, Zeta potential, Electrostatic repulsion.

INTRODUCTION

As introduced in 1991 for the 1st time, SLNs are the systems of medication carriers in the nanometer range and contain nanometer biophysical solid lipids and active pharmaceutical ingredients mainly scattered in fluid surfactant arrangements or water. These lipids are solid at the body or room temperature.[1] For intravenous injection of drugs, SLNs possess several advantages including size, capacity of high drug loading, large surface area, non-toxicity, high stability and bioavailability, and specific interaction with the receptors of the target site. In addition, they are practical for their potential to improve pharmaceutical performances.[2] fig 1

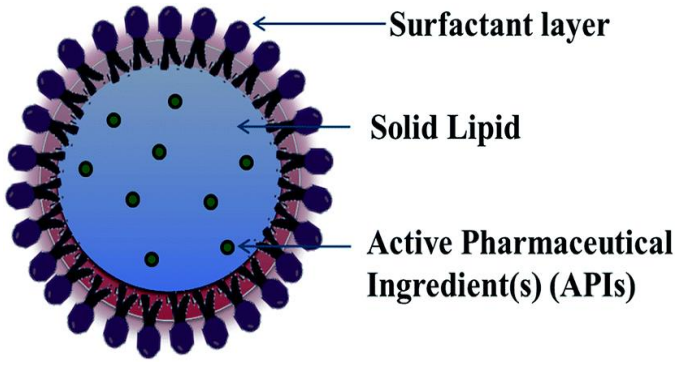

Fig. 1: Structure of solid lipid nanoparticle.

Because of some drawbacks of the liquid state of the oil droplet, solid lipids are preferred over liquid lipids. This replacement had some significant advantages, for example, high biocompatibility and low toxicity. Furthermore, lipophilic drugs are delivered effectively by SLNs, and the system is physically stable in the biological media.[2][3] Drug delivery systems are divided into different groups based on the degree of biodegradability and routes of administration, etc. The way of administration for SLNs is flexible and almost all routes of administration, such as parental, ocular, pulmonary, dermal, and topical administrations are compatible with SLNs.[1] A unique SLN system should have these parameters: 1) High drug bioavailability, 2)

Minimum immune response, 3) Controlled release kinetic, 4) Tissue targeting, 5) Good patient compliance, 6) High capacity for drug loading, 7) Capability of deliver traditionally difficult drugs such as biomolecules. fig 2

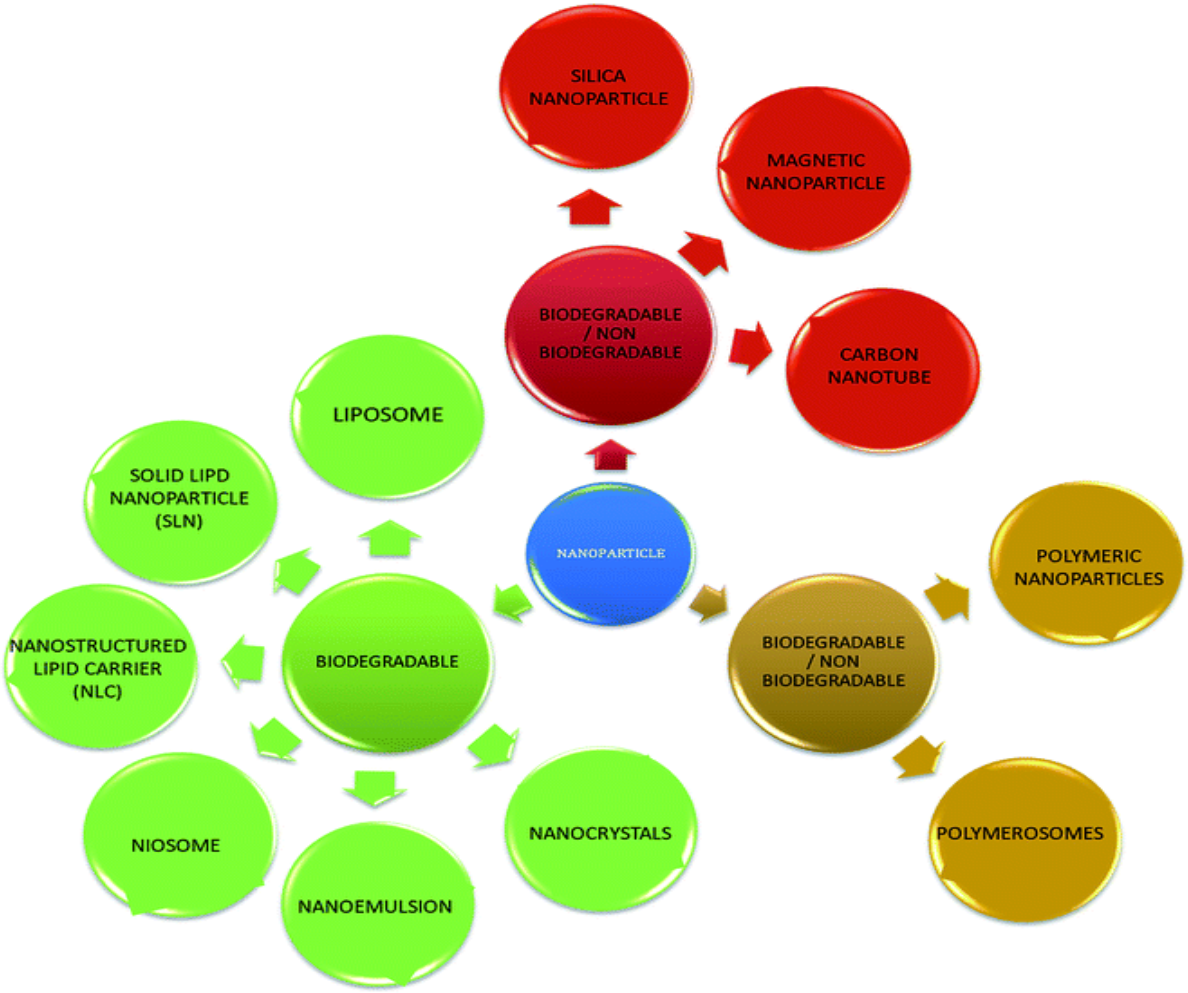

Fig. 2: Classification of nanoparticles.

Advantages of SLN

Utilizing biodegradable physiological lipids reduces the risk of both acute and long-term toxicity, and using chemical solvents in the production process is avoided.

- Better bioavailability of compounds that are poorly soluble in water.
- Drugs are delivered to specified sites, and dermal application improves drug penetration into the skin.
- The potential for both medication targeting and controlled release.
- Preventing sensitive molecules from the external environment and chemically labile substances from degrading in the stomach.
- SLNs have superior stability in contrast to liposomes.
- Increase the chemical synthesis of labile incorporated compounds and the bioavailability of entrapped bioactives.
- A high level of the functional chemical was attained.
- Possible lyophilisation,[24,25,26]

Disadvantages of SLN

- Poor drug loading capacity.
- Drug expulsion after polymeric transition during storage.
- Relatively highwater content of the dispersions (70-99.9%).
- The low capacity to load water soluble drugs due to partitioning effects during the production process[28] Eccentric gelation propensity.
- Unforeseen motion of polymeric transition.[29,30]

Preparation methods

1. **High pressure homogenization or HPH (cold/hot)[4]**

With HPH, a liquid or dispersion is forced through a few micrometers of space at high pressure (100–2000 bar) to create particles that are smaller than microns. The particles are broken down by cavitational forces and a strong shear stress, which reduces the particle size. There are two types of HPH: hot-HPH, which is done at a high temperature, and cold-HPH, which is done below room temperature.[5] To dissolve or disperse the medication in

the melted lipid, the lipids and medicines are heated to a temperature that is 5–10 °C above the lipid's melting point in the first phase of both procedures.[6] Lipids typically range in content from 5% to 20% w/v. The aqueous phase containing the amphiphile molecules is added to the lipid phase in the second step of the HPH process (at the same temperature as the lipid melting), and a high-speed stirring device is used to create the hot pre-emulsion. Depending on the formulation and desired outcome, the lipid (more is added for homogenization) is driven three to five times through a small area (few µm) at high pressure (100–1000 bar). The medication is dissolved or distributed throughout the lipid melt prior to homogenization. Nevertheless, this approach has the following disadvantages: Drugs that are heat-sensitive cannot be employed due to their deterioration, and increasing the number of rotations or pressure of homogeneity frequently causes the particle size to rise.[7]

However, by preparing SLNs with cold-HPH, these limitations can be addressed. As was previously mentioned, the first stage entails creating a suspension of medicines and melting lipids, which is then quickly cooled in liquid nitrogen and dry ice. The third step involves grinding the powder to create microparticles. The microparticles are then dissolved in a cold solution of aqueous surfactant. In the last phase, homogenization is typically carried out for five cycles at 500 bars in order to produce SLNs.[8] fig 3

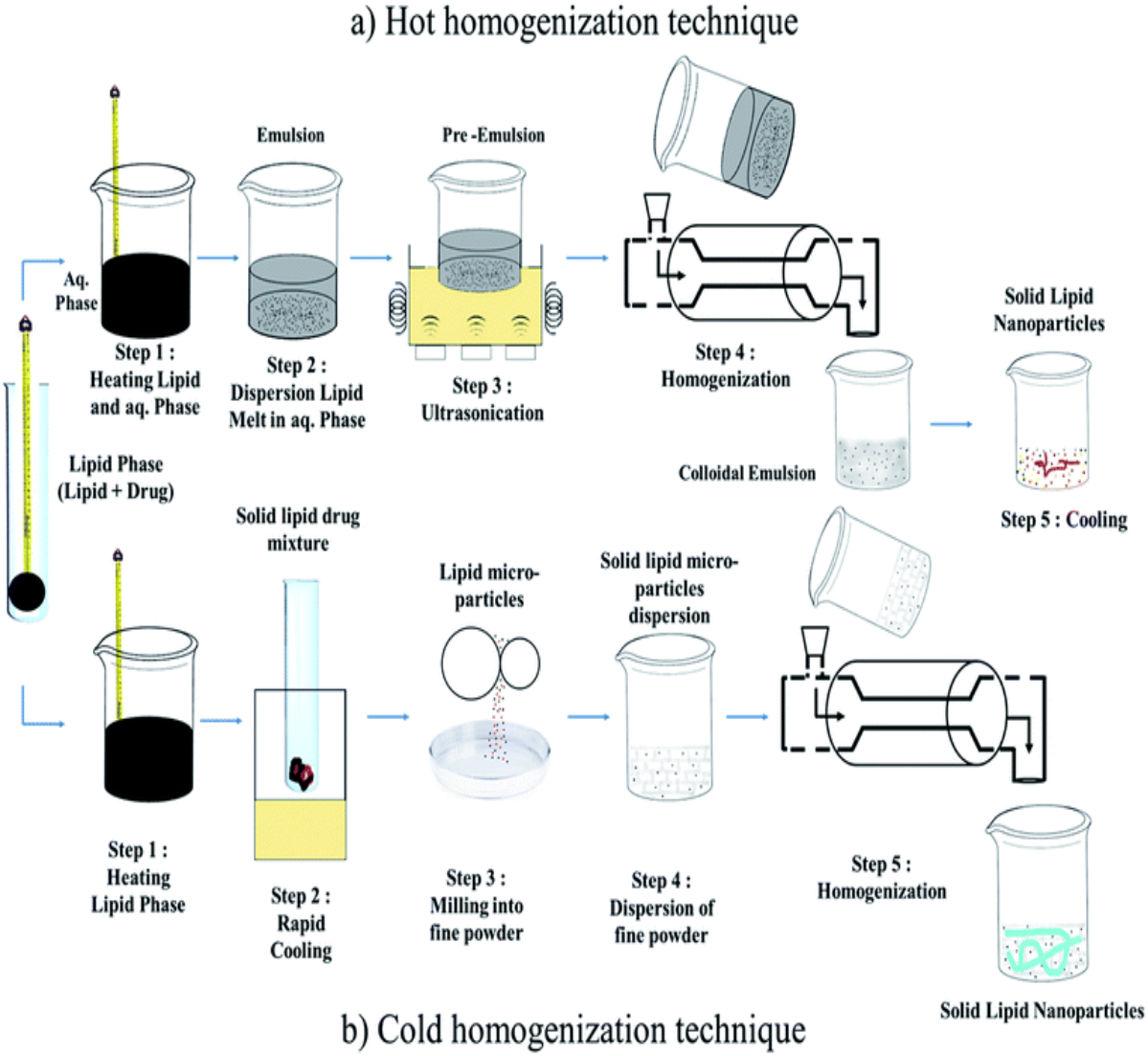

Fig. 3: Homogenization technique.

2. Oil/water [o/w] microemulsion breaking technique

The process for splitting oil/water (o/w) microemulsions Gasco developed this technique. In order to create the microemulsion, the lipid melt is first combined with a drug, surfactant, and co-surfactant mixture that has been heated to the lipid's melting point. The resulting microemulsion is then dissolved in water that is between 2 and 10 °C.fig 4

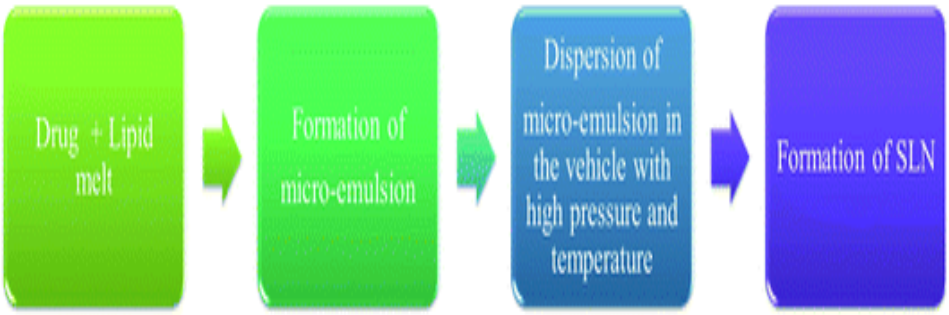

Fig. 4: Microemulsion technique.

3. Solvent-emulsification diffusion technique[9]

The diffusion method of solvent-emulsification, solvent-emulsification diffusion method for creating solid lipid nanoparticles is depicted in This process involves dissolving the lipid in an organic solvent that has been saturated with water. The resulting solution is then further emulsified with water and saturated with organic solvent while being continuously stirred. By adding water to the created emulsion, which subsequently causes the organic phase to diffuse into the continuous phase, lipid nanoparticles are produced. It is possible to purify the SLN dispersion by ultra-filtration with a dialysis membrane that has a cut-off of roughly 100,000 kDa.fig 5

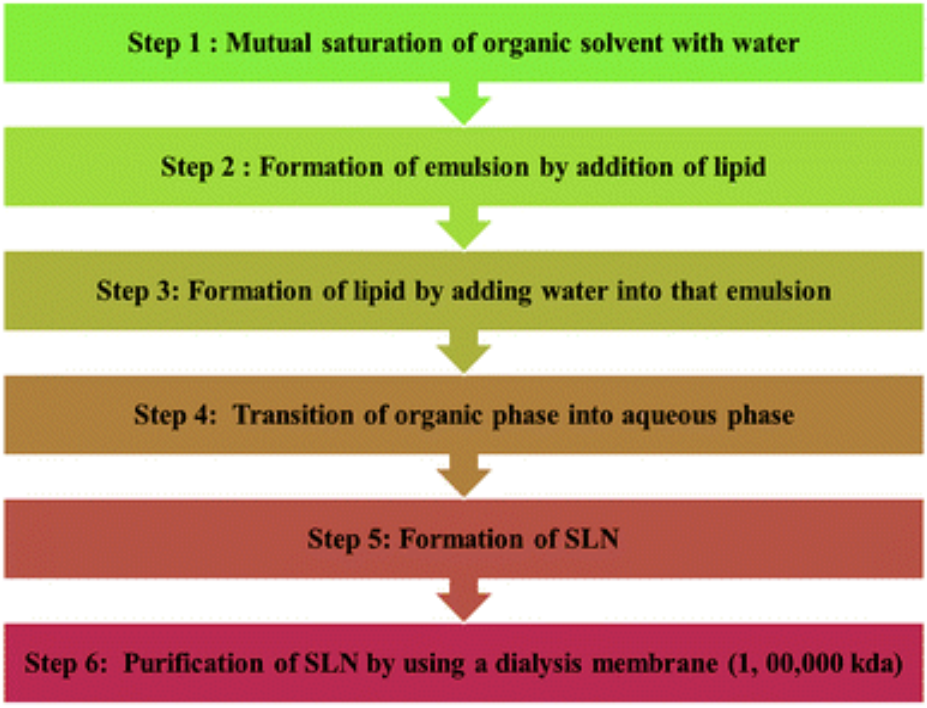

Fig. 5: Solvent emulsion diffusion method.

4. Solvent injection method[10]

Injecting a solvent This technique involves dissolving the lipids in a solvent that dissolves in water, then injecting the dissolved lipids—with or without surfactant—through an injection needle into a swirling aqueous solution. The kind of injected solvent, lipid concentration, injected volume of lipid solution, viscosity, and the diffusion of the lipid solvent phase into the aqueous phase are the parameters of the process for the production of nanoparticles using this approach.[10]

5. Water/oil/water[w/o/w] double emulsion method[11]

The double emulsion method of water/oil/water (w/o/w)[11] The double emulsion method for creating SLNs is depicted. The creation of SLNs loaded with hydrophilic medications and some biological molecules, such peptides and insulin, is the primary use for this technique. The solvent in water emulsion diffusion technique is used to create SLNs from w/o/w multiple emulsions. Insulin dissolves in the inner acidic phase of the w/o/w multiple emulsion, while lipids dissolve in the water while lipids dissolve in the water-miscible organic phase. The w/o/w emulsion is then diluted in water to create SLNs. As a result, the SLNs precipitate and the organic solvent diffuses into the aqueous phase. The preparation procedure utilizing this method is influenced by the solvent's characteristics as well as how the hydrophilic medication interacts with the solvent and excipients. fig 6

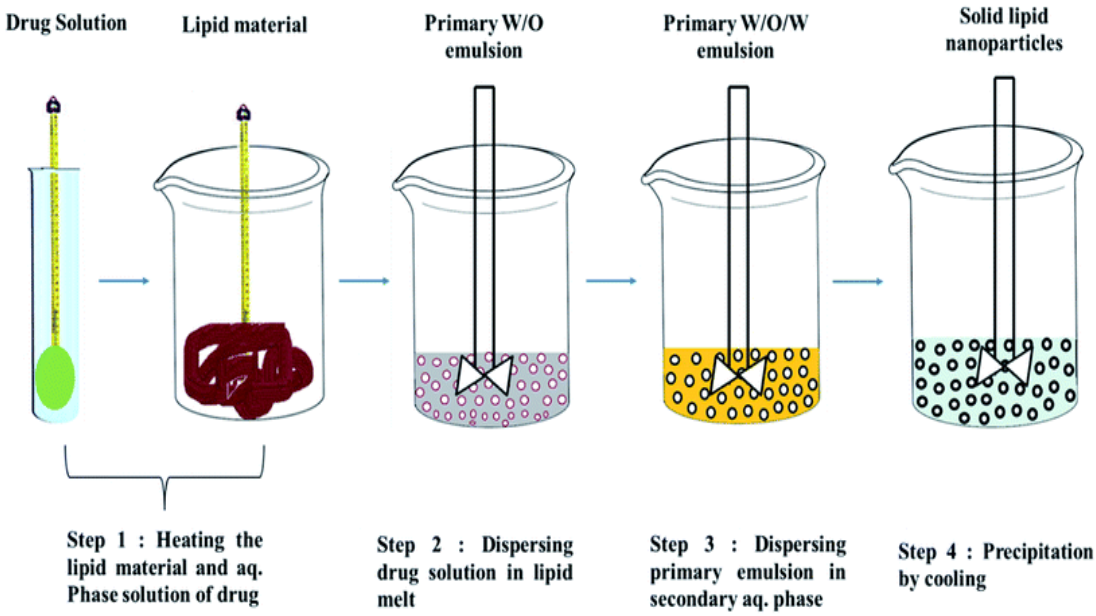

Fig. 6: Double emulsion method.

6. Ultrasonication[11]

The use of ultrasound[11] The idea behind this technique is to use sound waves to reduce particle size. This technique prepares SLNs with a size range of 80–800 nm by simultaneously using high pressure homogenization and ultrasonication.

7. Super critical fluid technique[13]

The technology of super critical fluid[13] When utilized in conjunction with the ultrasonication procedure, super critical carbon dioxide has the ability to dissolve lipophilic medicines and can be used to create SLNs. Ultrasonication and super critical carbon dioxide fluid extraction have been used to create Xionggui-loaded SLNs. Fig 7

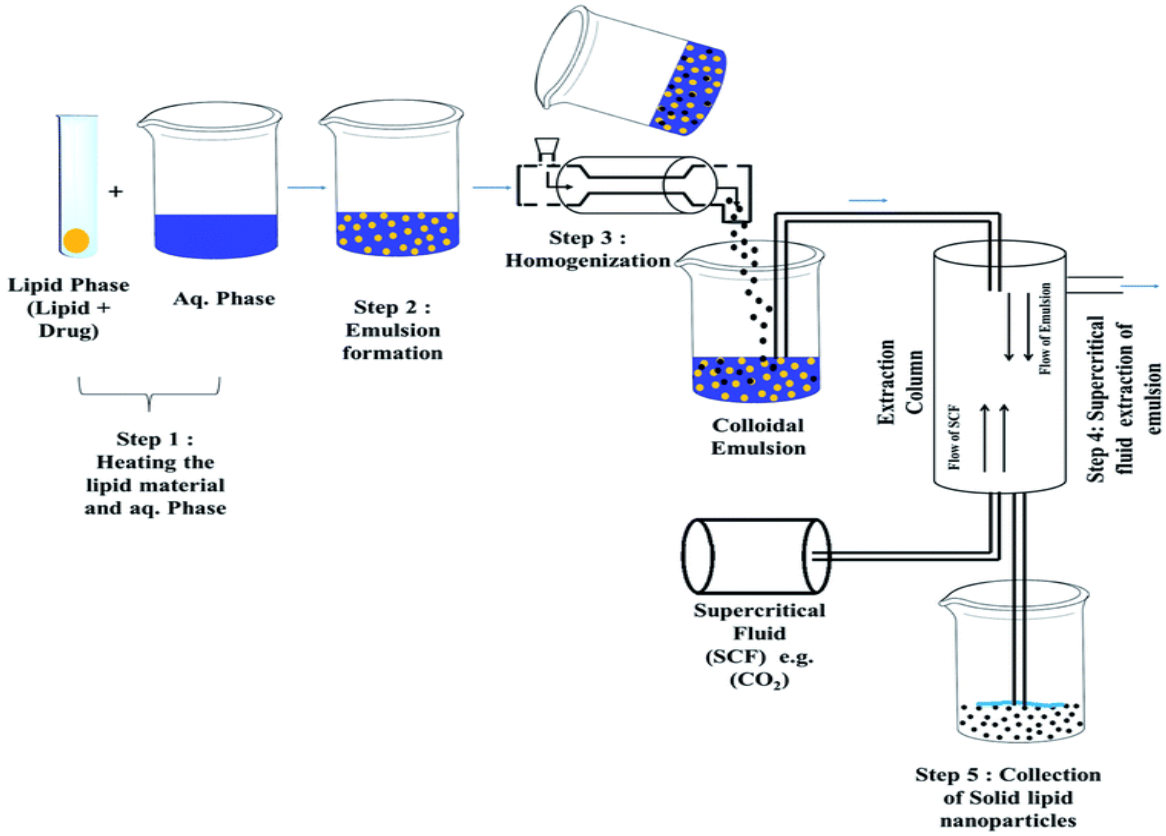

Fig. 7: Super critical fluid technique.

8. Membrane contractor technique[14]

The technique of membrane contractors.[14] This process creates SLNs by pressing a lipid through membrane pores at a temperature higher than its melting point. Water that circulates outside the pores flows with the melted lipid droplets that are then cooled to room temperature.

9. Electrospray technique[15]

The electrospray method[15] Electrodynamic atomization is a new and recent method for creating SLNs. It creates spherically dispersed SLNs that are smaller than 1 µm. SLNs are directly obtained in powder form using this approach.

Preparation of semisolid solid lipid nanoparticles

Making solid lipid nanoparticles that are semisolid A single-step, more efficient method was created to produce SLNs, particularly semisolid formulations.The procedure involves melting a lipid, dispersing it in a heated surfactant solution that is about 10 °C above its melting point, and then rotating it for one minute at 9500 rpm. After that, three dispersion cycles are carried out at 500 bar of pressure and 85 °C. The dispersion turns viscous once the first cycle is finished and is used for the next two cycles. The heated, viscous nanoemulsion is then allowed to cool to ambient temperature. The SLNs become semi-solid compatible as a result of the lipid droplets recrystallizing and forming a gel network. This method requires a lipid content of 30 to 50 percent w/v.[16]

Characterization

Characterization of SLN analytically Controlling the product's quality requires a sufficient characterization of the SLNs. A number of factors that directly affect stability and release kinetics must be taken into account:

- Zeta potential and particle size.
- Level of lipid modification and crystallinity
- Co-existence of other structures and dynamic processes.

Zeta Potential and Particle size measurement[17,18]

The most effective methods for everyday particle size measurements are laser diffraction (LD) and photon correlation spectroscopy (PCS). PCS, which is another name for dynamic light scattering, quantifies the variation in scattered light intensity brought on by particle motion. The size range covered by this technique is a few nanometers to roughly three microns.

- **Dynamic light scattering (DLS)[18,19]**

DLS, also called PCS, records the variation in the intensity of the scattered light on the microsecond time scale. 92 P. Ekambaram et al.: Solid Lipid Nanoparticles.

- **Static light scattering (SLS)/fraunhofer diffraction**

SLS is an ensemble method in which the light scattered from a solution of particles is collected and fit into fundamental primary variables.

- **Acoustic methods**

It measures the attenuation of the scattered sound waves as a means of determining size through the fitting of physically relevant equations.

- **Nuclear magnetic resonance (NMR)[20]**

Both the size and qualitative nature of nanoparticles.

- **Microscopy of electrons[21,22]**

Nanoparticles can be directly measured and physically characterized using scanning electron microscopy (SEM) and transmission electron microscopy (TEM), with the former being utilized for morphological analysis. The size limit of detection for TEM is smaller.

- **AFM or atomic force microscopy**

A topological map is created by rastering a probe tip with atomic scale sharpness across a sample, taking into account the forces acting between the tip and the surface.

- **Diffraction of powdered X-rays with differential scanning calorimetry (DSC)[18,23]**

The degree of crystallinity can be evaluated by determining whether or not there are crystal planes in a solid by the geometric scattering of their radiation. The type and species of crystallinity in nanoparticles can be ascertained via DSC.the speciation of crystallinity within nanoparticles through the measurement of glass and melting point temperature.

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Drug Name	Lipid	Surfactant	Co Surfactant	Method of preparation	Technique for Characterization	Size(nm)
Amphotericin B	Compritol ® ATO 888, Precirol ATO 5 and stearic acid, Compritol® ATO 888 (glyceryl behenate), glyceryl palmitostearate (Precirol ® ATO 5), medium chain triglyceride.	Pluronic® F-68, Pluronic® F-127, Tween 20, Pluronic® F-127, Cremophor RH40, polyoxy ethylene (40) stearate (Myrj 52)		Solvent diffusion method HPH	DLS, DSC, zeta potential DLS, zeta potential, HPLC, TEM, FTIR, DSC, PXRD, ^{1}H NMR	111–415.8 90–260
Baclofen	Stearic acid	Epikuron 200 (92% phosphatidylcholine)	Propionic acid, butyric acid, and sodium taurocholate	Multiple (w/o/w) warm, microemulsion	DLS	161.4
Buspirone HCl	Cetyl alcohol, Spermaceti	Pluronic® F-68, Tween 80		Emulsification-evaporation followed by ultrasonication	DLS	86–123

Application of solid lipid nanoparticals

1. SLN as potential new adjuvant for vaccines

SLN as a Possible Novel Vaccine Adjuvant In order to boost the immune response, adjuvants are utilized in vaccinations. Effective adjuvants are necessary since the safer modern subunit vaccinations are less effective at immunizing. Emulsion systems are new innovations in the adjuvant field. These are emulsions of oil and water that break down quickly in the body.

2. Solid lipid nanoparticles in chemotherapy for cancer

It has been demonstrated that the results of these investigations increase the effectiveness of chemotherapeutic medications while also lowering their negative effects. The key characteristics of SLN that make them an appropriate carrier for delivering chemotherapeutic agents are improved drug stability, encapsulation of chemotherapeutic agents with a variety of physicochemical properties, increased medication efficacy, improved pharmacokinetics, and reduced in vitro toxicity.

Delivering the molecule SLN at least partially overcomes a number of challenges commonly faced by anticancer drugs, including normal tissue toxicity, poor selectivity and stability, and a high rate of drug-resistant tumor cells.

3. SLN as a specific anticancer drug delivery system for solid tumors[31,32,33]

4. SLN in lymph node metastases and breast cancer[33]

5. Solid Lipid Nanoparticles for Protein and Peptide Delivery[34]

It is possible to integrate or adsorbed therapeutic proteins and antigens onto SLN. Improved protein stability, prevention of proteolytic degradation, and prolonged release of the integrated molecules are all benefits of formulation in SLN. Important peptides that have been integrated into solid lipid particles that are presently being studied include insulin, calcitonin, somtostatin, cyclosporine A, and others.Numerous systemic or local therapies are available.

6. SLN for topical application

Topical use of SLN In addition to their colloidal carrier system properties, SLN and NLC have a number of positive skin benefits that make them highly appealing colloidal carrier systems for skin applications. Active ingredients like vitamin E, tocopherol acetate, retinol, ascorbyl palmitate, clotrimazole, triptolide, phodphyllotoxin, and a nonsteroidal antiandrogen called RU 58841 have been used in studies of SLN and NLC in recent years.

7. SLN for possible use in agriculture

When added to SLN, essential oil from Artemisia arborescens L. was able to slow down evaporation more quickly than emulsions, and the systems were employed in agriculture as an appropriate vehicle for environmentally safe pesticides

8. Stealth nanoparticles

These offer a fresh and distinctive method of medication delivery that avoids the immune system's rapid clearance.Such nanoparticles have the potential to target particular cells. Increased delivery to the target tissue in accessible places has been demonstrated in studies using antibody-labeled stealth lipobodies.

9. SLN as cosmeceuticals

The SLNs have been used as an active carrier agent for UV blockers and molecular sunscreens as well as in the manufacturing of sunscreens. According to the in vivo study, adding 4% SLN to a regular cream will boost skin moisture by 31% after 4 weeks. Innovative occlusive topicals with controlled release have been demonstrated by SLN and NLCs.

CONCLUSION

As suggested, solid lipid nanoparticles do not "avoid the drawbacks of other colloidal drug carriers and combine their advantages." The outcomes are more complex than just solid-core nano emulsions. The composition (physiological compounds), the quick and efficient production process, which allows for large-scale production, and the avoidance of organic 98 are all obvious benefits of SLN.Solid lipid nanoparticles, solvents, and the potential to create carriers with improved encapsulation efficiency Low drug-loading capacities, the existence of alternative colloidal structures, the intricacy of the lipid's physical state), and the potential for supercooled melts that result in stability issues during administration or storage are some drawbacks.Colloidal dispersions with altered characteristics of other nanoparticles, including liposomes, suspensions, microemulsions, and polymeric nanoparticles, are known as solid lipid nanoparticles. With the help of SLNs, the main issues with nanoparticles can be avoided one at a time, leading to a drug delivery system that is both physiologically appropriate and chemically stable with fewer restrictions. The primary issue appears to be their propensity to gel, but nanostructured lipid carriers may be able to address this issue. Additionally, the heat and stress produced during the hot homogenization technique of manufacture may cause the drug's active ingredient to deteriorate. Selecting a suitable production method is so essential.

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