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SOLID LIPID NANOPARTICLES

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***Abstract*:** Solid lipid nanoparticles is a rapidly developing topic of applied science with a wide range of potential uses in research and pharmaceutical delivery. Solid lipid nanoparticles are colloidal spherical particles with a diameter of approximately 10 to 1000nm, made up of physiological lipid suspended in a liquid or an aqueous surfactant solution. Solid lipid nanoparticles are composed of lipid and stabilizers mostly surfactants, cosurfactants and coating materials. Applications are also found for antioxidants, electrolytes, preservatives, viscosity-enhancing compounds, adhesives, absorption enhancers, and other excipients. Majority of the formulation ingredients are secure and have been given the Food and Drug Administration's (FDA), Generally Recognized As Safe (GRAS). They offer distinctive characteristics such as a large surface area, various sizes, high drug loading, and phase interaction at the interface, and are appealing for their potential to increase pharmaceutical efficacy. This review describes the benefits, limitations and method of preparations and characterization of solid lipid nanoparticles.

Key Words: Solid lipid Nano particles, Lipids, Stabilizers.

Introduction: Solid lipid nanoparticles (SLN) were first developed in 1991 as an alternative to colloidal transporters which including emulsions, liposomes, and polymeric micro- and nanoparticles shown on Fig 1. [1]. Solid lipid nanoparticles are attracting more and more attention as a novel colloidal pharmaceutical carrier. Intravascular applications, as an alternate particle carrier method, has been proposed. Physiological lipid-based sub-micron colloidal carriers with diameters ranging from 50 to 1000 nm. In aqueous surfactant solution or distributed in water SLN has unique characteristics such as a tiny size and a lot of capacity, surface area, high drug loading, and phase interactions. They have the ability to improve their performance [2,3,4].

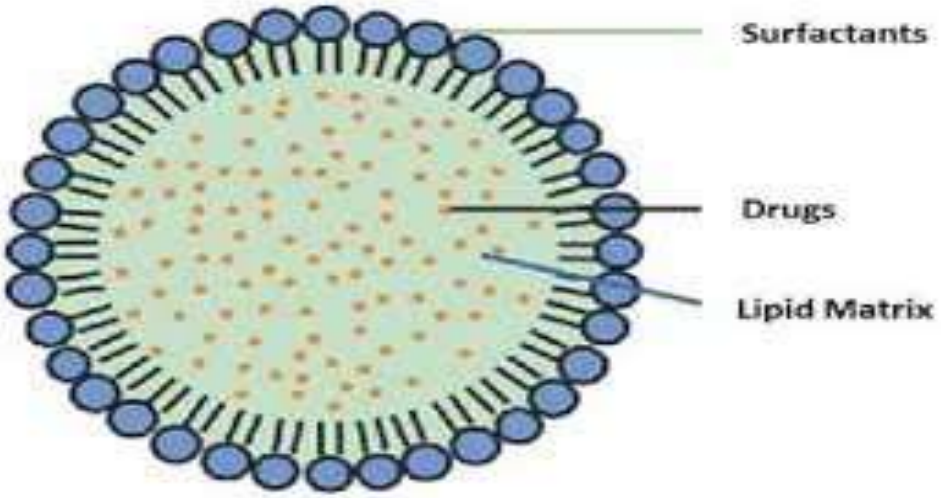

Figure 1: Chemical structure of solid lipid nanoparticles

***Advantages*:** SLNs have a number of benefits for drug delivery, including lipid chemical stability, increased permeability through biological membranes, ability to modify their surface and capability to co-deliver a large number of pharmaceuticals, and drug degradation changes [5]. The matrix of the SLN protects drug-loaded carriers from a variety of chemical degradations, resulting in increased drug stability. It is possible to extend drug release by lowering the fluctuations in the therapeutic zone, resulting in a controlled drug release profile with minimal toxicity [6]. The use of potentially toxic additives such as organic solvents or toxic monomers are excluded when lipid particles are made. The lipid matrix inhibits drug leakage from the carrier, thus the rigid solid particles generated are stable against flocculations [7].

***Disadvantages*:** Drug leakage, high water content, and inadequate drug loading may cause solid lipid nanoparticles to transform into nanostructured lipid carriers [8,9,10]. Drug ejection during storage is one of the drawbacks of SLNs. During storage, the reestablishment of lipid molecules into a perfect crystal lattice limits the area available for drug integration, resulting in drug discharge [11,12].

***Preparation of solid lipid nanoparticles*:** Various techniques are given below for producing solid lipid nanoparticles from lipids, emulsifiers, and water solvents.

METHODS OF PREPARATION OF SOLID LIPID NANOPARTICLES:

***High pressure homogenization*:** High-Pressure Homogenization (HPH), which could also operate at low or high temperatures, is the most widely used production technology. HPH has been reported to be the technology utilized for the manufacturing of parenteral nutrition products such as Intralipid and Lipofundin for more than fifty years [13,14,15] shown on Fig.2

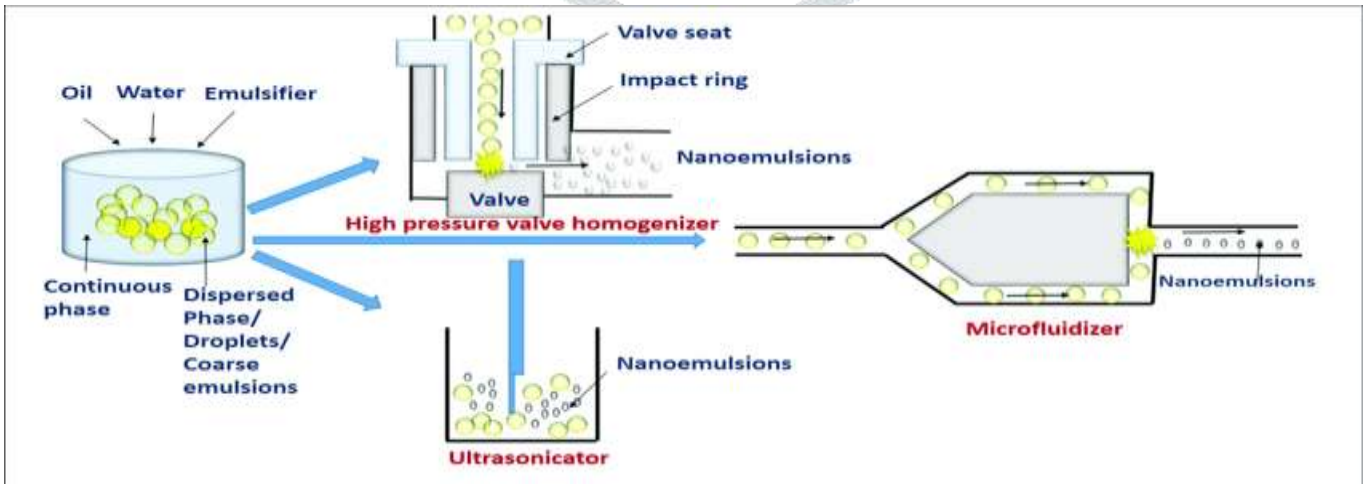

FIGURE 2: High pressure homogenization

Hot homogenization: Hot homogenization occurs at temperatures over the lipid's melting point and is consequently referred to as emulsion homogenization. A high-shear mixing mechanism creates a pre-emulsion of the drug-loaded lipid melt and the aqueous

emulsifier phase (at the same temperature). HPH of the pre-emulsion is done at temperatures over the lipid's melting point. Higher temperatures cause the inner phase's viscosity to drop, resulting in smaller particle sizes. High temperatures, on the other hand, hasten the deterioration of both the medicine and the carrier. Due to the high kinetic energy of the particles, increasing the homogenization pressure or the number of cycles frequently leads to an increase in particle size [16,17,18] shown on Fig.3.

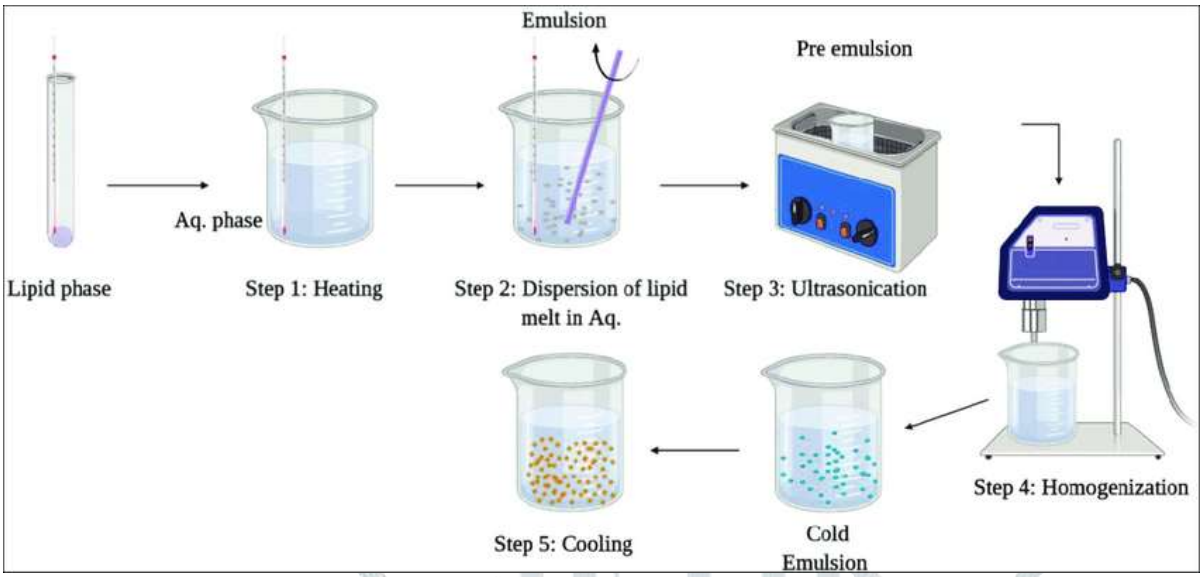

Figure 3: Hot homogenization

Cold homogenization: The initial stage in this approach is the same as in hot homogenization: the medication is dispersed, dissolved, or solubilized in the melted lipid. The drug-lipid combination is then quickly solidified using liquid nitrogen or dry ice. To make a pre-suspension, the drug-loaded solid lipid is milled to a micron size range of 50 micron to 100 micron in a chilled emulsifier solution. The pre-suspension is then homogenized at high pressure at room or below ambient temperature, where the cavitation force is capable of breaking the microparticles down to SLN [19] shown in figure 4.

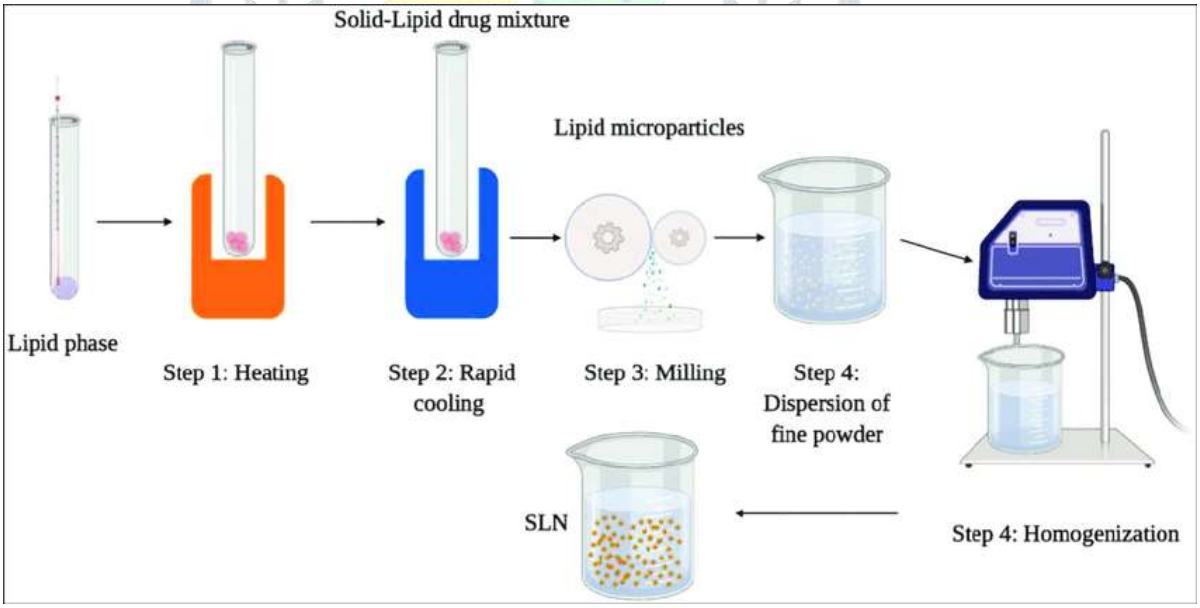

Figure 4: Cold homogenization

***High-speed homogenization and ultrasonication*:** This approach is used to generate a dispersion of saturated lipid nanoparticles [20]. The addition of a medication to melted lipid is the initial step in this approach. This approach is based on dispersing the melted lipid in a warm aqueous solution (approximately 5°C to 10°C above its melting point to avoid recrystallization during the procedure), incorporating surfactants, and homogenizing the emulsion with high shear homogenization. On a laboratory scale using a water bath (at 0°C), the resulting pre-emulsion was ultrasonicated using only a probe sonicator. To eliminate contaminants introduced during ultrasonication, the resultant nano emulsion (o/w) was filtered via a 0.45 m membrane. Then they got SLN, which is kept at 4 degrees Celsius [21].

Solvent evaporation method: A solvent evaporation approach can be used to make SLNs. The lipophilic substance is dissolved in a water-insoluble organic solvent (for example, cyclohexane) and emulsified in an aqueous phase. Nanoparticle dispersion is created by the precipitation of the lipid in the aqueous medium following the evaporation of the solvent, resulting in nanoparticles with a mean size of 25 nm. High-pressure homogenization was used to emulsify the solutions in an aqueous phase. Evaporation under lower pressure (40–60 bar) was used to extract the organic solvent from the dispersion [16].

Spray drying: It is a method of lyophilization that can be used instead. This involves the use of lipids having a melting point greater than 70 degrees Celsius. The best results were obtained using a 1% SLN concentration in a liquid solution or a 20% trehalose concentration in an ethanol-water mixture [16,22].

Double emulsion method: The hydrophilic medication is dissolved in an aqueous solution and then emulsified in melting lipid in the double emulsion process. Suitable stabilizers, including such gelatin and poloxamer-407, were added to this initial emulsion to make it more stable. The initial emulsion was then stabilized and disseminated in an aqueous solution containing a hydrophilic emulsifier such as PVA. The double emulsion was also agitated and filtered to separate it [23]. Shown on figure.5

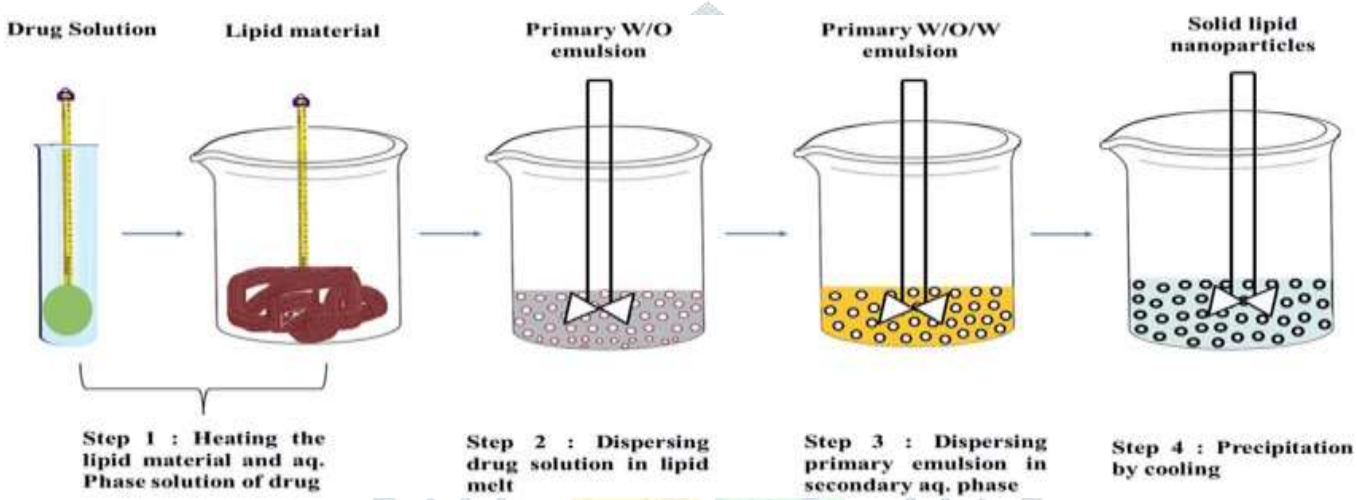

FIGURE 5: Double emulsion method

***Solvent injection method*:** The solid lipid was dissolved in a water-miscible solvent (for example, ethanol, acetone, isopropanol) or a water-miscible solvent mixture, and the lipid solvent mixture was delivered into a stirred aqueous medium with or without the addition of a surfactant using an injection needle. A filter paper was used to remove any extra lipid from the resulting dispersion. The inclusion of an emulsifier within the aqueous solution causes the development of lipid droplets at the injection site, which helps to stabilize SLN until solvent diffusion is accomplished by lowering the surface tension between both the organic solvent and the dispersion medium [24,25,26]. Shown on figure.6

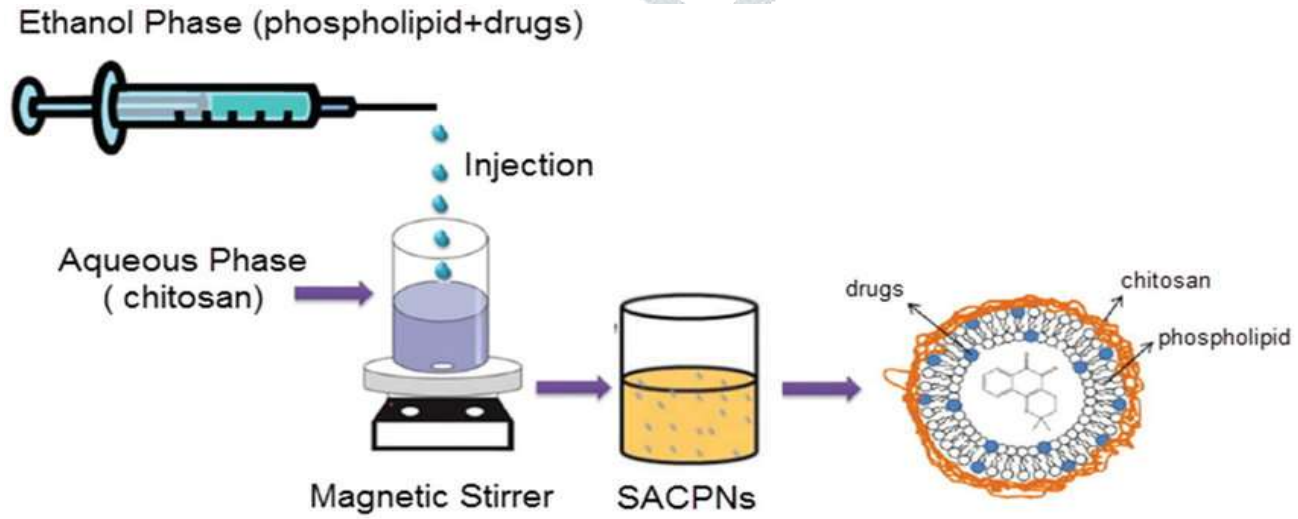

Figure 6: solvent injection method

Film ultrasound dispersion: The lipid and medications were dissolved in suitable organic solutions, then an aqueous phase including surfactant solution was given to the lipid phase with vigorous stirring, and a lipid film was created following evaporation of the organic solutions. Continue stirring with the probe solicitor and ultrasound until the SLN with small and polydispersed particle size is generated [27].

Membrane Contractor technique: The SLN is prepared using a unique process. The lipid was squeezed through the porous membrane to create smaller droplets using this approach at a temperature above the melting point of the lipid. The aqueous phase was cycled tangentially inside the membrane module with continual stirring at the same time, bowing the droplets forming at the pore outputs. SLN is created after it cools to room temperature. Both components were placed in a thermostate bath to maintain a constant temperature, and nitrogen gas was used to create pressure in the liquid state [27,28].

CHARACTERIZATION OF SOLID LIPID NANOPARTICLES:

Nanoparticle systems' size and distribution are essential features. They study the in vivo distribution, physiological function, and targeting properties of nanoparticle medication delivery. They can also control drug loading, drug release, and nanoparticle stability, among other things. In terms of medicine, several studies have proven that sub-micron nanoparticles exceed tiny particles.

DETERMINATION OF PARTICLE SIZE:

Zeta potential: The surface charge of solid lipid nanoparticles is determined using a Zetasizer and electrophoretic mobility in a U type tube at 25°C. The zeta potential indicates the amount of charge on suspended particles in a distribution. Because particles inhibit aggregation, the high value of zeta potential confers stability. The value of zeta potential ranged from 15.9 to 22.1[29].

Degree of crystalline: X-ray diffraction (powder X-ray diffraction) can be used to determine it. The presence or absence of a crystalline phase within a solid can be evaluated via geometric scattering of radiation, allowing the degree of crystallinity to be quantified. Differential Scanning Calorimetry (DSC) can be used to identify the type and speciation of crystallinity inside nanoparticles by measuring glass and melting point temperatures and their related enthalpies, which is a little different from how it's performed with bulk materials [30,31,32].

Drug incorporation and loading capacity: The particle size, loading capacity, and size and shape of SLNs are observed to vary depending on the lipid (triglycerides, fatty acids, steroids, waxes, etc.), surfactant (anionic, cationic, non-ionic), and manufacturing process, among other factors [33,34].

Polydispersity index: The polydispersity index (PI), which is vital to understanding the size and distribution of nanoparticles, is determined by the polydispersity of SLNs/NLCs. The more monodispersed the nanoparticle dispersion is, the lower the PI value. Many researchers consider a Value obtained of less than 0.3 to be ideal [35,36].

Differential scanning calorimetry (DSC): It is a widely used method for determining how much heat is needed to raise a sample's temperature in comparison to a reference. Positive or negative variations in heat flow are shown as functions of temperature. There are differences between the sample and the reference at the phase transition. DSC can provide information on the sample structure and interactions between the components because different lipid modifications have distinct melting points and melting enthalpies. It is strongly advised to check the DSC results using a different method, particularly when high melting Active Pharmaceutical Ingredients (APIs) are present because they can dissolve in the melted lipid blend but tend to crystallize in the solid lipids [36,37].

Powder x-ray diffraction (PXD): This method involves illuminating the sample with X-rays of a fixed wavelength and measuring the intensity of the reflected radiation. The inter-atomic gap is calculated using this data. Researchers frequently employ PXD to examine the SLN and NLC crystal structures. The water from the colloidal suspension must be removed because it is carried out on powders. Following sample dehydration, many polymorph changes can develop. As a result, PXD cannot be used to determine the crystallinity of particles that were created as colloidal suspensions and are being stored. PXD helps characterize helpful in characterizing lyophilized and spray-dried of SLN [37,38].

Conclusion: The study stated clearly that SLNs have become a potential new medication delivery mechanism in recent years. This review highlights the excellent therapeutic activity of pharmaceuticals including solid lipid nanoparticles, which maximizes efficacy while minimizing side effects on tissues other than the target tissue. The choice of constituents that affect the formulations' stability, prolonged release of the drugs, and drug loading capacity are all covered in the current study. According to the review report, SLNs are intricate systems with rapidly evolving nanotechnology that may be used for oral delivery to enhance GI absorption of weakly water-soluble medicines.

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