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A Comprehensive Review on Solid Lipid Nanoparticles

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ABSTRACT

Polymeric nanoparticles can be used as an alternative compared to other classic colloidal carriers like liposomes, and emulsions due to their benefits such as controlled delivery of drugs, focused drug delivery, and enhanced stability, solid lipid nanoparticles were created in the early 1990s. This page provides a overview of the possible benefits and drawbacks of solid lipid nanoparticles, excipients, and all of the many techniques used to make them, including the membrane contractor approach. aspects of the stability of SLN and the impact of different excipients (used in the manufacturing of SLN) on stability, as well as other secondary stages involved in their stabilization, such as freeze drying, spray drying, etc. The issues surrounding SLN manufacture as well as the instrumental methods employed are extensively examined.

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INTRODUCTION:

As an efficient carrier method for correcting effective medicine and water-soluble drug, solid nanoparticles of lipids (SLNs) are proposed. Nanoparticles are colloidal molecules with a size among 10 and 1000 nm. These are made of synthetic distinctive polymers and designed to improve drug delivery and reduce mortality.[1]

They have designed as a flexible alternative to lipid nanoparticles as a drug delivery system. They are ideally suited to maximise sedate release and decrease lethality since they are produced using artificial or special polymers.[2]

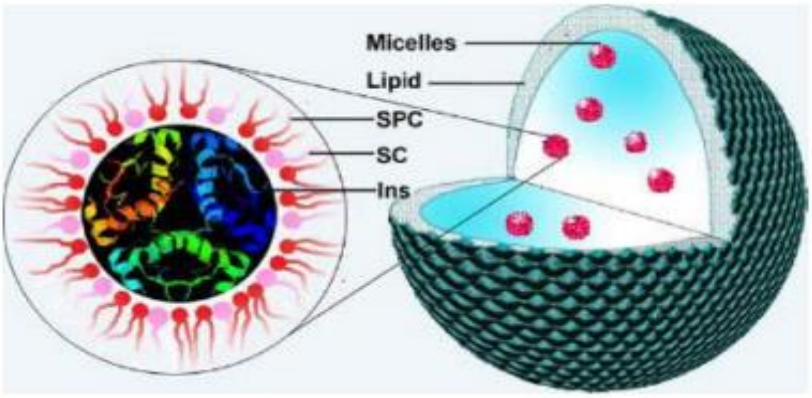

Figure No. 1: Structure of Solid Lipid Nanoparticles

SLN are attractive for their ability to improve the implementation of medicines and have intriguing qualities including small size, large surface zone, high medicament mounting, and stages interacting at the interface.[3]

Aqueous colloidal dispersions called SLN's have Solid biodegradable lipids as their matrix. SLNs include the advantages of some colloidal carriers in their class while preventing few of their disadvantages, including physicochemical parameters, the guarantee of integrated labile drug preservation against degradation and integration with other labile pharmaceuticals, controlled delivery, and excellent tolerability. SLN formulations were created and exhaustively characterised in-vitro and in-vivo for a broad range of application routes.[4]

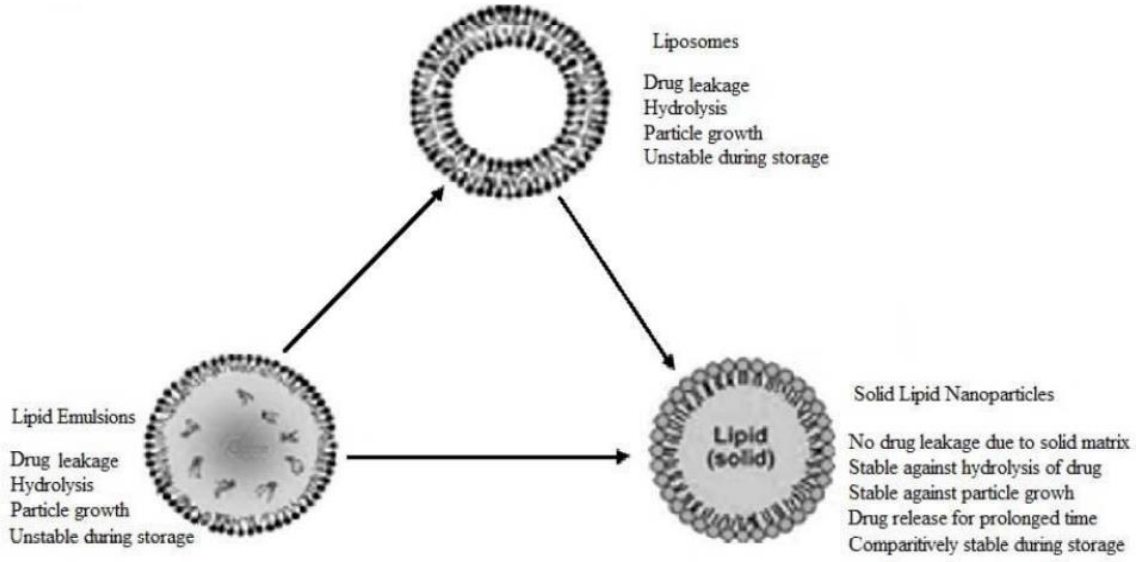

Figure No. 2: A diagram showing SLN across emulsions and liposomes

SLNs are a cutting-edge colloidal delivery system that may be used as a substitute to an oil-in-water emulsion for intravenous delivery. But a SLNs has taken the place of the emulsion's liquid lipid.[5]

1.1 Advantages of SLNs[6-11]

- Short estimation and typically limited measurement dispersion that provides natural opportunities for SLNs to deliver site-specific medicine.
- Useful are traditional emulsion-making methods.
- Powdered detailing may be shaped after being stop dry.
- Dynamic medicine can be introduced gradually over a lengthy period of time.
- Outstanding biocompatibility
- Enhance medications' stability.
- Excellent repeatability using as the readiness process a clever high-weight homogenization procedure.
- Significantly increased drug content.
- The possibility of combining drugs that are both hydrophilic and hydrophobic.

- The biodegradable nature of the transporter lipids provides protection. staying away from natural solvents atoms that are only partially soluble in water have increased bioavailability.
- Strategies for avoiding natural solvents are in place.
- Possibility of mass production and clean-up.

1.2 Disadvantages of SLNs:[12,13]

- Sedative stacking limit is poor.
- Drug ejection following a polymeric motion in a crowded area.
- Variable tendency for gelation.
- The inability to combine hydrophilic drugs due to apportioning effects during the production process.

2. Aim of SLN's:[14-20]

- Possibility of administering banned substances and drugs that target
- Moderate (less expensive than transporters based on polymers or surfactants).
- Steer clear of organic solvents.
- Issues with large scale scale creation and sanitization
- Enhanced tranquillizer security.
- Since most lipids may be broken down by biodegradation, the transporter has little biotoxicity.
- Increasing the bioavailability of bioactive mixtures that are caught.

3. Method of Preparation of Solid Lipid Nanoparticles:[21-24]

High shear homogenization, ultrasonication, microemulsion-based SLN design, supersonic fluid invention, splash drying, soluble emulsification/vanishing, soluble infusion technique, and soluble emulsification-dissemination are all part of the SLN preparedness strategy.[25]

Recently, this technique has also been used to create lipid nanoparticles.[26] The precipitation of lipids that have been arranged broken down is what drives this process. In this method, lipid synthesis and soluble removal occur simultaneously. Dissolvable ejection is essential

and can be accomplished by refining or another approach if it is not completed within the specified conditions. After the naturally occurring water-immiscible dissolvable has vanished, the organisation of lipid nanoparticles takes place. Particle size depends on a number of factors, such as the amount of additive, the concentration of lipid, the temperature, the mixing process, the kind of natural dissolvable, and the emulsifier.[27] SLNs are made from lipid, emulsifier, and water/dissolvable using various methods, and they are enrolled under.

3.1 High pressure homogenization:[28,29]

It is a trustworthy and effective approach that is being utilised for the first time to produce SLNs. High pressure homogenizers force a fluid via a small opening at higher pressure. Cavitation pressures and extremely high shear stresses cause the particles to break up into submicron sizes. Although up to 40% lipid content has also been researched, 5-10% lipid content is often utilised.

Cold homogenization and hot homogenization are the two forms of HPH. In both situations, a preliminary phase entails the medication being dissolved or dispersed in the lipid melt in order to be incorporated into the bulk lipid.

A. Hot Homogenization:

Hot homogenization, which is performed at temp. over the lipid's melting point, is sometimes referred to as emulsion homogenization. By using a high-shear mixing apparatus, the lipid with a medication load liquified and the watery emulsifier phase are combined into a pre-emulsion at the same temperature. Pre-emulsion quality has a significant impact on the end product's quality, hence it is preferable to obtain droplets that are only a few micrometres in size. Higher temperatures often lead to smaller particle sizes because the inner phase's viscosity is reduced.

Multiple iterations of the homogenization process are possible. Never forget that the temp of the sample increases during homogenization at higher pressure. 3-5 homogenized cycles between 500 and 1500 bar are frequently adequate. The increased velocity of the particles causes particle coalescence, which results in an increase in particle size when the homogenization pressure or cycle count are increased. Due to the lipid's liquid condition, the main result is a nano-emulsion, which solidifies upon cooling at room temperature. Lipid crystallisation may be greatly slowed down by the tiny particle size and the existence of emulsifiers, and the sample may stay in the form of a super-cooled melting for a few months.

B. Cold Homogenization:

In contrast, the cold homogenization involves grinding a suspension at higher pressure while using a solid lipid. Due to a rise in temperature during homogenization, effective temperature management and regulation are required to guarantee the lipid is in an unmolten form.

The following three drawbacks of the hot homogenization method have led to the development of cold homogenization.

1. Equipment that can degrade drugs due to temperature.

2. During homogenization, drug dispersion into the aqueous medium

3. The nanoemulsions complex crystallisation process, which can result in multiple alterations or super-cooled melt pressure.

3.2 Ultra sonication and high speed homogenisation

SLNs can also be made using high-speed homogenization or ultrasonication methods. It is necessary to combine ultrasonication and high speed homogenization for lower particle sizes. Although it lowers shear stress, there are several drawbacks, including the possibility of metal contamination and physical instability such particle development during storage. It uses a bath sonicator or a probe sonicator.

3.3 Solvent evaporation method

The lipophilic substance is dissolved in a water phase of an organic solvent that is water-immiscible (such as cyclohexane). After the solvent has evaporated, lipid precipitates as nanoparticles with a mean size of 25 nm, giving rise to a dispersion of nanoparticles. The solution has been homogenised under high pressure and emulsified in a water phase. Under lower pressure, the organic solvent was evaporated out of the emulsion.

3.4 Solvent emulsification diffusion method

This technique allows for the production of particles with typical diameters between 30 and 100 nm. The lack of heat during preparation is the key advantage of this procedure. In this procedure, the lipid is normally dissolved in the organic phase in a water bath heated to 50 °C, and the zeta potential is changed by an acidic aqueous phase to produce coacervation of SLN. Centrifugation is then used to easily separate the two phases. The SLN suspension had

been created swiftly. After centrifuging it, the entire dispersed system may be re-dissolved in distilled water.

3.5 Supercritical fluid method

This method of producing SLN is very fresh and offers the benefit of processing without the use of solvents. This platform technology for the creation of powder and nanoparticles comes in a variety of forms. The RESS technique can be used to make SLN. It was wise to use carbon dioxide (99.99 percent) as the solvent in this approach.

3.6 Microemulsion based method

Techniques for SLN preparation that Gasco and colleagues created are based on diluting microemulsions. To make an optically clear mixture, a low melting fatty acid, an emulsifier (polysorbate 20, polysorbate 60, soy phosphatidylcholine, co-emulsifiers, and water are often employed). The heated microemulsion is dissolved in cold water (2–3 °C) while being stirred. According to the literature, since the microemulsion already has a droplet structure, no energy is required to create particles with a diameter of less than one micron. Fessi made polymer particles by adding water to polymer solutions. De Labouret et al. claim that the distribution processes' velocity plays a key role in determining the particle size. Only acetone, a solvent that diffuses into the water phase relatively quickly, may form nanoparticles; more lipophilic solvents provide bigger particle sizes. Similar to how acetone forms polymer nanoparticles, the hydrophilic co-solvents of the microemulsion aid in the production of lipid nanoparticles.

3.7 Double emulsion-based method

Double warm/o/w microemulsions may be made in two phases. First, to create a transparent system, a drug-containing aqueous solution is added to a combination of melted lipid, a co-surfactant at a temperature slightly over the lipid's melting point. In the second stage, water, surfactant, and cosurfactant are combined with the created w/o microemulsion to create a clear w/o/w system. Warm micro double emulsions can be cleansed with dispersion medium using an ultrafiltration machine, then dispersed in cold water to create SLNs. The internal aqueous droplets inside the oil phase coalesce as a result of the coalescing oil droplets, and the layer on top of the internal droplets rupturing, multiple emulsions exhibit intrinsic instability. In order to produce SLNs, the transparent double microemulsions must be stable

for a short period of time, which can be achieved between their formation and their quenching in cold aqueous media.

3.8 Precipitation technique

Another way of producing solid lipid nanoparticles is through precipitation, which is distinguished by the requirement for solvents. An organic solvent (like chloroform) will be used to dissolve the glycerides, and an aqueous phase will be used to emulsify the result. Once the lipid has melted, it will precipitate out of the organic solvent, producing nanoparticles.

3.9 Film ultrasound dispersion

After adding the lipid and the medication to the appropriate organic solutions, which were then rotated, decompressed, and evaporated to create a lipid film, The emulsions-containing water phase was next added. Last but not least, the production of the SLN with tiny and uniform particle sizes utilising ultrasound and the probe to diffuser.

3.10 Solvent injection technique

It is a revolutionary method for making SLN that has the benefits listed below over previous production techniques: use of an organic solvent that is pharmacologically acceptable, simple handling, and a quick manufacturing process without the need for technical equipment. Its foundation is the precipitation of lipid from a mixture of dispersed lipids. This method involved dissolving the solid lipid in a water-miscible solvent (such as ethanol, acetone, or isopropanol) or a combination of water-miscible solvents. Then, with or without the addition of a surfactant, this lipid solvent combination was injected by an injection needle into the stirring aqueous phase. After that, a filter paper was used to eliminate any extra lipid from the resulting dispersion. By lowering the surface tension between water and solvent, the emulsifier in the aqueous phase aids in the production of lipid droplets at the injection site and stabilises SLN until solvent diffusion is complete.

3.11 Membrane contractor method

In order to enable large-scale production, the current work examines a novel method for producing SLN utilising a membrane contactor.

Small droplets are created when the lipid phase is forced through the membrane pores at a temperature higher than the lipid's melting point. The droplets that develop at the pore outputs are swept away by the aqueous phase as it circulates inside the membrane module. The formulation is subsequently cooled to room temperature to create SLN. On the size of the SLN and on the lipid phase flux, it is explored how the process variables affect these variables.

4. Characterization of Solid Lipid Nanoparticles (SLNs)

Characterizing SLN's is a real measure because of the microscopic size of the molecules and complexity of the framework. Particle size, zeta potential, the amount of lipid and crystallinity change, the addition of other colloidal structures, the duration of circulation processes, tranquillizer, in vitro drug release, and surface shape are all factors, are the critical parameters that should be assessed for the SLNs.[30] The following are some criteria that must be taken into account while characterizing anything.

4.1 Particle Size and Zeta Potential[31-35]

The size of nanoparticles may be determined using a number of methods, including photon-connection spectrometry, TEM, and SEM, as well as SEM coupled with energy dispersive X-Beam spectrometry, filtered test microscopy, and fraunhofer diffraction. Between them, PCS and electron microscopy techniques are the most frequently used methods. SEM and TEM are quite beneficial for morphology and fit as a fiddle of lipid nanoparticles. They also provide for assurance of particle size and dispersion. Nuclear drive microscopy is another advanced small technique used to characterise nanoparticles. This is an additional tool for visualising the particles' initial, undisturbed form and surface characteristics. The drive in this method between the surface and the inspection tip results in a spatial determination of up to 0.01 m. The refractive index of the scattering medium, water, and the lipid particles determine the figures for the laser diffraction process, which is suitable for sub micro-meter sized particles.

4.2 Determination of Incorporated Drugs[36]

After separating the free medicine and Solid lipids from the fluid medium and completing the separation by ultracentrifugation, centrifugation filtration, or gel penetration chromatography, the amount of medication fused is determined. Additionally, tranquillizer material may be

particularly resolved by taking the drug out with the proper dissolvable under perfect circumstances, followed by an examination of the resultant item in SLNs.

Models have been put up to illustrate how the number of drug atoms in SLNs is limited. The enhanced shell model is characterised by medicine particularly positioned at the interface, either via rapid network lipid hardening or by efficient medication competition for the interface. Such a model's sedative dispersion may have a positive burst effect during medicine release. Medication is distributed evenly across the lattice in the homogeneous framework paradigm, much like a Solid arrangement. Medication selectivity located in the centre of Solid lipid nanoparticles, maybe as a result of the medication hardening more quickly than the grid material, describes the advanced centre model.

4.3 In-vitro Drug Release Studies[37]

Studies on in-vitro tranquillizer discharge are often useful for quality assurance and for predicting in-vivo energy. Medication discharge profiles can be conducted with or without dialysis tubing. Another technique that relies on switch dialysis and avoids the fenced-in region of the colloidal drug carrier in a dialysis sac was reported by Impose and Benita in 1990. This method is insufficiently delicate to characterise the colloidal transporter's rapid medicine discharge rate.

4.4 Storage Stability[38-40]

Observing variations in particle estimation, tranquillizer ingredient, appearance, and viscosity, the physical solidity of the SLNs during delayed stockpiling may be managed. Thin layer chromatography should also be able to accomplish this.

For long-term stability, external factors like temp and light seem to be of the utmost important. For a scattering to continue to be physically stable, the zeta potential should typically be higher than - 60mV. The best stockpiling temperature is 4°C. 20°C- Long-term storage had no effect on the amount of medicine stacked in SLNs or on drug loss. 50°C - A rapid increase in particle size was observed.

4.5 The Propensity for Crystallization and Polymorphic Behaviour of SLNs[41,42]

Paid that lipid crystallisation is associated with drug fuse and discharge rates, uncommon consideration must be given to this phenomenon. The solid state of the particles is extremely important since it decreases the movement of combined medications, prevents the carrier

from leaking drugs. Warm research and X-beam diffraction are fundamental techniques to establish the physic-substance condition of particles [41,42]. The most often used techniques in warm investigation are differential warm evaluation and differential filtering calorimetry.

5. Evaluation of SLN's[23,43]

5.1 Electronic Microscopy of SLN's[44]

Transmission electron microscopy revealed solid lipid nanoparticles. SLN tests were 10 times weakened before being placed on gold plate. Without using any form of dye, the mounted plates had been dried and examined under a transmission electron microscope. The transmission electron magnifying tool was used in conjunction with the CCD camera and sensitive picture framework to see SLN.

5.2 Zeta potential of Solid Lipid Nanoparticles[45,46]

Zetasizer established the definitions for the SLN's zeta potential. For the estimates, Deionized water was used to properly weaken the tests to get 50 and 200 Kcps. Testing was done in the cubit that could be reached by the equipment, and zeta potential was carefully measured.

5.3 SLN's size and polydispersity index[29,45]

Zetasizer DTS was used to estimate the normal particle size and polydispersity file of the SLN information. Deionized water was used to attenuate the SLN scattering specimens. Instrumental-based calculation system results for normal particle size and polydispersity were obtained.

5.4 Efficiency of SLN's Encapsulation[47]

The production of testosterone was calculated to be characterised by solid lipid nanoparticles. Solid lipid nanoparticles were dialyzed while being retained in a dialysis tube. The dialyzing medium consisted of 30 millilitres of 30% v/v PEG 400 in a phosphate buffer (pH-6) setup. Solid lipid nanoparticles underwent two hours of dialysis. The 100 mg of dialyzed SLN's were extracted from the dialysis pack and were broken down by Shimadzu's HPLC system at 254 nm to determine their drug content. The samples were separated and weakened as necessary using a Millipore film channel (0.2 m).

5.5 Viscosity of Solid Lipid Nanoparticles[48]

By using shaft number 63 at 30 r/m under ambient conditions, a Brookfield viscometer (DV-E viscometer, Brookfield, USA) was used to assess the viscosity of testosterone containing solid lipid nanoparticles.

5.6 *In Vitro* Study of SLN's[49]

The concentrate for in vitro release, Franz dispersion sort cell, a privately developed device, was used to create solid lipid nanoparticles. The evaluation was conducted in a 30–2°C environment. The disseminated cell's receptor segment usually contains 30 ml of PEG 400 mixed at 50 r/m in phosphate cradle setups with a pH of 6. The dialysis layer, which had a sub-atomic weight cut off of 12 KD, was used as a discharge barrier between the receptor and beneficiary compartments, which had previously been filled with purified water and covered with a 30 percent v/v PEG 400 arrangement. 5 ml tests were periodically drawn back via the examination port of the dissemination cell every hour or more. The same amount of 30 percent v/v PEG 400 arrangement was immediately replaced. The collected samples were suitably attenuated and subjected to HPLC analysis at 254 nm.

6. Route of Administration

SLNs are provided by following the institution's procedure.

6.1 Oral Organization[50-52]

It is possible to provide SLN orally as watery scattering or, alternatively, following transformation into a standard measuring form, such as pills, pellets, containers. Instead of using a granulation fluid in the granulation process for the creation of tablets, SLN scattering can be used. Fluid scatterings are one of the types of SLNs planning that are covered in the oral course. SLNs come in stacked dosage forms such pills, pellets, and cases. The causticity and high ionic quality of the stomach's microenvironment encourage Particle aggregation. It is not unusual for nutrition to have a significant effect on SLN production.

6.2 Parenteral Organization[50-53]

SLNs are often administered intravenously to animals. In contrast, the arrangements led to increased drug dissemination into the liver and kidneys. In comparison to a business sedate setup after intravenous, SLN showed greater blood levels. SLN scatterings must be sterile for

parenteral organisation. In these situations, the mean particle size makes sterile filtering unfeasible.

6.3 Transdermal Application[54]

The thinness and poor clustering of the distributed lipid are drawbacks of cutaneous organisation. To get a plan that can be controlled to the skin, the SLN scattering must be combined with a therapy or gel.

6.4 Pulmonary Administration[55]

A highly intriguing application appears to be the SLN's aspirational organisation. Because the SLN powders' particles are too small and will be exhaled, it is impossible to direct them to the lung. The fluid SLN scatterings are aerosolized, which is a very simple method. The crucial aspect is that the SLN shouldn't completely during aerosolization. By colliding an airborne mass of beads with a mass of glass in a measuring glass, the vaporised beads were collected.

6.5 Rectal Organization[56-58]

For paediatric patients, the usual rectal route of administration is used as much as feasible due to its ease of usage. When compared to drugs given orally or intravenously, the plasma levels and beneficial adequacy of rectally administered drugs were shown to be superior. Through SLN, a few reports on the rectal medicine organisation are available. Diazepam was concentrated into SLN for rectal organisation in order to provide a quick response. They focused on the fact that lipid networks, which are solid at body temperature, are not an effective method for delivering diazepam through the rectal route. They decided to use lipids that dissolve at body temperature in their upcoming experiments. PEG coating is unquestionably a reliable method for rectal delivery, improving bioavailability.

CONCLUSION

This study covers a wide range of solid lipid nanoparticles, outlining the objectives, methods of manufacture, benefits, drawbacks, and potential solutions. This study discusses the manufacturing process, characterisation, and route of administration of solid lipid nanoparticles (SLNs) in general. As an alternative to other conventional colloidal carriers such liposomes, polymeric nanoparticles, and emulsions due to their benefits such as controlled drug release, focused drug delivery, and enhanced stability, solid lipid

nanoparticles were created in the early 1990s. This page provides a summary of the possible benefits and drawbacks of solid lipid nanoparticles, excipients, and all of the many techniques used to make them, including the membrane contractor approach.

CONFLICT OF INTEREST

The authors have no conflict of interest.

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