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A REVIEW ON: SOLID LIPID NANOPARTICLES

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ABSTRACT

The ability to incorporate drugs into nanocarriers offers a new prototype in drug delivery that could be used for secondary and tertiary levels of drug targeting. Hence, solid lipid nanoparticles hold great promise for reaching the goal of controlled and site specific drug delivery and hence have attracted wide attention of researchers**.** Solid lipid nanoparticles are one of the developed technologies for addressing the bioavailability and targeting issues of drug delivery. In this review article, we attempted to incorporate all the essential details of SLNs like method of preparation, lipids use in SLNs advantages and disadvantage. Solid lipid nanoparticles (SLNs) are made from lipids that are safe for the body. These nanoparticles have been shown to help drugs dissolve better, be taken up by cells more effectively, and stay stable for longer. They also protect drugs from being broken down by enzymes and help them stay in the bloodstream for a more extended period. SLNs have been carried out within the oral, parenteral, transdermal, intranasal, ocular, and pulmonary drug delivery of various drugs, with more suitable safety, bioavailability, and normal healing outcomes.

KEYWORDS: solid lipid nanoparticles, bioavailability, hydrophilic, bioactive, lipophilic, biotoxicity, homogenization, biocompatible.

- **INTRODUCTION**

Solid lipid nanoparticles (SLNs) are used as a carrier system for water-soluble medications and for delivering drugs that need to be adjusted dynamically. Colloidal particles with sizes ranging from 10 to 1000 nanometers are called nanoparticles. These are made from specially

designed polymers and are useful for better drug delivery and can help reduce harmful effects.[1] SLN offers interesting features, such as small size, a large surface area, high drug loading capacity, and effective communication between different layers at the interface, making them attractive for their potential to improve the performance of pharmaceuticals.[2] Solid lipid nanoparticles are one of the new and promising colloidal transport systems that can be used as alternative materials to polymers. They are different from oil-in-water emulsions, which are commonly used for parenteral nutrition. However, the liquid lipid in these emulsions has now been replaced by solid lipid nanoparticles.[3] SLNs have nonetheless been taken into consideration as quite biocompatible, and in vitro research have showed this element of SLNs characteristics.[4] SLNs were proven to load better portions of the drug (drug volumes) than the polymeric NPs and nanoemulsions that are not normally lipid based. additionally, from the manufacturing and commercial stand-factor, the low production expenses without using any natural solvents, with improved feasibility of upkeep of the sterility of SLNs formulations[5] have brought to the SLNs' benefits. on the contrary, the longer storage time and lengthy duration sitting time of the drug in SLNs formulations have the tendency to result in several dangers,[6] which include changes in drug launch styles and particles' size increase, and occurrence of polymorphic transition are too high, together with gelation occurrences which are pretty frequently encountered and are of excessive occurrence for SLNs.

- **Purpose of SLN's[7,8]**

Possibility of controlled medication release and medication focus includes:

- Using more moderate options (less expensive than polymeric or surfactant-based transporters).
- Ability to incorporate both lipophilic and hydrophilic medications.
- Avoidance of natural solvents.
- Issues related to significant scale formation and sanitization.
- Enhanced drug safety.
- No biotoxicity from the transporter since most lipids are biodegradable.
- Higher bioavailability of trapped bioactive.

- **Merits**

The chronic and acute poisoning of drug can be minimized by the production process involved in the manufacturing of SLNs and it utilize the organic solvents and biodegradable physiological lipids.

1. It improves the bioavailability of compounds that are poor water soluble.
2. It governs both the probability of drug delivery and drug targeting.
3. SLNs have a higher stability than liposomes.
4. It promotes trapped bioactive bioavailability and a labile chemical synthesis compound that is incorporated.
5. Lyophilization is a viable option.[5-7]

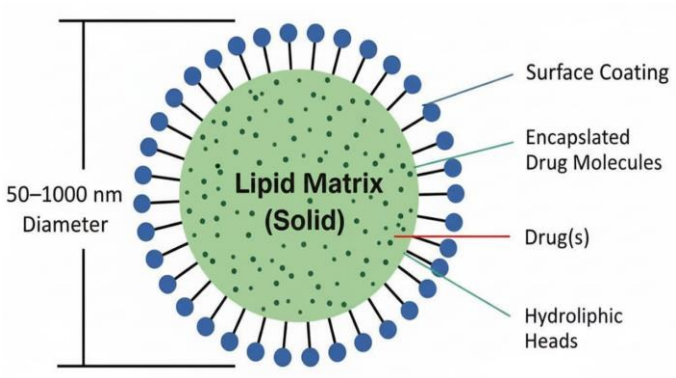
- **Demerits[9,10,11]**

1. Bad sedate stacking restriction.
2. Drug ejection after polymeric circulate amid potential.
3. Unpredictable gelation propensity.
4. The low capacity to stack hydrophilic medicines because of apportioning influences amid the technology process.[12]

Table 1: Lipid Used for Solid Lipid Nanoparticle Preparation.

Sr.No	Lipids	Example
1	Triglycerides(13,14)	Trilaurin, Tricaprin, Hydrogenated coco glycerides (Softisan®142), Tripalmitin [Dynasan® 116, Tristearin [Dynasan® 118, Trimyristin[Dynasan®114]
2	Fatty Acids(15)	Dodecanoic acid,Myristic acid,Palmitic acid, Stearic acid
3	Monoglycerides(15)	Glyceryl monostearate, Glyceryl hydroxyl stearate, Glycerylbehenate
4	Waxes(14)	Cetyl palmitate, Beeswax, Carnauba wax

Solid lipid nanoparticles



- **PREPARATION TECHNIQUES**

1. 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. A pre-emulsion of the drug loaded mixing device (like silversion-type homogenizer). 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. High pressure homogenization of the pre-emulsion is done above the lipid melting point. Usually, lower particle sizes are obtained at higher processing temperatures because of lowered viscosity of the lipid phase,[16] although this might also accelerate the drug and carrier degradation. Better products are obtained after several passes through the high-pressure homogenizer (HPH), typically 3-5 passes. High pressure processing always increases the temperature of the sample (approximately 10° at 500 bar).[17] In most cases, 3-5 homogenization cycles at 500-1500 bar are sufficient. Increasing the homogenization leads to an increase of the particle size due to particle coalescence, this occurs because of the high kinetic energy of the particles.

2. Cold homogenization

The cold homogenization process is carried out with the solid lipid and therefore is similar to milling of a suspension at elevated pressure. To ensure the solid state of the lipid during homogenization, effective temperature regulation is needed.[17] Cold homogenization has been developed to overcome the following problems of the hot homogenization technique such as: Temperature mediated accelerated degradation of the drug payload, Partitioning and hence loss of drug into the aqueous phase during homogenization, Uncertain polymorphic transitions of the lipid due to complexity of the crystallization step of the nanoemulsion leading to several modifications and/or super cooled melts. 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. However, the subsequent steps differ. The drug containing melt is cooled rapidly (using dry ice or liquid nitrogen) to favor homogenous drug distribution in the lipid matrix. In effect, the drug containing solid lipid is pulverized to micropaticles ball/mortar milling. Typical particle sizes attained are in the range 50-100 microns. Chilled processing further facilitated particle milling by increasing the lipid fragility. The SLNs are dispersed in a chilled emulsifier solution. The dispersion is subjected to high pressure homogenization at or below room temperature with appropriate temperature control keeping in view the usual rise in temperature during high pressure processing. However, compared to

hot homogenization, larger particle sizes and a broader size distribution are typical of cold homogenized samples.[18] The method of cold homogenization minimizes the thermal exposure of the sample, but it does not avoid it due to the melting of the lipid/drug mixture in the initial step.

3. Ultrasonication or high speed homogenization

SLN were also developed by high speed stirring or sonication.[19,20] A most advantages are that, equipments that are used here are very common in every lab. The problem of this method is broader particle size distribution ranging into micrometer range. This lead physical instability likes particle growth upon storage. Potential metal contamination due to ultrasonication is also a big problem in this method. So for making a stable formulation, studies have been performed by various research groups that high speed stirring and ultrasonication are used combined and performed at high temperature.

4. Spray drying method

It's an alternative procedure to lyophilization in order to transform an aqueous SLN dispersion into a drug product. It's a cheaper method than lyophilization. This method cause particle aggregation due to high temperature, shear forces and partial melting of the particle. Freitas and Mullera[21] recommends the use of lipid with melting point >700 for spray drying. The best result was obtained with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol-water mixtures (10/90 v/v).

5. Double emulsion method

For the preparation of hydrophilic loaded SLN, a novel method based on solvent emulsification evaporation has been used.[22] Here the drug is encapsulated with a stabilizer to prevent drug partitioning to external water phase during solvent evaporation in the external water phase of w/o/w double emulsion.

6. Micro emulsion based SLN preparations

Gasco and co-workers developed SLN preparation techniques which are based on the dilution of microemulsions.[23] They are made by stirring an optically transparent mixture at 65-700 which is typically composed of a low melting fatty acid (stearic acid), an emulsifier (polysorbate 20, polysorbate 60, soy phosphatidylcholine, and sodium taurodeoxycholate), co-emulsifiers (sodium monooctylphosphate) and water. The hot microemulsion is dispersed in cold water (2-30) under stirring. Typical volume ratios of the hot microemulsion to cold

water are in the range of 1:25 to 1:50. The dilution process is critically determined by the composition of the microemulsion. According to the literature,[24,25] the droplet structure is already contained in the microemulsion and therefore, no is required to achieve submicron particle sizes. With respect to the similarities of the production procedure of polymer nanoparticles described by French scientists, different mechanisms might be considered. Fessi produced polymer particles by dilution of polymer solutions in water. According to De Labouret et al.[26] the particle size is critically determined by the velocity of the distribution processes. Nanoparticles were produced only with solvents which distribute very rapidly into the aqueous phase (acetone), while larger particle sizes were obtained with more lipophilic solvents. The hydrophilic co-solvents of the microemulsion might play a similar role in the formation of lipid nanoparticles as the acetone for the formation of polymer nanoparticles.[27]

7. SLN preparation by using supercritical fluid

This is a relatively new technique for SLN production and has the advantage of solvent-less processing.[28,29] There are several variations in this platform technology for powder and nanoparticle preparation. SLN can be prepared by the rapid expansion of supercritical carbon dioxide solutions (RESS) method. Carbon dioxide (99.99%) was the good choice as a solvent for this method.[30]

- **Evaluation of Solid Lipid Nanoparticles**

Electron Microscopy of Solid Lipid Nanoparticles

Solid lipid nanoparticles were seen by transmission electron microscopy. Tests of SLN were weakened to ten time and after that mounted on gold plate. The mounted plates were dried and inspected under a transmission electron magnifying instrument without utilizing any sort of stain. The CCD camera and delicate picture framework was utilized with the transmission electron magnifying instrument to envision SLN.[31]

Zeta potential of Solid Lipid Nanoparticles

Zeta potential of SLN definitions were dictated by Zetasizer. Tests were fittingly weakened with deionized The after effects of normal Partical size and polydispersity record were gotten from instrumental based computation system.[25]

Encapsulation Efficiency of Solid Lipid Nanoparticles

Measure of testosterone epitomized in Solid lipid nanoparticles were figured as typified productivity (EE). Solid lipid nanoparticles were kept in dialysis tube and dialyzed. Thirty

milliliter of 30% v/v PEG 400 in phosphate cushion (pH-6) arrangement was utilized as dialyzing medium.[32] Dialysis of Solid lipid nanoparticles was performed for two hours. The one hundred milligram of dialyzed Solid lipid nanoparticles were taken from dialysis pack and broke down for medication content by elite fluid chromatography (HPLC), (Shimadzu, Japan) at 254 nm. The examples were appropriately weakened and separated through Millipore film channel (0.2 µm).

Viscosity of Solid Lipid Nanoparticles

Viscosity of testosterone containing Solid lipid nanoparticles was measured by Brookfield viscometer (DV-E viscometer, Brookfield, USA) utilizing shaft no 63 at 30 r/m in surrounding condition. The shaft speed no 63 was settled in viscometer nob and most extreme torque was measured before watching Viscosity. Viscosity of testosterone containing Solid lipid nanoparticles was measured specifically from the viscometer computerized show.[33]

In Vitro Release Study of Solid Lipid Nanoparticles

The in vitro sedate discharge concentrate Solid lipid nanoparticles was performed by privately created Franz dispersion sort cell. The review was performed at 30±2°C temperature. Receptor compartment of dissemination cell contained 30 ml 30% v/v PEG 400 in phosphate cradle (pH-6) arrangement and was always mixed by an attractive stirrer at 50 r/m. Dialysis layer (sub-atomic weight cut off 12 KD was utilized as discharge hindrance in the middle of receptor and benefactor compartment which was beforehand was with refined water and doused with 30% v/v PEG 400 arrangement. Time to time 5 ml tests was pulled back through the examining port of the dissemination cell in interims one h, more than 8 h. Same measure of 30% v/v PEG 400 arrangement was supplanted instantly. The gathered examples were reasonably weakened and examined by HPLC at 254 nm.[34]

- **CONCLUSION**

In the early days of the 20th century, Paul Ehrlich envisioned his magic bullet concept; the idea that drugs reaches the right site in the body, at the right time, at right concentration. It should not exert side effects, neither on its way to the therapeutic target, nor at the target site, nor during the clearance process. The SLNs have the potential to achieve, at least partially, these broad objectives. Apart from these, the regular objective of controlled drug delivery is aptly achieved with SLNs. They are relatively young drug delivery systems, having received primary attention from the early 1990s and future holds great promise for its systematic

investigation and exploitation. We can expect many patented dosage forms in the form of SLNs in the future.

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