Review Article

Solid Lipid Nanoparticles- an Innovative approach for Improving the Solubility and Bioavailability

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ABSTRACT

Purpose: The purpose of this study is to give a general review on solid lipid nanoparticles (SLNs) as a novel drug carrier for improving the solubility and bioavailability of drugs.

Approach: Among the various colloidal drug carriers, SLNs have been emerged as next generation drug delivery system for incorporating lipophilic drugs. They are relatively nontoxic and nonirritant. The review insight on the various methods of preparation, characterization and also the application of SLNs for improving the solubility and bioavailability is explained here.

Findings: SLNs is used as a novel carrier for improving the solubility of poorly soluble drugs which may results in enhanced bioavailability and stability of drug can also be improved by incorporating drug in the form of solid lipid nanoparticles.

Conclusion: This review presents an overview of SLNs which includes SLN and its properties, excipients, techniques used in preparation of SLNs, characterization, and their applications.

Keywords: *Bioavailability, Solubility, Lipophilic, Stability, Advantages, Disadvantages.*

INTRODUCTION

Nanosized drug delivery system such as micelles, polymer nanoparticles, nanoemulsions, solid dispersion, nanocapsules have been developed to overcome one or several of the following problems such as low or highly variables drug concentrations after per oral administration due to poor absorption, rapid metabolism and elimination, poor drug solubility, which includes I.V injections containing aqueous drug solutions, drug distribution to other tissue combined with high toxicity (e.g. cancer drugs).[1,2]

Among the various drug carriers, SLNs are colloidal carriers developed in the last decade (1990s), an alternative means to the existing traditional carriers (emulsions, liposomes, and polymeric nanoparticles). Nanoparticles made from lipids provide an attractive means as a novel colloidal drug carrier due to the presence of natural lipids. Due to their unique size dependent properties, lipid nanoparticles offer the possibility to develop a new therapeutics.

They are submicron colloidal carriers (50-1000 nm) which are composed of physiological lipids, dispersed in water or in aqueous surfactant solution. Generally they are made up of solid hydrophobic core having a monolayer of phospholipid coating. The diagrammatic representation of SLNs is given in figure 1.[3]

SLN also possesses good stability and is able to control the release of

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incorporated drug, the physiological lipid made SLNs can be better tolerated by human body and also its lipophilic nature allows easy penetration of drugs through the biological membrane.[4]

Embedded bioactive compounds

Solid lipid core

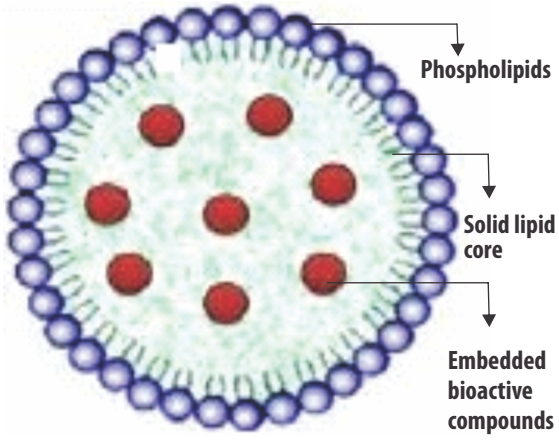
Phospholipids

They enhance the oral bioavailability of poorly aqueous soluble drugs due to their potential to enhance gastrointestinal solubilization, selectively through lymphatic uptake. These properties can be applied to enhance the therapeutic efficacy of the drugs.[5]

Advantages of SLNs:[6]

- Use of biodegradable physiological lipids decreases both acute and chronic toxicity.
- SLNs possess better stability and are able to control release of incorporated drug in comparison with polymeric nanoparticles and liposomes.
- Improves solubility and bioavailability of poorly soluble drug molecules.

Fig. 1: Structure of SLN



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- SLNs have better stability compared to liposomes.
- High concentration of functional compound can be achieved.

Disadvantages of SLNs:[7,8]

Table 1: Excipients used in SLNs preparation.[9]

Lipids	Surfactants
Triglycerides	Phospholipids
Tricaprin	Soy lecithin (LipoidÒ S 75, LipoidÒ S 100)
Trilaurin	Egg lecithin (LipoidÒÒE 80)
Trimyristin (Dynasan 114)	PhosphatidylCholin (EpikuronÒÒ170, Epikuron 200)
Tripalmitin (Dynasan 116)	Ethylene oxide/propylene oxide copolymers
Tristearin (Dynasan 118)	Poloxamer 188
Hydrogenated coco-glycerides (SoftisanÒ 142)	Poloxamer 182
Hard fat types	Poloxamer 407
WitepsolÒ W 35	Poloxamine 908
WitepsolÒ H 35	Sorbitan ethylene oxide/propylene oxide copolymers
WitepsolÒ H 45	Polysorbate 20
WitepsolÒ E 85	Polysorbate 60
Acyl glycerols	Polysorbate 80
Glyceryl monostearate (ImwitorÒ900)	Alkyl aryl polyether alcohol polymers
Glyceryl distearate(Precirol)	Tyloxapol
Glyceryl monooleate(Peceol)	**Bile salts**
Glyceryl behenate (CompritolÒ 888 ATO)	Sodium cholate
Glyceryl palmitostearate (PrecirolÒ ATO 5)	Sodium glycocholate
Waxes	Sodium taurocholate
Cetyl palmitate	Sodium taurodeoxycholate

Fatty acids	**Alcohols**
Stearic acid	Ethanol
Palmitic acid	Butanol
Decanoic acid	Butyric acid
Behenic acid	Dioctyl sodium sulfosuccinate
Cyclodextrin	Monooctylphosphoric acid sodium
Para-acyl-calix-arenes	

- Unpredictable gelation tendency.
- Coexistences of several colloidal species.
- Drug expulsion after polymeric transition during storage.

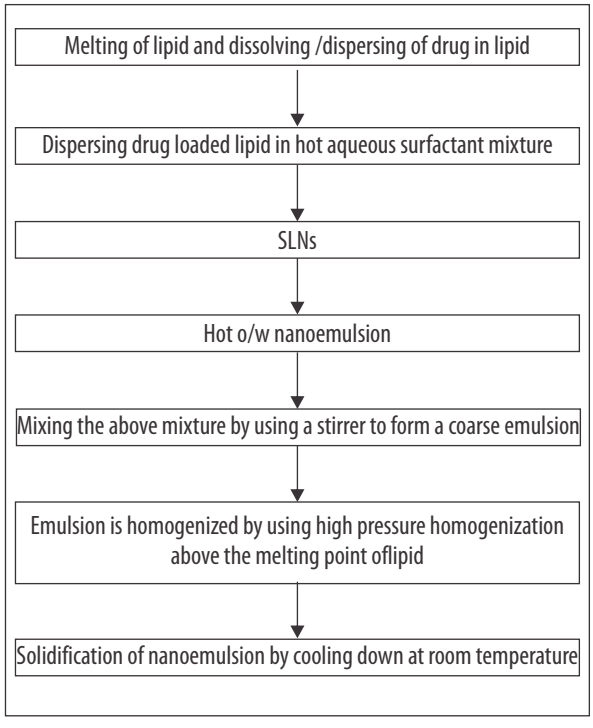
The following excipients which can be used in SLNs preparation is mentioned in Table 1

Methods of preparations.

Solid lipid nanoparticles are prepared by various methods which include:

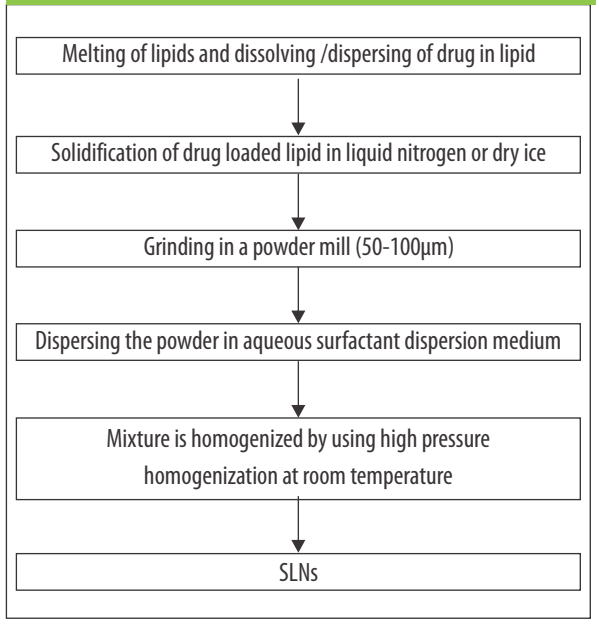
1. Hot homogenization technique.[10]

Fig. 2: Schematic procedure of hot homogenization technique



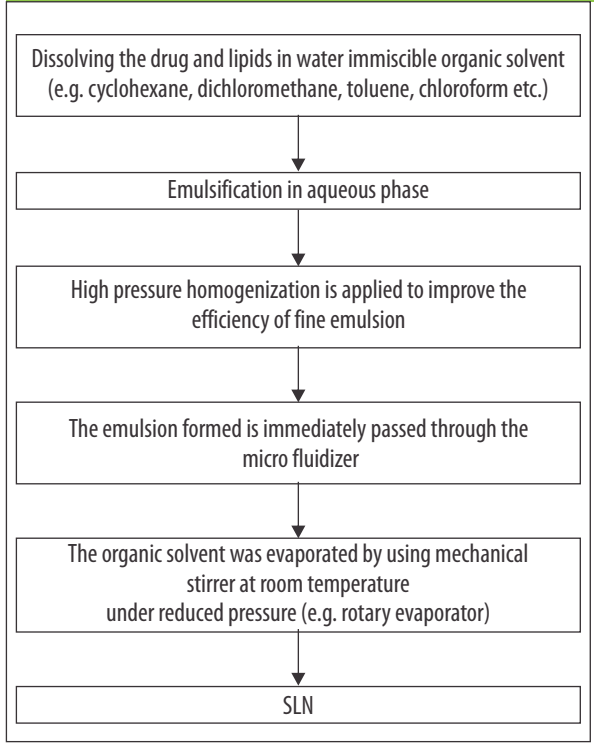
2. Cold homogenization technique.[10]

Fig. 3: Schematic procedure of cold homogenization technique



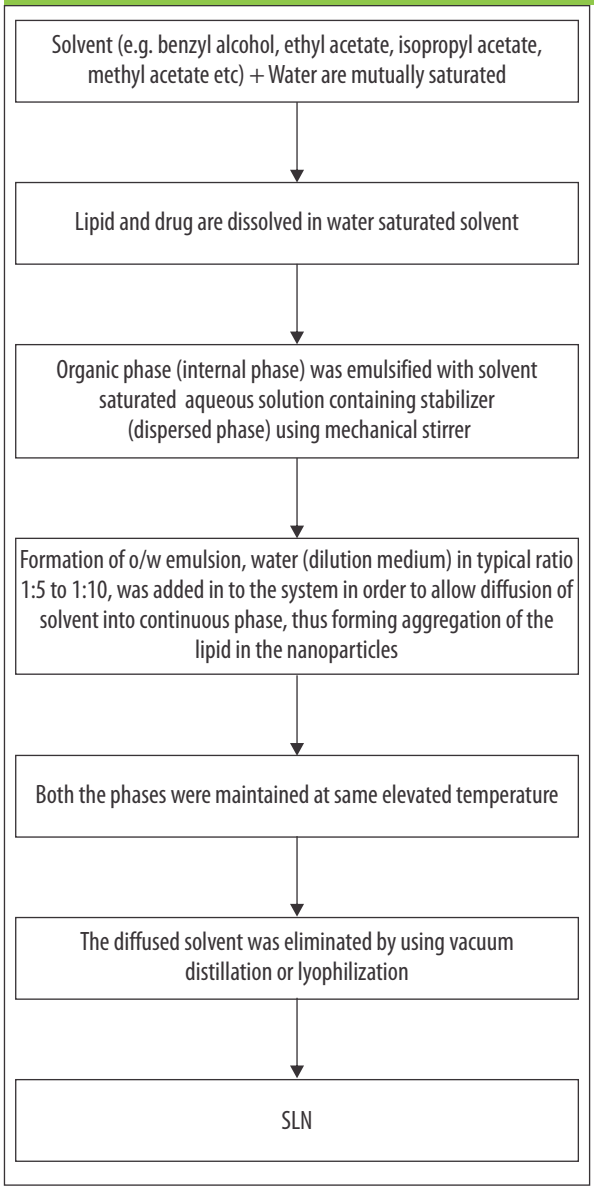
3. Solvent emulsification evaporation technique.[11]

Fig. 4: Schematic procedure of solvent emulsification evaporation technique



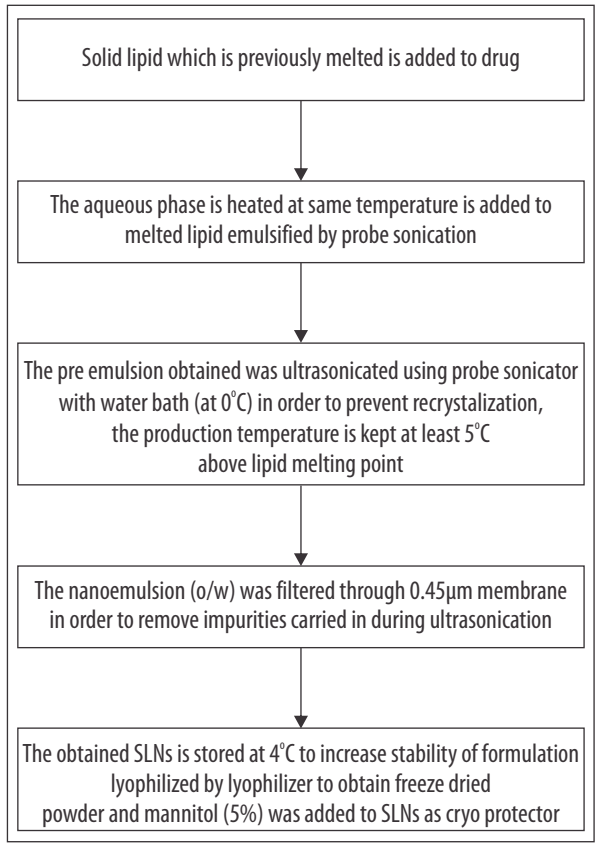
4. Solvent emulsification diffusion technique.[11]

Fig. 5: Schematic procedure of solvent emulsification diffusion technique



5. Ultrasonication technique.[12]

Fig. 6: Schematic procedure of ultrasonication technique



Characterization of solid lipid nanoparticles:

1) Measurement of particle size and zeta potential

Photon correlation spectroscopy (PCS) and Laser diffraction (LD) are most widely used techniques for measurements of particle size. PCS measures fluctuation of intensity of scattered light source which is caused by particle movement and covers a size range from few nanometers to 3µm.[13]

One of the disadvantages of PCS is that it will not be able to detect the particles of large microns size but it can detect the particles of size ranging from 3nm to 3µm.

LD method depends upon the diffraction angle on particle size and it can detect the particles of size ranging from 100nm to 180µm.

Zeta potential measurements are carried out by using zetameter. SLNs dispersions are diluted first 50 fold before measurement of zeta potential, higher value of zeta potential is an indication of de-aggregation of particles in absence of factors such as stearic stabilizers.[9]

2) Electron microscopy

Scanning electron microscopy (SEM) and Transmission electron microscopy (TEM) are most widely used for measuring the shape and morphology of lipid nanoparticles.SEM uses electrons transmitted from surface of sample and TEM uses electrons transmitted through the sample.[13]

3) Atomic force microscopy

It is an advanced microscopic technique where a probe tip along with atomic scale sharpness is rastered across a sample to produce a topological map which depends on the force acting between surface of sample and tip of probe, when the probe is kept in close proximity to the sample results in special resolution up to 0.01nm.[9,13]

4) *In vitro* drug release

Dialysis tubing

In vitro drug release could be achieved using dialysis tubing. The solid lipid nanoparticle dispersion is placed in pre washed dialysis tubing which can be hermetically sealed. The dialysis sac then dialyzed against a suitable dissolution medium at room temperature; the samples are withdrawn from the dissolution medium at suitable intervals, centrifuged and analyzed for the drug content using a suitable analytical method.[13]

5) Rheology

Rheological measurements can be carried out by use of Brookfield viscometer containing suitable spindle number. Viscosity depends on the dispersed lipid contents, as lipid contents increases the flow becomes Non-Newtonian from Newtonian.[13]

6) Nuclear magnetic resonance (NMR)

NMR is used for determination of size and qualitative nature of nanoparticles, which is selectively, afforded by chemical shift that complements the selectivity towards mobility and they provide information on the physicochemical status of components within the nanoparticles.[13]

Applications of solid lipid nanoparticles in improving solubility and bioavailability:

- SLN reduces the particle size, modify the crystal habit, which modifies physiochemical, micrometrics, and biopharmaceutical properties of poorly soluble drugs, there by improves the solubility.

  E.g. All trans retinoic acid (ATRA) possess anticancer activity which is poorly aqueous soluble drug, by formulating in the form of SLN loaded with ATRA the solubility can be improved.[14,15]

- Cefpodoxime proxetil (CP) is a prodrug which posses poor bioavailability, due to its low aqueous solubility and preabsorption luminal conversion of CP into Cefpodoxime acid (CA). The bioavailability of CP can be improved by increasing solubility or by eliminating preabsorption conversion of CP to CA. Hence SLN are prepared which can bypass the passage of drug through epithelial cell and provides sufficient protection to the drug from luminal cholinesterase thereby bioavailability is improved.[16]

CONCLUSION

SLN as colloidal drug carrier combines the advantage of polymeric nanoparticles and fat emulsions due to various advantages, including feasibility of incorporation of lipophilic and hydrophilic drugs, good physical stability, they are available at low cost, ease of scale-up, and easy to manufacture etc.

As many drugs are successfully marketed as solid lipid based formulations, the solid lipid based drug delivery system has a wide scope in terms of solubility and bioavailability enhancement. This review focused on the current trends in formulation development and their characterization. However, there are few limitations proper regulatory guidelines for lipid based formulations still need to be addressed in depth to advance the technology.

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