SOLID LIPID NANOPARTICLES A POTENTIAL APPROACH FOR DELIVERY OF LIPOPHILIC DRUGS: A REVIEW

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ABSTRACT
A pharmaceutical formulation development study requires a detailed understanding of the relationship between the drug entity, excipients, process parameters and its quality attributes. Development of new drug entities is posing real challenge to formulators, particularly due to the poor aqueous solubility of drugs which in turn is a major factor responsible for poor oral bioavailability. To overcome these problems lipid based oral drug delivery system has taken a new dimension with application for lipophilic drugs. One such lipid based system is Solid Lipid Nanoparticles (SLN) in which the lipid serves as a carrier to drugs in their various forms, have the potential of providing endless opportunities to enhance the gastrointestinal solubilization and absorption via selective lymphatic route. The current review discusses the various approaches of lipid drug delivery system, different methods of preparation, characterization and applications of Solid lipid Nanoparticles.

KEYWORDS: Colloidal particles, Nanoparticles, Lipid Based Drug Delivery, Solid Lipid Nanoparticles (SLN).

INTRODUCTION
Oral route has been the major route of drug delivery for the chronic treatment of many diseases. However, oral delivery of 50% of the drug compounds is hampered because of the high lipophilicity of the drug itself. Nearly 40% of new drug candidates exhibit low solubility in water, which leads to poor oral bioavailability, high intra- and inter-subject variability and
lack of dose proportionality. Following oral administration, dissolution of the drug molecule in the gastrointestinal (GI) milieu is a prerequisite for the absorption process.\cite{1} According to the Biopharmaceutical Classification System (BCS), poorly water soluble compounds are classified as either class 2 or class 4 compounds. For class 2 compounds, which have high intestinal permeability properties, absorption level is dictated by the dissolution properties of the molecule in the gastrointestinal fluids. BCS class 4 compounds, which are characterized by both low solubility and poor intestinal wall permeability, are generally poor drug candidates (unless the dose is very low). The solubilization of the lipophilic molecule occurs mostly at the upper part of the GI tract, where pancreatic fluids and biliary lipids (including bile salts, phospholipid and cholesterol ester) are secreted and enhance the solubilization process. The absorption of these molecules usually takes place in the small intestine. The residence time of a molecule in the upper GI is limited, and the transit time in the small intestine is 3.5–4.5 h in healthy volunteers. Fat can cause a modest extension of the short intestinal transit time (30–60 min). The short transit time in the small intestine limits the absorption of a lipophilic compound, and in the case where the lipophilic molecule reaches the colon prior to solubilization its bioavailability is low.\cite{2,3} The layer of water adjacent to the absorptive membrane of the enterocyte is essentially unstirred. For BCS class 2 compounds the rate of permeation through the intestinal brush border is fast and the diffusion across the unstirred water layer (UWL) is the rate limiting step in the permeation process. The second mechanism by which the UWL functions as a barrier to drug absorption is its effective surface area. When a drug molecule enters the enterocyte, it faces biochemical barriers that affect the magnitude of its absorption. The enterocyte cytochrome P-450 3A4 (CYP3A4) enzymes are located in the endoplasmic reticulum of the enterocyte and are responsible for most of drug metabolism in the intestinal wall. This iso-enzyme accounts for more than 70% of all small intestinal CYP450s. While some transporters located in the apical wall of the enterocyte facilitate absorption, there are others that serve as efflux transporters. These are considered as the Multiple Drug Resistance (MDR) transporters and they play an important role in the disposition of many drugs. Following absorption into the blood capillaries and before reaching the systemic blood circulation, the drug molecules transfer through the liver and hence are exposed to metabolic enzymes. This first pass hepatic metabolism has been shown to be a major barrier to the absorption of lipophilic drugs.\cite{1}
Lipid Based Drug Delivery

To overcome these problems, lipid-based oral drug delivery system (LBODDS) for oral drug delivery has taken a new dimension with the increasing application for lipophilic drugs.\[4\] By eliminating the variables of pre-absorptive gastrointestinal (GI) solubilization and the effects of dietary status, lipid-based formulations improve normalized drug absorption, which is particularly beneficial for low therapeutic index drugs. These formulations enhance drug absorption by a number of ancillary mechanisms, including inhibition of P-glycoprotein-mediated drug efflux and preabsorptive metabolism by gut membrane-bound cytochrome enzymes, promotion of lymphatic transport, which delivers drug directly to the systemic circulation by avoiding hepatic first-pass metabolism and by increasing GI membrane permeability. These unique properties of lipids have made them a very attractive candidate for oral bioavailability of poorly water soluble drug candidate.\[5,6\]

A normal adult diet includes a daily intake of about 60–80 g of fat. Additionally, 40–60 g of fat is of endogenous origin, which consists of phospholipids, cholesterol and membrane lipids from desquamated intestinal cells and bacteria. This indicates that an adult digestive system is powerful enough to hydrolyze approximately 100–140 g of lipid every day. The solubilisation of drug in the GI tract and its bioavailability depend predominantly on the intra-luminal processing to which lipids are subjected prior to absorption is divided into three distinct phases(1) Digestive phase, (2) absorption phase, (3) circulatory uptake. The *in-vivo* fate of lipids in body is shown in figure 1.

![Figure 1: In vivo fate of lipids in body](image-url)
1) Digestive Phase
The digestive phase initiates with the physical breakdown of lipid formulation into a coarse emulsion of high surface area due to shear produced by antral contraction, retropulsion and gastric emptying. This is accompanied with hydrolysis of the fatty acid glyceryl esters by gastric lipase secreted from chief cells in the stomach (capable of functioning in an acidic environment) which act at the oil/water interface. The enzymatic hydrolysis reduces the TGs (triglycerides) into its more polar products monoglycerides (MGs) and FAs.

2) Absorption Phase
The colloidal species produced, in the form of micelles, mixed micelles, vesicles and free FAs as a result of lipid digestion, are taken up by passive diffusion, facilitated diffusion and active transport through the enterocyte membrane.

3) Circulatory uptake
The majority of orally administered drugs gain access to the systemic circulation by absorption into the portal blood. However, some extremely lipophilic drugs (log P > 5) gain access to the systemic circulation via lymphatic route, which avoids hepatic first-pass metabolism. Therefore, highly metabolized lipophilic drugs may be potential candidates for lipid based drug delivery. Compounds showing increased bioavailability in the presence of lipids (dietary or lipid-based formulation) are absorbed via the intestinal lymph as they are generally transported in association with the long-chain TGs lipid core of intestinal lipoproteins formed in the enterocyte after re-esterification of free FAs and MGs. Drug transport via the lymphatics, therefore, requires co-administration of lipid to stimulate lipoprotein formation. The main mechanism of intestinal lymphatic drug absorption is via intracellular association of the drug with the lipidic core of the chylomicron, a lipoprotein that is synthesized in situ inside the enterocyte. Following this association, the chylomicron is packaged in the Golgi, secreted from the basolateral membrane of the enterocyte to the intracellular space, absorbed into the porous mesenteric lymph vessels and travels, with the lipophilic molecule in it, along the lymphatics until it drains into the systemic blood circulation.

The drug being transported in the circulatory system, in the form of either micelles or mixed micelles, may then be available in its free form, since upon dilution with a large volume of the lymph/blood, surfactant concentration may reduce below its cmc value and micelle may dissociate into monomers. The drug transported as lipid vesicles may remain intact for
extended periods and thereby, can result in prolonged release of the encapsulated drug. Figure 2 is a diagrammatic presentation of the various mechanisms by which lipids enhance the bioavailability of drug.

![Diagram of Various mechanisms of enhancement of drug bioavailability in the presence of lipids](image)

**Figure 2: Various mechanisms of enhancement of drug bioavailability in the presence of lipids**[^3]

**Nanoparticles**

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000nm.[^7] The major goals in designing nanoparticles as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen.[^8] The successful implementation of nanoparticles for drug delivery depends on their ability to penetrate through several anatomical barriers, sustained release of their contents and their stability in the nanometer size. They have some limitations due to their high cost and scarcity of safe polymers with regulatory approval.[^9] To overcome this limitation of polymeric nanoparticles, lipid is used as an alternative carrier. These nanoparticles are known as solid lipid nanoparticles (SLNs). Solid lipid nanoparticles (SLN) have attracted increasing attention as a potential drug delivery carrier owing to their advantages such as the possibility of simple and large scale production and low toxicity.[^10] The features of lipid nanoparticles for oral and peroral delivery are related with their adhesive properties. Once adhered to the GIT wall, these particles are able to release the drug exactly where it should be absorbed.[^11]
Solid Lipid Nanoparticles

SLN’s are colloidal carriers made up of lipids, emulsifiers and water with a mean photon correlation spectroscopy (PCS) diameter between approximately 50-1000 nm. They are made up of solid hydrophobic core having a monolayer of phospholipid coating stabilized by surfactants (emulsifiers).\textsuperscript{[10]} Solid lipid core contains the drug dispersed or dissolved in lipid matrix. They have potential to carry lipophilic or hydrophilic drugs. Figure 3 shows structure of SLN.\textsuperscript{[13]}

![Lipid (solid)](image)

Figure 3: Structure of Solid Lipid Nanoparticles.\textsuperscript{[13]}

Advantages of solid lipid nanoparticles\textsuperscript{[14]}
1. Possibility of controlled drug release and drug targeting
2. Increased drug stability
3. High drug payload
4. Incorporation of lipophilic and hydrophilic drugs feasible
5. No biotoxicity of the carrier
6. No problems with respect to large scale production and sterilization.

Components for the preparation of solid lipid nanoparticles

Various types of lipids, surfactants and co-surfactants are used for the preparation of solid lipid nanoparticles are summarized in the Table 1 and 2 respectively.\textsuperscript{[14]}

Table 1: Different types of lipids used for preparation of SLN

<table>
<thead>
<tr>
<th>LIPIDS</th>
<th>Acyglycerol</th>
<th>Fatty acids</th>
<th>Waxes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triacylglycerides</td>
<td>Acyglycerol</td>
<td>Fatty acids</td>
<td>Waxes</td>
</tr>
<tr>
<td>Triarcarpin</td>
<td>1) Glycerolmonostearate (Imwitor 900)</td>
<td>1) Stearic acid</td>
<td>1) Cetyl Palmitate</td>
</tr>
<tr>
<td>Trilaurin</td>
<td>2) Glycerol behenate (Compritol 888 ATSO)</td>
<td>2) Palmitic acid</td>
<td></td>
</tr>
<tr>
<td>Tripalmitin</td>
<td>3) Glycerol palmitostearate(Precirol ATO5)</td>
<td>3) Decanoic acid</td>
<td></td>
</tr>
<tr>
<td>Tristearin</td>
<td></td>
<td>4) Behenic acid</td>
<td></td>
</tr>
</tbody>
</table>

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Table 2: Different types of surfactants and co-surfactants used for preparation of SLN

<table>
<thead>
<tr>
<th>SURFACANTS</th>
<th>Ethylene oxide/Propylene oxide copolymer</th>
<th>Sorbitan ethylene oxide</th>
<th>Bile salts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phospholipids</td>
<td>1) Poloxamer 188</td>
<td>1) Polysorbate 20</td>
<td>1) Sodium cholate</td>
</tr>
<tr>
<td>1) Soy lecithin (Lipoid S 75, S 100)</td>
<td>2) Poloxamer 182</td>
<td>2) Polysorbate 60</td>
<td>2) Sodium taurocholate</td>
</tr>
<tr>
<td>2) Egg lecithin (Lipoid E80)</td>
<td>3) Poloxamer 407</td>
<td>3) Polysorbate 80</td>
<td>3) Sodium taurodeoxycholate</td>
</tr>
<tr>
<td>3) Phosphatidylcholine (Epikuron 170, 200)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CO-SURFACTANTS</th>
<th>Ethanol</th>
<th>Butanol</th>
</tr>
</thead>
</table>

Different methods of SLN preparation

1. Primary Production Techniques

A. High pressure homogenization
   (I) Hot homogenization.
   (II) Cold homogenization.

B. Micro emulsion based SLN preparations.

C. Solvent emulsification-diffusion technique.

D. Solvent emulsification-evaporation technique.

E. Double Emulsion technique.

2. Secondary Production Techniques

1. Lyophilization (Freeze Drying)
2. Spray drying method.

A. High pressure homogenization technique

High pressure homogenization (HPH) has emerged as a reliable and powerful technique for the preparation of SLN. Homogenizers of different sizes are commercially available from several manufacturers at reasonable prices. High pressure homogenizers push a liquid with high pressure (100–2000 bar) through a narrow gap (in the range of a few microns). The fluid accelerates on a very short distance to very high velocity (over 1000 km/h). Very high shear stress and cavitation forces disrupt the particles down to the submicron range. Typical lipid contents are in the range 5–10%. Two general approaches of the homogenization the hot and the cold homogenization techniques, can be used for the production of SLN. In both cases, a
preparatory step involves the drug incorporation into the bulk lipid by dissolving or dispersing the drug in the lipid melt.\textsuperscript{[14]}

\textbf{(I) Hot high pressure homogenization}

Hot homogenization is carried out at temperatures above the melting point of the lipid and can therefore be regarded as the homogenization of an emulsion. A pre-emulsion of the drug loaded lipid melt and the aqueous emulsifier phase (same temperature) is obtained by high-shear mixing device (Ultra-Turrax). HPH of the pre-emulsion is carried out at temperatures above the melting point of the lipid. In general, higher temperatures result in lower particle sizes due to the decreased viscosity of the inner phase. However, high temperatures may also increase the degradation rate of the drug and the carrier. The homogenization step can be repeated several times.\textsuperscript{[14]}

\textbf{(II) Cold high pressure homogenization}

In contrast, the cold homogenization is carried out with the solid lipid and represents, therefore, a high pressure milling of a suspension. Effective temperature control and regulation is needed in order to ensure the un molten state of the lipid due to the increase in temperature during homogenization.

The Cold homogenization has been developed to overcome the following three problems of the hot homogenization technique: temperature-induced drug degradation, drug distribution into the aqueous phase during homogenization and 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 dispersing of the drug in the melt of the bulk lipid. The drug containing melt is rapidly cooled (e.g. by means of dry ice or liquid nitrogen). The high cooling rate favors a homogenous distribution of the drug within the lipid matrix.

The solid, drug containing lipid is milled to microparticles. Typical particle sizes obtained by means of ball or mortar milling are in the range 50–100 microns. Figure 4 shows comparison of hot and cold homogenization.\textsuperscript{[14,15]}
Figure 4: Comparison of hot and cold high pressure homogenization processes.

B. Microemulsions based SLN
The microemulsion technique was developed by Gasco. The microemulsion is formed above the melting point of the lipid. It is a two-phase system composed of an inner and outer phase (e.g. o/w-microemulsions). They are made by stirring an optically transparent mixture at 65–70°C which is typically composed of a low melting fatty acid (e.g. stearic acid), an emulsifier (e.g. polysorbate 20, polysorbate 60, soy phosphatidylcholine, taurodeoxycholic acid sodium salt), co-emulsifiers (e.g. butanol, sodium monooyctylphosphate) and water. The hot microemulsion is dispersed in cold water (2–3°C) 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. The droplet structure is already contained in the microemulsion and therefore, no energy is required reduction for the average particle size to achieve submicron particle sizes.[14,29]

C) Solvent emulsification-diffusion technique
In solvent emulsification-diffusion technique, the solvent used (e.g. benzyl alcohol, butyl lactate, ethyl acetate, isopropyl acetate, methyl acetate) must be partially miscible with water and this technique can be carried out either in aqueous phase or in oil. Initially, both the solvent and water are mutually saturated in order to ensure the initial thermodynamic equilibrium of both liquid. When heating is required to solubilize the lipid, the saturation step is performed at that temperature. Then the lipid and drug were dissolved in water saturated
solvent and the organic phase (internal phase) is emulsified with solvent saturated aqueous solution containing stabilizer (dispersed phase) using mechanical stirrer.[16]

D) Solvent emulsification-evaporation technique
Sjostrom and Bergenstahl described a production method for preparing SLN by precipitation in o/w emulsions. The lipophilic material is dissolved in a water-immiscible organic solvent (e.g. cyclohexane) that is emulsified in an aqueous phase. Upon evaporation of the solvent, a nanoparticle dispersion is formed by precipitation of the lipid in the aqueous medium. The mean diameter of the obtained particles was 25 nm with cholesterol acetate as model drug and by using a lecithin /sodium glycocholate blend as emulsifier. The advantage of this procedure over the cold homogenization process is the avoidance of any thermal stress. A clear disadvantage is the use of organic solvents.[16]

E) Double emulsion technique
In double emulsion technique the drug (mainly hydrophobic drugs) is dissolved in aqueous solution, and then is emulsified in melted lipid. This primary emulsion was stabilized by adding stabilizer (e.g. gelatin, poloxamer-407). Then the stabilized primary emulsion was dispersed in aqueous phase containing hydrophilic emulsifier (e.g. PVA). Thereafter, the double emulsion is stirred and is isolated by filtration. This technique is mainly used to encapsulate hydrophilic drug (peptides). A major drawback of this technique is the formation of high percentage of microparticles.[16]

1.8.2. Secondary Production Techniques
1. Lyophilization
Lyophilization is a promising way to increase chemical and physical SLN stability over extended periods of time. Lyophilization also offers principle possibilities for SLN incorporation into pellets, tablets or capsules. Transformation into the solid state would prevent the Oswald ripening and avoid hydrolytic reactions. Addition of cryoprotectors is necessary to decrease SLN aggregation and to obtain a better redispersion of the dry product. Cryoprotectors are place holders which prevent the contact between discrete lipid nanoparticles. Cryoprotectors like glucose, mannose, maltose and trehalose in concentrations between 10 and 15% is used.[13,14,18]
2) Spray Drying
Spray drying might be an alternative procedure to lyophilization in order to transform an aqueous SLN into a dry product. This method has been used scarcely for SLN formulation, although spray drying is cheaper compared to lyophilization.\textsuperscript{[14,19]}

Characterization of SLN\textsuperscript{[10, 14, 15, 30, 26]}
Nanoparticulate formulations are usually characterized in terms of size, morphology, drug content and in-vitro drug release. Wide ranges of techniques are available for physico-chemical characterization of nanoparticles and are listed in the following Table 3.

Table 3: Physico-chemical characterization of nanoparticles

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particle size and morphology</td>
<td>Transmission Electron Microscopy</td>
</tr>
<tr>
<td></td>
<td>Scanning(electron,force,tunnelling)Microscopy</td>
</tr>
<tr>
<td></td>
<td>Freeze Fracture Electron Microscopy</td>
</tr>
<tr>
<td></td>
<td>Photon Correlation Spectroscopy</td>
</tr>
<tr>
<td>Drug content</td>
<td>Ultracentrifugation / Ultrafiltration / Sephadex column/Dialysis bag.</td>
</tr>
<tr>
<td></td>
<td>Separation followed by quantitative analysis</td>
</tr>
<tr>
<td>Crystallinity</td>
<td>X-Ray Diffraction Differential Scanning Calorimetry</td>
</tr>
<tr>
<td>Surface charge</td>
<td>Zeta potential measurement</td>
</tr>
<tr>
<td>Surface chemical analysis</td>
<td>Fourier Transform Infrared Spectroscopy</td>
</tr>
<tr>
<td></td>
<td>Nuclear Magnetic Resonance</td>
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</tbody>
</table>

Application of SLN

Oral administration
Per oral administration forms of SLN may include aqueous dispersions or SLN-loaded traditional dosage forms such as tablets, pellets or capsules.\textsuperscript{[15, 25,26]}

Parenteral administration
SLN have been administered intravenously to animals. Pharmacokinetic studies of doxorubicin incorporated into SLN showed higher blood levels in comparison to a commercial drug solution after i.v. injection in rats. Regarding distribution, SLN were found to have higher drug concentrations in lung, spleen and brain, while the solution led to more distribution into liver and kidneys.\textsuperscript{[15, 26,28]}

SLNs for Topical use
SLNs and NLCs have been used for topical application for various drugs such as tropolide, imidazole antifungals, anticancers, isotretinoin, ketoconazole and glucocorticoids. The
penetration of podophyllotoxin-SLN into stratum corneum along with skin surface lead to the epidermal targetin. By using glyceryl behenate, vitamine A-loaded nanoparticles can be prepared. The methods are useful for the improvement of penetration with sustained release. The isotretinoin-loaded lipid nanoparticles was formulated for topical delivery of drug. The soyabean lecithin and Tween 80 are used for the hot homogenization method for this. The methodology is useful because of the increase of accumulative uptake of isotretinoin in skin.\textsuperscript{[15,27]}

**SLN for Nasal Application**

Nasal administration was a promising alternative noninvasive route of drug administration due to fast absorption and rapid onset of drug action, avoiding degradation of labile drugs (such as peptides and proteins) in the GI tract and insufficient transport across epithelial cell layers. In order to improve drug absorption through the nasal mucosa, approaches such as formulation development and prodrug derivatization have been employed. In a recent report, coating polymeric nanoparticles with PEG gave promising results as vaccine carriers. The role of PEG coating of polylactic acid nanoparticles in improving the trans mucosal transport of the encapsulated bioactive molecule reported to be successful by Tobio et al, 1998. This concept can be useful for solid lipid nanoparticles.\textsuperscript{[23]}

**SLN for Ocular Application**

Ocular drug administration via SLN has been reported several times. Biocompatibility and mucoadhesive properties of SLN improve their interaction with ocular mucosa and prolong corneal residence time of the drug, with the aim of ocular drug targeting. Cavalli et al., (2002) evaluated SLN as carriers for ocular delivery of tobramycin in rabbit eyes. As a result SLN significantly enhanced the drug bioavailability in the aqueous humor. Cavalli et al., (1995) also studied pilocarpine delivery via SLN, which is commonly used in glaucoma treatment, earlier. They reported very similar results in order to enhance the ocular bioavailability of drug.\textsuperscript{[23]}

**SLNs as Cosmeceuticals**

The SLNs have been applied in the preparation of sunscreens and as an active carrier agent for molecular sunscreens and UV blockers.\textsuperscript{[15,27]}
SLNs as a targeted carrier for Anticancer drug to solid tumors
SLNs have been reported to be useful as drug carriers to treat neoplasms. Tamoxifen, an anticancer drug incorporated in SLN to prolong release of drug after i.v. administration in breast cancer and to enhance the permeability and retention effect.[15]

Oral SLNs in Antitubercular chemotherapy
Antitubercular drugs such as rifampicin, isonizide, pyrazinamide-loaded SLN systems, were able to decrease the dosing frequency and improve patient compliance. By using the emulsion solvent diffusion technique antitubercular drug loaded solid lipid nanoparticles are prepared.[25]

SLNs for targeted Brain drug delivery
The extremely small particle size of solid lipid nanoparticles, which are less than 50 nm, might be beneficial with respect to drug targeting. Small carrier size generally favors reduced uptake by the reticuloendothelial system. Drug targeting might also be possible by surface modification of solid lipid nanoparticles. SLNs can improve the ability of the drug to penetrate through the blood-brain barrier and is a promising drug targeting system for the treatment of central nervous system disorders. In a study to overcome the limited access of the drug 5-fluoro-2’-deoxyuridine (FUdR) to the brain, 3’,5’-dioctanoyl-5- fluoro-2’- deoxyuridine (DO-FUdR) was synthesized and incorporated into solid lipid nanoparticles (DOF UdR-SLN)43. The state of the art on surfactant coated poly (alkylcyanoacrylate) nanoparticles specifically designed for brain targeting is given by emphasizing the transfer of this technology to solid lipid matrices. The potential advantages of the use of solid lipid nanoparticles over polymeric nanoparticles are accounted on the bases of a lower cytotoxicity, higher drug loading capacity and best production scalability. Solid lipid nanoparticles physicochemical characteristics are also particularly regarded in order to address the critical issues related to the development of suitable brain targeting formulations.[26]

CONCLUSION
One of the most prominent and effective Lipid based drug delivery is Solid lipid nanoparticles (SLNs). SLN formulations enhance the drug absorption by inhibition of P-glycoprotein-mediated drug efflux and pre-absorptive metabolism by gut membrane-bound Cytochrome enzymes which increases the GI membrane permeability and delivers drug directly to the systemic circulation via lymphatic transport thus, surpassing the hepatic first-
pass metabolism. The SLNs have the potential to achieve, at least partially, these broad objectives. We can expect many patented dosage forms in the form of SLNs in the future.

REFERENCES


