REVIEW ARTICLE

Solid Lipid Nanoparticles: A Trending Slant for Drug Delivery System

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Abstract

Drug delivery systems have opened various doors to fulfill the requirements of chemotherapy. It improves therapeutic effects of already efficient molecules by delivering it to the targeted site. Research area achieved a high peak in the aspect of lipid-based nano-drug delivery system. Conventional oral therapy has various problems especially lower oral bioavailability of a drug. To overcome such problems, researcher found a way in the form of solid lipid nanoparticles (SLNs). Newest form of medication carrier system, that is, SLN concept firstly introduced in December 1991. It is a system of medication carrier over the traditional colloidal carriers. It mainly includes nanoparticles ranges of spherical stable lipid cells, scattered in fluid surfactant. It includes of nanometer ranges of spherical stable lipid cells, which are often scattered in fluid surfactant arrangement or in water. The main issues raised in previous type of carrier systems are poor water soluble and under development; absolutely having low bioavailability. In this type we have to prepare medicine with physiologically well tolerated lipids is the main advantage of this system to achieve good therapeutic outcomes. Lipid-based nanoparticles are SLNs which has size in between 10 and 1000 nm. This review will focuses on SLNs and their applications in various aspects. Applications comprise targeted therapy in brain tumors. Along with this treatment of metastatic breast cancer can also achieve using SLNs.

Key words: Brain targeting, chemotherapy, solid lipid nanoparticles, targeted drug therapy

INTRODUCTION

Nowadays, the targeted drug delivery system became a main system to achieve therapeutic purpose. Research area achieved a high peak in the aspect of lipid-based nano-drug delivery system. The main components of human cell include carbohydrates, proteins, and lipids. Carbohydrates provide energy to the body; Lipids have three major roles in cells. First, they provide an important form of energy storage. Second, and of great importance in cell biology, lipids are the major components of cell membranes. Third, lipids play important roles in cell signalling; convey signals from cell surface receptors to targets within the cell.[1]

Newest form of medication carrier system, that is, SLN concept firstly introduced in December 1991. It is a system of medication carrier over the traditional colloidal carriers. It mainly includes nanoparticles ranges of spherical stable lipid cells, scattered in fluid surfactant. It includes of nanometer ranges of spherical stable lipid cells, which are often scattered in fluid surfactant arrangement or in water.[2]

Recently one of the main streams evolved, that is, targeted drug delivery system. According to new stream's applications, improvement of drug delivery can be achieved using various carriers such as nanoparticles and liposomes. Along with some poor properties of SLN such as it encompasses the polymeric nanoparticle's superiority, lipid emulsion, and liposomes but at the same time, the SLN have many advantages such as good biocompatibility, non-harmful, stable against mixture, sedate spillage, hydrolysis, biodegradable, physical table, and good carrier for lipophilic drugs. The new one system of medication carrier, that is, SLN is beneficial over traditional carrier system with the aspects such targeting drug therapy in brain tumors, topical drug delivery: Parenteral, dermal, pulmonary, and topical. For dose form development process, the dosage form developed in such a way that no hypersensitivity occurs after administration. Furthermore, worthy of mention they

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introduced a strong program in the field of transferring gene and in industrializing cosmetic and food materials. However, due to the above said limits and associated to them, the entire quantity of production in the markets is still inadequate, and in a narrow range. SLN works by solving all the issue that are raised in traditional carrier system.[3]

The main issues raised in previous type of carrier system are poor water soluble and under development; absolutely having low bioavailability. In this type, we have to prepare medicine with physiologically well-tolerated lipids is the main advantage of this system to achieve good therapeutic outcomes. Lipid-based nanoparticles are SLNs which have size in between 10 and 1000 nm^3.

In traditional era, many problems were found by scientist during formulation of dosage form of particular drug. The problems are low solubility and bioavailability. It became a thought by accepting these problems scientist started work and found most relevant carrier system for the required target in the form of SLNs. The structure of SLN is spherical (diameter 10–1000 nm) as shown in Figure 1. SLNs contain a solid lipid core matrix. It is helpful to solubilize lipophilic molecules. The surfactants (emulsifiers) play a key role in the stabilization of lipid core.[4]

Nano-sized drug delivery systems having following problems:

- Low absorption, quick metabolism, and elimination; if orally administered
- Poor drug solubility that includes IV injections of aqueous drug solutions
- Drug delivery associated with high toxicity of other tissues. (Ex: Medicines for Cancer).

Several processes done to incorporate a drug into lipid core to form SLN mediated drug delivery system for therapeutic purpose. Various methods of preparation nowadays implemented, namely, high pressure homogenization (HPH), dissolvent emulsification/evaporating, supercritical extracting of emulsion fluid, and ultrasonic or fast-moving homogenization in addition to spray drying.[5,6]

Lipid nanoparticles (LNPs) are the oldest drug carrier system. A liposome is known as a spherical vesicle surrounded by a lipid bilayer membrane, with an aqueous internal cavity. The name liposome originates from the following two Greek terms, “Lipid” is fat and also its definition, “Soma” means body.[7]

In this day, the both types of nanoparticles are used to formulate and evaluate cosmetic, dermal, and medicinal studies. It is true that liposomes are lipid core that releases drug from core matrix but with that we have to monitor drug release also.[8]

Classification of nanoparticlesNanoparticles can be categorized into different types as per the size, morphology, physical, and chemical properties as shown in Figure 2. In that main types are polymeric nanoparticles, LNPs, dendrimer, hydrogel, and inorganic nanoparticles. The LNPs are further divided into nanostructured lipid carriers (NLC) and SLN as shown in Figure 3.[10] The use of lipids as a certain carrier for polymeric nanoparticles, mainly for lipophilic medication and LNPs are known as SLNs.

SLN has structure as their particles scattered over surfactant or water. SLN originates from solid hydrophobic heart with a single layer of phospholipids. Fat matrix comprises phospholipid hydrophobic chain and it possess the ability to carry hydrophilic or lipophilic medication as shown in Figure 4.[7]

Composition and structure of SLNs

Components of SLNs are totally depends on which drugs to be incorporated since it has to be solubilized in the lipid matrix to have good entrapment efficiency. SLNs are versatile nanocarriers that have been applied to improve the therapeutic effect of different molecules. In this, crystal structure of lipid matrix is a crucial characteristic to obtain high quality SLN formulations. The most frequently used components in the preparation of lipid core are mono, di, triglycerides, fatty acids, fatty alcohols, and waxes. These types of substances are highly biocompatible and their melting point is higher than body temperature hence used in the preparation of SLN. Formulation method is also essential to determine drug release from lipid core. Hence, preparation method, component as well as proportion of components has a great impact on the quality and characteristics of SLNs, the appropriate composition should be chosen to each particular case.[11]

PREPARATION OF SLNs

Release of medicaments from SLN is depends on how SLN is processed or what method is being apply to formulate or incorporate medicament with SLN. There are various methods for preparation of finely detached LNPs dispersions for targeted therapy.[5,6]

Homogenization at high pressure: (Hot HPH and cold HPH)

In general, SLNs contains solid lipids, surfactants, and water. It consists of solid lipids with a mean diameter of about 10–1000 nm. Solid lipids generally comprise triglycerides, fatty acids, hormones (such as, cholesterol), and waxes (such as cetyl palmitate). The surfactant forms (respect for charge and molecular weight) are aimed at settling lipid diffusion.[5]

SLN is also regarded as beneficial medication conveyer systems because of constant release of medicaments. SLN has constant physicochemical properties although it never changes in any condition. As polymeric nanoparticles have better biocompatibility because they are composed of lipids who are physiologically stable. The all reasons

helpful to polymeric nanoparticles to become poisonousness (decreased). Similarly, SLN is also physiologically stable; hence, it will show better biocompatibility.[6]

SLN has greater atom bulk (>1000 nm). Various methods for preparation of nanoparticles and microparticles with solid lipid are exist. Emulsions (hot homogenization method, dissolve scattering process, PIT strategy, and dissolvable dissipation dispersion from emulsions), microemulsions (diluting microemulsion and microemulsion cooling procedures), and solutions of micelle (cooling method) are the most important precursors. Certain preparing ways are grounded on supercritical liquids. The most significant methods including utilizing a specific device consist of: Membrane contactor method, spray-drying, spray-congealing, and electrospraying.[13]

The two most common production techniques for preparation of SLN are hot homogenization and cold homogenization. Medication is melted for both of them in the lipid at temperature 5 ± 108°C above fusion level.[14,15]

SLN formulated with microemulsion technology

Microemulsion means small particles emulsified in aqueous or lipid media. It is a pale blue arrangement comprising of lipophilic stage with surfactant and also water in various cases. By adding water to the microemulsion, it accumulates small particles in the lipid process. This type of advantage taken into consideration for the preparation of SLN by Gasco's SLN preparation method.[13]

Microemulsion must be formed at temperature over the softening purpose of lipid. The gentle mixing of all the components is done by heating to the unsaturated fats, glycerides, a blend of water, and co-surfactants (heated all the components with similar temperature). When the all the mixes are blended in the accurate proportion then microemulsion is ready to form. This microemulsion is then distributed under a moderate mechanical mixture in a cold aqueous medium (2 ± 38°C), thereby guaranteeing that the little volume of the particles is because of precipitation and not precisely brought about by a blending strategy.[16,17]

Membrane contactor technique

In this type of preparation method, two layers are being separated in that one layer is might be aqueous and other organic. The separation takes place at high temperature. The temperature raised up to or higher than melting point of fat molecules that fat molecule crystallizes in their form when the temperature is reduced to 20°C.

The aqueous and organic layers can be isolated to be used in the liquid phase where nitrogen and high pressure are used to maintain the aqueous and organic layers of the next stage.

The steps are involved in the membrane contactor technique:

1. Dissolve the matrix consisting of a mixture of fats, surface materials, polymers, and medicine at a temperature of 55–70°C
2. Add hot water with continuous vibratory stirring to form a small emulsion
3. Cooling to 20°C with continuous stirring until the SLNs are formed.[6]

Spray drying

This is another method to convert aqueous formulation of SLN into dried drug product. This type of method has more advantages than lyophilization as it comprises use of solid lipid having melting point more than 70°C. It includes aggregation of nanoparticles somewhat due to excessive heating and half way melting of the nanoparticles.[6]

Solvent injection technique

In this method, lipid (solid) is liquefying in organic solvent which is miscible in aqueous phase. The organic solvent consists of lipid added into aqueous phase with or without surfactant during stirring. Then, the formulation filtered as to remove extra lipid from the formulation. Aqueous phase emulsion supports to form the small drops of lipid added and balance the SLN formulation up till the of solvent diffusion gets finished.[1,8]

Supercritical fluid technique

This is different technique that newly applied for the SLN preparation. A fluid is called as supercritical while pressure and temperature of the fluid are go beyond appreciated critical values.

In this method, the capability of fluid to get liquefies increased. The technique composed of few steps of nanoparticles preparation such as supercritical solution expansion and supercritical fluid extraction of emulsion. It has several advantages, namely, lack of solvents and dry formulation depends upon minimum temperature and pressure condition.[16,17]

THE MAIN ADVANTAGES AND DISADVANTAGES OF SLNs

SLN's advantages

1. It has several advantages as it may reduce the chance of risk of acute and chronic poisonousness
2. It improves poor water soluble molecules bioavailability
3. It enhances medication entrance into the skin through applying dermal by what called site specific distribution of medications

4. It controls drug release possibility and also drug targeting
5. It protects chemically labile reducing agents in the intestine and also it safeguards delicate molecules from external world
6. SLNs are more stable compared to liposomes
7. It fosters the trapped bioactive bioavailability and integrated labile chemical production compound
8. Highly focuses on functional compound accomplished
9. Lyophilization is possible.[8,17]

SLN's disadvantages

1. Low medicine packing capacity
2. Medication exclusion following polymeric change during storing
3. Comparatively high dispersed water volume (70–99.9%)
4. The bounded capacity of loading of water-soluble drugs during the manufacturing cycle due to partitioning effects
5. Gelation tendency
6. Incredible motion of polymeric transition.[8,17]

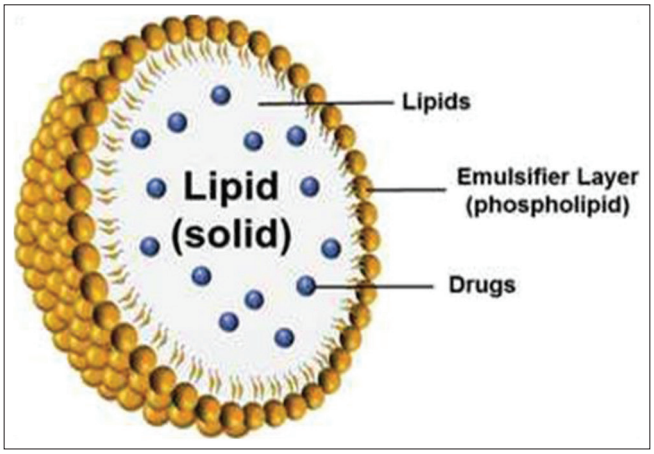

Figure 1: Solid lipid nanoparticle chemical structure

APPLICATIONS OF SLN

SLNs for chemotherapy

SLNs are widely used to deliver chemotherapeutic agent at their respective target site to treat various stages of cancer. Some nanoscale devices can be used as instruments to confront the cancer cells. This varies the drugs' selectivity to the cancer cells and it would certainly diminish the normal tissue poisonousness. Many reports are created to be devoted to describe LNPs possibilities for parenteral delivery particularly for the cancer treatment. Since two decades' scientists achieved a great deal of extensive data for an essential biological procedure that is disrupted by cancer, for example, development factor restricting disruptions, gene transcription, signal transduction regulation, cell cycle checkpoints, apoptosis, and angiogenesis which in their turn contributed to the quest for appropriate anti-cancer medications and created a record number of novel ingredients that are now utilized in cancer treatment studies.[8]

In another study, tamoxifen citrate loaded nanoparticles were injected in intravenously into rats and the parameters of pharmacokinetics were established. The t1/2 and mean residence time of TC-loaded SLNs in plasma was approximately 3.5-fold ($P < 0.001$) and 3-fold ($P < 0.001$) higher than free tamoxifen, suggesting the capacity of TC-loaded SLNs as a long blood circulation system. Accordingly, the aforesaid strong LNPs might be a useful method for delivering tamoxifen of tissues of cancer by improved porousness and maintenance impact (EPR).[18-21]

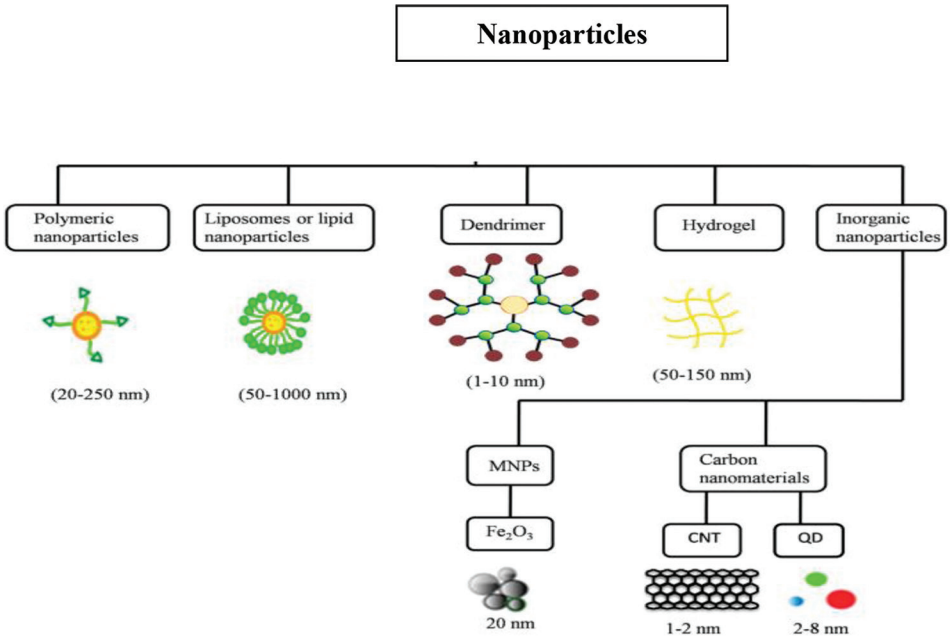

Figure 2: Classification of nanoparticles (size, morphology, physical, and chemical properties)[9]

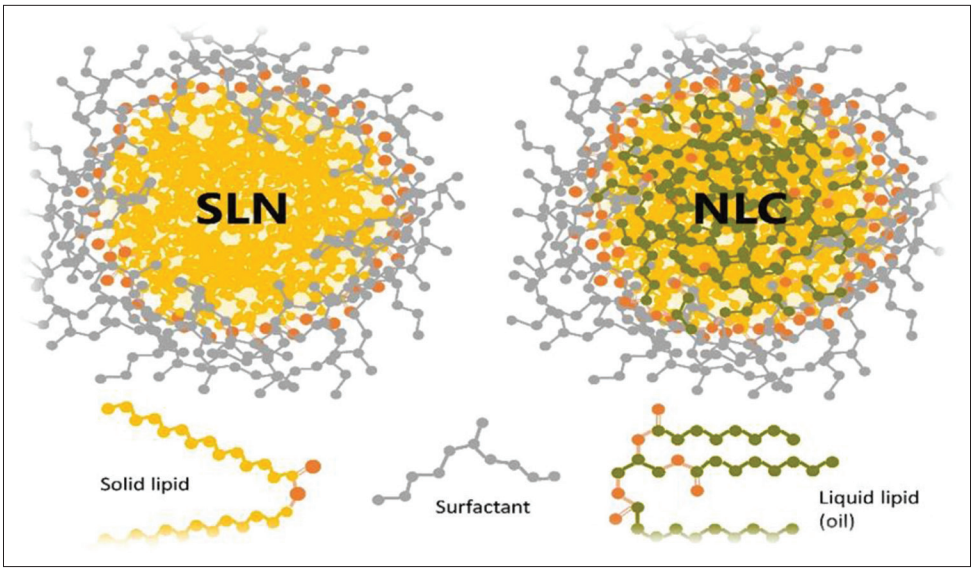

Figure 3: Classification of lipid nanoparticles[9]

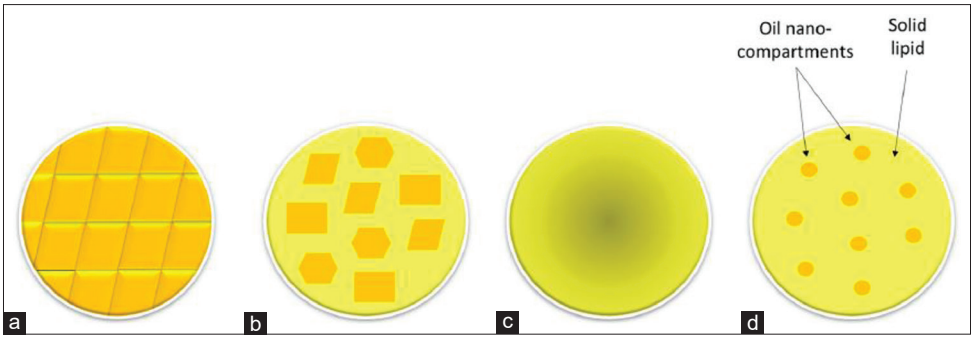

Figure 4: Schematic representation of solid lipid nanoparticles and different nanostructured lipid carrier (NLC type). (a) Solid lipid nanoparticles; (b) imperfect nanostructured lipid carrier; (c) structure less nanostructured lipid carrier; (d) multiple oil in solid fat in water[12]

SLN/NLC for parenteral use

SLNs are composed of physiologically completely-tolerated components; hence, it is largely acceptable. They have fine storage potential after lyophilization and/or sterilization. SLNs are usually tiny to disperse in the micro vascular system and stop macrophage intake in the event of deliquescent coating. With all the above aspects, SLNs have been proposed for viral and non-viral gene delivery. Hence, it is used in targeted gene therapy in treatment of cancer. Treatment of brain tumors, AIDS, neurological, and psychiatric disorders is frequently constrained by the inability of drugs to pass blood brain barrier. Possibly SLNs are became best option for targeted therapy to treat brain tumors.[8,20]

For nasal application

Nasal administration was an optimistic choice noninvasive route for drug administration due to quick absorption and immediate onset of drug action, bypass degradation of reactive drugs (such as peptides and proteins) in the gastrointestinal tract and inadequate transport beyond epithelial cell layers. With regard to enhance drug absorption by the nasal mucosa, perspectives such as formulation development and derivatization of prodrug have been hired. SLN has been suggested as substitute transmucosal delivery systems for macromolecular therapeutic ingredients and diagnostics by different research groups. In a current report, polyethylene glycol (PEG) -coated polymeric nanoparticles gave hopeful results as vaccine carriers. The function of PEG coating polylactic acid nanoparticles in enhancing the transmucosal transport of the enclosed active molecule described to be fruitful. This approach can be convenient for SLNs.

Inhalational drug delivery has several advantages over conventional (parenteral and oral) dosage forms such as non-invasiveness; negligible first-pass effects, and reduced systemic toxicity. Inhaled drugs may reach directly to the lung epithelium, enhancing local drug concentrations. Particles smaller than 500 nm may enhance pulmonary deposition due to an increased diffusional mobility.[8]

SLNs as cosmeceuticals

Cosmeceuticals are growing since these carriers' vital goal for application. Carrier systems such as SLNs and NLC have been designed to meet production criteria such as scale-up, certification and authentication, clear technology, and low cost. The SLNs were used in sunscreen preparation and as an active carrier agent for molecular sunscreens and ultraviolet blockers. SLN and NLCs have proved to be controlled release innovative occlusive topicals. Better localization has been accomplished for Vitamin A in upper layers of skin with glyceryl behenate SLNs compared to conventional formulations. In early 2005, the initial two beautifying production items comprising LNPs appeared on the market.[7]

SLNs as gene vector carrier

SLN can be used in formulating gene vectors. Several reports recently appeared about SLN bearing genetic/peptide constituents for example deoxyribonucleic acid (DNA), plasmid DNA, and other nucleic acids. The gene transfer was identified when a diametric HIV-1 HAT peptide was inserted into the SLN gene vector. The lipid nucleic acid nanoparticles were set up from a fluid nanoprocess comprising water and a non-miscible natural dissolvable where lipid and DNA are melted separately by extracting the organic solvent, stable, and homogeneous lipid nucleic acid nanoparticles (70-100 nm). It is known as geosphere. It is directly attacked by injecting in the particle an antibody-lipopolymer conjugated.[7]

SLNs as a targeted carrier for solid tumor anticancer drugs

SLNs have been accounted for as being valuable as medication bearers for treating neoplasms. Tumor goal was reached with drug-stacked SLNs, for example, methotrexate and camptothecin. Tamoxifen an anticancer medication is integrated in SLN to lengthen medication discharge after IV.[7]

CONCLUSION

Solid lipid nanoparticles are the fore front for the controlled drug delivery system. SLN and NLCs as colloidal drug carrier merges the advantage of liposomes, polymeric nanoparticles and fat emulsions. They were widely accepted, this review will focuses on composition, advantages, disadvantages, method of preparation, and SLNs are having vast applications in therapeutics. So in future research can be accomplish on formulation of NLC and LDC to achieve better drug loading, site specificity and low toxic effects.

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