Review Article

Solid lipid nanoparticles: A drug carrier system

Abstract

Solid lipid nanoparticles (SLN) are a type of nanoparticles. They are submicron colloidal carriers which are composed of physiological lipids, dispersed in water or in aqueous surfactant solutions. SLN have wide range of advantages over other types of nanoparticles. These include availability of large-scale production methods and no signs of cytotoxicity, which are main hindrances in the application of other types of nanoparticles. Hot and cold homogenization techniques are mainly employed for its production. They are mainly evaluated on the basis of their drug release profile and particle internal structure. The products based on SLN are under development. They have a very wide range of applications in cosmetics and pharmaceuticals. They can be applied for any purpose, for which nanoparticles have a distinct advantage. Thus, SLN can be used extensively as an alternative to the existing drug carrier systems, providing more flexibility with respect to the area of applications and also aspects for commercialization.

Key words:
Applications, drug carrier system, solid lipid nanoparticles

Introduction

Over the past few years, significant research has been carried out on nanoparticles with their applications in medicine. Nanotechnology can be defined as "the design, production and application of structures, devices and systems by controlled management of size and shape at the nanoscale that produces structures, devices and systems with at least one new property."[1] The nanosize of these particles has a profound influence on their properties and characteristics. This influence is probably because at the nanolevel, there is increase in volume to surface area ratio which eventually attributes to their high reactivity. In addition, quantum effects are more prominent with decrease in size, thereby having effect on the properties of these nanoparticles. Nanotechnology has had a huge impact on the drug delivery- and drug discovery-related areas.

Nanomaterials may be produced in one dimension, two dimensions, or in three dimensions.

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Nanomaterial in One Dimension

Nanomaterial in one dimension may include engineered surfaces and thin films. For example, thin films in silicon-integrated circuit industry. Further advances are being made to control the composition and smoothness of surfaces.

Nanomaterials in Two Dimensions

These include nanotubes (organic and inorganic) and nanowires.

Carbon nanotubes

These organic nanotubes were first observed by Sumjo lijima in 1991. Carbon nanotubes (CNTs) may be single walled (one tube) or multiwalled (several concentric tubes). CNTs are few nanometers in diameter and several nanometers to centimeters long. Their high conductivity and mechanical strength can be utilized for a variety of purpose.[2,3]

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Inorganic nanotube

Inorganic nanotubes are based on layered compounds such as molybdenum disulfide, silicon. They have excellent lubricant properties. Additionally, they have very high catalytic reactivity and high capacity for hydrogen and lithium storage.[4]

Nanowires

Nanowires are semiconductor wires made from a wide range of materials like silicon, gallium nitride, indium phosphide, etc. They have excellent optical, electrical, and magnetic properties. These are prepared by self-assembly techniques.

Nanomaterials in Three Dimensions

Fullerenes (C60)

Kroto and Richard Smalley discovered a new class of carbon compounds, carbon 60, and named it "buckminsterfullerene."[5] C60 are spherical molecules about 1 nm in diameter. They are applied as miniature ball bearings to lubricate surfaces, drug delivery vehicles, and electronic circuits.

Dendrimers

Dendrimers are spherical polymer molecules formed through self-assembly process. They can be used as drug-delivery carrier.[6]

Quantum dots

Quantum dots are semiconductor particles made small enough so that quantum effects begin to dominate. There is change in chemical, optical, and electrical properties.

Nanoparticles

Nanoparticles have diameter less than 100 nm. They may be made up of polymers (polymeric nanoparticles), lipids (lipid nanoparticles), or other such materials.

Solid lipid nanoparticles (SLN) are a type of nanoparticles. The present article deals in detail with SLN, including its definition, potential advantages, preparation techniques, and applications in medicine.

Definition of Solid Lipid Nanoparticles

Definition of Solid Lipid Nanoparticles (SLN) are nanoparticles that are made from solid lipids or lipid blends. It is similar to an oil-in-water emulsion where the liquid lipid (oil) of the emulsion has been replaced by solid lipid in SLN. Lipids used for the synthesis of SLN may include various types of waxes, triglycerides, and complex glycerides.[7]

Advantages of SLN as a Drug Carrier System

First of all, SLN are made up of physiologically compatible and tolerable lipids, and hence they are not toxic to the body. Depending upon the incorporation model, the drug release can be controlled as immediate release or sustained release. In addition, they offer protection to the encapsulated drug within them which may be labile and thereby prevent their degradation. They also have advantages of site-specific targeting and of being stable over a period of time.[8]

Preparation Techniques

One of the important advantages of SLN is its cost-effective large-scale production. Various different methods for the production of SLN include high-pressure homogenization method, SLN production through microemulsions, double emulsion method, solvent emulsification-evaporation technique, and sonication method.[8]

Of the above methods, high-pressure homogenization method is commonly used.[9] This method is performed at elevated temperatures or at or below room temperature. The former is called as hot high-pressure homogenization technique, while the latter is called as cold high-pressure homogenization technique. In hot high-pressure homogenization, drug and lipids are melted and added to a surfactant solution to form a pre-emulsion which is then subjected to high-pressure homogenization and subsequently cooled form SLN. In cold high-pressure homogenization, drug and lipids are melted and then subjected to high-pressure homogenization at or below the room temperature. This is normally utilized for thermolabile drugs.

The second method of production of SLN is through microemulsions.[10] In this method, a hot microemulsion containing the lipids and surfactants is prepared and dispersed into cold water. Excess of water is removed by different techniques like lyophilization, and SLN is formed.

In emulsion formation-solvent evaporation method,[8] a lipid containing solution is emulsified with an aqueous phase and then solvent is evaporated, which leads to the precipitation of lipids and SLNs. Even double emulsification method can be used for the production of SLN. However, appreciation of size is a major concern while using this method.

SLN have also been synthesized with the help of high-speed stirring in combination with ultrasonication. This method is normally performed at higher temperatures. An advantage of using this method is that stirrers and sonicators are easily available and hence this method is cost effective. However, contamination with metal particles while performing probe sonication still remains one of the hurdles in this method.

Applications of SLN in Medicine

Topical administration

SLN can be effectively utilized for pharmaceutical products

administered topically. They are made up of well-tolerated lipids and other excipients. Due to extremely small size, they have excellent adhesive properties on the skin, and hence its application for topical administration is enormous. In addition, with the help of SLN, the drug release can be controlled more effectively. SLN solid matrix also protected the active ingredients incorporated within them and thereby protected them from degradation. This was observed with active ingredients like retinol. SLN can also be used as a carrier system in cosmetics. SLN matrix can be used in sunscreens formulations. One of the biggest disadvantages of using sunscreen is its penetration into the skin, which eventually leads to irritation. It has been found that this penetration has decreased immensely while the sunscreen was formulated in a SLN matrix. In addition, SLN themselves were found to posses some sun protective effects.[11, 12]

Parenteral administration

The advantages of SLN, as already discussed, make it suitable as a drug carrier through parenteral administration. They can be injected intravenously, intramuscularly, subcutaneously, or directly to the affected organ. Because of their extremely small size, they can be used systemically with very minimum risk of embolism. It has also been found that SLN are having very prolonged stability as long as 1 year. Various different drugs have been incorporated into the SLN system and intended for parenteral application. These may include anticancer drugs like paclitaxel and doxorubicin, antibiotics like tetracaine and tobramycin, CNS acting drugs like diazepam, to list a few. This shows the versatility of SLN to be drug carrier through parenteral administration in different therapies.[8]

As a drug delivery system for proteins and peptides

Under prerequisite conditions, SLN can be used to incorporate and deliver both hydrophobic and hydrophilic proteins. The protein incorporated within SLN is free from exposure to external environment. Thereby, the proteins delivered through SLN avoid proteolytic degradation and their bioavailability is enhanced greatly. Various different proteins like cyclosporins, insulin, and somatostatin have been successfully incorporated within SLN matrix and studied. This system can be utilized then for different therapies through different routes of administration. These proteins or antigens can be incorporated within the SLN matrix or absorbed onto it. Even vaccines can effectively be administered with the help of SLN system.[13]

Miscellaneous applications

In addition, SLN system can also be applied to deliver drugs through oral and pulmonary routes of administration. The final product may be dispersion or a traditional dosage form like tablets or capsules. For example, camptothecin-loaded SLN particles were successfully synthesized and stabilized with the help of stearic acid and poloxamer 188.[12]

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