

Review Article

Solid lipid nanoparticles- Novel drug delivery system – A Review

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ARTICLE INFO

Received 01 Feb 2018

Revised 26 Feb 2018

Accepted 18 Mar 2018

Keywords:

- Solid lipid nanoparticles
- Colloidal drug carriers
- Homogenization
- Manufacturing techniques
- Polymer
- Spray drying

ABSTRACT

Nanotechnology is prominent field in the past few decades due to its wide range of application as a novel drug delivery, in clinical medicine and research. The solid lipid nanoparticles (SLN) is an excellent drug delivery system and has broad prospects in the pharmaceutical field. SLN was firstly introduced in 1991 represents an alternative carrier system to traditional carrier system, such as liposome's, emulsion, microemulsion and nanoparticles. This novel colloidal drug carrier system combines the advantages of traditional drug delivery system by eliminating their disadvantages. This article reviews the present state of the art regarding manufacturing techniques for SLN, advantages and disadvantages, characterization methods and applications in delivery of drug molecules and therapeutic genes.

1. INTRODUCTION

Nanotechnology and nanoscience have a great potential to bring benefits to many areas of research and application. The prefix Nano is derived from the Greek word dwarf. One nanometer is equal to one billionth of a meter, that is, 10^{-9} m. The term nanotechnology was first used in 1974, when Norio Taniguchi, a scientist at the University of Tokyo, Japan, referred to material in nanometers. The colloidal particles between 10-1000 nm are known as nanoparticles. They are composed of synthetic or natural polymers which give optimized drug delivery and reduce toxicity [1-6]. The popularity of nanoparticles as a drug delivery depends on their ability to penetrate through several anatomical barriers, sustained release of their contents and stability in the nanometer size [7]. In order to overcome the disadvantages associated with the liquid state of the oil droplet, the liquid lipid was replaced by solid lipid which eventually known as solid lipid nanoparticles

Solid lipid nanoparticles (SLN) (Fig. 1) dispersions have been proposed as a new type of colloidal drug carrier system suitable for intravenous administration. The system consists of spherical solid lipid particles in the nanometer ranges, which are

dispersed in water or in aqueous surfactant solution. Generally, they have solid hydrophobic core coated with a monolayer of phospholipids. The solid core contains the drug dissolved or dispersed in the solid high melting fat matrix. The hydrophobic chains of phospholipids are embedded in the fat matrix. They have potential to carry lipophilic or hydrophilic drugs or diagnostics [3-10].

SLN have unique properties such as small size, large surface area, high drug loading, and interaction of phases at the interface and are attractive for their potential to improve performance of pharmaceuticals [11]. The lipid based system has increased interest many – fold as:

- Lipids enhance oral bioavailability and reduce plasma profile variability.
- Better characterization of lipoid excipients.
- An improved ability to address the key issues of technology transfer and manufacture scale-up [11].

SLN formulations are for various application routes like parenteral, oral, dermal, ocular, pulmonary, rectal and characterized by *in vitro* and *in vivo* technique [12].

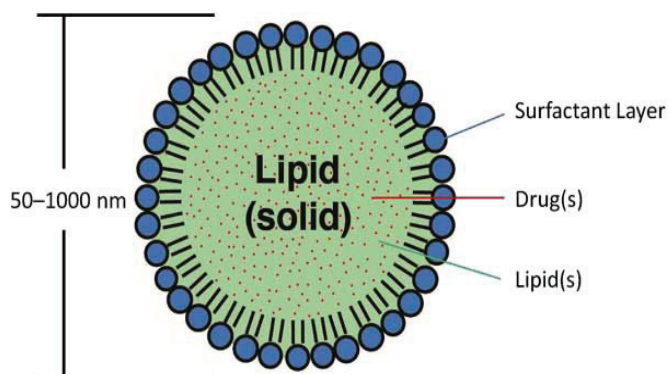


Fig 1. Solid lipid nanoparticle

1.1 SLN versus other colloidal carriers

SLN have been proven to be a better alternative carrier system than conventional o/w emulsion in the following aspects. If protection of drug against chemical degradation is required. Incorporation of drug in the solid lipid matrix surely offer a better protection than can be achieved in the oily internal phase of emulsion and liposome's. [4, 5] Prolonged release of drug from emulsion is not feasible which can be achieved to a certain extent from SLN. SLNs is found to be a better carrier than polymeric nanoparticles in the following aspects:

- Lower cytotoxicity due to the absence of solvents
- Low cost of excipients
- Large scale production is possible by the simple process of high-pressure homogenization

1.2 SLNs versus liposome

In comparison with liposome's SLNs offer better protection to drug against chemical degradation there is no or little access of water to the inner core of lipid particles Depending upon the nature of the drug higher payload might be achieved [13].

1.3 Advantages of SLN

- Particle size and surface characteristics of nanoparticles can be easily modified to achieve both passive and active drug targeting after parenteral administration.
- Controlled release of poorly water soluble active drug in the solid lipid matrix over a long period can be achieved.
- Incorporation of drug can reduce distinct side effects of drug, e.g. Thrombophlebitis that is associated with i.v. injection of diazepam.
- Very high long-term stability.
- Application versatility.
- Can be subjected to commercial sterilization procedures and lyophilization.
- Excellent biocompatibility and bioavailability.
- Improve stability of pharmaceuticals

1.4 Disadvantages

- Their small size and large surface area can lead to particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms.
- In addition, small particles size and large surface area readily result in limited drug loading and burst release.

2. PREPARATION OF SOLID LIPID NANOPARTICLES [11]

2.1 High pressure homogenization

It is a reliable and powerful technique, used for the preparation of SLNs. 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) which disrupts the particles down to the submicron range. Generally 5-10% lipid content is used but up to 40% lipid content has also been investigated. Two general approaches of HPH are hot homogenization (performed at elevated temperature) and cold homogenization (performed at or below room temperature), work on the same concept of mixing the drug in bulk of lipid melt.

2.1.1 Hot homogenization: Hot 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. The resultant product is hot o/w emulsion and the cooling of this emulsion leads to crystallization of the lipid and the formation of SLNs. In general, higher temperatures result in lower particle sizes due to the decreased viscosity of the inner phase. However, high temperatures increase the degradation rate of the drug and the carrier. Increasing the homogenization pressure or the number of cycles often results in an increase of the particle size due to high kinetic energy of the particles. Generally, three to five homogenization cycles at a pressure of 500-1000 bar are used [12, 14]

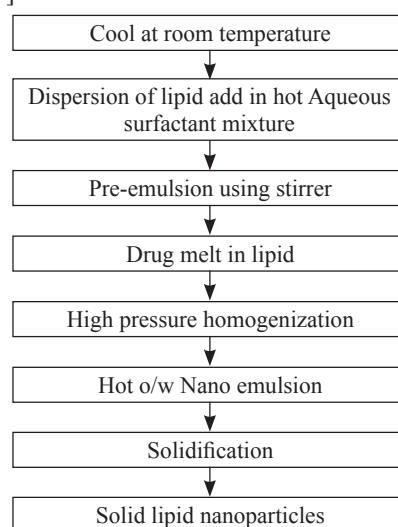


Fig. 2. Flow chart of manufacturing of sln by hot homogenization

2.1.2 Cold homogenization method: Cold homogenization has been developed to overcome various problems associated with hot homogenization such as temperature induced drug degradation, drug loss into the aqueous phase and partitioning associated with hot homogenization method. In cold homogenization, the drug containing lipid melt is cooled rapidly using dry ice or liquid nitrogen. The solid lipid is ground to lipid microparticles and these lipid microparticles are dispersed in a cold surfactant solution yielding a pre-suspension. Then this pre-suspension is homogenized at or below room temperature, the gravitation force is strong enough to break the lipid microparticles directly to solid lipid nanoparticles. The temperature should be regulated effectively to ensure the solid state of the lipid during

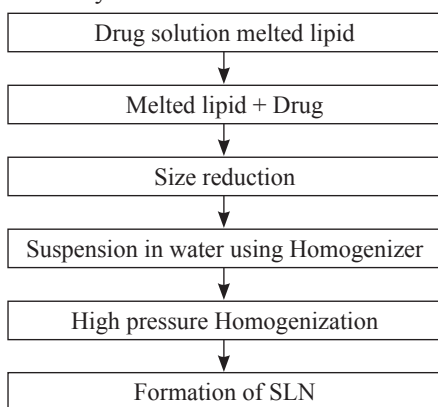


Fig. 3. Flow chart of manufacturing of SLN by cold homogenization

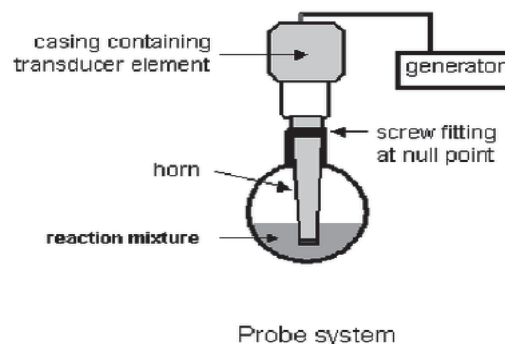
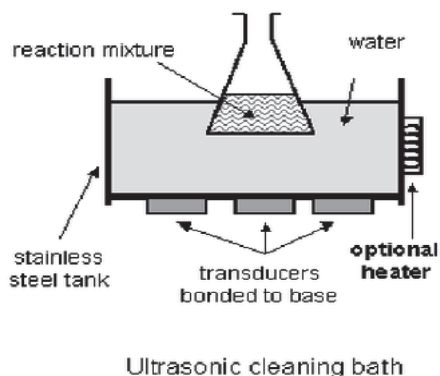


Fig. 4. Probe ultrasonicator and bath ultrasonicator

Advantages:

- (a) Reduced shear stress.

Disadvantages:

- (a) Potential metal contamination.
- (b) Physical instability like particle growth upon storage

2.3 Solvent Evaporation

SLN can also be prepared by solvent evaporation method. 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, nanoparticles dispersion is

homogenization. Larger particle size and a broader size distribution are typical characteristics of cold homogenization samples [11, 12]

Advantages Cold homogenization

- (a) Low capital cost.
- (b) Demonstrated at lab scale.

Disadvantages

- (a) Energy intensive process.
- (b) Demonstrated at lab scale Biomolecule damage.
- (c) Polydisperse distributions.
- (d) Unproven scalability.

2.2 Ultrasonication

SLN were also developed by ultrasonication or high speed homogenization. The equipment used for ultrasonication are commonly available at lab scale However, the major problem associated with 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. [7, 11, 12]

formed by precipitation of the lipid in the aqueous medium by giving the nanoparticles of 25 nm mean size. The solution was emulsified in an aqueous phase by high pressure homogenization. The organic solvent was removed from the emulsion by evaporation under reduced pressure (40–60 mbar) [5, 14].

Advantages

- (a) Scalable.
- (b) Mature technology.
- (c) Continuous process.
- (d) Commercially demonstrated.

Disadvantages

- (a) Extremely energy intensive process.
- (b) Polydisperse distributions.
- (c) Biomolecule damage

2.4 Solvent Emulsification Diffusion Method

Solvent emulsification diffusion method gives the particles with average diameters of 30-100 nm. The particle size depends upon lipid concentration in the organic phase and the emulsifier used. Heat is avoided during the preparation which is the most important advantage of this technique. Here, the lipid matrix is dissolved in water-immiscible organic solvent followed by emulsification in an aqueous phase. The solvent is evaporated under reduced pressure resulting in nanoparticles dispersion formed by precipitation of the lipid in aqueous medium [12, 14]

2.5 Micro Emulsion Based Method

This method is based on the dilution of micro emulsions which is a two phase system composed of an inner and outer phase (o/w micro emulsion) These are prepared by stirring an optically transparent mixture at 65-75°C, which is composed of low melting fatty acid (stearic acid), an emulsifier (polysorbate 20, polysorbate 60, soy phosphatidylcholine, and sodium taurodeoxycholate), co-emulsifiers (sodium monooleylphosphate) 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 macro emulsion. The SLNs dispersion can be used as granulating fluid for transferring into solid product like tablets and pellets by granulation process. To obtain low particles content too much of water need to be remove. The solvent which have the susceptibility to distribute with in aqueous phase (e.g. acetone) were more preferable for SLNs formulation. More lipid solvent produce larger particle size. Considering micro emulsions, the temperature gradient and pH value fix the product quality in addition to the composition of the micro emulsion. High temperature gradients facilitate rapid lipid crystallization and prevent aggregation [11, 15].

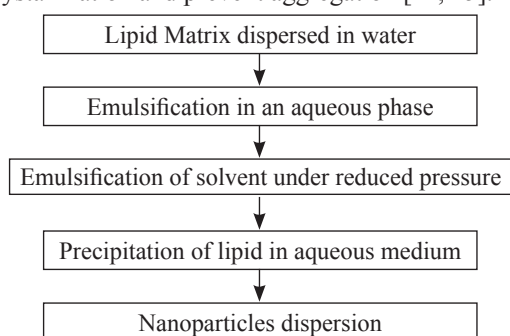


Fig. 5. Flow chart of manufacturing of SLN by microemulsion based

Advantages

- Low mechanical energy input.
- Theoretical stability.

Disadvantages

- Extremely sensitive to change.
- Labor intensive formulation work.
- Low nanoparticles concentrations

2.6 Supercritical fluid method

When the pressure and temperature of the liquid exceeds their respective critical value, the fluid is known as supercritical fluid, which increases the ability of fluid to dissolve the compounds. The rapid expansion of supercritical solution (RESS), particle gas saturated solutions (PGSS), aerosol solvent extraction solvent (ASES), supercritical fluid extraction of emulsions (SFEE) are the various technique used to formulate SLNs in this technique [16].

Advantages

- Avoid the use of solvents.
- Particles are obtained as a dry powder, instead of suspensions.
- Mild pressure and temperature conditions.
- Carbon dioxide solution is the good choice as a solvent for this method

2.7 Spray Drying Method

It's a cheaper and alternative technique to lyophilization method in order to transform an aqueous SLN dispersion into a drug product. It recommends the use of lipid with melting point more than 70 C. 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). This method causes particle aggregation due to high temperature, shear forces and partial melting of the particle [7, 11].

2.8 Double emulsion method

It is a novel method based on solvent emulsification evaporation method which is used for preparation of hydrophilic loaded SLNs. 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 [7, 12].

2.9 Precipitation technique

The glycosides are dissolved in organic solvent (eg: chloroform, dichloromethane) and the solution are further emulsified in aqueous phase. After evaporation of organic solvents the lipid would be precipitated out as a SLNs [16].

2.10 Film ultrasound dispersion

A lipid film is formed after decompression of organic solvents consisting of lipid and drug then the aqueous solution which includes the emulsion was added. By using the ultrasound with the probe to diffuser at last, the SLN with the little and uniform particle size is formed [14].

3. CHARACTERIZATION OF NANOPARTICLES

3.1 Transition electron microscopy and spectroscopy of nanoparticles

SEM and TEM provide a way to directly observe nanoparticles, physical characterization of nanoparticles TEM is a versatile tool which provide not only atomic resolution lattice image but also chemical information at spatial resolution of 1 nm or better, allowing direct identification of the chemistry of single nanocrystal. Although some structural features can be revealed by X-ray and neutron diffraction, direct imaging of nanoparticles is only possible using transmission electron microscopy [4, 17]

3.2 Differential scanning calorimetry (DSC)

The degree of crystallinity of the particle dispersion is performed by DSC and powder X-ray diffractometry (PXRD). The rate of crystallinity using DSC is estimated by comparison of the melting enthalpy/g of the bulk material with the melting enthalpy/g of the dispersion [12].

3.3 Zetapotential

It is an important product characteristic of SLN which measure charge on the surface of the particles. It is usually measured by zetameter It imparts colloidal stability due to particle particle repulsion. A zeta potential measurement also helps in designing particles with reduced reticuloendothelial system (RES) uptake. In order to divert SLNs away from the RES or lymphatic system, the surface of the particles should be hydrophilic and non- charged [12].

3.4 Nuclear magnetic resonance (NMR)

Particle size and nature of nanoparticles is determined by NMR. The selectivity afforded by chemical shift complements the sensitivity to molecular mobility to provide information on the physicochemical status of components within the nanoparticles [2,12].

3.5 Dynamic light scattering (DLS)

The variation in the intensity of scattered light on the microsecond time scale is recorded by DLS, also known as PCS or quasi-elastic light scattering (QELS). This variation results from interference of light scattered by individual particles under the influence of Brownian motion, and is quantified by compilation of an autocorrelation function. This function is fit to an exponential, or some combination or modification thereof, with the corresponding decay constant(s) being related to the diffusion coefficient(s). Using standard assumptions of spherical size, low concentration, and known viscosity of the suspending medium, particle size is calculated from this coefficient. The advantages of the method are the speed of analysis, lack of required calibration, and sensitivity to sub micrometer particles [17].

3.6 Atomic force microscopy (AFM)

A probe tip with atomic scale sharpness is rastered across a sample to produce a topological map based on forces at play between the tip and the surface [15].

3.7 *In-vitro* drug release studies

In-vitro drug release studies are advantages to quality control as well for evaluation of the influence of process parameters on the release rate of active compounds. Unfortunately, due to the very small particles size, the release rate observed *in vivo* can differ greatly from the release obtained in a buffer solution. Release profile of drug can be conducted in dialysis tubing or without tubing. Samples from dissolution medium are taken at discrete times, centrifuged, and assayed for drug content. The sink conditions must be maintained during release studies. The potential drawback of this method is that it is not 'sensitive' enough to characterize rapid release rate of drug from colloidal carrier. However, it can be assumed that if the drug is released over much more than one hour, then this method can be used for *in vitro* release profile investigation from colloidal carriers. The *in vitro* kinetic methods based on dilution and separation [3].

3.8 Rheology

Viscosity of formulation is detected by rheological measurement which is conducted in a Brookfield Viscometer, using an appropriate spindle number. The viscosity of formulation depends upon the dispersed lipid content. Generally flow of formulation is Newtonian but it becomes non-Newtonian when lipid content is high [3].

3.9 Storage stability

The physical stability of the SLNs is determined by monitoring changes in panicle size, drug content, appearance, and viscosity as a function of time. Since with the passage of time the PC components can be hydrolyzed to lyso-PCs, the chemical changes of SLNs also need to be monitored which is accomplished by thin -layer chromatography [3].

4. APPLICATIONS

4.1 SLN for Ocular Application

SLN for ocular drug administration has been reported many times. SLN gives ocular drug targeting due to bio-compatibility and mucoadhesive properties, which improve their interaction with ocular mucosa and prolong corneal residence time. As a result SLN significantly enhanced the drug bioavailability in the aqueous humor Cavalli et al., (2002) evaluated SLN as carriers for ocular delivery of to bramycin in rabbit eyes. 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 [12].

4.2 Topical applications

Tropolide, imidazole antifungals, anticancers, vitamin A, isotretinoin, ketoconazole, DNA, flurbiprofen and glucocorticoids are formulated in SLN for topical application. The penetration of podophyllotoxin-SLN into stratum corneum along with skin surface lead to the epidermal targeting [18]. Vitamin A-loaded nanoparticles can be prepared by using glyceryl behenate.

This method is useful for the improvement of penetration with sustained release. The soyabean lecithin and Tween 80 are used for the hot homogenization method for formulation of isotretinoin-loaded lipid nanoparticles for topical use. The methodology is useful because of the increase of accumulative uptake of isotretinoin in skin. Topical application of flurbiprofen-loaded SLN gel delivers the drug directly to the site of action, which will produce higher tissue concentrations. Polyacrylamide, glycerol and water were used for the preparation of SLN gel.

4.3 SLNs as gene vector carrier

SLN for biological macromolecules like DNA and peptides is considered as an efficient and non-toxic alternative lipophilic colloidal carriers. They are biodegradable and stable for prolonged period and can be scale up easily as compared to other colloidal system. SLN drug delivery to the liver cells are actively phagocytic. Their colloidal dimensions and the controlled release actions facilitate drug protection and administration by both parenteral and non-parenteral routes. The gene transfer was optimized by incorporation of a diametric HIV-1 HAT peptide (TAT 2) into SLN gene vector. The lipid nucleic acid nanoparticles were prepared from a liquid nano phase containing water and a water miscible organic solvent in which both lipid and DNA are separately dissolved by removing the organic solvent, which results in stable and uniform sized lipid-nucleic acid nanoparticles (70-100 nm). It's called genospheres. It is targeted specific by insertion of an antibody-lipo polymer conjugated in the particle. There are many recent reports of SLN carrying genetic/peptide materials such as DNA, plasmid DNA and other nucleic acid [13,19]

4.4 SLNs as cosmeceuticals

Many sunscreen formulations contains SLN as an active carrier agent for molecular sunscreens and UV blockers. The *in vivo* study reveals that hydration of skin is increased by 31% by addition of 4% SLN to a conventional cream after. SLN have proved to be controlled release innovative occlusive topical. Glycerin behenate SLNs gives better localization for vitamin A in upper layers of skin as compared to conventional formulations [13].

4.5 SLNs for potential agriculture application

Essential oil extracted from *Artemisia arborescens* L when incorporated in SLN, were able to reduce the rapid evaporation compared with emulsions and the systems have been used in agriculture as a suitable carrier of ecologically safe pesticide. The SLN were prepared here by using Compritol 888 ATO as lipid and poloxamer 188 or Miranol Ultra C32 as surfactant [15].

4.6 Pulmonary administration

SLN by pulmonary administration is one of the important application of SLN. The aerosolization of aqueous SLN dispersions is used for pulmonary administration because particle size of SLN powder is too small and may get exhaled. The major advantage is that SLN should not aggregate during

aerosolization. The aerosol droplets were collected by collision of aerosol with a glass wall of a beaker. This basically interprets that SLN are suitable for lung delivery. The drug can be released in a controlled way from the lipid particles after localization into the bronchial tube and in the alveoli [15].

4.7 Solid lipid nanoparticles in cancer chemotherapy

Several chemotherapeutic agents were formulated in SLN and their *in-vitro* and *in-vivo* efficacy have been evaluated which shows to improve the efficacy of chemotherapeutic drugs along with reduction in side effects, improved stability of drugs, encapsulation of chemotherapeutic agents of diversified physicochemical properties, improved pharmacokinetics and less *in-vitro* toxicity which make them a suitable carrier for delivering chemotherapeutic drugs. Several problems associated with anticancer compounds, such as normal tissue toxicity, poor specificity and stability and a high incidence of drug resistant tumor cells, are partially overcome by delivering them using SLN. The major obstacle to targeting tissues elsewhere in the body, such as bone marrow and solid tumors is the rapid removal of colloidal particles by the macrophages of the RES [11, 20].

4.7.1 SLN as targeted carrier for anticancer drug to solid tumor: SLN have been most commonly used as drug carriers for anticancer treatment. Tamoxifen is used in breast cancer, to prolong the release of drug after IV administration. Tumor targeting has been achieved with SLN loaded with drugs like methotrexate and camptothecin.

4.7.2 SLN in breast cancer and lymph node metastases: Mitoxantrone SLN local injections were formulated to reduce the toxicity and improve the safety and bioavailability of the drug.

4.8 Oral SLNs in antitubercular chemotherapy

Antitubercular drugs such as rifampicin, isoniazide, pyrazinamide-loaded SLN systems, were able to decrease the dosing frequency and improve patient compliance. Emulsion solvent diffusion technique is used to prepare antitubercular drug loaded solid lipid nanoparticles [7]. The nebulization in animal by incorporating the above drug in SLN also reported for improving the bioavailability of the drug.

4.9 Stealth nanoparticles

These provide a novel and unique drug-delivery system they evade quick clearance by the immune system. Stealth SLNs have been successfully tested in animal models with marker molecules and drugs which can target specific cells. Studies with antibody labelled stealth lipobodies have shown increased delivery to the target tissue in accessible sites [17].

4.10 SLNs for parental applications

SLNs can be administered intravenously, intramuscularly, subcutaneously or to the target organ, because of their small size. SLNs are very suitable in parental use due to its good drug storage capability after freeze drying and consisting physiologically well tolerable ingredients. It can easily circulate in micro vascular

system due to its size and prevent macrophage uptake (in case of hydrophilic coating). In viral and non-viral gene, genes delivery it is extensively used. In the treatment of cancer cationic SLNs have potential benefit in targeting cancerous cells. Treatment of central nervous system diseases such as brain tumors, AIDS, and neurological psychiatric disorders is often constrained by the inability of potent drugs to pass blood brain barrier (BBB). Hydrophilic coating of colloids improves the transport of these through BBB and tissue distribution (Kreuter 2001; Wang et al., 2002). Fundaro et al, 2000, prepared doxorubicin loaded stealth and non-stealth SLN and observed that the stealth nanoparticles were present in blood at higher concentrations than non-stealth SLN, after 24 h following intravenous administration. Camptothecin (CA)-loaded SLN were produced by HPH [16, 21].

5. CONCLUSION

Solid lipid nanoparticle drug delivery technology presents considerable opportunities for improving medical therapeutics, but the technology's potential remains unrealized. The review has focused on the variety of aspects of SLNs and their applicability in the encapsulation of various drugs. This review article covers different methods of preparation their advantages and evaluation, characterization parameters along with their applications in different fields. Because of the SLN potential for facilitating controlled drug delivery to a target tissue and its biocompatibility, there will be much investigation in improvement of quality, efficacy, and safety profile of drugs using them in the future.

REFERENCES

- [1] Mohanraj VJ, Chen Y. Nanoparticles-a review. Tropical journal of pharmaceutical research. 2006; 5(1): 561-73.
- [2] Reddy AP, Parthiban S, Vikneswari A, Senthilkumar GP. A modern review on solid lipid nanoparticles as novel controlled drug delivery system. Int. J. Res. Pharm. Nano Sci. 2014; 3: 313-25.
- [3] Shah Chandni V, Viral S, Umesh U. Solid Lipid Nanoparticles: A Review. Current Pharma Research 2011; 1(1): 351-68.
- [4] Maruthi G, Smith AA, Manavalan R. Nanoparticles--A Review. Journal of Advanced Scientific Research. 2011; 2(4) 52-67.
- [5] Patidar A, Thakur DS, Kumar P, Verma JH. A review on novel lipid based nanocarriers. International Journal of Pharmacy and Pharmaceutical Sciences. 2010; 2(4): 30-5.
- [6] Pandya J. Solid Lipid Nanoparticles: Overview on Excipients, Asian Journal of Pharmaceutical Technology & Innovation 2013; 01(03): 01-09
- [7] Pallerla SM, Prabhakar B. A review on solid lipid nanoparticles. Int. J. Pharm. Sci. Rev. Res. 2013; 20(2): 36.
- [8] Mullar RH, Runge SA. Solid lipid nanoparticles (SLN) for controlled drug delivery, Benita (Ed), Submicron emulsions in drug targeting and delivery, Amsterdam: harwod Academic Publishers: 1998, pp 219-34.
- [9] Jenning V, Schäfer-Korting M, Gohla S. Vitamin A-loaded solid lipid nanoparticles for topical use: drug release properties. Journal of controlled release. 2000; 66(2-3): 115-26.
- [10] Thasu D, Pathak Y, Deleers M. Nanoparticulate drug delivery system An overview; Drugs and the pharmaceutical Science, Volume-1 pp 166-168
- [11] Ekambaram P, Hasan A, Sathali A. Solid lipid nanoparticles: a review; sci. Revs. Chem. Commun. 2012; 2(1) 28-30.
- [12] Garud A, Singh D, Garud N. Solid lipid nanoparticles (SLN): Method, characterization and applications. International Current Pharmaceutical Journal 2012, 1(11): 384-393.
- [13] Sailaja AK, Amareshwar P, Chakravarty P. Formulation of solid nanoparticles and their application. Current Pharma Research 2011; 1(2): 197-203.
- [14] Kamble MS, Vaidya KK, Bhosale AV, Chaudhari PD. Solid lipid Nanoparticles and nanostructured Lipid Carriers- An Overview. International Journal of Pharmaceutical, Chemical and Biological Sciences. 2012; 2(4): 681-691
- [15] Yadav NE, Khatak SU, Sara UV. Solid lipid nanoparticles-a review. Int. J. Appl. Pharm. 2013; 5(2): 8-18.
- [16] Bhattacharya S. A review on solid lipid nano particles (slns, international journal of pharmaceutical research and bio-science 2014; 3(6): 445-465
- [17] Mukherjee S, Ray S, Thakur RS. Solid lipid nanoparticles: a modern formulation approach in drug delivery system. Indian journal of pharmaceutical sciences. 2009; 71(4): 349.
- [18] Hajare AA, Mali SS, Ahir AA, Thorat JD, Salunkhe SS, Nadaf SJ, Bhatia NM, Chitranagari K. Lipid nanoparticles: A modern formulation approach in topical drug delivery systems. J Adv Drug Deliv. 2014; 1: 30-7.
- [19] Dolatabadi JE, Valizadeh H, Hamishehkar H. Solid lipid nanoparticles as efficient drug and gene delivery systems: recent breakthroughs. Advanced pharmaceutical bulletin. 2015 ; 5(2): 151.
- [20] Mathur V, Satrawala Y, Rajput MS, Kumar P, Shrivastava P, Vishvkarma A. Solid lipid nanoparticles in cancer therapy. International Journal of Drug Delivery. 2010; 2(3) 44-48.
- [21] Kamboj S, Bala S, Nair AB. Solid lipid nanoparticles: an effective lipid based technology for poorly water soluble drugs. Int J Pharm Sci Rev Res. 2010; 5(2): 78-90.