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A GUIDE TO SOLID LIPID NANOPARTICLES

Komal Sanjay Mande*[1], Anuja Vilas Barve[2], Vijay R. Mahajan[3] and Amol S. Deshmukh[4]

Department of Pharmaceutics, S.M.B.T. College of Pharmacy, Dhamangaon, Tel- Igatpuri, Dist- Nasik, Maharashtra. India.

***Corresponding Author: Komal Sanjay Mande**

Department of Pharmaceutics, S.M.B.T. College of Pharmacy, Dhamangaon, Tel- Igatpuri, Dist- Nasik, Maharashtra. India.

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ABSTRACT

Solid lipid nanoparticle (SLN) are proposed as a replacement sort of colloidal drug carrier system. It consists of spherical solid lipid particles within the nanometer ranges, which are dispersed in water or in aqueous surfactant solution. Solid lipid nanoparticle technology represents a promising new approach to deliver hydrophilic also as lipophilic drugs. Thanks to their unique size dependent property, lipid nanoparticles offer to develop the new therapeutics. Scaling from the assembly process from lab scale to industrial scale are often easily achieved. This review focuses on the utility of solid lipid nanoparticles in terms of their advantages, production methodology, characterization and applications. Solid lipid nanoparticles hold a novel platform for reaching the goal of controlled and targeted drug delivery and subsequently pulled wide attention of researchers in the field of nanotechnology.

KEY WORDS: Solid lipid nanoparticles, Colloidal system, Drug release, Homogenization, Particle size.

INTRODUCTION

Nanoparticles are solid colloidal particles starting from 10 to 1000 nm in which the active pharmaceutical ingredient are dissolved or entrapped and or to which active medication is adsorbed or attached. The nanotechnology in pharmaceutical field could also be applied through the drug delivery systems like solid lipid nanoparticles, nanosuspensions, nanoemulsions, nano structured lipid carriers and nanocrystals. Solid lipid nanoparticles are colloidal carriers developed at the start of 1990s as an alternate novel carrier system to liposomes, emulsions and polymeric nanoparticles. Generally, they're made from solid hydrophobic core having a monolayer of phospholipid coating. Solid lipid nanoparticles are sub micron colloidal carrier 50-1000 nm size range. The solid core contains the drug dissolved or dispersed within the solid high melting fat matrix. The various sorts solid lipid nanoparticles are at the forefront of the quickly creating field of nanotechnology with few potential applications in drug delivery, clinical medicines and research. This one among the foremost popular approach to enhance the oral bioavailability of poorly water soluble drug.[1] In the following years SLN proved as a blockbuster in nanotechnology because many believed that SLN "offer a number of the benefits of polymeric nanoparticles, fat emulsions and liposomes along side the likelihood to successfully resolve problems associated with drug physical and chemical stability, drug delivery and absorption".[2]

STRUCTURE

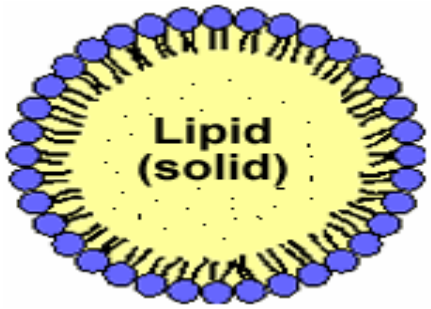

Fig 1: Structure of Solid Lipid Nanoparticles.

COMPOSITION

SLN are composed of lipids and of stabilizers – in most cases surfactants, co-surfactants and coating materials. Antioxidants, electrolytes, preservatives, viscosity enhancing agents, adhesives, absorption enhancers and other excipients also find application. Most of the formulation ingredients are safe and under the widely Recognized as Safe (GRAS) status issued by the Food and Drug Administration (FDA).[2]

Commonly used lipids in the preparation of SLN

- Triglycerides- Glyceryl tristearate, Glyceryl tripalmitate Glyceryl trimyristate.
- Monoglycerides- Glyceryl monostearate.
- Mixtures- Glyceryl behenate.
- Free fatty acids- Behenic acid, Stearic acid, Palmitic acid, Myristic acid, Oleic acid.
- Free fatty alcohols- Stearyl alcohol, Cetyl alcohol, Myristyl alcohol.

- Waxes- Beeswax, Carnauba wax.
- Others- Castor oil, Hydrogenated castor oil, Hydrogenated palm oil, Cacao butter.

Commonly used surfactants and co-surfactants in SLN formulations.

- Nonionic-
  - Poloxamers- Poloxamer 188, Poloxamer 407,
  - Polyoxyethylene alkyl/aryl ethers- Polyoxyethylene(20)cetyl ether.
  - Ethoxylated castor oils- PEG-35 castor oil, PEG-40 hydrogenated castor oil.
- Anionic- Sodium taurocholate, Sodium glycocholate, Sodium cholate, Sodium lauryl sulphate
- Cationic- Cetrimonium bromide, DOTAP, DOTMA
- Amphoteric- L-α –phosphatidyl- choline, Soya lecithin, Egg lecithin.

Co-surfactants- Propylene glycol, Low molecular weight PEG.[2]

ADVANTAGES

- Very high long-term stability.
- Better control over release kinetics of encapsulated compound.
- Staple which are to be required are same as that of emulsion.
- High concentration of functional compound are often achieved.
- Lyophilization possible.
- SLNs particularly ranging between 120 nm and 200 nm aren't haunted readily by the cells present within the res (reticulo endothelial system), thereby bypassing liver and spleen filtration.
- It's suitable for lipophillic also as hydrophilic compounds.
- Organic solvents are avoided.
- It's less toxic than some polymeric nanoparticles because used lipids are physiological and biocompatible.
- Low cost for solid lipid as compared to biodegradable polymers and phospholipids.
- Simple manufacture and proportion. It's easy to manufacture than bipolymeric nanoparticles
- The SLNs have enhanced stability as compared to the opposite colloidal carrier systems.
- Solid lipid nanoparticle is suitable for various routes of administration like oral, pulmonary, rectal, ophthalmic, dermal and parenterals administration, etc.
- Protection of medicine sensitive and responsible for photochemical, chemical or oxidative degradation.[1,3]

DISADVANTAGES

- Poor drug loading capacity.
- Drug expulsion after polymeric transition during storage.
- The low capacity to load hydrophilic drugs thanks to partitioning effects during the assembly process.
- Particle growth.
- Unpredictable gelation tendency.[1,3]

DRUG RELEASE

Depending upon the drug solubility and drug / lipid ratio, method of preparation, the drug is found within the core of the particles, within the shell or molecularly dispersed throughout the matrix. There are three drug incorporation models which describe the principle of drug release from SLN.

a) Homogenous Matrix Model.
b) Drug Enriched Shell, Core Shell Model.
c) Drug Enriched Core, Core Shell Model.

a) Homogenous Matrix Model – The most acquired solid solution model with drug being present in amorphous clusters or molecularly dispersed is especially obtained when incorporating highly lipophilic drugs into SLN utilizing hot homogenization technique or applying cold homogenization method or by avoiding potentially drug solubilizing surfactants. Within the cold homogenization technique the drug (in molecularly dispersed form) is dispersed in bulk of melted lipid, then the mechanical force of high homogenization results in the breakdown of molecules to form nanoparticles and offering homogenous matrix model.

b) A Drug Enriched Shell Model – This may be obtained when performing the assembly. During the assembly, the drug partitioned to water phase. Upon cooling, the lipid precipitates first, forming a practically drug free lipid core thanks to phase separation. At an equivalent time, the drug re-partitions into the remaining liquid-lipid phase and drug concentration within the outer shell increasing gradually. Finally drug enriched shell crystallizes. The quantity of drug partitioning to the aqueous phase will increases with the rise of solubility of drug within the aqueous phase. For the most part two factors, increasing temperature of the aqueous phase and increasing surfactant concentration focuses increasing the saturation solubility of drug in water phase.

c) A Drug Enriched Core Model – This model is obtained when dissolving a drug within the lipid melts at or on the brink of its saturation solubility. In this model, cooling of the formed nanoemulsion will cause supersaturation of drug in melted lipid and it further leads to drug precipitation before lipid precipitation. Further cooling will cause precipitation of lipid surrounding the drug enriched core as a membrane. Thanks to increased diffusional distance and hindering effect of surrounding solid lipid shell, the carrier system shows sustained release profile.[3]

Principles of Drug Release From SLN

Following are the principles of drug release from the SLN

- There is an inverse relationship between drug release and the partition coefficient of the drug.
- Higher area thanks to smaller particle size in nanometer range gives higher drug release.
- Slow drug release are often achieved when the drug is homogenously dispersed within the lipid matrix. It depends on type and drug entrapment model of SLN.
- Crystallinization behaviour of the lipid carrier and high mobility of the drug cause fast drug release. there's an inverse relationship between crystallization degree and mobility of drug.[4]

METHODS OF PREPARATION

1. High Pressure Homogenization

In this technique a liquid is pushed at high through a narrow gap. Both the high (in the range of 100-2000 bar) and therefore the small size of the gap (in the range of few microns) cause a really high acceleration and pressure drop. As a result a really high shear stress and cavitation forces disrupt particles/drops within the liquid. A rise within the temperature during the method (usually around 10 °C for each 500 bar) is additionally possible thanks to the high acceleration and friction. The tactic is straightforward accessible and scalable.

a) Hot Homogenization

b) Cold Homogenization

In the "hot" method the procedure is carried at temperatures above the melting temperature of the lipid. A pre-emulsion is made usually with the assistance of high shear mixers. This emulsion is skilled a narrow orifice – valve or nozzle. Usually several cycles are applied to realize submicron size with low polydispersity. The merchandise obtained after the homogenization may be a hot microemulsion. The latter should be cooled fast in order that the liquid lipid droplets can solidify and form the intrinsic structure of the SLN. The first stage of the cold homogenization approach is that the formation of a hot lipid melt mixture of the substances that form the lipid matrix and therefore the APIs. Then the melt is cooled right down to a solid state and grinded in powder mill to get particles within the size range of 50 - 100 micrometers. The obtained lipid powder is dispersed in solution of surfactant to make a pre-suspension. This pre-suspension is then skilled a homogenize. The cold approach is desirable in formulations with drugs that aren't stable at high temperatures or can distribute within the aqueous phase during the preparation.[2]

2. Solvent Injection

The method is analogous to the emulsification solvent diffusion method but the organic solvents used are selected from the group of the very miscible with water solvents (DMSO, ethanol) thus eliminating the prospect for emulsion to be formed. Firstly, the lipid(s) and API(s) are dissolved within the organic solvent. Then the organic solution is injected in solution of surfactant under stirring. This causes a rapid migration of the organic solvent within the water and precipitation of the lipids. The obtained particle size depends strongly on the speed of extraction respectively on the lipophilicity of the solvent. The more hydrophilic solvents gives the smaller particle size but the less its ability to dissolve lipids. The tactic offers advantages like low processing temperatures and low shear stress.[2]

3. Membrane Contactor

Within the production of SLN this system is modified and therefore the gaseous phase is replaced with a melted lipid blend. This blend is forced to undergo the membrane. Small droplets are formed spontaneously. On the opposite side of the membrane a hot surfactant solution is circulating and swapping away the droplets. The liquid lipid droplets are enveloped and stabilized by the surfactant molecules. After cooling down the dispersion the droplets transform into solid particles. The tactic is scalable and therefore the particle size are often tuned by using membranes with different pore size.[2]

4. Microemulsion Method

Microemulsion formation is employed as a stage within the production of SLN since the first 90s. During this method the microemulsion is spontaneously formed thanks to the high surfactants/lipid ratio. The proportions of the excipients are essential and in most cases pseudo ternary diagrams are wont to study and describe the areas of microemulsion formation. This method is straightforward and is performed by several common steps.[2]

Gasco and coworkers (1997) developed SLNs supported the dilution of microemulsions. These are made stirring an optically transparent mixture at 65-70°C which is usually composed of a coffee melting carboxylic acid like octadecanoic acid , an emulsifier (e.g, polysorbate 60, soyaphosphatydylcholine, Polysorbate 20 and taurodeoxycholic acid sodium salt), co-emulsifiers (e.g. Butanol, sodium monooctylphosphate) and water.[5] The recent microemulsion is dispersed in cold water (2-3°C) under stirring.[6] Typical volume ratios of the recent microemulsion to cold water are within the range of 1:25 to 1:50. The dilution process is fundamentally controlled by the composition of the microemulsion. The nanoparticles were created uniquely with solvents which disperse quickly into the aqueous phase (acetone), while larger molecule sizes were acquired with increasingly lipophilic solvents.[7]

5. Coacervation Method

A replacement solvent-free method (named coacervation) for the preparation of carboxylic acid SLN has recently been developed. This system allows, even thermo sensitive, drugs to be incorporated without using very complex equipment or dangerous solvents. It's therefore an inexpensive method for laboratory and industrial applications. "It is predicated on the slow

interaction that happens between a micellar solution of a carboxylic acid sodium salt and an acid solution (coacervating solution) within the presence of a correct amphiphilic polymeric stabilizing agent". Carboxylic acid nanoparticles are often precipitated by lowering the pH.[8]

6. Phase Inversion Temperature

The phase inversion temperature (PIT) method is typically employed for the preparation of nanoemulsions. Hell concept exploits the specific ability of some polyethoxylated surfactants to vary their affinities for water and oil as a function of temperature. "The utilization of such a surfactant type prompts in an emulsion inversion from an O/W macroemulsion to a W/O emulsion when the temperature is increased above the PIT". An O/W nanoemulsion is then formed when the temperature decreases below Hell. It's recently been adapted for SLN preparation, too. The aqueous phase, containing NaCl, and therefore the oil phase, made from solid lipids and nonionic surfactants, are separately heated at ~90°C (above the PIT). "The aqueous phase is then added dropwise, at constant temperature and under agitation, to the oil phase, so as to get a W/O emulsion. The mixture is then cooled to temperature under slow and continuous stirring. The turbid mixture becomes clear at Hell, and, below Hell, an O/W nanoemulsion is made, which turns into SLN below the lipid melting point".[8]

7. Spray Drying and Nano Spray Drying Technology

The nano spray-drying technology (NSD) has been recently employed for transforming preformed SLN into dry powders with the support of suitable excipients, giving rise to dry SLN embedding MP. Compared to standard spray-drying equipment, nano spray dryers produce much smaller droplets, with high yields, at much lower atomization temperatures that allow manufacturing of dry micro- and nanoparticulates. Albeit not yet scaled, this system is extremely promising for processing heat-sensitive materials and polymorphic substances producing fine respirable powders.[9]

It is an alternate tool to lyophilization so as to rework an aqueous SLN dispersion into a drug product. This is often an economic method than lyophilization and recommends the utilization of lipid with freezing point >70°C. This method causes particle agglomeration thanks to heat, shear forces and partial melting of the particle. The conversion of the liquid dispersion into a dry product is beneficial, or often necessary. SLN granulates or powders might be put into capsules, pressed into tablets or incorporated into pellets. Nevertheless, a protracted long-term stability especially for i.v. Administered systems are often achieved when stored as a dry product. This might be of interest for SLN containing drugs that are vulnerable to hydrolysis or are exposed to elevated temperatures or light in aqueous dispersion.[10]

8. Microwave Assistance

Microwaves can assist in forming the microemulsion template used for nanoparticle preparation and within the direct production of nanoparticles. During this second case, employing a microwave reactor is straightforward, quick, cheap, and sustainable. This technology facilitates the one-pot production of the particles, in one or two steps and during a closed system. Furthermore, it doesn't use organic solvents or large volumes of water.[11]

9. Spray-Congealing

In the spray-congealing method, lipids are heated to a temperature above their freezing point. Hot lipids are atomized through a pneumatic nozzle into a vessel, which is held during a CO_2 ice bath. The microparticles that are obtained (50-500μm) are then dried under vacuum at temperature.[12]

10. Solvent Emulsification - Diffusion Technique

Another strategy which is proposed for production of solid lipid nanoparticles is solvent emulsification-diffusion method. During this technique, the solvent used like e.g. Benzyl alcohol, butyl lactate, ester, isopropyl acetate, methyl acetate must be partially miscible with water. This system are often administered either in aqueous phase or in oil phase. Initially, both the solvent and water were mutually saturated so as to determine the initial thermodynamic equilibrium of both liquid. When heating is required to solubilize the lipid, saturation step was performed at that temperature. Then the lipid and drug were disintegrated in water saturated solvent and this organic phase which is internal phase was emulsified with solvent saturated solution containing stabilizer i.e. Dispersed particles using mechanical stirrer. After the formation of o/w emulsion, water may be a dilution medium in typical ratio ranges from 1:5 to 1:10, added to the system so as to permit solvent diffusion into the continual phase, and forming aggregation of the lipid within the nanoparticles. Avoidance of warmth during the preparation is that the most vital advantage of this system.[13]

11. Solvent Emulsification or Evaporation

In this method, the assembly of nanoparticle dispersions by precipitation in o/w emulsions. The lipophilic material and hydrophobic drug is dissolved in water-immiscible organic solvents like e.g. cyclohexane, dichloromethane, toluene, chloroform etc. then that's emulsified in an aqueous phase using high speed homogenizer. Upon evaporation of the solvent, nanoparticle dispersion is made by lipid precipitation within the aqueous medium. Thereafter, the organic solvent was evaporated by mechanical stirring at temperature and decreased pressure (e.g. rotary evaporator) leaving lipid precipitates. Very small particle size might be obtained with low lipid content (5%) associated with organic solvent.[13]

12. Melting Dispersion Technique

In this technique drug and solid lipid were melted in an organic solvent which is termed as oil phase and simultaneously water phase was also heated to same temperature as oil phase. Then the oil phase is added slowly in to a little volume of water phase with stirring at higher rpm for few hrs. Then, it had been cooled right down to temperature to supply SLNs. Reproducibility was quite ultrasonication method but lesser than that of solvent emulsification evaporation method.[13]

13. Electro-Spray Technique

In this relatively new technique an electrodynamic atomization is employed to supply SLN directly in powder form. The obtained particles by this strategy have restricted distribution and size underneath one micrometre. However the tactic remains under investigation for its applicability within the production of larger quantities of dispersions. (14)

14. Ultrasonication

Ultrasonication is another strategy for the creation of SLNs. The advantage of this method is that the equipment used is usually available at lab scale. However, this method suffers from problems like broader size distribution ranging into micrometer range. Potential metal contaminations, physical instability like particle growth upon storage are other drawbacks related to this system.[15]

15. Supercritical Fluid (SCF) Technique

This is a completely unique technique recently applied for the assembly of SLNs. This technology comprises of several processes for nanoparticle production like rapid expansion of supercritical solution (RESS), particles from gas saturated solution (PGSS), aerosol solvent extraction solvent (ASES), supercritical fluid extraction of emulsions (SFEE). The benefits of this system includes avoidance of the utilization of solvents, particles obtained as a dry powder, rather than suspensions, requires mild pressure and temperature conditions. CO_2 solution is that the good selection as a solvent for this method.[15]

16. Double Emulsion Method

The double emulsion (w/o/w) method is predicated on solvent emulsification–evaporation method. This method is especially for the assembly of lipid nanoparticles loaded with hydrophilic drugs. During this case, the drug and stabilizer are encapsulated within the inner aqueous phase of the w/o/w double emulsion. A stabilizer is important to stop drug partitioning to the outer aqueous phase during solvent evaporation. This sort of formulations is typically named as 'lipospheres' thanks to their comparatively larger particle size than SLNs.[16]

STERILIZATION OF SLN

SLN dispersions also can be sterilized by filtration almost like emulsions for parenteral nutrition. It's highly important to filter them within the liquid state, this enables even particles with a size larger than the pores within the filter to be filtered. This technology is documented from parenteral emulsions and straightforward to use to SLN. Alternatively, the SLN are often produced aseptically, again just like parenteral emulsions. To sum up, SLN dispersions are often sterilized or prepared aseptically using already established techniques within the pharmaceutical industry.[17]

CHARACTERIZATION OF SLN

Estimation of Incorporated Drug

Entrapment Efficiency: The entrapment efficiency of the drug is decided by measuring the concentration of free drug within the dispersing phase by HPLC or UV spectrophotometer. This separation are often administered using the techniques like ultracentrifugation, centrifugation filtration and gel permeation chromatography. In Centrifugation Filtration, filters like ultra free – mc or ultra sort – 10 are used along side classical centrifugation techniques. Ultracentrifugation was administered using Centrisart, which contains filter membrane (molecular weight cutoff 20,000 Da) at the bottom of the sample recovery chamber.[18]

% Entrapment efficiency =
[(Initial drug weight–weight of free drug) /Weight of initial drug] × 100%

Measurement of Particle Size: The physical stability of SLNs depends on their size. The particle size determination by photon correlation spectroscopy (PCS) detects size range of three nm to three µm and by laser diffraction in size range of 100 nm to 180 µm. Although PCS may be a good tool to characterize nano-particles, but is capable for the detection of larger microparticles. PCS (also referred to as dynamic light scattering) measures the fluctuation of the intensity of the scattered light which is caused by particle movement.[18]

Zeta Potential: Stability of the nanodispersion during storage are often predicted form the ZP value. Zeta potential analyzer or zetameter is employed to live the zeta potential. Before measurement, SLN dispersions are diluted 50 times with the first dispersion preparation medium for size determination and zeta potential measurement. A high value of zeta potential may prompt deaggregation of particles within the absence of other complicating factors example hydrophilic surface appendages or steric stabilizers. ZP measurements allow predictions about the storage stability of colloidal dispersion.[18]

Nuclear Magnetic Resonance (NMR): NMR are often wont to determine both the dimensions, their topology, dynamics and therefore the qualitative nature of nanoparticles. The selectivity managed by chemical shift components the affectability to sub-atomic versatility to

give data on the physicochemical status of segments within the nanoparticle.[19]

Static Light Scattering (SLS)/ Fraunhofer Diffraction: This method studies the pattern of sunshine scattered from an answer of particles is collected and fit fundamental electromagnetic equations during which size is that the primary variable. It's fast and rugged method, but requires more cleanliness than DLS, and advance knowledge of the particles optical qualities.[15]

Electron Microscopy: Microscopy methods like Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are wont to measure the general shape and morphology of lipid nanoparticles. It permits the determination of particle size and distributions. SEM uses electrons transmitted from the surface of the sample while TEM uses electrons transmitted through the sample[20]. Transmission Electron Microscopy (TEM) and Scanning electron Microscopy (SEM) provide thanks to directly observe nanoparticles. However, SEM is best for morphological examination. TEM features a small size limit of detection.[21]

Atomic Force Microscopy (AFM): AFM measures the force which is acting between surface of the sample and therefore the tip of the probe, when the probe is kept in close proximity to the sample which ends up during a spatial resolution of up to 0.01 nm for imaging.[22] In this technique ultra-high resolution is obtainable with this approach, which along side the power to map a sample consistent with properties additionally to size, e.g., colloidal attraction or resistance to deformation, makes AFM a valuable tool.[23]

In Vitro Methods For The Assessment of Drug Release From SLN

1. **Dialysis Tubing**: In vitro drug release might be achieved using dialysis tubing. The SLNs dispersions are placed during a prewashed dialysis tubing which may be hermetically sealed. The dialysis tube is then analyzed against an appropriate dissolution medium at room temperature; the samples are withdrawn from the medium at regular intervals, centrifuged and analyzed for drug content utilizing an appropriate technique such as U.V. spectroscopy, HPLC etc. The upkeep of sink condition is important.[24]
2. **Reverse Dialysis**: In this system, variety of Small dialysis sac containing 1 ml of dissolution medium are placed in SLN dispersion. The SLNs are then placed into the dissolution medium. The direct dilution of the SLNs is feasible with this method; however the rapid release can't be quantified using this method.[24]
3. **Franz Diffusion Cell**: The SLNs dispersion is placed within the donor chamber of a Franz diffusion cell fitted with a cellophane membrane. The sample dispersion is then analyzed against an appropriate dissolution medium at room temperature; the samples are withdrawn from the dissolution medium at suitable intervals and analyzed for drug content employing a suitable method (U.V. spectroscopy, HPLC etc.). The upkeep of sink condition is important.[13]

Measurement of Crystallinity And Lipid Modifications

DSC and powder X-ray diffractometry (PXRD) is performed for the assurance of the degree of crystallinity of the particle dispersion. The speed of crystallinity using DSC is estimated by comparison of the melting enthalpy/g of the majority material with the melting enthalpy/g of the dispersion.[25]

APPLICATIONS

1. SLNs for Topical Use

SLNs mean an choice to facilitate dermal penetration. Additionally nano size range provides a high specific area for drug absorption through the skin thereby providing greater efficacy as a delivery system.[26] They are also ready to attach themselves on to the skin surface, promoting adhesiveness and increasing hydration, even realizing lipid exchange between the lipid-based carriers and therefore the outermost layers of skin. Several researchers are administered for safe and effective transdermal delivery of skin though solid lipid nanoparticles.[27]

SLNs used for topical application for various drug like podophyllotoxin[28], vitamin-A[29], flurbiprofen.[30]

2. SLNs in Anti Tubercular Chemotherapy

Anti tubercular drugs like rifampicin, isonizide, pyrazinamide-loaded SLN systems, were ready to decrease the dosing frequency and improve patient compliance. By using the emulsion solvent diffusion technique this antitubercular drug loaded solid lipid nanoparticles are prepared.[31]

3. SLNs as Cosmeceuticals

The SLNs are applied within the preparation of sunscreens and as a lively carrier agent for molecular sunscreens and UV blockers. SLN and NLCs have proved to be controlled delivery for innovative occlusive topical formulations. Better localization has been achieved for vitamin A in upper layers of skin with glyceryl behenate SLNs compared to standard formulations.[32]

4. SLNs as Gene Vector Carrier

SLN are often utilized in the gene vector formulation. There are several recent reports of SLN carrying genetic/peptide materials like DNA, plasmid DNA and other nucleic acids.[33]

5. SLNs In Carcinoma And Lymph Node Metastases

Efficacy of doxorubicin (Dox) has been reported to be increased by incorporation in SLNs. Mitoxantrone-loaded SLN local injections were formulated to scale back the toxicity and improve the security and bioavailability of dru.[34]

6. SLNs as a Targeted Carrier for Anticancer Drug to Solid Tumors

Tamoxifen an anticancer drug is incorporated in SLN to prolong release of drug after i.v. SLNs are reported to be useful as drug carriers to treat neoplasm's.[35] Tumour targeting has been achieved with SLNs loaded with drugs like methotrexate[36] and Camptothecin.[37]

7. Stealth Nanoparticles

These provide a completely unique and unique drug-delivery system they evade quick clearance by the system. Such nanoparticles can target specific cells. Stealth SLNs are successfully tested in animal models with marker molecules and medicines. Antibody labelled stealth Lipobodies have shown increased delivery to the target tissue in accessible sites.[38]

8. SLNs for Potential Agriculture Application

Essential oil extracted from Artemisia arboreseens L when fused in SLN, were ready to decrease the rapid evaporation compared with emulsions and therefore the frameworks are utilized in the agriculture as an appropriate carrier of ecologically safe pesticides.[39]

9. Ophthalmic Administration

It had been shown by Gasco that SLN have a protracted retention time at the attention. This was affirmed by utilizing radiolabiled formulations and γ-scintigraphy. The lipids of SLN are easy to metabolize and open a replacement ways for ophthalmological drug delivery without impairing vision.[40] Ocular drug administration via SLN has been reported several times.[41] Biocompatibility and mucoadhesive properties of SLN improve their interaction with ocular mucosa and prolong corneal duration of the drug, with the aim of ocular drug targeting. Cavalli et al in 2002 evaluated SLN as carriers for ocular delivery of tobramycin in rabbit eyes. As a result SLN significantly enhanced the drug bioavailability within the aqueous humour.[42] Cavalli et al in 1995 also studied pilocarpine delivery via SLN, which is usually utilized in glaucoma treatment, earlier.They reported very similar leads to order to reinforce the ocular bioavailability of drug.[43]

10. Pulmonary Administration

The lungs offer a high area for drug absorption by avoiding first-pass effects. Rapid drug absorption by aerosolization of medicine (in the 1-3 μm size range) occurs since the walls of alveoli within the deep lung are extremely thin.[44,45] SLN are often proposed as carriers of anticancer drugs in carcinoma treatment or peptide drugs to enhance their bioavailability. Assessment of inhaled radio-labeled SLN bio distribution has been described and therefore the data showed a crucial and significant uptake of the radio-labeled SLN into the lymphatic after inhalation.[46] During a recent study, antitubercular drugs (rifampicin, isoniazid and pyrazinamide) were incorporated into various formulations of solid lipid particles ranged from 1.1–2.1 μm and formulations were nebulized to guinea pigs orally for direct pulmonary delivery.[31,47]

11. SLN for Parenteral Application

Wissing et al. reviewed that parenteral use of SLN is sort of safe and well tolerated as they contains physiologically well-tolerated ingredients and that they have good storage capabilities after lyophilization or sterilization. When injected intravenously, SLN are very small to circulate within the microvascular system. Therefore, SLN are suggested for viral and non-viral gene delivery. Cationic SLN have potential benefits in targeted gene therapy in treatment of cancer. Treatment of central systemic nervous diseases like brain tumors, AIDS, neurological and psychiatric disorders is feasible via SLNs as hydrophilic coating of colloids improves the transport of those through BBB and tissue distribution.[48]

12. SLN for Nasal Application

SLN were proposed as alternative transmucosal delivery systems by various research groups. The role of PEG coating of polylactic acid nanoparticles in improving the transmucosal transport of the encapsulated bioactive molecule reported to achieve success by Tobio et al, 1998.[49]

13. SLN for Rectal Application

Sznitowska et al. incorporated diazepam into SLN for rectal administration so as to supply a rapid action. They applied SLN dispersions on rabbits and performed bioavailability studies. They found that lipid matrix which is solid at blood heat isn't an advantageous system for diazepam rectal delivery. They decided to use lipids which melt around blood heat in their next experiments.[50,51] PEG coating seems to be a promising methodology on rectal conveyance and consequently, enhancement of bioavailability.

14. SLN as potential new adjuvant for vaccines

Adjuvants are utilized in vaccination to reinforce the immune reaction. The safer new subunit vaccines are required.[52]

15. SLN for delivery of peptides and proteins

Proteins and antigens are proposed for therapeutic resolutions could also be incorporated or adsorbed onto SLN. Formulations in SLN convers improved protein stability, avoids proteolytic degradation, also as sustained release of the incorporated molecules. Important peptides for example insulin, cyclosporine A, calcitonin and somatostatin are have been incorporated into solid lipid nanoparticles and are presently under investigation.[53]

CONCLUSION

SLN as colloidal drug carrier combines the advantage of polymeric nanoparticles, liposome; like improved physical stability, feasibility of incorporation of lipophilic and hydrophilic drugs, economic, simple scale-up, and manufacturing. SLNs are used extensively for applications in drug discovery, drug delivery, and diagnostics and for several others in medical field. SLNs may open new vistas in treatment of complex illness.

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