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# SOLID LIPID NANOPARTICLES: AN EFFECTIVE AND PROMISING DRUG DELIVERY SYSTEM- A REVIEW

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**ABSTRACT:** Solid lipid nanoparticles (SLN) have been reported to be an alternative system to emulsions, liposomes, microparticles and their polymeric counterparts for various application routes since the early 1990s due to their advantages. Solid lipid nanoparticles colloidal drug carrier system gained a lot of popularity among researcher as colloidal drug carriers for incorporating hydrophilic or lipophilic drugs. Solid lipid nanoparticles are the rapidly developing field of nanotechnology with several potential applications in drug delivery, clinical medicine and research, as well as in other varied sciences. Due to their unique size-dependent properties, lipid nanoparticles offer the possibility to develop new therapeutics. The present review focuses on the utility of SLN in terms of their introduction, advantages, disadvantages, general ingredients used, production methodology, characterization and current applications.

**INTRODUCTION:** Solid lipid nanoparticles (SLN) are colloidal carriers developed at the beginning of the 1990s. Generally, they are made of solid hydrophobic core having a monolayer of phospholipids coating. 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 [1]. Nanoparticles are colloidal particles ranging from 10 to 1000 nm, in which the active principles (drug or biologically active material) are dissolved, entrapped, and/or to which the active principle is adsorbed or attached [2].

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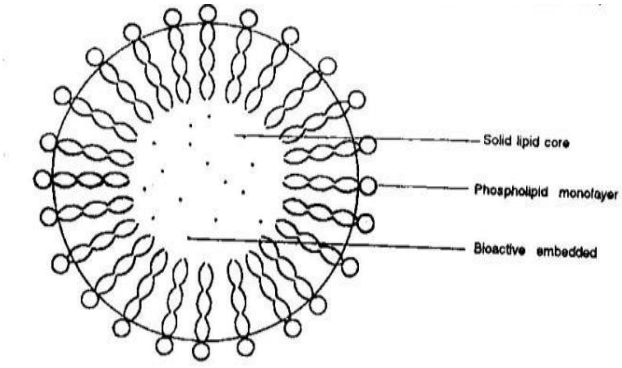


**FIG. 1: PROPOSED STRUCTURE OF SLN.**

The solid lipid nanoparticles are sub-micron colloidal carriers (50-100 nm) which are composed of physiological lipid, dispersed in water or in aqueous surfactant solution. SLNs as colloidal drug carrier combine the advantage of polymeric nanoparticles fat emulsions and liposomes [3]. The development of drug delivery carriers is often very challenging, due to the physico-chemical properties of the drug: poor solubility, low permeability, short

half-life, and high molecular weight is the commonest challenges for those involved in formulation. The importance of carriers is well known, not only to academics but also to managers of the pharmaceutical industry [4].

**Advantages of SLNs:**

1. Small size and relatively narrow size distribution which provide biological opportunities for site-specific drug delivery by SLNs.
2. Incorporation of drug can reduce distinct side effects of drug, e.g. Thrombophlebitis that is associated with i.v. injection of diazepam or etomidate.
3. Ease of industrial scale production by hot dispersion technique.
4. Surface modification can easily be accomplished and hence can be used for site-specific drug delivery system
5. Controlled release of active drug over a long period can be achieved.
6. Protection of incorporated drug against chemical degradation.
7. Possible sterilization by autoclaving or gamma irradiation.
8. SLNs can be lyophilized as well as spray dried.
9. No toxic metabolites are produced.
10. Avoidance of organic solvents, relatively cheaper and stable [5].
11. Better control over release kinetics of encapsulated compounds.
12. Enhanced bioavailability of entrapped bioactive compounds.
13. Chemical protection of labile incorporated compounds.
14. Much easier to manufacture than biopolymeric nanoparticles.
15. Conventional emulsion manufacturing methods applicable.
16. Excellent biocompatibility, Improve stability of pharmaceuticals.
17. High and enhanced drug content, No special solvent required.
18. Application versatility [1].
19. Reduce the number of doses required [5].

**Disadvantages of SLN:**

1. Limited drug loading capacity due to crystalline structure of solid lipid.
2. Adjustment of drug release profile.
3. Drug expulsion during storage due to the formation of a perfect crystal.
4. Particle growing, Unpredictable gelation tendency.
5. Unexpected dynamics of polymorphic transitions.
6. High water content of SLN dispersions [6].

**General ingredients of SLN's:** Lipids and emulsifiers are generally used for preparation of solid lipid nanoparticles. The matrixes of SLN are the natural or the synthetic lipids which can be degraded, including triglyceride (Tricaprin, Trilaurin, Trimyristin, Tripalmitin, Tristearin), Hydrogenated coco-glycerides (SoftisanÒ 142), Hard fat types (WitepsolÒ W 35, WitepsolÒ H 35, WitepsolÒ H 42, WitepsolÒ E 85), Glyceryl monostearate (ImwitorÒ 900), Glyceryl behenate (CompritolÒ 888 ATO). Glyceryl palmitostearate (PrecirolÒ ATO 5), Cetyl palmitate, Fatty acids (e.g., Stearic acid, Palmitic acid, Decanoic acid, Behenic acid), steroid (e.g., cholesterin) waxes (e.g., microcrystal paraffin wax, whale ester wax, cetyl palmitate).

Emulsifiers include the phospholipids [Soybean lecithin (LipoidÒ S 75, LipoidÒ S 100), Egg lecithin (LipoidÒ E 80)], Phosphatidylcholine (lecithin, EpikuronÒ 170, Epikuron 200), Pluronics F 68, 127, Nonionic wetting agent (e.g., poloxamer 188, 182, 407, 908), cholate (e.g., sodium cholate, sodium glycocholate, sodium taurocholate, deoxy-sodium taurocholate) short-chain spirits (e.g., butanol, butanoic acid), Polysorbate 20, Polysorbate 60, Polysorbate 80,

Dioctyl sodium sulfosuccinate, Mono-octylphosphoric acid sodium. Amphipathic materials (e.g., ionic and nonionic type) can stabilize the dispersion of SLN, on the surface of SLN, hydrophobic parts stretch to the core, hydrophilic parts stretch to the disperse medium, so drug with low water-solubility can be entrapped in the SLN to form the colloidal drug system [5, 7].

**Preparation of Nanoparticles:**

1. High pressure homogenization
   A. Hot homogenization
   B. Cold homogenization
2. Ultrasonication/high speed homogenization
   A. Probe ultrasonication
   B. Bath ultrasonication
3. Solvent evaporation method
4. Solvent emulsification-diffusion method
5. Supercritical fluid method
6. Microemulsion based method
7. Spray drying method
8. Double emulsion method
9. Precipitation technique
10. Film-ultrasound dispersion

1. **High pressure homogenization (HPH):** It is a reliable and powerful technique, which is used for the production 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). Very high shear stress and gravitation forces disrupt 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 and cold homogenization: work on the same concept of mixing the drug in bulk of lipid melts (given in **table 1**) [8].

**TABLE 1: SCHEMATIC REPRESENTATION FOR THE PRODUCTION OF SOLID LIPID NANOPARTICLES BY THE HOT AND COLD HOMOGENIZATION TECHNIQUES**

| Steps used | Hot Homogenization Technique | Cold Homogenization Technique |
|---|---|---|
| **Step 1.** | Melt lipid; dissolve or solubilize active ingredients in the lipid. | |
| **Step 2.** | Disperse melted lipid in hot aqueous surfactant solution. | Cooling and recrystallization of the active lipid mixture using liquid nitrogen or dry ice. |
| **Step 3.** | Preparation of a pre-emulsion by means of a rotor-stator homogenizer. | Milling of the active lipid mixture by means of a ball mill or a jet mill. |
| **Step 4.** | High-pressure homogenization above the melting point of the lipid. | Disperse lipid microparticles in cold aqueous surfactant solution. |
| **Step 5.** | Cooling and recrystallization. | High-pressure homogenization at or below room temperature. |

2. **Ultrasonication or high speed homogenization:** Drug and Phospholipid are dissolved in methanol and mixed with an acetone solution containing a blend of fatty acids. The mixture is then added dropwise to Pluronic solution at 70°C. A pre-emulsion is obtained by homogenization using an Ultra-Turrax T25 (IKA-werke GmBH, Germany), at 15000 rpm for 10 minutes at 70°C. This pre-emulsion is ultrasonicated (20w) for 15 minutes to prevent the crystallization of lipids. The o/w emulsion obtained is subsequently cooled down to room temperature with continuous stirring, and the lipid is recrystallized to form SLN.

3. **SLN prepared by solvent emulsification /evaporation:** The lipophilic materials are dissolved in a water-immiscible organic solvent (e. g., cyclohexane, toluene, chloroform, and dichloromethane) that is emulsified in an aqueous phase.

   Upon evaporation of the solvent, nanoparticle dispersion is formed by precipitation of the lipid in the aqueous medium. This solution was emulsified in an aqueous phase by HPH. The organic solvent was removed from the emulsion by evaporation under reduced pressure (40-60mbar) [1].

4. **Solvent emulsification-diffusion method:** The particles with average diameters of 30-100 nm can be obtained by this technique. Voidance of heat during the preparation is the most important advantage of this technique (given in **fig. 2**) [8].

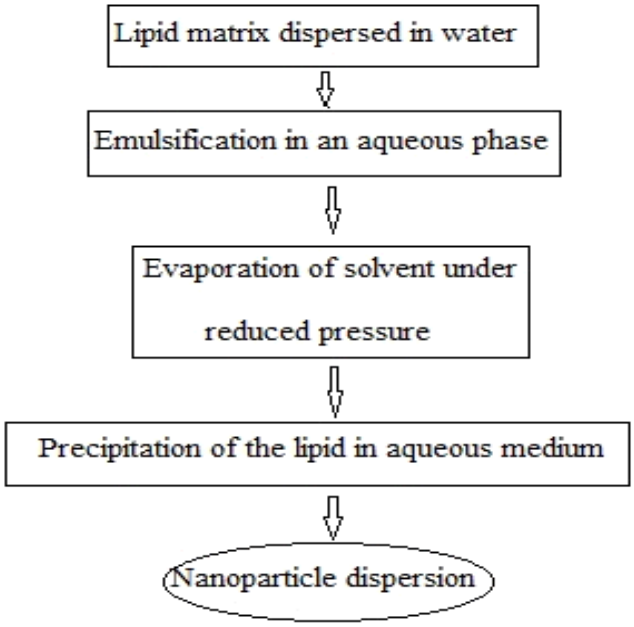


**FIG. 2: SYSTEMATIC REPRESENTATION FOR SOLVENT EMULSIFICATION-DIFFUSION METHOD**

5. **SLN preparation by using supercritical fluid:** This is a relatively new technique for SLN production and has the advantage of solvent-less processing. There are several variations in this platform technology for powder and nanoparticle preparation. SLN can be prepared by the rapid expansion of supercritical carbon dioxide solutions (RESS) method.

6. **SLN produced by microemulsion technique:** Microemulsions are two-phase systems composed of an inner and outer phase (e.g. o/w microemulsions). They are made by stirring an optically transparent mixture at 65-78$^{o}$c which is typically composed of a low melting fatty acid (e.g. stearic acid), an emulsifier (e.g. polysorbate 20, polysorbate 60, soy phosphotidylcholine, and taurodeoxycholic acid sodium salt), co-emulsifiers (e.g. butanol, sodium monooctylphosphate) and water. The hot microemulsion is dispersed in cold water (2-38$^{o}$c) under stirring. Typical volume ratios of the hot microemulsion to cold water are in the range of 1:25 to 1:50 [9].

7. **Spray drying method:** It's an alternative procedure to lyophilization in order to transform an aqueous SLN dispersion into a drug product. It's a cheaper method than lyophilization. This method cause particle aggregation due to high temperature, shear forces and partial melting of the particle.

8. **Double emulsion method:** For the preparation of hydrophilic loaded SLN, a novel method based on solvent emulsification-evaporation has been used. Here 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 [10].

9. **Precipitation method:** Solid lipid nano-particles can also be produced by a precipitation method which is characterized by the need for solvents. The glycerides will be dissolved in an organic solvent (e.g. chloroform) and the solution will be emulsified in an aqueous phase. After evaporation of the organic solvent the lipid will be precipitated forming nanoparticles [11].

10. **Film-ultrasound dispersion:** The lipid and the drug were put into suitable organic solutions, after decompression, rotation and evaporation of the organic solutions, a lipid film is formed, then the aqueous solution which includes the emulsions was added. Using the ultrasound with the probe to diffuser at last, the SLN with the little and uniform particle size is formed [8].

**Types of Solid Nanoparticles:** The types of SLNs depend on the chemical nature of the active ingredient and lipid, the solubility of actives in the melted lipid, nature and concentration of surfactants, type of production and the production temperature.

1. **Type I or Homogenous Matrix Model**: It is derived from a solid solution of lipid and active ingredient. A solid solution can be obtained when SLN are produced by the cold homogenation method. A lipid blend can be produced containing the active in a molecularly dispersed form. After solidification of this blend, it is ground in its solid state to avoid or minimize the enrichment of active molecules in different parts of the lipid nanoparticles.

2. **Type II or drug enriched Shell Model:** It is achieved when SLN are produced by the hot technique and the active ingredient concentration in the melted lipid is low during the cooling process of the hot o/w nanoemulsion the lipid will precipitate first, leading to a steadily increasing concentration of active molecules in the remaining melt, an outer shell will solidify containing both active and lipid. The enrichment of the outer area of the particles causes burst release. The percentage of active ingredient localized in the outer shell can be adjusted in a controlled shell model is the incorporation of coenzyme Q 10.
3. **Type III or drug enriched Core Model:** Core model can take place when the active ingredient concentration in the lipid melt is high & relatively close to its saturation solubility. Cooling down of the hot oil droplets will in most cases reduce the solubility of the active in the melt. When the saturation solubility exceeds, active molecules precipitate leading to the formation of a drug enriched core [10]. Table 2 explained the list of drugs and polymers used for the preparation of SLNs using different methods in various research papers.

**TABLE 2: A LIST OF DRUGS AND POLYMERS USED FOR THE PREPARATION OF SLNS USING DIFFERENT METHODS**

| Drug | Polymer | Method of preparation | Reference |
|---|---|---|---|
| Olanzapine | Hydrogenated soyaphosphatidyl choline | Modified high pressure homogenization | 12 |
| Rizatriptan | Tristearin, Phospholipon80 | Modified solvent injection method | 13 |
| Alendronate NP | PLGA, Ethyl acetate, PF68 | Double emulsion solvent diffusion | 14 |
| Clozapine | Dynasan114,116 | Hot homogenization | 15 |
| Tetracaine | Tristearin, Dynasan112 | | 16 |
| Etomidate | Campritol 888ATO | | 17 |
| Vitamin A | Compritol 888ATO, Miglyol 812 | Hot homogenization | 18 |
| Retinol | Dynasan 116 | | 19 |
| Gatifloxacin | Chitosan-Na aliginate | Modified Coacervation | 20 |
| Insulin | PEG'Glycolgrafted chitosan | Ionic gelation | 21 |
| Paclitaxel | Tripalmitin, phosphatidylcholine | Microemulsion | 22 |
| Insulin | Hydrophobized cholesterol bearing pullulan | Ultra sonication | 23 |
| Mitoxantrone | Glyceryl behenate, Campritol 888ATO, lecithin | | 24 |
| Vinpocetine | Glyceryl monostearate, DCM, soyalecithin | Ultrasonic solvent emulsification | 25 |
| Insulin | Cetyl palmitate | Solvent emulsification evaporation | 26 |
| 5-Fluorouracil | Dynasan 114, 118, triglyceride, soyalecithin | Double emulsion Solvent evaporation | 27 |
| Methotrexate | Cetyl alcohol, Campritol 888 ATO, Tween 80 | Microemulsion congealing technique | 28 |
| Domperidone | Dynasan 114, cetyl resinoleate, soy phosphotidylecholine 99% | Hot homogenization | 29 |
| Itraconazole | Pluronic, tween | Microemulsion dispersion technique | 30 |
| Lamivudine | Stearic acid, PVA | Emulsion solvent diffusion technique | 31 |
| Nimesulide | Lecithin, sodium taurocholate, tween80 | Emulsification and low temperature solidification method | 32 |
| Amikacin | Cholesterol, Tween 80 | Solvent diffusion technique and homogenization | 33 |
| Ciprofloxacin | Cetyl palmitate, polysorbate 80 | Microemulsion technique | 34 |
| Adefovir, dipivoxil | poloxamer 188, stearic acid, | Solvent diffusion method | 35 |
| Atazanavir | Pluronic®F-68 | Thin film hydration technique | 36 |
| Tetrandrine | Precirol® ATO 5, glyceryl monostearate, stearic acid | Melt–emulsification and ultrasonication technique | 37 |
| Ofloxacin | Palmitic acid, poly vinyl alcohol | Hot homogenization and ultrasonication method | 38 |
| Miconazole | Compritol 888 ATO, propylene glycol, tween 80, and glyceryl monostearate | Hot homogenization method | 39 |
| Doxorubicin | Glyceryl caprate, curdlan | Solvent emulsification-diffusion method | 40 |
| Risperidone | Compritol 888 ATO, sodium lauryl sulphate | Solvent evaporation method | 41 |
| Diazepam | Compritol® 888; glyceryl palmitostearate | High-shear homogenization and ultrasound techniques | 42 |
| Terbinafine | Sodium alginate, Chitosan | Microemulsion technique | 43 |

**Characterization of SLN:** Characterization of SLN is a serious challenge due to the small size of the particles and the complexity of the system. Several parameters have to be considered which have direct impact on the stability and release kinetics [1].

1. **Measurement of particle size and zeta potential:** Photon correlation spectroscopy (PCS) and laser diffraction (LD) are the most powerful techniques for routine measurements of particle size. The Coulter method is rarely used to measure SLN particle size because of difficulties in the assessment of small nanoparticle and the need of electrolytes which may destabilize colloidal dispersions. PCS is a good tool to characterize nanoparticles, but it is not able to detect larger microparticles. They can be visualized by means of LD measurements. It should be kept in mind that both methods do not 'measure' particle size. Rather, they detect light scattering effects which are used to calculate particle size [44].

2. **Measurement of Crystallinity and Lipid modifications:** Special attention must be paid to the characterization of the degree of lipid crystallinity and the modification of the lipid, because these parameters are strongly correlated with drug incorporation and release rates. Due to the small size of the particle and the presence of emulsifiers, lipid crystallization and modification changes might be highly retarded. For example, it has been observed with Dynasan 112. SLN that if crystallization is not artificially induced, it may remain as a supercooled melt over several months and polymorphic transition occur very slowly.

3. **Drug content and drug release:** A very important point to judge the suitability of a drug carrier system is its loading capacity. The loading capacity is generally expressed in percent related to the lipid phase (matrix lipid + drug). Drugs loading capacities vary from typically 1% to 5% for hydrophilic drugs, for liphophilic drug loading capacity between 10%-30% was reported. For tetracaine and intimidate capacities of 10-20% for Ubidecarenone loading capacities of up to 50% was reported. For coenzyme Q10 it was 20% and 20%-25% drug loading found for cyclosporine.

   Factors determining the loading capacity of drug in the lipid are, for example:

   - Solubility of drug in melted lipid.
   - Miscibility of drug melt and lipid melt.
   - Chemical and physical structure of solid lipid matrix.
   - Polymorphic state of lipid material [5].

4. **Static Light Scattering/Fraunhofer Diffraction:** Static light scattering (SLS) is an ensemble method in which the pattern of light scattered from a solution of particles is collected and fit to fundamental electro-magnetic equations in which size is the primary variable. The method is fast and rugged, but requires more cleanliness than DLS, and advance knowledge of the particles' optical qualities.

5. **Nuclear Magnetic Resonance:** NMR can be used to determine both the size and the qualitative nature of nanoparticles. The selectivity afforded by chemical shift complements the sensitivity to molecular mobility to provide information on the physicochemical status of components within the nanoparticle.

6. **Electron Microscopy:** SEM and TEM provide a way to directly observe nanoparticles, physical characterization of nanoparticles with the former method being better for morphological examination. TEM has a smaller size limit of detection, is a good validation for other methods, and affords structural required, and one must be cognizant of the statistically small sample size and the effect that vacuum can have on the particles.

7. **Atomic Force Microscopy (AFM):** In this technique, a probe tip with atomic scale sharpness is restored across a sample to produce a topological map based on the forces at play between the tip and the surface. The probe can be dragged across the sample (contact mode), or allowed to hover just above (noncontact mode), with the exact nature of the particular force employed serving to distinguish among the sub techniques. That ultrahigh resolution is obtainable with this approach, which along with the ability to map a sample according to properties in addition to size, e.g.,

colloidal attraction or resistance to deformation, makes AFM a valuable tool [10]

8. **Differential Scanning Calorimetry:** Differential scanning Calorimetry (DSC) (yields information on melting behavior and crystallization behavior of solid and liquid constituents of the particles) are performed. DSC analysis is performed using Mettler DSC 822e/200 (Mettler Toledo). The instrument is calibrated with indium (calibration standard, purity >99.999%) for melting point and heat of fusion. A heating rate of 10°C/min is employed in the range of 20–220°C. Analysis is performed under a nitrogen purge (50 ml/min). A standard aluminum sample pans (40 Al) are used. About 10 mg sample are taken for analysis.

9. **Powder X-ray Diffractometry (PXRD):** PXRD studies are performed on the samples by exposing them to CuKa radiation (40 kV, 30 mA) and scanned from $2^o$ to $70^o$ 2h at a step size of $0.045^0$ and step time of 0.5 s. Samples used for PXRD analysis are same as those of DSC analysis [15].

10. ***In-vitro* drug release studies:** *In-vitro* drug release studies are mainly useful for quality control as well as for the prediction of *in-vivo* kinetics. Release profile of drug can be conducted in dialysis tubing or without tubing. In dialysis, the SLNs dispersion is introduced into prewashed dialysis tubing, which is then hermetically sealed and then dialyzed against dissolution medium at constant temperature with constant stirring. Samples were taken at different times, centrifuged and assayed for drug content. Levy and Benita (1990) have reported a new technique which avoids the enclosure of the colloidal drug carrier in a dialysis sac and is based on reverse dialysis. This method is not sensitive enough to characterize rapid release rate of drug from colloidal carrier [45].

**Principles of drug release from SLN:** The general principles of drug release from lipid nanoparticles are as follows:

- There is an inverse relationship between drug release and the partition coefficient of the drug.
- Higher surface area due to smaller particle size in nanometer range gives higher drug release.
- Slow drug release can be achieved when the drug is homogenously dispersed in the lipid matrix. It depends on type and drug entrapment model of SLN.
- Crystallization behavior of the lipid carrier and high mobility of the drug lead to fast drug release. There is an inverse relationship between crystallization degree and mobility of drug.

**Sterilization of SLNS:** For intravenous and ocular administration SLN must be sterile. The high temperature reach during sterilization by autoclaving presumably causes a hot o/w microemulsion to form in the autoclave, and probably modifies the size of the hot nanodroplets. On subsequent slow cooling, the SLN reformed, but some nanodroplets may coalesce, producing larger SLN than the initial ones. Since SLN are washed before sterilization, amounts of surfactant and cosurfactant present in the hot system are smaller, so that the nanodroplets may be not sufficiently stabilized. For parenteral administration, SLN dispersions must be sterile. The mean particle diameter of SLNs is often more than 200 nm, so sterile filtration is not possible in these cases. Options are therefore limited to aseptic manufacturing processes following sterilization of the starting materials (gamma or e-beam irradiation of the final dispersion) or exposure to ethylene oxide gas (EO) [10].

**Current applications of SLN:**

1. **SLN in Cosmetic and Dermatological preparations:** An area of big potential for SLN and with a short time-to market are topical products based on the SLN technology, that means pharmaceutical but also cosmetic formulations. SLN are considered as being the next generation of delivery system after liposomes. Due to the lower risk of systemic side effects topical treatment of skin disease appears favourable, yet the stratum corneum counteracts the penetration of xenobiotics into viable skin. Besides liposomes, solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) have been studied intensively.

2. **SLN as potential new adjuvant for Vaccines:** Adjuvants are used in vaccination to enhance the immune response. The safer new subunit vaccines are less effective in immunization and therefore effective adjuvants are required.

3. **Solid Lipid Nanoparticles in Cancer Chemo-therapy:** The prospect of improved cancer chemotherapy using solid lipid nanoparticles (SLN) as a drug delivery system is promising. Several obstacles frequently encountered with anticancer compounds, such as normal tissue toxicity, poor specificity and stability and a high incidence of drug resistant tumor cells, are at least partially overcome by delivering them using SLN. The emergence of the newer forms of SLN such as polymer lipid hybrid nanoparticles, nanostructured lipid carriers and long-circulating SLN may further expand the role of this versatile drug carrier in cancer treatment.

4. **Solid Lipid Nanoparticles for delivering Peptides and Proteins:** Solid lipid particulate systems such as solid lipid nanoparticles (SLN), lipid microparticles (LM) and lipospheres have been sought as alternative carriers for therapeutic peptides, proteins and antigens. The research work developed in the area confirms that under optimized conditions they can be produced to incorporate hydrophobic or hydrophilic proteins and seem to fulfil the requirements for an optimum particulate carrier system. Proteins and antigens intended for therapeutic purposes may be incorporated or adsorbed onto SLN, and further administered by parenteral routes or by alternative routes such as oral, nasal and pulmonary. Formulation in SLN confers improved protein stability, avoids proteolytic degradation, as well as sustained release of the incorporated molecules.

5. **Solid Lipid Nanoparticles for Targeted brain drug delivery:** The available literature on solid lipid nanoparticles and related carriers for brain drug targeting is revised as well. The Potential advantages of the use of solid lipid nanoparticles over polymeric nanoparticles are accounted on the bases of a lower cytotoxicity, higher drug loading capacity, and best production scalability. Solid lipid nanoparticles physicochemical characteristics are also particularly regarded in order to address the critical issues related to the development of suitable brain targeting formulations.

6. **Solid Lipid Nanoparticles for Ultrasonic drug and Gene delivery:** Ultrasound, traditionally used in diagnostic medicine, is finding a place in drug delivery in connection with these nanoparticles. In addition to their non-invasive nature and the fact that they can be focused on targeted tissues, acoustic waves have been credited with releasing pharmacological agents from nanocarriers, as well as rendering cell membranes more permeable. Ultrasonic drug delivery from micelles usually employs polyether block copolymers and has been found effective in vivo for treating tumors. Ultrasound releases drug from micelles, most probably via shear stress and shock waves from the collapse of cavitation bubbles. Liquid emulsions and solid nanoparticles are used with ultrasound to deliver genes in vitro and in vivo. The small packaging allows nanoparticles to extravasate into tumor tissues.

7. **SLN applications for improved delivery of Antiretroviral drugs to the Brain:** Human immunodeficiency virus (HIV) can gain access to the central nervous system during the early course of primary infection. Once in the brain compartment the virus actively replicates to form an independent viral reservoir, resulting in debilitating neurological complications, latent infection and drug resistance. Current antiretroviral drugs (ARVs) often fail to effectively reduce the HIV viral load in the brain. This, in part, is due to the poor transport of many ARVs, in particular protease inhibitors, across the blood-brain barrier (BBB) and blood-cerebrospinal fluid barrier (BCSBF). Studies have shown that nanocarriers including polymeric nanoparticles, liposomes, solid lipid nanoparticles (SLN) and micelles can increase the local drug concentration gradients, facilitate drug transport into the brain via endocytotic pathways and inhibit the ATP-binding cassette (ABC) transporters expressed at the barrier sites.

8. **SLN applied to the treatment of malaria:** Nanosized carriers have been receiving special attention with the aim of minimizing the side effects of drug therapy, such as poor

bioavailability and the selectivity of drugs. Several nanosized delivery systems have already proved their effectiveness in animal models for the treatment and prophylaxis of malaria. A number of strategies to deliver antimalarials using nanocarriers and the mechanisms that facilitate their targeting to *Plasmodium* spp-infected cells are discussed in this review. Taking into account the peculiarities of malaria parasites, the focus is placed particularly on lipid-based (e.g., liposomes, solid lipid nanoparticles and nano and microemulsions) and polymer-based nanocarriers (nanocapsules and nanospheres) [46].

9. **SLNs used Topically:** SLNs have been used for topical application for various drugs such as Tropolide, vitamin A, isotretinoin, ketoconazole, etc

   - **SLNs as Gene Vector Carrier:** SLN can be used in the gene vector formulation. In one work, the gene transfer was optimized by incorporation of a diametric HIV-1 HAT peptide (TAT 2) into SLN gene vector. There are several recent reports of SLN carrying genetic/peptide materials such as DNA and other nucleic acids.

   - **SLNs in Cosmetics:** Solid lipid nanoparticles (SLN) are novel delivery systems for pharmaceutical and cosmetic active ingredients.SLN possesses some features which make them promising carriers for cosmetic applications.

   - The protection of labile compounds against chemical degradation has been shown, e.g. for retinol and tocopherol.

   - Depending on the produced SLN-type, controlled release of the active ingredients is possible. SLN with a drug-enriched shell show burst release characteristics whereas SLN with a drug-enriched core lead to sustained release.

   - SLN act as occlusive, i.e. they can be used in order to increase the water content of the skin.

   - SLN show a UV-blocking potential, i.e. they act as physical sunscreens on their own and can be combined with molecular sunscreens in order to achieve improved photoprotection.

The SLNs have been applied in the preparation of sunscreens and as an active carrier agent for molecular sunscreens and UV blockers. The in vivo study showed that skin hydration will be increased by 31% after 4 weeks by addition of 4% SLN to a conventional cream. SLN and NLCs have proved to be controlled release innovative occlusive topical [5].

10. **Oral SLNs in Antitubercular Chemotherapy:** Antitubercular drugs such as rifampicin, isoniazid, pyrazinamide-loaded SLN systems, were able to decrease the dosing frequency and improve patient compliance. By using the emulsion solvent diffusion technique this anti tubercular drug loaded solid lipid nanoparticles are prepared. The nebulization in animal by incorporating the above drug in SLN also reported for improving the bioavailability of the drug [47].

11. **Stealth Nanoparticles:** These provide a novel and unique drug-delivery system they evade quick clearance by the immune system. Theoretically, such nanoparticles can target specific cells e.g. antibody 19 labelled stealth lipobodies have shown increased delivery to the target tissue in accessible sites [48, 49].

**CONCLUSION:** SLN constitute an attractive colloidal drug carrier system due to successful incorporation of active compounds and their related benefits. SLN offer an effective, promising, economical and patient-friendly device for administration of drugs by various routes.

**CONFLICT OF INTEREST STATEMENT:** We declare that we have no conflict of interest.

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