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A MODERN REVIEW ON SOLID LIPID NANOPARTICLES AS NOVEL CONTROLLED DRUG DELIVERY SYSTEM

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ABSTRACT

Solid lipid nanoparticles are at the forefront of the rapidly developing field of nanotechnology with several potential applications in drug delivery, clinical medicine and research as well as in other varied sciences. SLNs introduced in the beginning of the 1990s represent an alternative carrier system to traditional colloidal carrier systems. This review presents various production techniques for SLNs including their advantages and disadvantages, methods of characterizations, formulation variables, drug incorporation models and factors effecting loading capacity. Aspects of SLN route of administration and their applications in various fields are discussed.

KEY WORDS

SLNs, Colloidal drug carriers, Homogenization, SEM and Sterilization.

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INTRODUCTION

Targeted delivery of a drug molecule to specific organ sites is one of the most challenging research areas in pharmaceutical sciences. By developing colloidal delivery systems such as liposomes, micelles and nanoparticles, new frontiers have opened for improving drug delivery. Nanotechnology and nanoscience are widely seen as having a great potential to bring benefits to many areas of research and applications. Nanomaterials differ significantly from other materials due to the

following two major principal factors: the increased surface area and quantum effects. These factors can enhance properties such as reactivity, strength, electrical characteristics, and in vivo behaviour[1-2]. The solid lipid nanoparticles are submicron colloidal carriers (50-1000 nm) which are composed of physiological lipid, dispersed in water or in an aqueous surfactant solution. SLNs as a colloidal drug carrier combines the advantages of polymeric nanoparticles, fat emulsions and liposomes simultaneously and avoiding some of their disadvantages[3]. SLNs were invented at the beginning of 1990s and are produced either by high-pressure homogenization or by microemulsion technique and are considered to be the most effective lipid based colloidal carriers. Owing to their solid particle matrix, they can protect incorporated ingredients against chemical degradation and allow modification of release of the active compounds[4,5]. Since a decade, trials are being made to utilize SLNs as alternative drug delivery system to colloidal drug delivery systems such as lipid emulsions, liposomes and polymeric nanoparticles. SLN can be used to improve the bioavailability of drugs, e.g. cyclosporine A and to obtain sustained release of lipophilic drugs like camptothecin.

History and concept of SLN's[6- 7]

Nanosized drug delivery systems have been developed to overcome one or several of the following problems;

- Low or highly variables drug concentrations after per oral administration due to poor absorption, rapid metabolism and elimination.
- Poor drug solubility which includes i.v injections of aqueous drug solutions
- Drug distribution to other tissue combined with high toxicity. (eg: Cancer drugs).

Several systems, including micelles, liposomes, polymer nanoparticles, nanoemulsions, solid dispersion and nanocapsules have been developed. A promising strategy to overcome these problems involves the development of suitable drug carrier system like solid lipid nanoparticles**.**

Aims of SLNs[8-10]

- Possibility of controlled drug release
- Possibility of controlled drug release and drug targeting
- Increased drug stability and high drug payload
- Incorporation of lipophilic and hydrophilic drugs feasible
- No biotoxicity of the carrier
- Avoidance of organic solvents
- No problems with respect to large scale production and sterilization

Advantages of SLNs[7-9]

- Small size and relatively narrow size distribution which provide biological opportunities for site-specific drug delivery by SLNs.
- Controlled release of active drug over a long period can be achieved.
- Protection of incorporated drug against chemical degradation.
- Possible sterilization by autoclaving or gamma irradiation an and subjected to commercial sterilization procedures.
- SLNs can be lyophilized as well as spray dried.
- No toxic metabolites are produced.

Disadvantages[10-11]

- Need to remove too much water in tablet / pellet production
- Dosing problems, relatively high water content of the dispersions (70-99.9%)
- Physical stability of aqueous solution, gel formation, particle aggregation
- Poor drug loading capacity, drug expulsion after polymeric transition during storage.
- The low capacity to load hydrophilic drugs due to partitioning effects during the production process (Table No.1).

Method of preparations of SLNs:

A. High pressure homogenization
1. Hot homogenization
2. Cold homogenization

B. Microemulsion
C. Emulsification solvent diffusion
D. Ionotropic gelation
E. Polyelectrolyte complex
F. Solvent emulsification/ evaporation technique

G. Double emulsion (w/o/w) solvent evaporation method
H. Lipid extrusion
I. Ultrasonic solvent emulsification technique
J. Solvent injection method
K. High shear homogenization

High pressure homogenization[15]

HPH is suitable method for preparation of SLN, NLC, and LDC and can be performed at elevated temperature (hot HPH technique) or at or below room temperature (cold HPH technique). The particle size is decreased by cavitations' and turbulences. Basically, there are two approaches for SLN production by high pressure homogenization, hot and cold homogenization techniques.

Hot homogenization[9]

For the hot homogenization technique the drug loaded melted lipid is dispersed under stirring by high shear device (e.g. Ultra Turrax) in the aqueous surfactant solution of identical (e.g. Macron LAB 40 or Macron. LAB 60 or APV-2000) and the produced hot o/w nanoemulsion is cooled down to room temperature. At room temperature the lipid recrystallizes and leads to formation of SLNs.

Cold homogenization[9-11]

Cold homogenization is carried out with the solid lipid containing drug and therefore called as milling of a suspension. Cold homogenization has been developed to prevent:

- Temperature induced drug degradation.
- Partitioning of hydrophilic drug from lipid phase to aqueous phase.
- Complexity of the crystallization step of the nanoemulsion leading to several modifications and/or super cooled melts.

Microemulsion based SLN preparation[6-7]

Gasco and other scientists had developed and optimized a suitable method for the preparation of SLN via micro emulsion. Microemulsion was an optically transparent mixture at 65-70°Cor a slightly bluish solution, which is typically composed of a low melting lipid, an emulsifier(s), co-emulsifier(s) and water. When the hot microemulsion is dispersed in cold water (2-3oc) under constant stirring, precipitation of the lipid phase takes place, forming fine particles smaller than 300nm. A typical volume ratio of the hot micro emulsion to cold water is usually in the range of 1:25 to 1:50.

Double emulsion method[17-18]

Novel method based on solvent emulsification evaporation has been 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.

Spray drying method[19]

It's a cheaper and alternative procedure to lyophilization in order to transform an aqueous SLN dispersion into a drug product. This method causes particle aggregation due to high temperature, shear forces and partial melting of the particle. 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).

Supercritical fluid method[10]

This is an alternative method of preparing SLN by particles from gas saturated solutions (PGSS). This is new technique and advantage of solvent less processing. SLN can be prepared by the rapid expansion of supercritical carbon dioxide solutions this method is called as RESS method. Carbon dioxide with 99.99% is good solvent. This technique has several advantages such as

- Avoid the use of solvents.
- Particles are obtained as a dry powder, instead of suspensions.
- Mild pressure and temperature conditions.

Solvent injection technique[20-21]

Solvent injection technique is a new approach to prepare SLN and it has following advantages like use of pharmacologically acceptable organic solvent, easy handling and fast production process without technically sophisticated equipment. In this technique, the solid lipid was dissolved in water-miscible solvent (e.g. ethanol, acetone, isopropanol) or a water-miscible solvent mixture. Then this organic solvent mixture was slowly injected through an injection needle in to stirred aqueous phase with or without surfactant. Then the dispersion was filtered with a filter paper in order to remove any

excess lipid. The presence of surfactant within the aqueous phase helps to produce lipid droplets at the site of injection and stabilize the formed SLNs until solvent diffusion was complete by reducing the surface tension.

Solvent emulsification-evaporation technique[11]

In solvent emulsification-evaporation method, the lipophilic material and hydrophobic drug was dissolved in a water immiscible organic solvent (e.g. cyclohexane, dichloromethane, toluene, chloroform) and then that is emulsified in an aqueous phase using high speed homogenizer. To improve the efficiency of fine emulsification, coarse emulsion was passed through the micro fluidizer. Thereafter, the organic solvents were evaporated by mechanical stirring at room temperature and reduced pressure (e.g. rotary evaporator) leaving lipid precipitates of SLNs.

Solvent emulsification-diffusion technique[16]

In solvent emulsification-diffusion technique, the solvent used (e.g. benzyl alcohol, butyl lactate, ethyl acetate, isopropyl acetate, methyl acetate) must be partially miscible with water and this technique can be carried out either in aqueous phase or in oil. Initially, both the solvent and water were mutually saturated in order to ensure the initial thermodynamic equilibrium of both liquid.

Formulation variables in the product quality[29]

Particle size

Any alteration in particle size significantly affects the physical stability, bio fate of the lipid particles, and release rate of the loaded drug. Hence the size of the SLNs has to be controlled within reasonable range. Well formulated systems (liposomes, nanospheres and nanoparticles) should display a narrow particle size distribution in the submicron size range (as having size below 1μm), according to the definition of colloidal particles.

Influence of the ingredients on product quality

The particle size of lipid nanoparticles is affected by various parameters such as composition of the formulation (such as surfactant/ surfactant mixture, properties of the lipid and the drug incorporated), production methods and conditions (such as time, temperature, pressure, cycle number, equipment, sterilization and lyophilization). Large particle size is obtained at lower processing temperature. The hot homogenization technique gives a smaller particle size, generally below 500 nm, and a narrow particle size distribution as compared to cold homogenization. Mean particle size as well as polydispersity index (PI) values are reported to be reduced at increasing homogenization pressure up to 1500 bar and number of Cycles (3-7 cycles).

Influence of the lipids

Using the hot homogenization, it has been found that the average particle size of SLN dispersions is increasing with higher melting lipids. However, other critical parameters for nanoparticle formation will be different for the different lipids. The examples include the velocity of lipid crystallization, the lipid hydrophilicity (influence on self-emulsifying properties and the shape of the lipid crystals (and therefore the surface area).Further, increasing the lipid content over 5-10% resulted in larger particles (including microparticles) and broader particle size distribution in most cases.

Influence of the emulsifiers

The concentration of the surfactant/surfactant mixture strongly affects the particle size of the lipid nanoparticles. In general, smaller particle sizes were observed when a higher surfactant/lipid ratio was chosen. The decrease in surfactant concentration resulted in increase of particle size during storage. Surfactants decrease the surface tension between the interface of the particles causing portioning of the particles and thereby increasing the surface area.

Drug incorporation models of SLN[29-31]

Drug incorporation models:

- Homogenous matrix model
- Drug enriched shell, core shell model.
- Drug enriched core, core shell model

A drug enriched core obtained when dissolving a drug (e.g. Prednisolone) in the lipid melts at or close to its saturation solubility. In this model, cooling of the formed nanoemulsion will lead to super saturation of drug in melted lipid and it further leads drug precipitation prior to lipid precipitation. Further cooling will lead to precipitation of lipid surrounding the drug enriched core as a membrane

as indicated in Figure No.4. Due to increased diffusional distance and hindering effect of surrounding solid lipid shell, the carrier system shows sustained release profile.

Homogenous matrix model or solid solution model with drug being present in amorphous clusters or molecularly dispersed is mainly obtained when incorporating highly lipophilic drugs into SLN with using hot homogenization technique or applying cold homogenization method or by avoiding potentially drug solubilizing surfactants. In the cold homogenization technique the drug is dispersed in bulk of melted lipid and then the mechanical force of high pressure homogenization leads to the breakdown of molecular form to nanoparticles and giving rise to homogenous matrix model as shown in Figure No.4.

The drug enriched shell with core shell model will be obtained when performing the production during this time the drug partitioned to water phase and upon cooling, the lipid precipitates first, forming a practically drug free lipid core due to phase separation. At the same time, the drug re-partitions into the remaining liquid-lipid phase and drug concentration in the outer shell increasing gradually. Finally drug enriched shell crystallizes as depicted in Figure No.4. The amount of drug partitioning to the aqueous phase will increases with the increase of solubility of drug in the aqueous phase because of two factors

- Increasing temperature of the aqueous phase
- Increasing surfactant concentration

Factors affecting loading capacity of a drug in lipid are:

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

Methods of characterization of SLNs[22- 24]

Adequate and proper characterization of the SLNs is necessary for its quality control. However, characterization of SLN is a serious challenge due to the colloidal size of the particles and the complexity and dynamic nature of the delivery system. Nanometrology is the science of measurements at the nano scale, and its application underlies all the nanoscience and nanotechnology. The ability to measure and characterize materials, as well as determine their shape, size, and physical properties at the nano scale is vital for nanomaterials and devices. These need to be produced to a high degree of accuracy and reliability, to realize the applications of nanotechnologies.

The important parameters which need to be evaluated for the SLNs are particle size, size distribution kinetics (zeta potential), time scale of distribution processes, drug content, *in vitro* drug release and surface morphology. The particle size/size-distribution may be studied using photon correlation spectroscopy (PCS), transmission electron microscopy (TEM), scanning electron microscopy (SEM) atomic force microscopy (AFM), scanning tunneling microscopy (STM), or freeze fracture electron microscopy (FFEM).

Particle size and zetapotential

There are so many techniques for the particle size and zeta potential (size distribution) like photon correlation spectroscopy (PCS), transmission electron microscopy (TEM), scanning electron microscopy (SEM), atomic force microscopy (AFM), scanning tunnelling microscopy (STM) or freeze fracture electron microscopy (FFEM). For the routine measurement of particle size Photon correlation spectroscopy (PCS) and laser diffraction (LD) are important techniques used.

Zeta potential is an important product characteristic of SLNs since its high value is expected to lead to de aggregation of particles in the absence of other complicating factors such as steric stabilizers or hydrophilic surface appendages. It is usually measured by zetameter.

Scanning Electron Microscopy

SEM uses the basic technology developed for TEM, but the beam of electrons is focused to a diameter spot of approximately 1 nm on the surface of the specimen and scanned repetitively across the surface. It reveals that the surface topography of the sample with the best spatial resolution currently achieved is on the order of 1 nm.

Transmission Electron Microscopy

TEM is used to investigate the internal structure of micro- and nanostructures. It works by passing electrons through the samples and then using magnetic lenses to focus the image of the structure. TEM can reveal the finest details of the internal structure, in some cases the individual atoms. TEM with high-resolution transmission electron microscopy is the important tool for the study of NP.

Freeze fracture electron microscopy (FFEM)

Freeze fracture electron microscopy is used for morphological examination of lipidic particles. Kalko et al., used FFEM for detection of the appearance of protein bound to the surface of intact and microfluidized liposomes and its influence on their surface morphology. Surface bound protein was observed by FFEM and was confirmed by immunogoldcryo- microscopy.

Dynamic Light Scattering (DLS)

DLS or quasi-elastic light scattering records the variation in the intensity of scattered light on the microsecond time scale. 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. The advantages of the process are the speed of analysis, lack of requisite calibration, and sensitivity to submicrometer particles.

Differential Scanning Calorimetry (DSC) and X-Ray Diffraction (XRD)

Among the large number of analytical techniques engaged for that purpose, DSC and XRD play an important role because they are able to afford structural information on the dispersed particles. DSC and XRD are renowned typical techniques in the area of pharmaceutics and since data evaluation from these methods is usually straightforward. In addition to XRD, the associated techniques of small angle X-ray and neutron scattering can give very attractive added information on the structure of the systems. Most popular applications are the identification of crystal structures, particle sizes and shapes as well as quantitative phase analysis and determination of crystallinity indices. Structural modifications of materials are accompanied by heat exchanges, e.g., uptake of heat during melting or emission of heat during crystallization. DSC is planned to measure these heat exchanges at some stage in controlled temperature programs and allows to draw conclusions on the structural properties of a sample. DSC and X ray/neutron diffraction and scattering techniques are crucial tools for SLN characterization and offer many possibilities to gain information on the properties of the dispersed particles.

Atomic force microscopy (AFM)

In this method, a probe tip with atomic scale sharpness is rastered across a taster 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 or allowed to hover just above, with the exact nature of the particular force employed helping to differentiate among the sub techniques. That ultrahigh resolution is available with this approach, which along with the capability to map a sample according to properties in addition to size, e.g., colloidal attraction or conflict to deformation, makes atomic force microscopy a valuable tool.

Nuclear Magnetic Resonance (NMR)

NMR is used to determine both size and 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.

Static light and scattering/Fraunhofer diffraction

The method is fast and rugged, but requires more cleanliness than DLS, and advance knowledge of the particles' optical qualities 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 electromagnetic equations in which size is the primary variable.

Acoustic methods

Acoustic spectroscopy measures the attenuation of sound waves as a means of determining size through the fitting of physically relevant equations. In addition, the oscillating electric field generated by the movement of charged particles under the influence of acoustic energy can be detected to provide information on surface charge.

Entrapment efficiency

The entrapment efficiency of the drug is determined by measuring the concentration of free drug in the dispersion medium. Ultracentrifugation was carried out using Centrisart, which consist of filter membrane (molecular weight cutoff 20,000 Da) at the base of the sample recovery chamber. The SLNs along with encapsulated drug remain in the outer chamber and aqueous phase moves into the sample recovery chamber. The amount of the drug present in the aqueous phase is determined by HPLC or UV spectrophotometer.

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

***In-vitro* drug release**

The SLNs dispersion is placed in prewashed dialysis tubing which can be hermetically sealed. The dialysis sac is then dialyzed alongside a appropriate dissolution medium at room temperature, the samples are withdrawn at suitable intervals from the dissolution medium, centrifuged and analyzed for drug content using a appropriate analytical method. This method however suffers from the disadvantage of a lack of direct dilution of the SLNs by the dissolution medium. The drug release of camptothecin SLN using a dynamic dialysis method in phosphate buffered saline has been reported. Secondly, in reverse dialysis technique a number of small dialysis sacs containing 1 ml of dissolution medium are placed in SLN dispersion. The direct dilution of the SLNs is attainable with this process; however the fast release cannot be quantified with this technique.

Sterilization of SLNs[26]

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. Autoclaving the finished dispersion is not practical as the lipids melt at temperatures used to terminally heat sterilize pharmaceutical products, and the molten lipid droplets coalesce as there is no applied shear to prevent this. Options are therefore limited to aseptic manufacturing processes following sterilization of the starting materials (gamma ore-beam irradiation of the final dispersion) or exposure to ethylene oxide gas (EO). Be monitored, especially when raw materials are of natural origin. It may be possible to lyophilize the SLN dispersion, and this lyophile can be irradiated or exposed to EO. We have demonstrated that lyophilized SLNs made of carnauba wax are readily redispersed, and the original particle size distribution is recovered. Of course, SLN with appropriately small particle size can be sterilized using filtration.

Stability[26]

The shelf-life stability of SLNs can be very good. Lipids can be chosen that do not hydrolyze in aqueous suspension (another advantage over nanoparticles made from polymers, such as PLGA, which hydrolyzes with a rate that is dependent on polymer structure, and therefore must be lyophilized for practical use). The very small particle size and density close to unity of SLNs means gravity has little effect on the particles in dispersion, and Brownian motion is sufficient to maintain colloidal dispersion without creaming or sedimentation. Any such separation can usually be completely reversed by gentle agitation, even if it is observed.

Route of administration[27]

SLNs are given by following route of administration

- Oral administration.
- Parenteral administration.
- Transdermal application.

Oral administration

Forms of SLNs preparation which are given by oral route are aqueous dispersions. SLNs loaded dosage form such as tablets, pellets and capsule. The microclimate of the stomach favors particle aggregation due to the acidity and high ionic

strength. It is to be expected that food will have a large impact on SLN performance.

Parenteral administration

SLNs generally administered intravenously to animals. Distributions of SLN were found to have higher drug concentrations in lung, spleen and brain, while the solution led to more distribution in to liver and kidneys[27]. SLN showed higher blood levels in comparison to a commercial drug solution after intravenous.

Transdermal application

The smallest particle sizes are observed for SLN dispersions with low lipid content (up to 5%).Disadvantages of dermal administration are low concentration of the dispersed lipid and the low viscosity. The incorporation of the SLN dispersion in an ointment or gel is necessary in order to achieve a formulation which can be administered to the skin.

Applications of SLN[29, 1, 31]

SLN for ocular application

SLNs are especially useful in ocular drug delivery as they can improve the corneal absorption of drugs and progress the ocular bioavailability of both hydrophilic and lipophilic drugs. Biocompatibility and mucoadhesive properties of SLN improve their interaction with ocular mucosa and prolong corneal residence time of the drug, with the aim of ocular drug targeting. SLNs have another benefit of allowing autoclave sterilization, an essential step towards formulation of ocular preparations.

Ocular drug administration via SLN has been reported several times. The most applications of drug-loaded ophthalmic delivery systems are for glaucoma therapy, especially cholinergic agonists like Pilocarpine. The short elimination half-life of aqueous eye drops (due to lachrymal drainage) can be extended from a very short time (1-3 min) to prolonged time (15-20 min) using nanoparticles.

SLN in cancer chemotherapy

Enhanced endocytic activity and leaky vasculature of the tumour favours accumulation of intravenously administered nanoparticles. From the last two decades several chemotherapeutic agents have been encapsulated in SLN and their *in-vitro* and *in-vivo* efficacy have been evaluated.

a) SLN as targeted carrier for anticancer drug to solid tumor

SLN have been to be useful as drug carriers. Tamoxifen is an anticancer drug incorporated in SLN to prolong the release of drug after i.v. administration in breast cancer. Tumor targeting has been achieved with SLN loaded with drugs like Methotrexate and Camptothecin.

b) 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.

Solid lipid nanoparticles for antimicrobial drug delivery

SLNs contain occlusive excipients that, upon appliance on skin, readily form a thin film to lessen water evaporation and retain skin moisture. This occlusive property promotes molecule penetrations into the skin. SLNs encapsulated antimicrobial agents such as retinol and retinylpalmitate have shown better drug penetration rate and slower drug expulsion than the free drug counterparts. SLNs can facilitate the delivery of anti-tuberculosis drugs such as Rifampin, Isoniazid and Pyrazinamide to the lungs as well as to the lymphatic systems. SLNs can provide a sustained release of the carried antimicrobial payloads, which then can effectively eliminate the infectious microbes harbored at these lymphatic sites.

SLN 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 pesticides. The SLN were prepared here by using Compritol 888 ATO as lipid and Poloxamer 188 or Miranol Ultra C32 as surfactant.

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, plasmid DNA and other nucleic acids.

SLN in cosmetics

Solid lipid nanoparticles (SLN) are novel delivery systems for pharmaceutical and cosmetic active ingredients.SLN possess 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's, 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 photo protection.

Table No.1: Common ingredients used in the preparation of SLN[13-14, 6]

Lipids	Emulsifiers/ Co- emulsifiers
Triglycerides: Tripalmitin, Tricaprin, Trimyristin, Tristearin. Hard fat types: Witespol® W35, H35, E85. Glycerylmonostearate, Glycerylbehenate, Cetylpalmitate, Stearic acid, Palmitic acid, Decanoic acid, Behenic acid.	Soybean lecithin Egg lecithin Phosphatidylcholine Poloxamer 182, 188, 407, 908. Polysorbate 20, 60, 80. Tyloxapol. Sodium cholate, Sodium glycholate Butanol, Butyric acid.

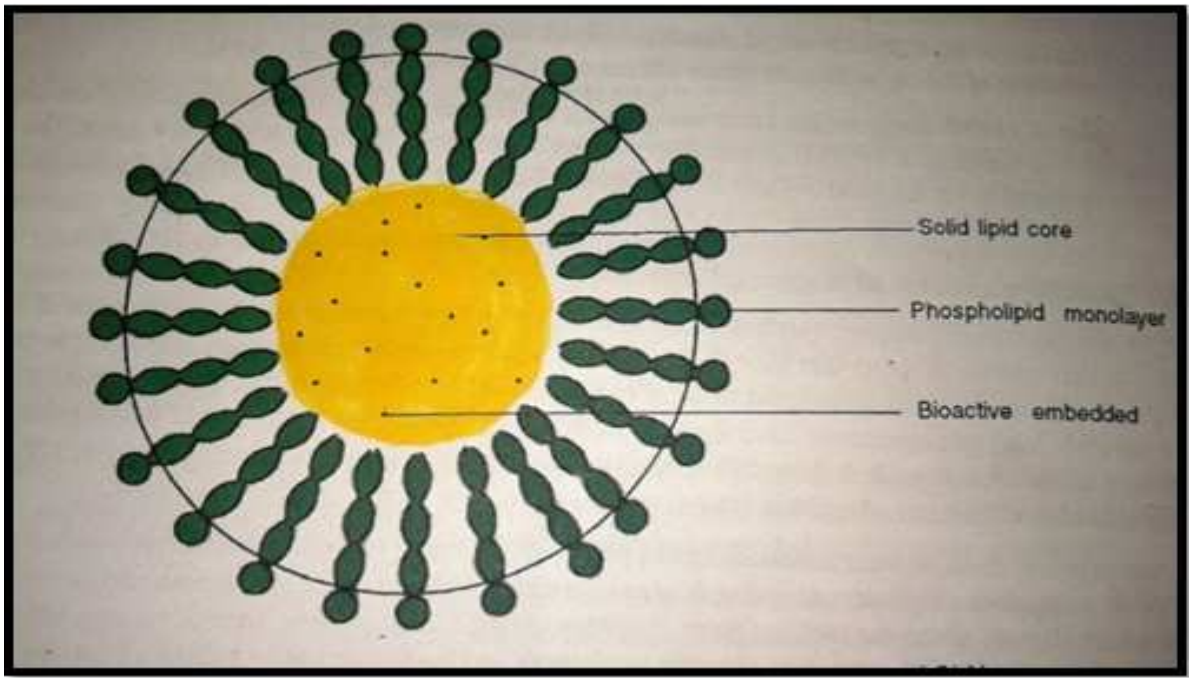

Figure No.1: The proposed structure of SLN

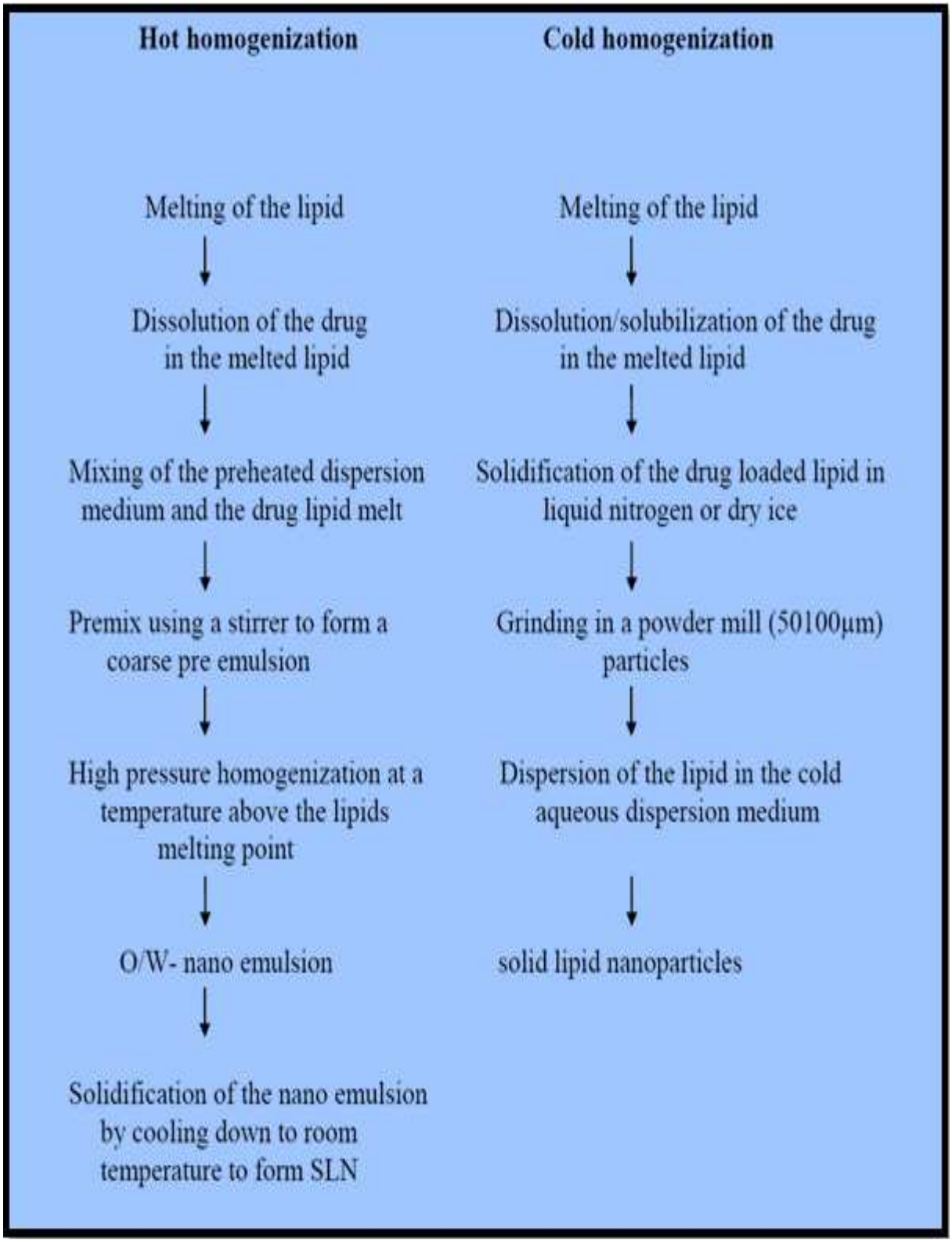

Figure No.2: Schematic procedure of hot and cold homogenization techniques for SLN Production

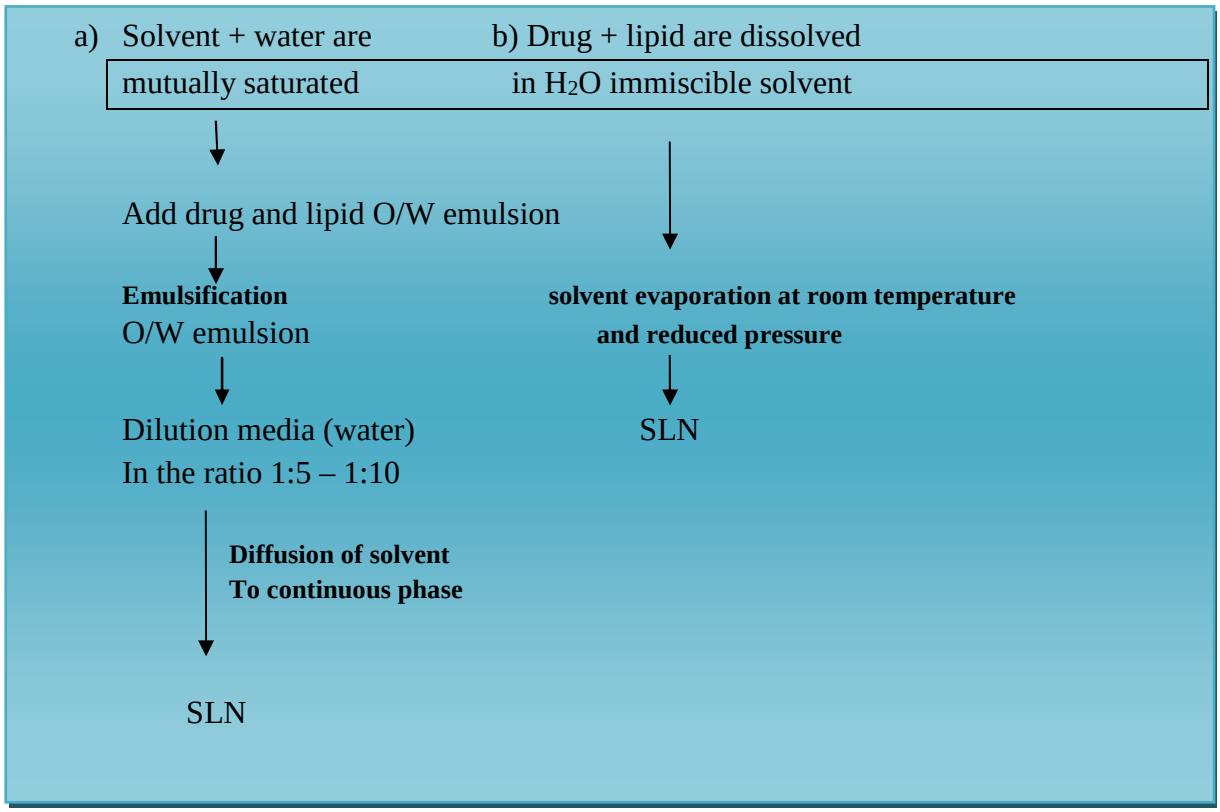

Figure No.3: Schematic diagram of (C) Solvent emulsification-diffusion technique (D) Solvent emulsification-evaporation technique

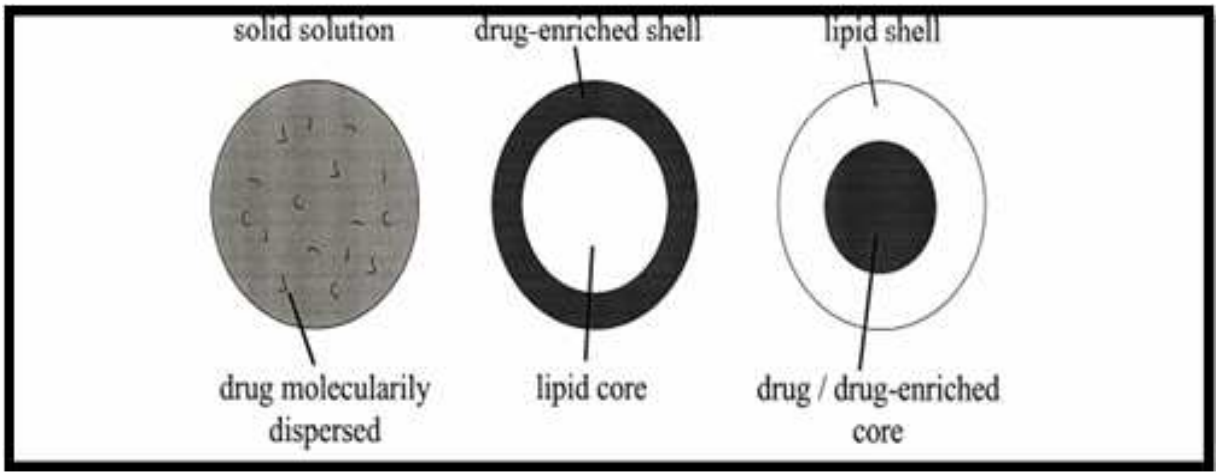

Figure No.4: Models of incorporation of API into SLN

CONCLUSION

SLN as colloidal drug carrier combines the advantage of polymeric nanoparticles, fat emulsions and liposome; due to various advantages, including feasibility of incorporation of lipophilic and hydrophilic drugs, improved physical stability, low cost, ease of scale-up, and manufacturing. SLNs have already been proven as good formulations in cosmeceuticals and other allied fields, they must occupy a considerable place in the pharmaceutical market. To exploit the broad applications of lipid based nanoparticulate formulations, it is essential that the pharmaceutical industries specialized in the development of new drug delivery systems should engage in novel formulation technology to promote their scale up and bring them onto the pharmacist's shelves. We can expect many patented dosage forms in the form of SLNs in the future.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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