Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2016, 8(8):102-114

Review Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Solid lipid nanoparticles: a comprehensive review

Verma Surender* and Makkar Deepika

Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra, India

ABSTRACT

Solid lipid nanoparticles (SLN) are most developing formulations of nanotechnology with several applications in different fields like drug delivery, clinical medicine and research as well as in other varied sciences. SLN are the spherical particles of nanometer range which immersed in water or aqueous surfactant solution either using lipophilic and hydrophilic drug. Even the enhancement of solubility and bioavailability of poorly soluble drugs should be carried out using different biodegradable and bioacceptable polymers which can also overcome the toxic effects of traditional drug carrier system. In this review article we focused on the various development techniques, their evaluation and comparison of different traditional carrier systems. This review also emphasize on methods to minimize the toxic and overdosing effects of drugs using sophisticated production techniques like homogenization and solvent evaporation. It pave the arena for the acceptance of solid lipid nanoparticles as novel or targeted drug delivery system through using recent analytical techniques like electron microscopy, dynamic light scattering (DLS), atomic force microscopy, differential scanning calorimetry (DSC), nuclear magnetic resonance and their evaluation parameters concurrent with application.

Keywords: Solid lipid nanoparticles, colloidal carriers, DLS, DSC

INTRODUCTION

Formulation scientists are facing the challenges in improving the low solubility and bioavailability of the newly invented drugs. One of the approaches to face the above problems is to formulate the new particulate carrier system. The existence of different colloidal drug carrier systems may raise the queries to the scientists' about which of these might be the most suitable carrier system for a desired purpose. The following aspects should be taken into consideration: [1, 19]

- Drug loading capacity
- Sufficient drug targeting
- In vivo fate of the carrier system (interaction with the surrounding biological fluid, degradation rate, accumulation in organs, etc.)
- Toxicity, acute as well as chronic
- Large scale production
- Overall cost of formulation.[5, 22, 25]

Nanoparticles are solid colloidal particles ranging from 10 to 1000 nm (1.0 μm), in which the active drug or biologically active material are dissolved, entrapped, and/or to which the active principle is adsorbed or attached [2]. As, nanotechnology may be defined:

- **Nanotechnology** is the preparation of nanosized structures containing the API as shown in **fig: 1**.
- Nanotechnology, as defined by the **National Nanotechnology Initiative** (NNI), is the study and use of structures roughly in the size range of 1 to 100 nm.
- Goal of nanotechnology is same as that of medicine: to diagnose as accurately and early as possible and to treat as effectively as possible without any side effects using controlled and targeted drug delivery approach [3].

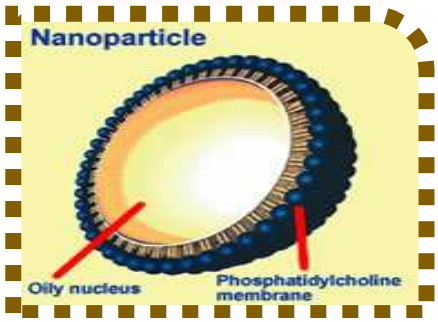


Fig.1

Drug Delivery System developed using Nanotechnology principles are:

❖Nanoparticles,
❖Solid Lipid Nanoparticles,
❖Nanosuspension,
❖Nanoemulsion,
❖Nanocrystals[14]

Classification of nanoparticles:

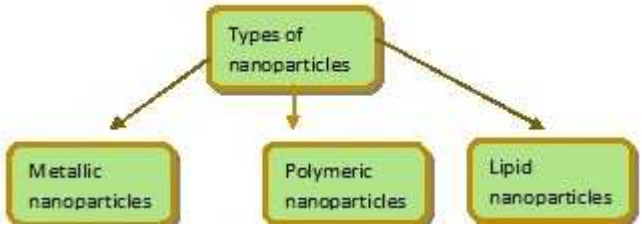


Fig: 2 Classification of nanoparticles

The major concern with the metallic and polymeric nanoparticles is the toxic effects of metals and polymers used in the preparation of nanoparticles. As the lipids used in the preparation are categorized as GRAS (Generally Recognised as Safe) substances [1].

Lipid Nanoparticles (LN) can be subdivided into two big groups – Solid Lipid Nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC).

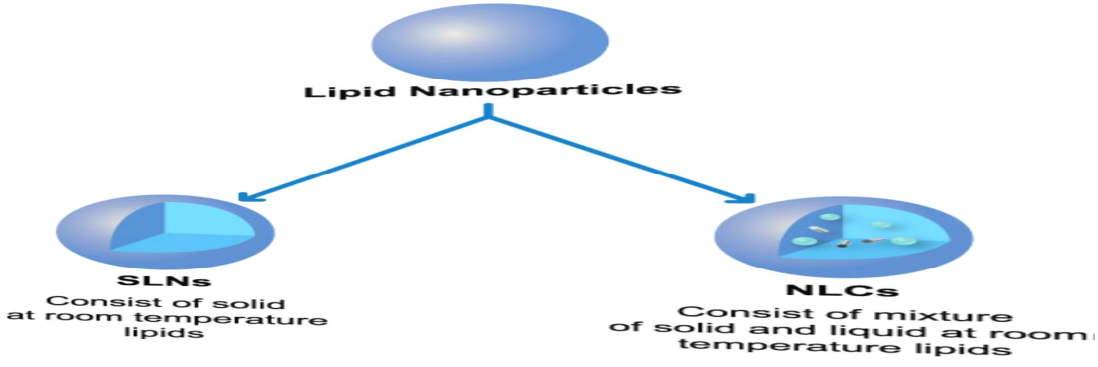


Fig: 3 Difference between the two basic types of lipid nanoparticles

Obtained from solid at room temperature lipids, SLN have the combination of the advantages of polymeric nanoparticles, fat emulsions and liposomes along with the capability to successfully resolve problems related to drug physical and chemical stability, drug delivery and absorption. [20]

Nanotechnology for drug delivery offers a suitable means of delivering small molecular weight drugs and macromolecules such as proteins, peptides or genes to cells and tissues and prevents them against enzymatic degradation. [2]

Solid lipid nanoparticles:
Lipids have been used as an alternative carrier for polymeric nanoparticles, particularly for lipophilic pharmaceuticals and lipid nanoparticles are known as solid lipid nanoparticles (SLNs) [4].

SLNs introduced in 1991 represent an alternative and suitable system to traditional colloidal carriers such as emulsions, liposomes and polymeric micro and nanoparticles [3].The system consists of spherical solid lipid particles in the nanometer ranges, which are dispersed in water or in aqueous surfactant solution. SLN are made of solid hydrophobic core having a monolayer of phospholipids coating. The hydrophobic chains of phospholipids incorporated in the fat matrix and have the potential to carry lipophilic or hydrophilic drugs or diagnostics [5].

The rationales for the increasing interest in lipid based system are:
1. Lipids enhance oral bioavailability and reduce plasma profile variability.
2. Better characterization of lipoid excipients.
3. An improved ability to address the issues of technology transfer and manufacture scale-up [12].

Advantages of SLN:

- Use of biodegradable physiological lipids which decreases the danger of acute and chronic toxicity and avoidance of organic solvents in production method.
- Improved bioavailability of poor water soluble molecules.
- Site specific delivery of drugs, enhanced drug penetration into the skin via dermal application.
- Possibility of controlled drug release and drug targeting.
- Protection of chemically labile agents from degradation in the gut and sensitive molecules from outer environment.
- SLNs have better stability compared to liposomes.
- Enhance the bioavailability of entrapped bioactive and chemical production of labile incorporated compound.
- High concentration of functional compound achieved.
- Lyophilization possible [2, 5, 25, 31].

Disadvantages of SLN

- Poor drug loading capacity.
- Drug expulsion after polymeric transition during storage.
- Relatively high water content of the dispersions (70-99.9%).
- The low capacity to load water soluble drugs due to partitioning effects during the production process(11)
- Eccentric gelation propensity.
- Unforeseen motion of polymeric transition.[12, 15]

Table: 1 Comparison between liposomes, lipid emulsions, and solid lipid nanoparticles: (6, 9)

PROPERTY	SLN	POLYMER NANOPARTICLES	LIPOSOMES	LIPID EMULSION
Systemic Toxicity	Low	> to SLN	Low	Low
Large scale production	Yes	No	Yes	Yes
Cytotoxicity	Low	> to SLN	Low	Low
Residues from organic solvents	No	Yes	may or may not	No
Sterlized by autoclaving	No	No	No	Yes
Sustained release	Yes	No	< to SLN	No
Avoidance of RES	No	No	Yes	Yes

Rationale for research of nanotechnologies in drug delivery includes:
- Decrease in toxicity while maintaining therapeutic effects.
- Specific drug targeting and delivery.
- Biocompatibile and greater safety.
- Development of safe medicine(8)

Principle of Drug Release from SLN:
The general standards of medication discharge from lipid nanoparticles are as per the following:
1. Higher surface territory because of little molecule measure in nanometer extent gives higher medication discharge.

2. Slow medication discharge can be accomplished when the medication is homogenously scattered in the lipid framework. It depends on sort and medication entanglement model of SLN.

3. Crystallinization conduct of the lipid carrier and high portability of the medication lead to quick medication discharge.

4. Fast initial drug release in the first 5 min in the drug –enriched shell model as a result of the outer layer of particle due to larger surface area of drug depositon on the particle surface.

5. The burst release is reduced with increasing particle size and prolonged release could be obtained when the particles were sufficiently large, i.e., lipid macromolecules.

6. The type of surfactant and its concentration, which will interact with the outer shell and affect its structure, should be noted as the outer factor which is important, because a low surfactant concentration leads to a minimal burst and prolonged drug release.

7. The particle size affect drug release rate directly depends on various parameters such as composition of SLN formulation (such as surfactant, structural properties of lipid, drug) production method and conditions (such as production time, equipment, sterilization and lyophilization [5].

There are three drug incorporation models which describe drug release from SLN as shown in fig. 4
A) Homogenous matrix model
B) Drug enriched shell with lipid core
C) Drug enriched core with lipid shell [5]

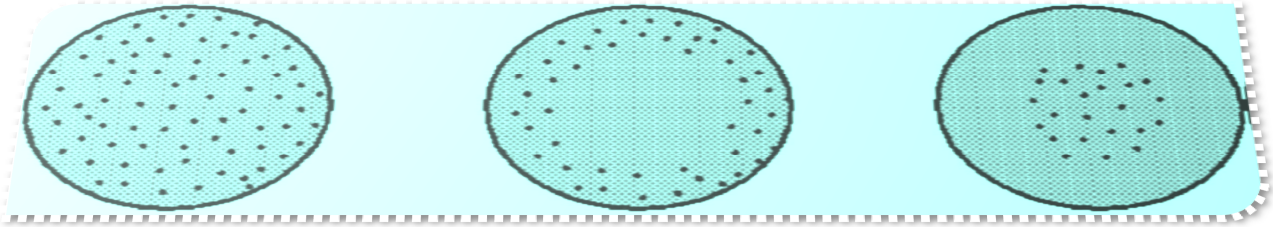


Fig.: 4 drug incorporation

Solid solution model	Core-shell model (drug-enriched shell)	Core-shell model enriched core)
Formation of this model in cold homogenization technique	Formation of this model in hot homogenization technique	Dispersion cooling leads to a super saturation of the drug which is dissolved in the lipid.
Using no drug-solubilizing surfactant	Formation of lipid core at recrystallization temperature of lipid	Precipitation of drug in melted lipid
Drug dispersed in lipid matrix	Cooling of the obtained dispersion leads to re-partitioning of the drug to the lipid phase	Finally, further cooling lead to recrystallization of the lipid
There is a strong interaction between lipid and drug	Concentration of drug in surrounding membrane	Formation of drug-enriched core

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.[13,22]

Challenges for formulation and delivery:
Problems frequently occurring with many drugs are:
✓Poor solubility
✓Insufficient in vitro stability (shelf life)
✓too low bioavailability
✓Too short in vivo stability (half-life)
✓Strong side effect
✓need for targeted delivery
✓Regulatory issues/hurdles
✓Lack of large scale production [12].

Methods of Preparation:
The performance of SLNs greatly depends on the method of preparation which in turn influences the particle size, drug loading capacity, drug release, drug stability etc. Different approaches exist for the production of finely dispersed lipid nanoparticle dispersions. Few of the production processes such as high pressure homogenization and microemulsion dilution have demonstrated scaling up possibility, a prerequisite for introduction of a product to the market [16, 17].

Composition of SLNs:
➢ ***LIPIDS:***

The lipid, itself, is the main ingredient of lipid nanoparticles that influence their drug loading capacity, their stability and the sustained release behavior of the formulations

Selection criteria for lipids:
Important point to be considered in the selection of drug carrier system (lipid) is its loading capacity and also the intended use.
- Lipids that form highly crystalline particles with a perfect lattice cause drug expulsion.
- More complex lipids containing fatty acids of different chain length form less perfect crystals with many imperfections. These imperfections provide the space to accommodate the drugs.
- **Role of Co-emulsifier:**
- Due to low mobility of the phospholipid molecules, sudden lack of emulsifier on the surface of the particle leads the particle aggregation and increase in the particle size of SLNs.
- To avoid this co-emulsifiers are employed.

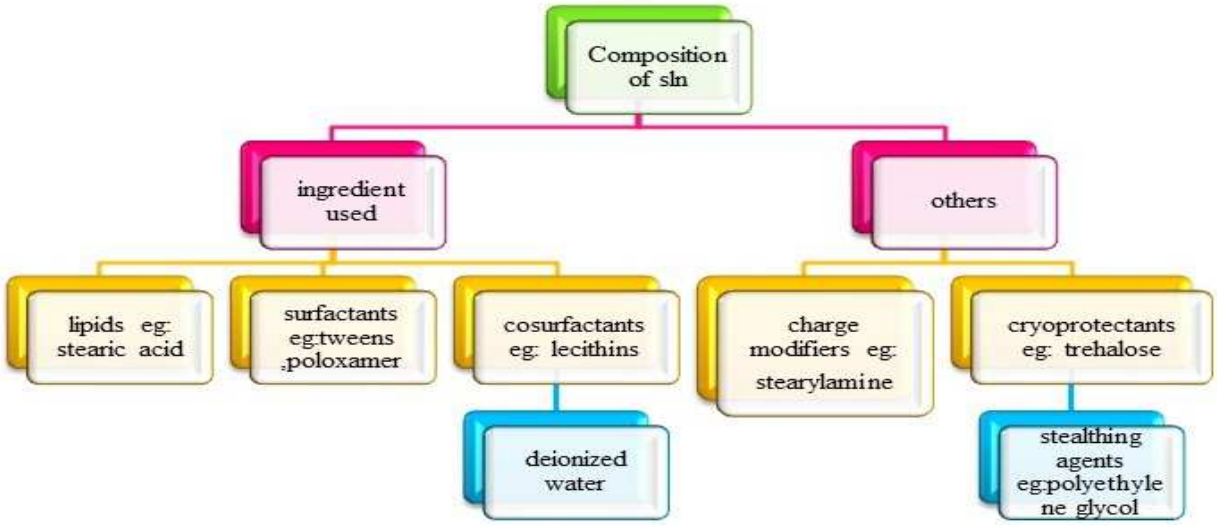


Fig 5: Composition of Solid lipid nanoparticles

Selection of Emulsifier:

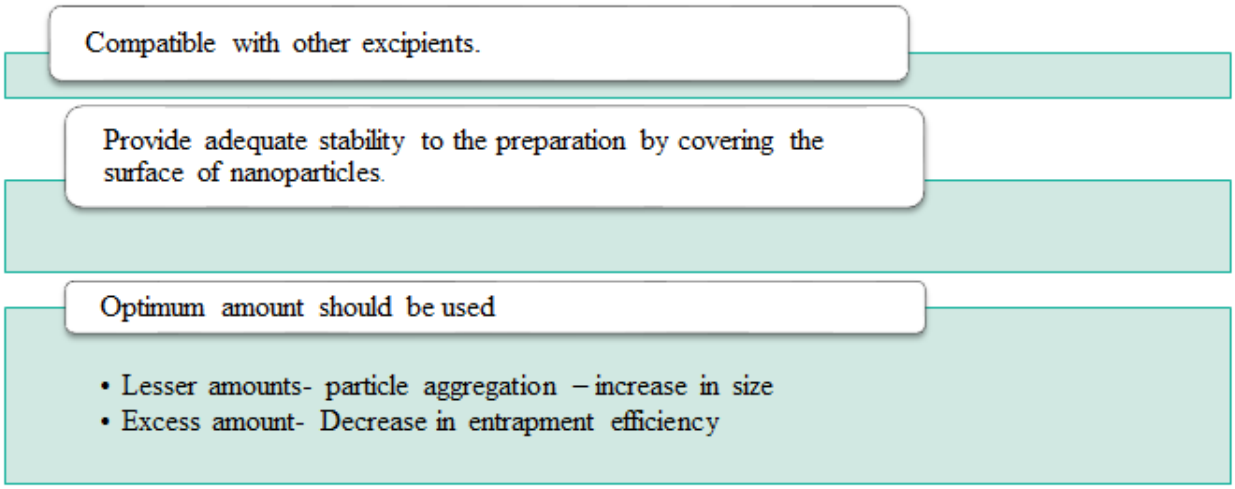


Table: 2 Different materials used for the preparation of SLNs

LIPIDS	SURFACTANTS and CO-SURFACTANTS
Triacylglycerols: Tricaprin Trilaurin Trimyristin Tripalmitin ,Tristearin	**Phospholipids:** Soy lecithin Egg lecithin Phosphatidylcholine
Acylglycerols: Glycerol monostearate Glycerol behenate Glycerol palmitostearate	**Ethylene oxide/propylene oxide copolymers:** Poloxamer 188 Poloxamer 182 Poloxamer 407 Poloxamine 908
Fatty acids: Stearic acid Palmitic acid Decanoic acid Behenic acid	**Sorbitan ethylene oxide/propylene oxide copolymers:** Polysorbate 20 Polysorbate 60 Polysorbate 80
Waxes: Cetyl palmitate	**Alkylaryl polyether alcohol polymers:** Tyloxapol
Cyclic complexes: Cyclodextrin	**Bile salts:** Sodium cholate Sodium glycocholate Sodium taurocholate Sodium taurodeoxycholate Taurocholic acid sodium salt
Hard fat types: Witepsol W 35 Witepsol H 35	**Alcohols:** Ethanol Butanol (11)

Other ingredients

Cryoprotectants	Trehalose, mannose mannitol, polyvinyl, pyrolidone, glucose, maltose, lactose, glycine, gelatin, etc.
Charge modifiers	Stearylamine, diacetyl phosphate, dipalmitoyl phosphatidyl choline (DPPC), dimyristoyl phosphatidyl glycerol (DMPG)
Stealthing agents (agents for improving circulation time)	Poloxamer, polyethylene glycol

Preparation of solid lipid nanoparticles:

The performance of SLNs greatly depends on the method of preparation which in turn influences the particle size, drug loading capacity, drug release, drug stability etc. Different approaches exist for the production of finely dispersed lipid nanoparticle dispersions [16].

Methods of preparation: [20]

- High pressure homogenization
  - Hot homogenization
  - Cold homogenization
- Ultrasonication/high speed homogenization
  - Probe ultrasonication
  - Bath ultrasonication
- Solvent evaporation method
- Solvent emulsification-evaporation method
- Supercritical fluid method
- Microemulsion based method
- Spray drying method
- Double emulsion method
- Precipitation technique
- Film-ultrasound dispersion[10, 17]

High Pressure Homogenization (HPH):

HPH is a reliable and suitable method for the 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). SLNs made from solid lipids or lipid blends produced by high pressure homogenization of melted lipids disperse in an aqueous as outer phase stabilized by surfactant as tween80, SDS, lecithin etc. (18)

✓High pressure homogenization pushes a liquid with high pressure (100-2000 bar) through a narrow gap.

✓The fluid accelerate on a very short distance to very high velocity(over 100 km / hr)
✓Very high shear stress and cavitation forces disrupt the particles down to the submicron range. 18
✓Generally 5-10% lipid content is used but up to 40% lipid content has also been investigated.19

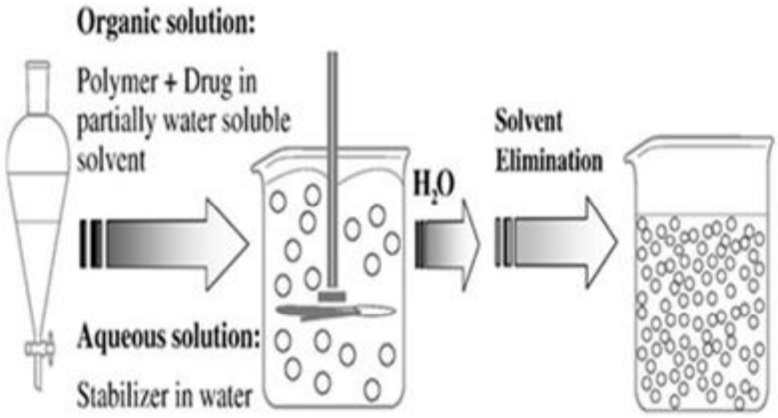
Table: 3 Hot Homogenization and Cold homogenization:

Steps	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 [11]

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 T 25, 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 [33].

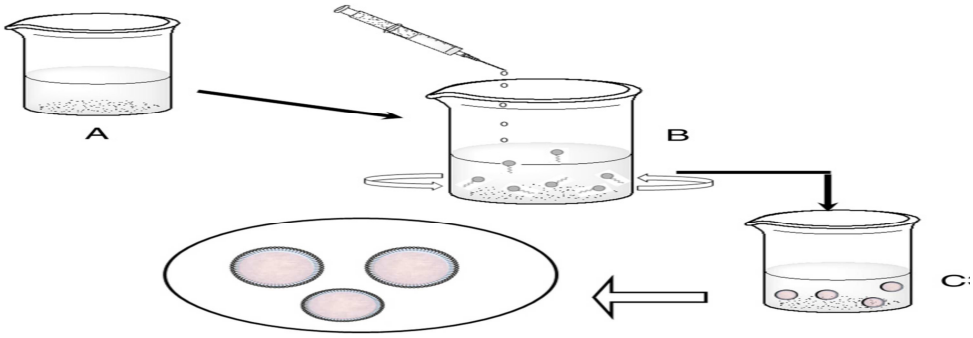
Spray drying method:
It's an alternative technique to lyophilization in order to transform an aqueous SLN dispersion into a drug product. It's a cheaper method than lyophilization. This method causes particle aggregation due to high temperature, shear forces and partial melting of the particle.[37].

Solvent evaporation – diffusion method:



SLN can also be prepared starting from emulsion precursor, whose organic phase is constituted by a solvent, which can be either volatile or partially water miscible. O/W or W/O/W emulsions can be prepared: O/W emulsions are used for lipophilic drugs that are dissolved in the inner organic phase of the system, together with the lipid. W/O/W emulsions are suitable for hydrophilic drugs, that are dissolved in the inner aqueous phase, while the lipid is dissolved in the intermediate organic phase of the multiple system. Nanoparticles are formed when the solvent is removed either by evaporation (solvent evaporation technique for volatile solvents) or by water dilution (solvent diffusion technique for partially water miscible solvents): owing to solvent removal lipid precipitates as nanoparticles encapsulating the drug as shown in **fig: 8** [36].

Solvent-injection method:
In solvent injection (or solvent displacement) method the lipid and the drug are dissolved in a water-miscible organic solvent (ethanol, acetone, isopropanol) and this solution is injected through a syringe needle in water under stirring: lipid precipitates as nanoparticles while contacting **fig: 9**



water, encapsulating the drug. Particle size can be influenced by lipid type, surfactant and solvent used, and from the viscosity of the outer phase **fig: 9** [36].

Double Emulsion Method:
The double emulsion (w/o/w) method is based on the solvent emulsification–evaporation method. It is mainly used for the production of lipid nanoparticles loaded with hydrophilic drugs. In this case, the drug and emulsifier are encapsulated in the inner aqueous phase of w/o/w double emulsion [32].

Supercritical Fluid Method
This is an alternative method of preparing SLNs using particles from gas-saturated solutions (PGSS). This technique has several advantages such as (i) avoiding the use of solvents; (ii) particles are obtained as a dry powder, instead of suspension; (iii) it required mild pressure and temperature conditions. Carbon dioxide solution is a good choice as a solvent for this method [32].

Membrane contactor technique:
The liquid phase was pressed at a temperature above the melting point of the lipid through the membrane pores allowing the formation of small droplets.. SLNs were formed by the cooling of the preparation at the room temperature. Here both the aqueous and organic phases were placed in the thermostated bath to maintain the required temperature and nitrogen was used to create the pressure for the liquid phase .

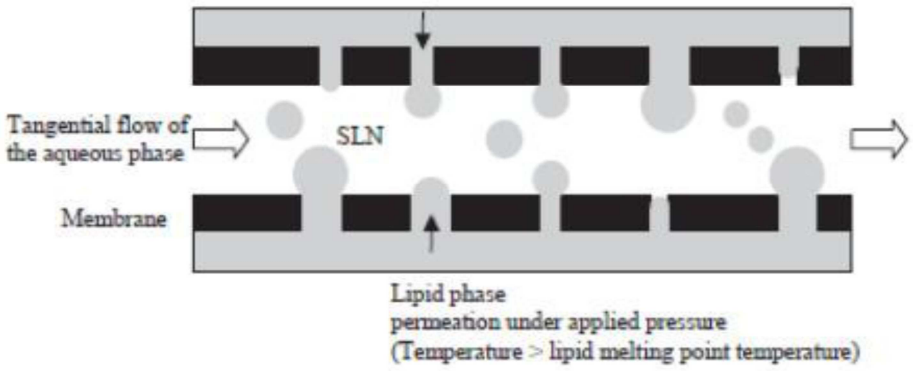


Fig: 10

Basically, the process consists of three steps:
1) Melting a pharmaceutically acceptable matrix comprised of lipid(s), surfactant(s), polymer(s), and drug at 55-70°C,
2) Adding pre-heated water with stirring to form the o/w microemulsion,
3) Cooling to room temperature with stirring to generate the SLNs.[25, 27]

Precipitation technique :
Solid lipid nanoparticles 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[5].

➢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[5, 8].

Table: 3 Advantages and Disadvantages of different methods

S. No	Method	Advantages	Disadvantages
1a	Hot HPH	Versatile, avoid use of organic solvent, easy scalability, Short production time, instruments easily available and no regulatory problems	High temperature lead to degradation, conformational changes in protein, coalescence of particles, burst release due to high emulsifiers
1b	Cold HPH	Minimizes thermal exposure of the drug but does not avoid it completely. Useful in temperature labile drugs or hydrophilic drugs	Higher Polydispersity index
2	Emulsification-solvent evaporation	Avoidance of heat during production thus useful for thermolabile drugs. Simple procedure	solvent residues
3	Emulsification-Solvent diffusion	Simple procedure, Fast drug release (drawback when slow release is required)	Low lipid content, Low EE and DL, organic solvent residue, Lack of scale up
4	Micro emulsion	No need for specialized equipment and energy for production	high concentrations of surfactants and co-surfactants, presence of large amounts of water in system
5	Membrane Contactor	Simple method, Control of particle size by selection of process parameters, and its scaling-up abilities	-
6	PGSS	one step procedure, no need of organic solvent, low processing temperature conditions	frequent nozzle blockage with hydro-phallic drugs, machinery is costly
7	Multiple emulsion	No need to melt lipids, high loading of hydrophilic drugs, useful for protein loading	Use of solvent and surfactant
8	Solvent injection	no need for high pressure homogenization, easy handling, fast production process, No need for specialized equipment	Use of solvent and surfactant
9	film Ultra-sonication dispersion	Simple, No need for specialized equipment	Metallic particle contamination, broader particle size
10	Phase inversion	Useful for thermolabile drugs, avoid organic solvent, No need for specialized equipment	-

Secondary Production Methods :

Freeze-drying:

Water can be removed in order to improve physical and chemical stability of these systems. Freeze-drying is the most commonly used process in the pharmaceutical field for conversion of solutions or suspensions into solids of sufficient stability for distribution and storage. Freeze-drying, also known as lyophilization, is an industrially scalable process, which consists of removing of frozen water by sublimation, and desorption under vacuum. [30].

Sterilization

For parenteral administration, SLNs dispersions must be sterile. Aseptic production, filtration, gamma irradiation and autoclaving are commonly used to achieve sterilization. Aseptic conditions can be used during production of sterile SLNs but requirements can be complex and expensive. Sterilization by autoclaving is popular and convenient but it has some disadvantages;the high temperaturesencountered during autoclaving can cause coalescence, as there is no applied shear to prevent this. [31].

CHARACTERIZATION PARAMETERS:

Physiochemical Characterization of SLN's:

1. Particle Size and Shape

SLNs are submicron sized, particle size and shape is determined by**:**

a) Photon Correlation Spectroscopy (PCS)

It is an established method which is based on dynamic scattering of laser light due to Brownian motion of particles in solution/suspension. This method is suitable for the measurement of particles in the range of 3 nm to 3 mm. The PCS device consists of laser source, a sample cell (temperature controlled) and a detector. Photomultiplier is used as detector to detect the scattered light. The PCS diameter is based on the intensity of the light scattering from the particles.

b) Electron Microscopy

Electron Microscopy methods such as Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are used to measure the physical characterization like overall 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. TEM has a smaller size limit of detection**.**

2. Measurement of zeta potential

Zeta potential is used to measure the charge on the particles . It allows prediction about the storage stability of colloidal dispersion because of repulsion between particles. Malvern Zetasizer is most widely used instrument for measurement of Zeta potential. A zeta potential measurement can also be helpful in designing particles with reduced RES uptake. Zeta potential below -25 mV and above + 25mV are required for full electrostatic stabilization of the formulation.

3. Determination of Incorporated Drug

Amount of drug incorporated in SLNs influences the release characteristics; hence it is very important to measure the amount of incorporated drug. The amount of drug encapsulated per unit weight of nanoparticles is determined after separation of the free drug and solid lipids from the aqueous medium by ultracentrifugation, centrifugation filtration or gel permeation chromatography. The drug can be assayed by standard analytical technique such as spectroscopy and HPLC methods.

4. Measurement of degree of crystallinity and lipid modification

Thermodynamic stability and lipid packing density increase while drug incorporation rates decrease in the following order:

Super cooled melt < α-modification < β'-modification < β-modification.

Due to the small size of the particles and the presence of emulsifiers, lipid crystallization and modification changes might be highly retarded. Differential scanning calorimetry (DSC) & X-ray scattering are used to investigate the status of the lipid. DSC uses the fact that different lipid modifications possess different melting points and melting enthalpies. By means of X-ray scattering it is possible to assess the length of the long and short spacings of the lipid lattice. It is highly recommended to measure changes of the SLN dispersion because solvent removal will lead to modifications. [26]

Drug incorporation and loading capacity:

The crucial ingredients for SLNs contain lipids, and a single or a combination of emulsifiers. Depending on the lipid, emulsifier and the method of preparation the particle size, and the surfactant used for the preparation of SLNs is found to vary.

Factors that influence the loading capacity of a drug in the lipid are:

1. Drug solubility in the melted lipid.
2. Miscibility of lipid melt and the drug melt.
3. Chemical and physical arrangement of solid lipid matrix.
4. Polymorphic condition of lipid material [35, 34].

Characterization Parameters:[26]

Table:4 Characterization Parameters:[26]

S.No.	Parameters	Importance	Methods
1.	Size and Shape	Determine skin penetration	Photon correlation spectroscopy, Scanning electron microscopy (SEM), Transmission electron microscopy (TEM)
2.	Zeta potential	Stability of particles	Zeta potentiometer, Laser droplet anemometry
3.	Entrapment efficiency	Suitability of method	Ultracentrifugation
4.	Drug content	Important in deciding the amount of nanoparticles preparation to be used	UV, HPLC
5.	In-vitro dissolution	Determine the drug release rate from particles.	Under physiologic and sink conditions.

Storage stability of SLN :
The physical properties of SLN's during prolonged storage can be determined by monitoring changes in zeta potential, particle size, drug content, appearance and viscosity as the function of time. External parameters such as temperature and light appear to be of primary importance for long term stability. The zeta potential should be in between -100 to + 100 mV for a dispersion to remain physically stable.
4°C - Most favorable storage temperature.
20°C - Long term storage did not result in drug loaded SLN aggregation or loss of drug.
50°C - A rapid growth of particle size is observed.[26]

EVALUATION PARAMETERS

Various methods used to study the in vitro release of the drug are:
In vitro drug release

Dialysis tubing:
In vitro drug release could be achieved using dialysis tubing. The solid lipid nanoparticle dispersion is placed in pre - washed dialysis tubing which can be hermetically sealed. The dialysis sac is then dialyzed against a suitable dissolution medium at room temperature, the samples are withdrawn from the dissolution medium at suitable intervals, centrifuged and analyzed for the drug content using a suitable analytical method.

Reverse dialysis:
In this technique a number of small dialysis sacs containing 1 ml of dissolution medium are placed in SLN dispersion. The SLN's are then displaced into the medium.

Franz Diffusion Cell:
The SLN's dispersion is placed in the donor chamber of Franz diffusion cell fitted with a cellophane membrane. The dispersion is then analyzed against a suitable dissolution medium; the samples are withdrawn from the dissolution medium at suitable intervals and analyzed for drug content using suitable methods like spectroscopy and HPLC methods.

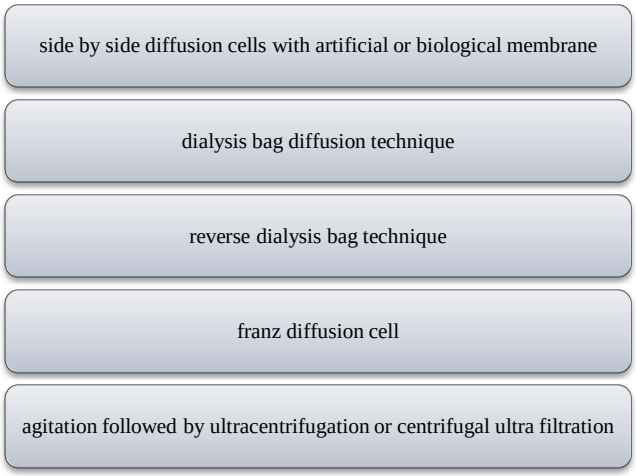


Figure 13: Schematic representation for in vitro release of the drug

Applications :

- **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. New developments in the adjuvant area are the emulsion systems. These are oil-in-water emulsions that degrade rapidly in the body.

- **Solid Lipid Nanoparticles in Cancer Chemotherapy**

Outcomes of these studies have been shown to improve the efficacy of chemotherapeutic drugs, simultaneously reduction in side effects associated with them. Improved stability of drugs, encapsulation of chemotherapeutic agents of diversified physicochemical properties, enhanced drug efficacy, improved pharmacokinetics and less in-vitro toxicity are the important features of SLN which make them a suitable carrier for delivering chemotherapeutic

drugs. 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 the musing SLN.

SLN as targeted carrier for anticancer drug to solid tumor [33, 35-37]

SLN in breast cancer and lymph node metastases [37]

- **Solid Lipid Nanoparticles for Delivering Peptides and Proteins**[38]

Proteins and antigens intended for therapeutic purposes may be incorporated or adsorbed onto SLN. Formulation in SLN confers improved protein stability, avoids proteolytic degradation, as well as sustained release of the incorporated molecules. Important peptides such as cyclosporine A, insulin, calcitonin and somtostatin have been incorporated into solid lipid particles and are currently under investigation. There are several local or systemic therapeutic.

- **SLN for Topical application**

SLN and NLC are very attractive colloidal carrier systems for skin applications due to their various desirable effects on skin besides the characteristics of a colloidal carrier system. During the last few years, SLN and NLC have been studied with active compounds such as Vitamin E, tocopherol acetate, retinol, ascorbyl palmitate, clotrimazole, triptolide, phodphyllotoxin and a nonsteroidal antiandrogen RU 58841 for topical application.

- **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 pesticide

- **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. Studies with antibody labelled stealth lipobodies have shown increased delivery to the target tissue in accessible sites.

- **SLNs as cosmeceuticals:**

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 topicals.

CONCLUSION

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

REFERENCES

[1]A Garud; D Singh; N Garud. *Int. curr. pharm. j*., **2012**, 1(11), 384-393.
[2]N Yadav; S Khatak; UVS Sara. *Int J Pharm.*, **2013**, 5(2), 8-18.
[3]S Mukherjee; S Ray; RS Thakur. *Indian J. Pharm. Sci.*, **2009**, 71(4), 1-30.
[4]PS Mahajan; KB Mahajan; AB Darekar. *IJPSR*, **2015**, 6(9), 3698-3712.
[5]KH Ramteke; SA Joshi; SN Dhole. *IOSRPHR*, **2012**, 2(6), 34-44.
[6]Li M; MR Zahi; Q Yuan; H Liang. *Eur J Lipid Sci Tech*, **2015**, 1-13.
[7]R Nair; KSA Kumar; KV Priya; M Sevukarajan. *J Biomed Sci. and Res.*, **2011**, 3(2), 368-384.
[8]S Nika; M Chavan; PH Sharma. *IPP*, **2014**, 2(3), 365-376.
[9]P Ekambaram; A Sathali; K Priyanka. *Scientific Reviews and Chemical*., **2012**, 2(1), 80-102.
[10]N Jawahar; SN Meyyanathan; G Reddy; S Sood. *J. Pharm. Sci. & Res*., **2012**, 4(7), 1848 – 1855.
[11]S Jaiswal; GD Gupta. *IAJPR*., **2013,** 3(12), 1601-1611.
[12]M Uner; G Yener. *Int J Nanomedicine*., **2007**, 2(3), 289–300.
[13]S Pragati; S Kuldeep; S Ashok; M Satheesh. *IJPSN*., **2009**, 2(2), 509-516.

[14] M Muchow; P Maincent; RH Müller. *Drug Dev. Ind. Pharm*., **2008**, 34, 1394–1405.
[15]KK Sawant; SS Dodiya. *Recent Pat Drug Deliv Formul.*, **2008**, 2, 120-135.
[16]S Nunes; R Madureira; D Campos; B Sarmento; A Gomes; M Pintado; F Reis.*Crit Rev Food Sci Nutr.,* **2015**, 1-49.
[17]S Das; A Chaudhury. *AAPS Pharm. Sci. Tech*., **2011**, 12(1), 62-76.
[18]J Patil; P Gurav; R Kulkarni; S Jadhav; S Mandave; M Shete; V Chipade. *Br. biomed bull.,* **2013**, 1(2),103-118.
[19]CT Tzache;, HL Svilenov. *Int. J. Pharm. Sci. Rev. Res.,* **2013**, 18(1), 103-115.
[20]J Kaur; G Singh; S Saini; AC Rana. *J. drug deliv. Ther.,* **2012**, 2(5), 146-150.
[21]C Pardeshi; P Rajput; V Belgamwar; A Tekade; G Patil; K Chaudhary; A Sonje. *Acta Pharm.,* **2012**, 62, 433–472.
[22]RL García; AG Rondero. *J. cosmet dermatol. sci. appl. J. cosmet*., **2015**, 5, 62-72.
[23]SP Chaturvedi; V Kumar. *Res J Pharm Biol Chem Sci*., **2012**, 3(3), 525-541.
[24]OM Bagade; RR Pujari; VS Raskar. *Int. J. Pharm. Sci. Rev. Res.,* **2014**, 29(1), 110-121.
[25]P Tayal. *Int J Pharm Sci Rev Res*., **2015**, 4(2), 301-316.
[26]A Tiwari; S Rashi; S Anand. *WJPPS*., **2015**, 4 (8), 337-355.
[27] SM Pallerla; B Prabhakar. *Int. J. Pharm. Sci. Rev. Res.*, **2013**, 20(2), 196-206
[28]B Mandal; H Bhattacharjee; N Mittal; H Sah; P Balabathula; LA Thoma; PharmDa. *Nanomed Nanotech Biol Med.*, **2013**, 1-18.
[29]W Abdelwahed. *Adv Drug Deliv Rev*., **2006**, 58(15), 1688-713.
[30]A Loxley. *WJPPS.,* **2009**, 9(8), 1-10.
[31]PG Kakadia; BR Conway. *AJPS*., **2014**, 2(5), 1-7.
[32]P Yadav; G Soni; A Mahor; S Alok; PP Singh; A Verma. *IJPSR*, **2014**, 5(4), 1152-1162.
[33]B Magenheim; MY Levy; S Benita. *Int. J. Pharm.,* **1993**, 94, 115–123.
[34] I Sarathchandiran. *IJPDT*., **2012**, 2(1), 45-61.
[35]L Battaglia; M Gallarate; PP Panciani; E Ugazio; S Sapino; E Peira; D Chirio. *Intech*., **2014**, 49-75.
[36]SM Pallerla; B Prabhakar. *Int. J. Pharm. Sci. Rev. Res.,* **2013**, 20(2), 196-206.