Introduction To Solid Lipid Nano Particles- An Overview

Divya Sanganabhatla, R. Shyam Sunder, Harshit Malpani

Abstract: ***Solid lipid nanoparticles are of major importance to the developing field of nano technology with applications in drug delivery, research and clinical medicine and other sciences. SLN dispersions have been proposed as a new type of colloidal drug carrier system suitable for intravenous administration. Solid lipid nanoparticles are submicron colloidal carriers composed of a single lipid core matrix that is solid at body temperature, and is coated with a surfactant acting as stabilizer. The conventional approaches such as use of permeation enhancers, surface modification, prodrug synthesis, complex formation and colloidal lipid carrier based strategies have been developed for the delivery of drugs to intestinal lymphatics. Aspects of solid lipid nanoparticles route of administration and their bio distribution are also incorporated. If appropriately investigated, solid lipid nanoparticles may open new vistas in therapy of complex diseases. It also discusses the potential of SLNs in brain targeting***

Index terms: Nano Particles, Solid Lipid Nanoparticles (SLNs), TEM, PCS, Bio Distribution.

I. INTRODUCTION

A high potential for drug delivery has been attributed to particulate drug carriers, especially small particles such as micro particles and colloidal system in nano meter range.[1]The lipids are a large group of organic compounds that has a fundamental role in life on Earth. Whether they act as the energy storage in our bodies or as the building blocks of the cell membranes they play a key role in different physiological and biochemical processes. Colloidal particles ranging in size between 10 and 1000 nm are known as nanoparticles. They are manufactured from synthetic/natural polymers and ideally suited to optimize drug delivery and reduce toxicity. Over the years, they have emerged as a variable substitute to liposomes as drug carriers. The successful implementation of nanoparticles for drug delivery depends on their ability to penetrate through several anatomical barriers, sustained release of their contents and their stability in the nano meter size. Biologics (proteins, peptides, oligo nucleotides, and SiRNAs) are water soluble but bring their own formulation and delivery challenges. Shelf-life stability and enzymatic degradation are two main areas of concern, and formulation design focuses on stabilizing the API in storage and protecting it from endogenous enzymes until it reaches its therapeutic target. In more advanced formulations, the API is formulated into a delivery vehicle that specifically targets tissue or cells to maximize the therapeutic index.

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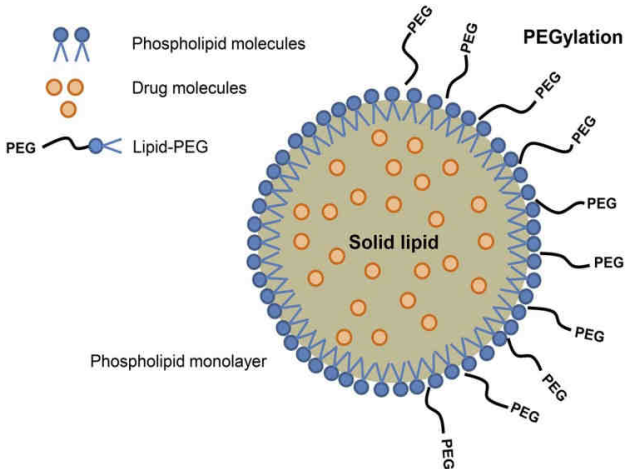

Fig1: Structure of Solid Lipid Nanoparticles

II. INGREDIENTS USED IN PREPARATION OF NANO PARTICLES

Table 1:

INGREDIENTS	CONCENTRATIONS
LIPID	3.3% w/v
PHOSPHOLIPIDS	1.2-1.5%
GLYCEROL	0.6%-1.4%
POLOXAMER 188	2-3.9%
SOY PHOSPHATIDYL CHOLINE	1.3-5%w/w
COMPRITOL	94.90%
CETYL PALMITATE	10.01%
TEGO CARE 450	10%w/w
PEG 2000	1.22%w/w
PEG 4500	0.25%
TWEEN 85	0.50%
ETHYL OLEATE	30%
NA ALGINATE	70%
ETHANOL	2%

III. LIST OF METHODS FOR SOLID NANO PARTICLES PREPARATIONS

There are various methods for preparation of solid lipid nanoparticles, some of them are described below.

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A. High Shear Homoginization

High shear homogenization technique is used to produce SLN by melt emulsification. Lipids used in this study included trimyristin, tripalmitin, a mixture of mono, di and triglycerides (Witepsol W35, Witepsol H35) with glycerol behenate and poloxamer 188 used as steric stabilizers (0.5% w/w). For Witepsol W35 dispersions the best SLN quality was obtained after stirring for 8 min at 20,000 rpm followed by cooling 10 min and stirring at 5000 rpm at a room temp. In contrast, the best conditions for Dynasan116 dispersions were a 10-min emulsification at 25,000 rpm and 5 min of cooling at 5,000 rpm in cool water (≈16°)[2]Two general approaches of the homogenization step, the hot and the cold homogenization techniques, can be used for the production of SLN. In both cases, a preparatory step involves the drug incorporation into the bulk lipid by dissolving or dispersing the drug in the lipid melt.[3]

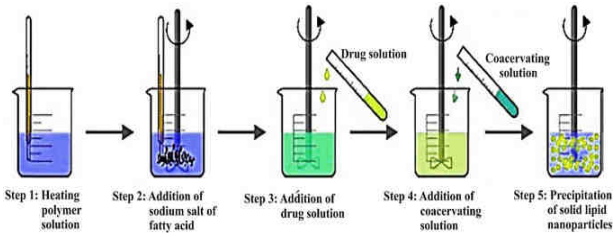


Fig 2: High Shear Homogenization

B. Hot Homogenization

One of the most used methods for the preparation of SLN , the lipids are melted by heating it at a slightly higher temperature than the melting point. The drug is dissolved , dispersed or solubilised in the lipid which is followed by dispersion of the drug lipid melt into an aqueous surfactant solution to form am o/w pre emulsion which is homogenised to obtain a nano emulsion. This is cooled to room temperature and recrystallization is performed and the product is obtained. (Figure: 2)

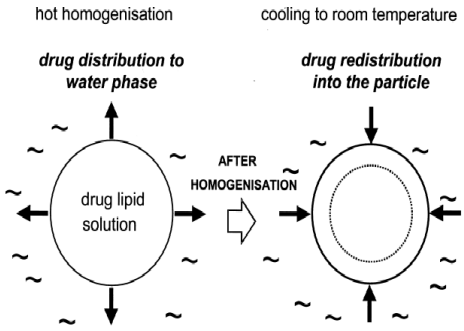
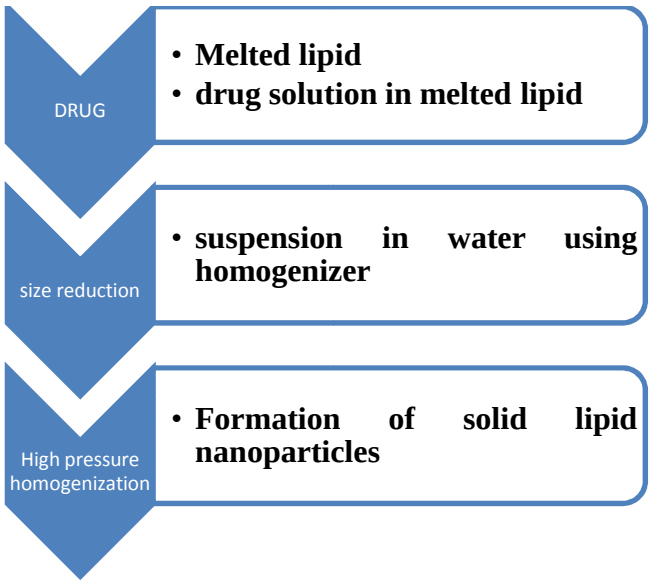


Fig 3: Hot Homogenization

C. Cold Homogenization:

The cold homogenization process is carried out with the solid lipid and therefore is similar to milling of a suspension at elevated pressure. To ensure the solid state of the lipid during homogenization, effective temperature regulation is needed. The first preparatory step is the same as in the hot homogenization procedure and includes the solubilization or dispersion of the drug in the lipid melt. However, the subsequent steps differ. The drug containing melt is cooled rapidly (using dry ice or liquid nitrogen) to favour homogenous drug distribution in the lipid matrix. In effect, the drug containing solid lipid is pulverized to micropaticles by ball/mortar milling. Typical particle sizes attained are in the range 50-100 microns. Chilled processing further facilitated particle milling by increasing the lipid fragility. The SLNs are dispersed in a chilled emulsifier solution. The dispersion is subjected to high pressure homogenization at or below room temperature with appropriate temperature control keeping in view the usual rise in temperature during high pressure processing. However, compared to hot homogenization, larger particle sizes and a broader size distribution are typical of cold homogenized samples[4]

Flowchart-1



D. Ultrasonication:

Ultrasonic Homogenization is a technique of dispersions processing, which utilizes ultrasonic waves for homogeneous distribution of the dispersed phase by the following actions: reducing the sizes of the dispersed particles/droplets (breaking); disintegrating the dispersed particles agglomerates; blending the dispersed phase in the liquid.Ultrasonication is based on the cavitation in aqueous dispersions caused by powerful *ultrasound* with wave frequency usually around and above 20kHz. In the production of SLN a mixture nof pre-emulsion from melted lipid and hot surfactant solution is first prepared . Then the ultrasound is applied with a sonotrode that is in contact with the liquid. The cavitation causes disintegration of the lipid phase into smaller droplets. The obtained hot micro emulsion is then cooled to form the solid particles.SLN were also developed by high speed stirring or sonication[5,.6] A most advantages is that, equipment whatever use here are very common in every lab. The problem of this method is broader particle size distribution ranging into micrometer range. This lead physical instabilities likes particle growth upon storage. Potential metal contamination due to ultrasonication is also a big problem in this method. So for making a stable formulation, studies have been performed by various research groups that high speed stirring and ultrasonication are used combined and performed at high temperature.

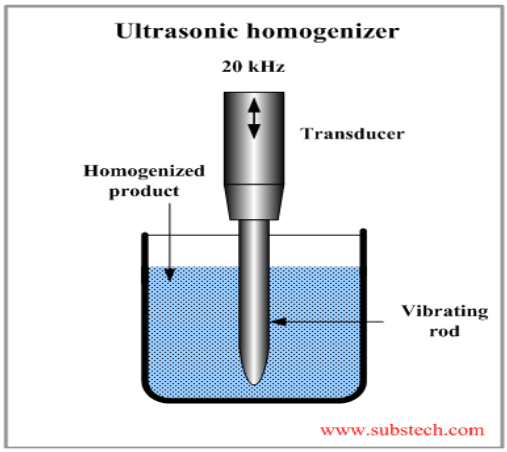


Fig 4: Ultrasonic Homogenizer

E. Solvent Emulsification:

Solvent emulsification of the lipid in the aqueous medium. The mean particle size depends on the concentration of the lipid in the organic phase. Very small particles could only be obtained with low fat loads (5 %) related to the organic solvent. With increasing lipid content the efficiency One of the methods of preparation of nanoparticles is by precipitation in o/w emulsions. The lipophilic material is dissolved in a water-immiscible organic solvent (e.g. cyclohexane) that is emulsified in an aqueous phase. Upon evaporation of the solvent nano particles dispersion is formed by precipitation of the homogenization declines due to the higher viscosity of the dispersed phase. For the production of nano particle dispersions by precipitation in o/w emulsions[7] the lipophilic material is dissolved in water-immiscible organic solvent (cyclohexane) that is emulsified in an aqueous phase. Upon evaporation of the solvent nano particle dispersion is formed by precipitation of the lipid in the aqueous medium. The mean diameter of the obtained particles was 25 nm with cholesterol acetate as model drug and lecithin/sodium glycocholate blend as emulsifier. The reproducibility of the result was confirmed by Siekmann and Westesen, who produced the cholesterol acetate nanoparticles of mean size 29 nm[8].

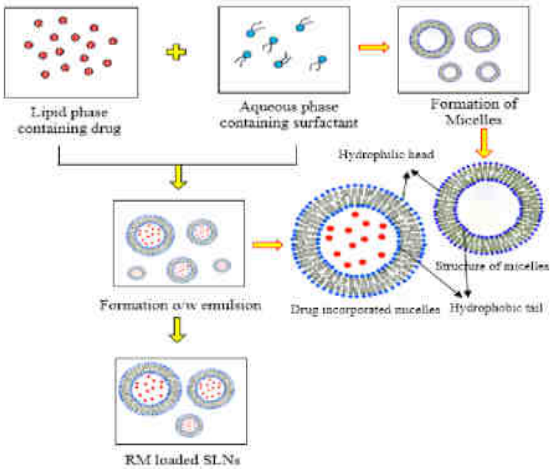


Fig 5: Solvent Emulsification

F. 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. Freitas and Mullera[9] recommends the use of lipid with melting point >70 0 for spray drying. The best result was obtained with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol-water mixtures (10/90 v/v). this feed is first atomised through various techniques (centrifugal, pneumatic, ultrasonic and electrostatic atomisation) to a spray form, that is put immediately into thermal contact with a hot gas, resulting in the rapid evaporation of the solvent to form dried solid particles [10].

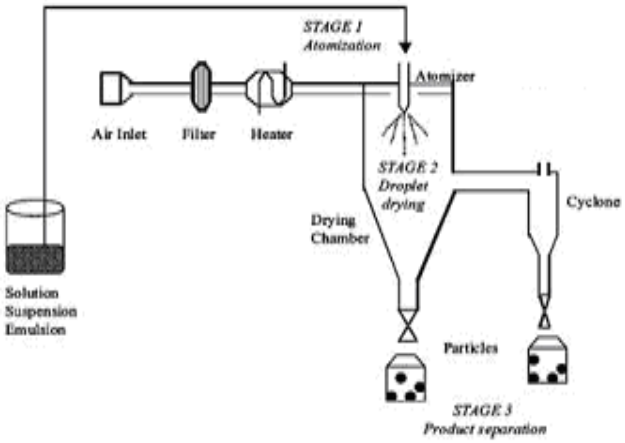


Fig 6: Spray Drying Method

IV. ADMINISTRATION ROUTE

Interactions of the SLN with the biological surroundings including: distribution processes (adsorption of biological material on the particle surface and desorption of SLN components into to biological surroundings) and enzymatic processes. Various administration routes are:

- Oral administration
- Parenteral administration
- Transdermal administration

V. APPLICATIONS

The applications of solid lipid nano particles are listed below:

- Gene vector carrier
- Topical use
- Cosmeceuticals
- Potential agriculture application
- Carrier for anticancer drug for tumors of solid type
- Used as a novel drug delivery system

VI. ADVANTAGES

- Target drug release
- Improved stability of pharmaceuticals
- Easy to gain regulatory approvals
- Non-organic solvents like water based technology is used
- Easy to sterilize

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VII. CONCLUSION

The solid lipid nano particles have revolutionized the drug based carrier system with its cheap production and easy to administer application. Their ability to provide low toxic effects has made it available to administer it in almost all drug delivery systems. A better understanding of the colloidal state of the lipids as a result of the more sensitive and modern analytical techniques will help the researches to overcome some of the limitations.

REFERENCES

1. Liversidge GG and Cundy KC: Particle size reduction for improvement of oral bioavailability of hydrophobic drugs. Absolute oral bioavailability of nanocrystallined danazol in beagle dogs. Int J Pharm 1995; 125:91-97.
2. Olbrich C, Gebner A, Kayser O, Muller RH. Lipid–drug conjugate (LDC) nanoparticles as novel carrier system for the hydrophilic antitrypanosomal drug diminazenediaceturate. J Drug Target. 2002;10:387–96.
3. Wolfgang Mehnert, Karsten Mader,; Solid lipid nanoparticles: Production,characterization and applications;Advanced Drug Delivery Reviews 47, (2001),165– 196
4. Mullen zur A. Feste Lipid-Nanopartikel mit prolongierter Wirkstoffliberation: Herstellung, Langzeitstabilitat, Charakterisierung, Freisetzungsverhalten und mechanismen. Ph.D. Thesis, Free University of Berlin. 1996
5. Eldem T, Speiser P, Hincal A. Optimization of spray-dried and congealed lipid microparticles and characterization of their surface morphology by scanning electron microscopy. Pharm Res 1991;8:47-54.
6. Speiser P. Lipidnanopellets als Tragersystem fur Arzneimittel zur peroralem Anwendung. European Patent No. EP 0167825; 1990.
7. 7.Sjostrom B, Bergenstahl B. Preparation of submicron drug particles in lecithin-stabilized o/w emulsions. I. Model studies of the precipitation of cholesteryl acetate. Int J Pharm 1992;88:53-.62.
8. Siekmann B, Westesen K. Investigations on solid lipid nanoparticles prepared by precipitation in o/w emulsions. Eur J Pharm Biopharm 1996;43:104-9.
9. Freitas C, Mullera RH. Spray-drying of Solid lipid nanoparticles (SLN TM). Eur J Pharm Biopharm 1998;46:145-51.
10. Killeen M.J. Spray drying and spray congealing of pharmaceuticals. In Encyclopedia of Pharmaceutical Technology. Edited by Swarbrick J. Boylan JC 2000