World Inventia Publishers

Journal of Pharma Research

http://www.jprinfo.com/

Vol. 8, Issue 5, 2019 ISSN: 2319-5622 USA CODEN: JPROK3

Review Article

SOLID LIPID NANOPARTICLE: A NOVEL APPROACH IN DRUG DELIVERY SYSTEM

Nida Parveen *

** Department of Pharmacy, MJP Rohilkhand University, Bareilly, U.P. INDIA.*

Received on: 10-04-2019; Revised and Accepted on: 21-05-2019

ABSTRACT

The solid lipid nanoparticles possess a lipid core matrix in a nanometer range, stabilized by a surfactant layer. These are bas on biocompatible lipids and provide sustained effect on the formulation either by diffusion or dissolution. SLN have several advantag over other colloidal carriers, such as the possibility of controlling drug release, long term stability, drug targeting, and good drug loadi of drugs may it be lipophilic or hydrophilic, free from biotoxicity due to the use of physiological lipids. The use of solid lipid instead of liqu lipid was much better idea to achieve controlled drug release, as the mobility of the drug in the solid is considerably lower as compar with liquid oils. Due to their biodegradable and biocompatible properties the solid lipid nanoparticles are used to deliver lipophilic dru macromolecules, proteins, peptides, genes, antigens, food molecules, hydrophilic drugs and diagnostic molecules.

KEYWORDS: *SLNs, Nanotechnology, Colloidal carriers.*

INTRODUCTION

Over the last few decade pharmaceutical field has registered most outstanding landmark in the field of medicine, especially in drug delivery. Nanotechnology is widely used for various drug delivery systems [1]. Nanotechnology is an art and science of manipulating matter at nanoscale that create new, unique material and products [2]. Nanotechnology has not only created a deep impression on medical field, but it also expanded its area in diagnosis, treatment, cure and patient monitoring. The effective use of nanotechnology in the drug delivery has been developed into a new branch of pharmacy that is called "Nanomedicine". The Nanomedicine include various categories like liposomes, niosomes, transfersomes, dendrimers, nanoshell, nanocapsules and solid lipid nanoprticles that are available in the market and all are gaining vital importance in comparison to conventional dosage form[3]. In the modern material science the field of nanotechnology is most active research area. Nanoparticle exhibits changed or improved properties that are based on specific characteristic such as size distribution and morphology [4, 5].

Amongst all the various nanocarriers, solid lipid nanoparticles have gained much attention from both the industrial and academic perspective. They can be simply prepared as a new epoch of colloidal carrier of submicron size, where liquid of emulsion is replaced by solid lipid. These solid lipids provide smaller size, larger surface area, high drug loading capacity and control drug release [6]. The pharmacokinetic and therapeutic index of drug can be significantly improved by loading drug into the nanoparticles through physical encapsulation, adsorption and chemical conjugation [7, 8].

1. Solid lipid nanoparticle (SLN):

Solid lipid nanoparticles (SLN) are characteristically spherical particles with an average diameter between 50-100 nm. SLN are particularly advantageous in ocular drug delivery as they have the ability to enhance the ocular bioavailability of both hydrophilic and lipophilic drugs [9].

The smaller size of solid lipid nanoparticles offers several advantages like larger surface area, high drug loading capacity, interaction with target site up to molecular level and they have enhanced the bioavailability of drug. The lipid core provides incorporation of wide variety of drug which gets dissolved, dispersed and entrapped in it. Solid lipid nanoparticles are used to deliver lipophilic drugs, macromolecules, proteins, peptide, genes, antigens, food molecules, hydrophilic drugs and diagnostic molecules [9-11].

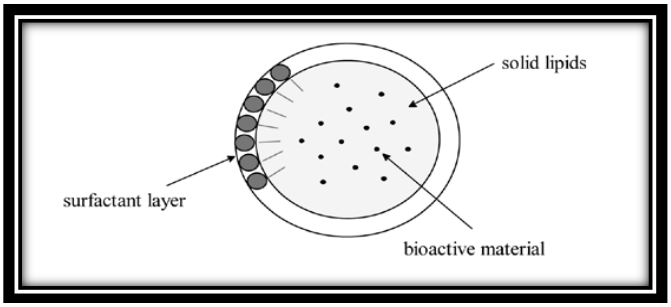

Fig. 1: Structure of SLN stabilized by surfactant layer [8]

*** Corresponding author:**

Nida Parveen

Department of Pharmacy,

MJP Rohilkhand University, Bareilly, U.P. INDIA.

** E-Mail: nida215788@gmail.com*

DOI:

1.1. Advantages:

- Control and target drug release
- Improve stability of pharmaceuticals
- High entrapment efficacy of contents as compared to other carrier
- Feasibility of carrying both lipophilic and hydrophilic drugs
- SLN can be lyophilized as well as spray dried
- No toxic metabolites are produced
- High drug payload
- Improved bioavailability of poorly water soluble drugs [12].

1.2. Disadvantages:

- Poor drug loading capacity
- Drug expulsion after polymeric transition during storage
- Relatively high water content of the dispersion have been observed (70-99%) [12].

Materials used in Formulation of SLN:

Solid lipid nanoparticles (SLN) are composed of lipids and stabilizers. In most of cases surfactant, co-surfactants are also added.

1. Lipids:

In the following years SLN provide a best technique in nanotechnology because SLN offers some of advantages of the polymeric nanoparticles, fat emulsion and liposomes. All these provide the possibility of successfully resolving problems related to physical and chemical stability of the drugs. These SLN are mainly comprised of lipids.

Lipid can be defined as fatty or waxy organic compounds. Generally they are soluble in non-polar solvents and insoluble in polar solvents. The typical constituents of lipids are free fatty acids, free fatty alcohols, glycerol esters of fatty acids and waxes. Lipids build the core / lipid matrix of the SLN. The lipid matrix determines the particles or structures that stores, transports and release the drugs.

2. Surfactants:

Those substance having both the hydrophilic and hydrophobic regions in their molecular structures are called as surface active agents. Surface active compounds due to their amphiphilic structure, exhibit a tendency to accumulate at phase boundary and form monomolecular layer around the droplets or particles. The choice of surfactant is essential to the final property of the formulation. They play a key role in stabilizing SLN.

Beside the main components of SLN (i.e., lipids and surfactants) a variety of different additives can be placed in each particular formulation. The examples of such additives are as follows:

Polysaccharide coating material: Coating to sln is imparted either to improve stability or to control drug release from SLN. Some of the materials employed for coating are: Chitosan, alternative polymeric emulsifiers- polyvinyl alcohol (PVA) and poly lactic glycolic acid (PLGA).

Tonicity adjusting agents: Electrolytes and glycerol are added in various preparations especially ophthalmic preparations and parenterals based SLN formulations.

Preservatives: In order to prevent microbial contamination preservatives are added. Substances which act as preservatives are: Parabens, thiomersal.

Other relevant examples of SLN with different viscosity enhancing excipients are carbopol and dextrin hydrogels [13, 14].

Table No. 1: List of Excipients used in SLN preparation [15, 16]

S. No.	Lipids	Surfactants
1	**Triglycerides** Glyceryl tristearate Glyceryl tripalmitate Glyceryl trimyristate	**Phospholipids** Soya lecithin Egg lecithin
2	**Acylglycerols** Glycerol monostearate Glycerol palmitostearate	**Propylene oxide co-polymers** Poloxamer 188 Poloxamer 182 Poloxamer 407 Poloxamine 908
3	**Fatty acids** Stearic acid Palmitic acid Oleic acid Behenic acid	**Polyoxyethylene sorbitan fatty ester** Polysorbate 20 Polysorbate 60 Polysorbate 80
4	**Waxes** Cetyl palmitate Bees wax	**Bile salts** Sodium cholate Sodium glycocholate Sodium taurocholate
5	**Cyclic complexes** cyclodextrin	**Alcohol** Ethanol Butanol
6	**Others** Cocao butter Anhydrous milk fat Hydrogenated castor oil	**Others** Polyoxyethylene-glycerine mono Stearate PEG caprylic/ capric triglycerides

Table No. 2: Ophthalmic friendly/ compatible surfactants used to prepare SLN [16, 17]

Amphoteric surfactant	Non-ionic surfactants	Ionic surfactants
Egg phosphatidylcholin	Poloxamer 188	Sodium cholate
Egg lecithin (lipoid E80)	Poloxamer 407	Sodium dodecyl sulfate
Soy phosphatidylcholine (SP)	Poloxamine 908	Sodium glycocholate
(Epikuron 200, 95% SP)	Span 20	Sodium oleate
(Lipoid S100)	Span 40	Sodium taurocholate
(Lipoid S75, 68% SP)	Span 60	
	Tween 20	
	Tween 40	
	Tween 80	

Method of Preparation of Solid Lipid Nanoparticles (SLN):

1. High pressure homogenization
   1.1. *Hot homogenization*
   1.2. *Cold homogenization*
2. Ultrasonication / high speed homogenization
3. Solvent evaporation method
4. Solvent emulsification-diffusion method
5. Double emulsion method
6. Precipitation technique
7. Solvent injection technique

1. High pressure homogenization (HPH):

It is a reliable and powerful technique, which is used for the first time for production of solid lipid nanoparticle. High pressure homogenizer pushes a liquid with high pressure (100-2000) through a narrow gap (in range of few microne).

HPH is of two type hot homogenization and cold homogenization [18].

1.1. *Hot homogenisation:* Hot homogenization is generally carried out at temperature above the melting point of lipid. A pre-emulsion of the drug loaded lipid melt and the aqueous emulsifier phase (same temperature) is obtained by high shear mixing device. The resultant product is hot o/w emulsion and the cooling of this emulsion leads to crystallization of the lipid and the formulation of solid lipid nanoparticles [18, 19].

1.2. *Cold homogenization:* It has been developed to overcome the temperature related degradation problem, loss of drug into the aqueous phase and partitioning associated with hot homogenization method. Drug is incorporated into melted lipid and the lipid melt is cooled rapidly using dry ice or liquid nitrogen [4, 11].

2. Ultrasonication / High speed homogenization:

It is another method for the production of solid lipid nanoparticles. The equipment used for this method is commonly available at the laboratory scale. For smaller particle size combination of both ultrasonication and high speed homogenization is required. It reduces shear stress but has some disadvantages like potential metal contamination, physical instability like particle growth upon storage [18, 19].

3. Solvent evaporation / emulsification:

In this method the lipophilic material is dissolved in a water immiscible organic solvent that is emulsified in an aqueous phase. Upon evaporation of the solvent, nanoparticle dispersion is formed by precipitation of the lipid in aqueous medium by giving the nanoparticle of 25 nm mean size [4, 11].

4. Solvent emulsification-diffusion method:

Particles with average diameter of 30-100nm can be obtained by this technique. Avoidance of the heat during the preparation is the most important advantage of this technique. In this method the lipid matrix is dissolved in water immiscible organic solvent followed by emulsification in an aqueous phase. The solvent is evaporated under reduced pressure resulting in nanoparticles dispersion which is formed by precipitation of the lipid in aqueous medium [18, 19].

5. Double emulsion:

In this method, 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. The w/o/w double micro emulsion can be prepared in two steps. Firstly, w/o micro emulsion is prepared by adding an aqueous solution containing drug to a mixture of melted lipid, surfactant and co-surfactant at a temperature slightly above the melting point of lipid to obtain a clear system. Then, formed w/o micro emulsion is added to a mixture of water, surfactant and co-surfactant and stirred gently, to obtain a clear w/o/w system [18, 19].

6. Precipitation technique:

Solid lipid nanoparticle can also be produced by precipitation method which is characterized by the need for solvent. The glycerides are dissolved in an organic solvent and the solution is emulsified in an aqueous phase. After the evaporation of the organic solvent the lipid gets precipitated forming nanoparticles [18, 19].

7. Solvent injection technique:

It is novel approach to prepare SLN, which has some advantages like use of pharmacologically acceptable organic solvent, is easily handled and is a fast process without usage of technically sophisticated equipment over the other production method. In this technique, the solid lipid is dissolved in water miscible solvent. The lipid solvent mixture is injected into stirred aqueous phase with or without surfactant. Finally the dispersion is filtered to remove excess lipid [18, 19].

Characterization of Solid Lipid Nanoparticles:

1. Particle size analysis:

The physical stability of solid lipid nanoparticle depends on their particle size. Particle size analysis of solid lipid nanoparticle is performed by Photon correlation spectroscopy (PCS) also known as dynamic light scattering (DLC) and laser diffraction (LD). These are the most powerful techniques for routine measurement of partical size [5, 20].

1.1. Zeta potential measurement: Zeta potential measurement can be carried out by using zeta potential analyzer or zeta

meter. Zeta potential measurements allow prediction about the storage stability of colloidal dispersion.

1.2. Electron microscopy: Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are providing the direct method to measure nanoparticles and physical characterization of nanoparticles. SEM is however better for morphological examination. TEM has a smaller size limit of detection.

1.3. Dynamic light scattering (DLS): DLS also known as photon correlation spectroscopy (PCS) or quasi-elastic light scattering (QELS) records the variation in the intensity of the scattered light on the microsecond time scale and thus asses the particle size.

2. Differential Scanning Calorimetry (DSC):

This technique is employed for ensuring the compatibility and stability of drug and lipid involved. The prepared SLN are taken in an aluminum pan and exposed to a temperature range from 20-200 ^{0}C. The temperature at which the lipid or drug melt, is recorded and reported in form of thermograms. The corresponding endothermic peaks determine the stability and purity of SLN [5, 8, 20].

3. Fourier Transform Infrared Spectroscopy (FTIR):

It is used to determine the lipid or drug modification during the formulating period or shelf life. It mainly measures the characteristic peak shift of functional groups. In this technique SLN is lyophilized, a pellet is made with potassium bromide and is allowed to scan from 4000 cm^{-1} to 400 cm^{-1} range. The corresponding absorbance is reported and interpreted from graph [5].

4. Acoustic method:

It measures the attenuation of the scattered sound waves as a means of determining size through the fitting of physically relevant equations. In addition, the oscillating electric field generates by the movement of charge particles under the influence of acoustic energy [8].

5. Drug content estimation:

In this technique the formulated SLN are digested with suitable surfactant solution so as to separate the drug from lipid and then centrifuge. After centrifugation the dense lipid settles down and the drug containing supernatant fluid is filtered out. The drug content is then determined by the use of U.V. Spectrophotometry or any other drug analysis method [5].

6. *In vitro* drug release:

It is usually determined by diffusion through a dialysis tube. A definite volume of SLN formulation is placed in the cellophane membrane dialysis tubing, both the ends of which are sealed and suspended in a dissolution vessel or beaker which have a definite volume of dissolution media at 37 ^{0}C. The medium is stirred with the help of a stirrer at 50-100 rpm and samples are collected at predetermined time intervals. The collected volume is replaced with equal quantity of fresh dissolution media and analyzed for the amount of drug released using U.V.Spectrophotometry or any other drug analysis method [5].

7. Stability Studies:

Stability studies are conducted as per ICH guidelines. The study is carried out in stability chamber which can provide varying temperature and relative humidity. The formulations are exposed to various temperature and humidity levels at different time intervals and effect of ageing, temperature and humidity on physicochemical characteristics and drug concentration is studied [5, 20].

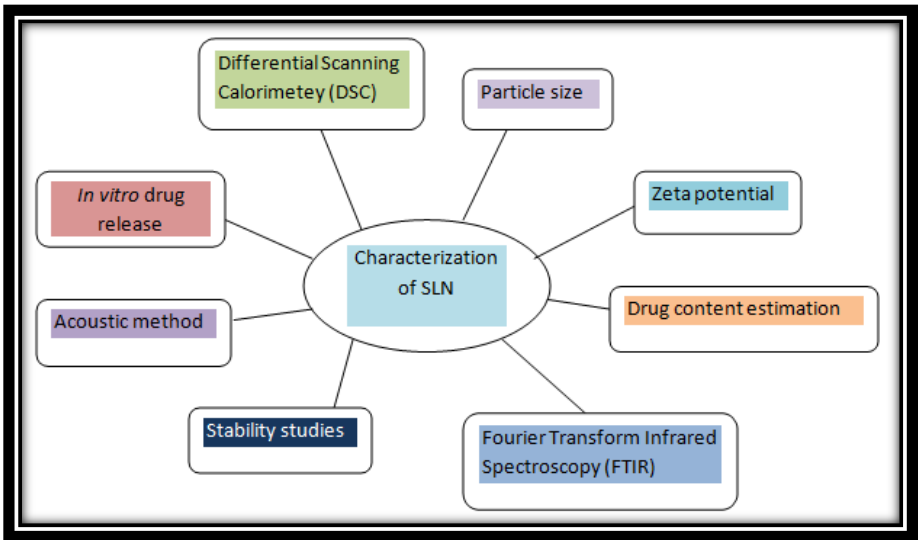

Fig. 2: Characterization parameter of SLN

Application of Solid Lipid Nanoparticle (SLN):

The various applications of solid lipid nanoparticles are as follows:

1. SLN for topical application:

It is a very attractive colloidal carrier system for skin application due to their various desirable effects on skin. It is well suited for use on damaged or inflamed skin because they are based on non-irritant and non-toxic lipids [8, 20].

2. SLN for parenteral application:

Parenteral application is a very wide field for SLN. SLN are most suitable dosage form for systemic delivery because they consist of physiologically well tolerated ingredients and they have good storage capabilities after lyophilization and

sterilization. Concerning the body distribution, SLN were found to cause higher drug concentrations in lungs, spleen and brain, while the solution led to a distribution more into liver and kidney. Subcutaneous injection of drug loaded SLN can be employed for commercial aspect, e.g., Erythropoietin (EPO), interferon-ß [8, 20].

3. SLN for ophthalmic application:

Many investigations have been made to use nanoparticles for prolonged release of drug to the eye. The basic problem of ocular formulation is the fast removal from the eye. Biocompatibility and mucoadhesive properties of SLN improve their interaction with ocular mucosa and prolong corneal residence time of drug, with the aim of ocular drug targeting [8, 20].

4. SLN for pulmonary application:

It is a very interesting application of SLN by nasal route. SLN powders cannot be administered to the lungs because the particle size is too small and they will be exhaled. A very simple approach is the aerosolization of aqueous SLN dispersion. The important point is that the SLN should not aggregate during the aerosolization. During the application, the localization into the bronchial tube and in the alveoli, the drug can be released in a controlled way from the lipid nanoparticles [8, 20].

5. SLN for cancer chemotherapy:

From the last two decades several chemotherapeutic agents have been encapsulated in the SLN. Tumor targeting has been achieved with SLN loaded drugs like Methotrexate and Camptothecin. Metoxantrone loaded SLN injections were formulated to reduce the toxicity and improve the safety and bio efficacy of the drug targeting in breast cancer and lymph node metastases [8, 20].

CONCLUSION

Solid lipid nanoparticles are relatively young drug delivery systems, having received primary attention from the early 1990s and future holds great promise for its systematic investigation and exploitation. It should not exert side effects, neither on its way to the therapeutic target, nor at the target site, nor during the clearance process. The SLNs have the potential to achieve, at least partially, these broad objectives. Apart from these, the regular objective of controlled drug delivery is aptly achieved with SLNs. We can expect many patented dosage forms in the form of SLNs in the future.

REFERENCES:

1. Zhang L, Pornpattananangkul D, Hu CMJ, et al. Development of nanoparticle for antimicrobial drug delivery. Curr Med Chem **2010**;17:585-594.
2. Maraicar KS. Hameed and Thirumoorthy N. Design and characterization of solid lipid nanoparticles by solvent evaporation followed by homogenization. Int J Biopharm **2014**;5:190-196.
3. Jain P, Mishra A, Yadav SK, Patil UK. and Baghel US. Formulation development and characterization of solid lipid nanoparticles containing nimesulide. Int J Drug Deliv Tech **2009**;1:24-27.
4. Lason E and Jan O. Solid lipid nanoparticles characterization, application and obtaining. Instit Org Chem and Tech CHEMIK **2011**;6:960-967.
5. P. Ekambaram and Abdul Hasan SA. Formulation and evaluation of solid lipid nanoparticles of Ramipril. J Young Pharm **2011**;3:216-220.
6. Chourasia MK, Jain NK and Chourasia M. Novel carrier for drug delivery. 3rd reprint 2016, Pharmamed Press Publisher, 4-4-309/316, Giriraj lane, sultan bazaar, Hyderabad-500095. **2016**;278-279.
7. http://www.nnin.org /nnin.edu.html.
8. Verma RS and Doshi A. Formulation development and characterization of nanostructured hetrolipid matrix of levofloxacin hemihydrates for ocular drug delivery. J Pharmacol & Clin Toxicol **2014**;2:1-5.
9. Yadav N, Khatak S. and Sara UVS. Solid lipid nanoparticles: A review. Int J Appl Pharm **2013**;5:8-18.
10. Svilenov H and Christo T. Solid lipid nanoparticles a promosing drug delivery system. Faculty of chemistry and pharmacy, Sofia University, Bulgaria, 188-213.
11. Vyas SP and Khar RK. Targeted and control drug delivery novel carrier system. First edition 2002, reprint 2007, CBS publishers and distributors, 11 darya ganj, New Delhi, **2002**;346.
12. Lason E and Jan O. Solid lipid nanoparticles characterization, application and obtaining. Instit Org Chem and Tech CHEMIK **2011**;6:960-967.
13. Ghanshyam UM, Patel PR and Patel JK. Formulation and characterization of SLP drug powder inhaler containing triamcinolone acetonide. Int J Res in Pharm Chem **2011**; 1:662-673.
14. Garud A, Singh D, Garud D. Solid lipid nanoparticle: Method, characterization and application. Int Curr Pharm J **2012**;1:384-39.
15. Okur UN and Evren HG. Lipid nanoparticle of ocular drug delivery. Int J Ophthalm Res **2015**;1:77-82.
16. Souto BE, Doktorovova S, Gonzalez-Mira E, Egea MA. and Garacia LM. Feasibility of lipid nanoparticles for ocular delivery of anti-inflammatory drugs. Curr Eye Res **2010**; 35:537-552.
17. Garud A, Singh D, Garud D. Solid lipid nanoparticle: Method, characterization and application. Int Curr Pharm J **2012**;1:384-39.
18. P. Ekambaram, A. Abdul Hasan Sathali & K. Priyanka. Solid Lipid nanoparticles: A review. Scient Rev & Communic **2012**;2(1):80-102.
19. Yadav P, Soni G, Mohar A, et al. Solid Lipid nanoparticles: an effective and promosing drug delivery system-A review. Int J Pharm Sci Res **2014**;5(4):1152-62.
20. Mukherjee S, Ray S. & Thakur S. Solid Lipid Nanoparticle-A modern formulation approach in drug delivery system. Ind J Pharm Sci **2009**;71(4):349-59.

How to cite this article:

Nida Parveen. SOLID LIPID NANOPARTICLE: A NOVEL APPROACH IN DRUG DELIVERY SYSTEM. J Pharm Res 2019;8(5):341-345.

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil