

Solid Lipid Nanoparticles: A Comprehensive Overview

Prankshi sharma^{1*}, Lovely Chaurasia^{1*}, Niharika², Sunayana Tyagi¹, Mojahidul islam¹

¹ IIMT College of Medical Science, IIMT University, Meerut, Uttar Pradesh, India.

² Department of botany. JamiaHamdard, New Delhi-110062

Submitted: 15-05-2022

Revised: 25-05-2022

Accepted: 28-05-2022

ABSTRACT

Solid lipid nanoparticles (SLN) are colloidal spheres with a diameter ranging from 10 to 1000 nanometers. Lipophilic substances can be solubilized by a solid lipid core in solid lipid nanoparticles. Solid lipid nanoparticles are also at the forefront of a burgeoning list of possible medication delivery and research uses. Lipid nanoparticles provide prospects for the development of novel therapeutic treatments due to their unique size-dependent characteristics. SLNs provide a number of advantages for topical drug delivery, including the capacity to deposit drugs into the skin with minimal systemic exposure and local adverse effects, as well as offering long term drug release. The capacity to encapsulate pharmaceuticals in nanocarriers is a revolutionary drug delivery prototype that can be used to deliver target drugs. As a result, researchers are particularly interested in solid lipid nanoparticles since they offer a lot of potential for achieving the goal of regulated and targeted drug delivery. This review examines the goal, production process, advantages and disadvantages, constraints, and various processing methods for solid lipid nanoparticles. Particle size, electron microscopy, dynamic light scattering, and crystallinity are all useful analytical approaches for assessing SLN. The mode of delivery of solid lipid nanoparticles as well as the carrier's in-vivo fate are also discussed. In conclusion, solid lipid nanoparticles are a complicated system with distinct advantages and disadvantages when compared to conventional colloidal carriers.

Keywords: Solid lipid nanoparticles, High Pressure Homogenization, Colloidal carriers, Ultrasonication, Controlled and site specific drug delivery, NDDS.

I. INTRODUCTION

a) Solid lipid nanoparticle:

In 1991, solid lipid nanoparticles were proposed as a viable alternative to typical liposome, micropolymers, nanoparticles, and other colloidal supports[1]. SLNs are one among the most extensively used ways to increasing the oral bioavailability of poorly soluble medications. They are the most potent colloidal carriers based on lipids. They're made up of lipid components that are physiologically suitable and solid at room temperature. They have a number of benefits, including minimal toxicity, good biocompatibility, and improved lipophilic drug delivery through SLNs, as well as a physically stable system [2]. Solid lipid nanoparticles (SLNs) are colloidal drug support systems compressed in aqueous surface active solution by a solid lipid diffuser, with particle ranging in size from 50 to 1000 nanometers[3]. Because of qualities such as good tolerability, bioavailability, and protection of the responsible drug from degradation, ease of manufacture, and low toxicity, SLNs are a good alternative to polymer systems, colloidal systems, and [4–6] desired drug, avoid drug degradation, and eliminate the use of organic solvents. This increased flexibility could be critical in the marketing of new items. As a result of this characteristic, SLN can be used as an alternate carrier system for improved drug delivery[7]. The most efficient lipid based colloidal carriers are SLNs, which were developed in the early 1990s. They are made via high-pressure homogenization or micro emulsion methods. Because of the solid particle matrix, the integrated material is protected from chemical degradation and the active ingredient's release can be altered[6][8].

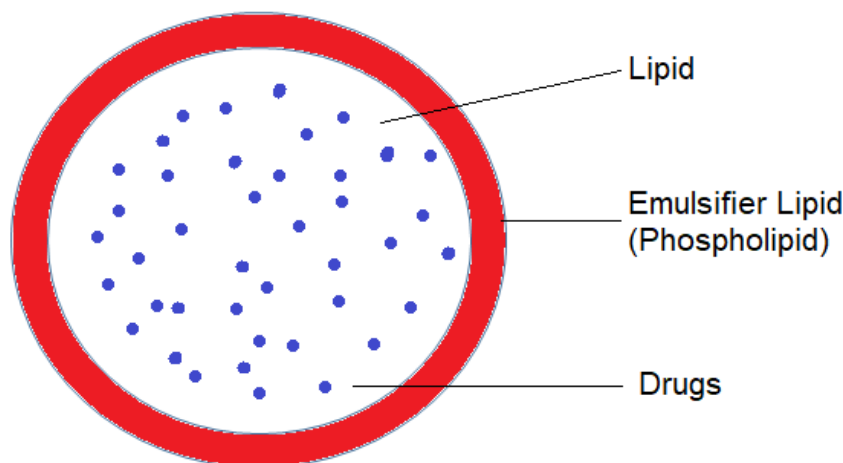


Figure 1. Structure of Solid Lipid nanoparticle

Merits of SLNs[9][3]:

- Improving drugs' long-term viability.
- Excellent biocompatibility.
- Organic solvents should be avoided.
- long-term consistency
- Increasing the bioavailability of bioactive chemicals that have been trapped.
- Sterilized and scalability is simple.
- Improved command of encapsulated drug kinetics of release.
- Chemical protection of substances included in the laboratory.
- It's a lot simpler to make than bio polymeric nanoparticles.
- Both the raw ingredient and the emulsion are required

Demerits of SLNs[10]:

- Drug loading capacity is limited.
- Hydrophilic medicines have a low compatibility.
- Gelatine tendency is precarious.

b) Aim of solid lipid nanoparticle(SLN)[11][12]:

- To improve the drug's stability.
- There is no biotoxicity in the carrier.
- Stay away from organic solvents.
- The SLN can contain both lipophilic and hydrophilic medications.
- Possibility of controlled drug release.

c) Formulation of Solid Lipid Nanoparticles:

SLN can be made from lipids, emulsifiers, and water/solvent in a number of ways, as detailed below.

- Homogenization under high pressure
 - a. Cold homogenization
 - b. Hot homogenization
- Solvent evaporation method
- Method of solvent emulsification diffusion
- High-speed homogenization and ultrasonic homogenization
 - a. Probe ultrasonic process
 - b. Bath ultrasonic process
 1. Supercritical fluid technique
 2. Using the spray drying method
 3. Method based on Microemulsions
 4. Double emulsion method
 5. Film ultrasound dispersion
 6. Precipitation method

I. High pressure homogenization (HPH):

HPH is a good approach for making SLN since it may be done on NDC and LDC (lipid drug conjugation) at high temperatures (hot homogenization) or at low temperatures (cold homogenization) (cold homogenization). Cavitation and turbulence both reduce particle size. Using a method known as high-pressure homogenization, SLN can be produced in two ways: hot and cold homogenization [13].

a. Cold homogenization:

Cold homogenization is performed with preparations containing solid lipids, so it is called suspension grinding. Cold homogenization is designed to prevent the separation of hydrophilic drugs from the lipid phase into the solvent phase; The nanoemulsion crystallization step is difficult, result in many variations and a very low melting point. The first manufacturing step is such like to hot homogenization, in which the drug is dispersed or dissolved in a liquid lipid. Liquid nitrogen or dry ice was used to rapidly cool the drug combination. The solid drug lipids are mixed to the micrometer size (50100 μm) using a mortar or ball mill, and these fine particles are dispersed in a cold emulsion to form a ready-made activating agent. Then, high-pressure homogenization is performed in a pre-compression chamber or at ambient temperature,

where the foaming force is capable of dismantling the fine particles in the SLN. This method avoids or minimizes lipid liquefaction and thus minimizes the loss of hydrophilic drugs in the aqueous phase. [14][2]. One more way to reduce the loss of hydrophilic drugs in the aqueous phase is to replace the water with another medium with low drug solubility (eg, oil and polyethylene glycol). Compared with hot symmetry, cold symmetry has a larger particle size and multidimensional index (wider size distribution). Cold homogenization not only reduces the thermal load on the drug but also should not melt the in the first step, lipid/drug mixture is created[8][3]. Merits: Costing is minimal, demonstrated on a laboratory scale. Demerits: Energy-intensive process, biomolecule damage demonstrated on a laboratory scale, polydisperse distribution [15].

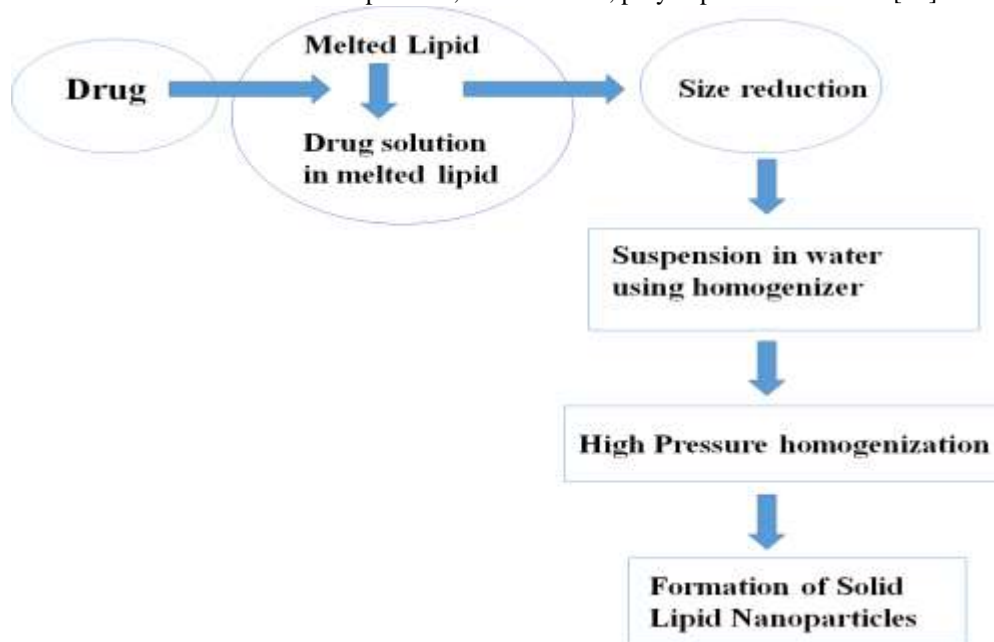


Figure 2: Creation of solid lipid nanoparticles(SLN) by cold homogenization process

b. Hot homogenization:

A homogenization emulsion is created by homogenizing at a temperature higher than the melting point of the lipid. Using high shear equipment, a pre-emulsion of a medication containing melt lipid and the aqueous emulsifier phase (both at identical temperatures) is created. High-pressure homogenization of pre-emulsion is performed at a temperature higher than the lipid's

melting point. Generally, the degradation of medicines and carriers caused the greater temperature resulted in smaller particle sizes. Due to the higher kinetic energy of the particle, when the homogenization pressure or the number of the cycles are increased, the particle size frequently grows [10][16].

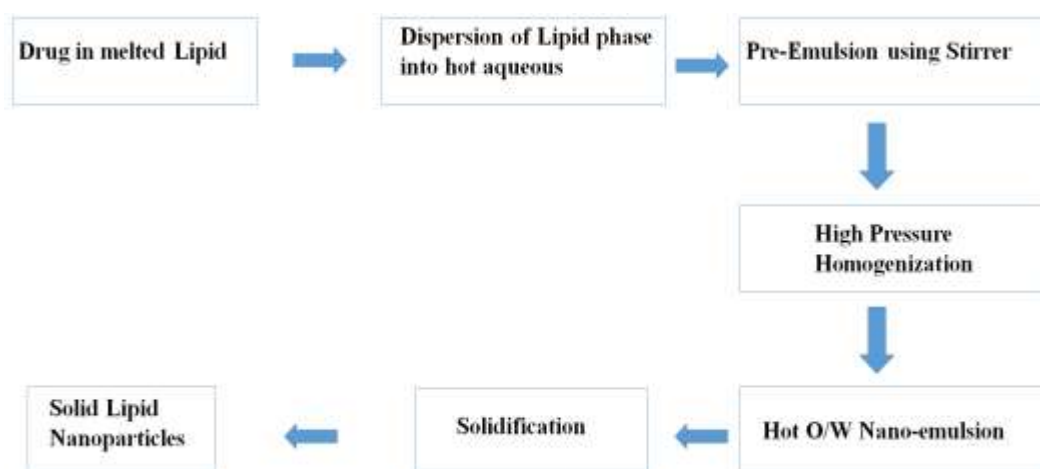


Figure 3: Preparation of SLN by hot homogenization technique

II. Solvent evaporation method

Solvent evaporation is another method for making solid lipid nanoparticles. The lipophilic substance is liquefied in a water-miscible organic liquid such as cyclohexane, and then emulsified in an aqueous phase. When solvent has evaporated, the dispersion of nanoparticles is created by the precipitate of lipids in an aqueous media, resulting in nanoparticles with an average diameter 25nm. High pressure homogenization was used to emulsify the solution in the aqueous phase. Under a lowered pressure of 4060 bar. The organic solvent evaporates from the emulsion. Merits: Measurable, continuous technology. Demerits: The process consumes a lot of energy, damage to biomolecules [8][13].

III. Solvent emulsification diffusion method:

The SLN can also be obtained from the solvent diffusion emulsion methodology. The mean particle size is calculated using the amount of lipid in the organic phase as well as the emulsifiers utilized. Particles having an average diameter of 30100 nm can be generated using this procedure. This technique has the advantage of avoiding heat during preparation. The lipid matrix is dissolved in an organic solvent that is water insoluble and then emulsified in an aqueous phase. Under reduced pressure, the solvent evaporated, allowing the nanoparticles to spread in an aqueous media through lipid precipitation [17][18].

IV. Ultrasonication homogenization & high-speed homogenization:

Solid lipid nanoparticles are also developed through ultrasonication or high-speed homogenization technology. A combination of ultrasonication and/or high speed homogenization is necessary to obtain tiny particle sizes. Merits: Reduce shear stress, Demerits: Possibility of metal defile, physical instability such as particle development during storage [19][20][16].

V. Supercritical fluid technique:

This is a new technique applied to generate SLNs. When the pressure and temperature of a liquid surpass their critical values, it is said to be supercritical. Increases the solubility of compounds in liquids. The technology includes several processes for the production of nanoparticles, e.g., supercritical fluid extraction of emulsions (SFEEs), rapid supercritical solution expansion (RESS), and solvent extraction. aerosol (ASES), particles from gas saturated solution (PGSS). The advantage of this method is that it avoids the use of liquids. Instead of a suspension, the granules are made as a dry powder that requires only moderate pressure and temperature. As a solvent for this process, carbon dioxide solution is a viable option Merits : Use solvents sparingly, granules were obtained in form of a powder and not in suspension, mild pressure and temperature conditions [21][22].

VI. Spray drying method:

Spray drying is a different technique from freeze-drying. He recommends using lipsticks with a melting point above 70°C. The finest results are achieved with a 1% SLN concentration in a

trehalose in water solution or 20% trehalose in an ethanol-water combination. [23][24]

VII. Microemulsion based approach:

This dilution of microemulsions is the basis for this approach. Microemulsion, like o/w microemulsion, are two phase systems consisting of an inner phase and an outer phase. They are created by stirring a translucent optical mixture including low melting fatty acids (stearic acid), emulsifiers (Polysorbate 20), emulsifier chemical (butanol), and water at 65-70°C. Under

displacement, the hot microemulsion was disseminated in cold water (23°C). To transform solid products (tablets, balls) by granulation, SLN dispersions can be employed as a granulating liquid, however too much water must be eliminated in the case of low particle content. The fast crystallization of lipid and prevention of agglomeration are aided by the high temperature gradient. The lipid levels achieved are much lower than with HPH based formulations due to the dilution[25].

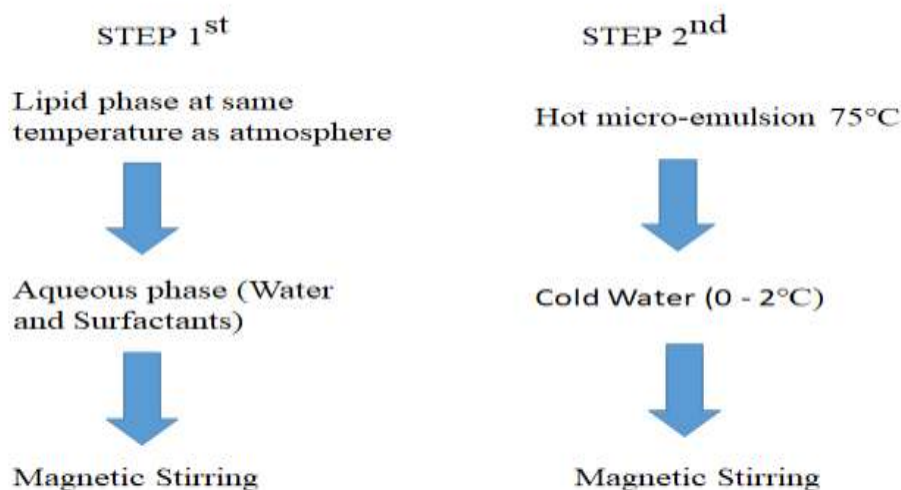


Figure 4: Microemulsion Method

VIII. Double emulsion method:

To prevent the active material from separating the outer aqueous phase during solvent evaporation, it is coated with a stabilizer, in the dual w/o/w emulsion's exterior aqueous phase [7][16][23].

IX. Ultra-Sonic dispersion film:

Lipids and drug substances are placed in the suitable organic medium after extracting, rotating, and evaporating the organic solution, after forming a lipid layer, an aqueous solution containing emulsion is added. Finally, using ultrasonic waves with a diffuser probe, SLNs with small and uniform particle sizes are formed[26][27].

X. Precipitation process.

Glycerides are dissolved in chloroform like organic solvent and then emulsified in water. The lipids precipitated and produced nanoparticles after the organic solvent evaporated[26].

II. PRODUCT QUALITY PARTICLE SIZE FORMULATING VARIABLES:

The Size changes have a significant impact on the physical durability of lipid molecules and the frequency of drug release. Therefore, the size of the SLN should be kept within reasonable control limits. The particle size distribution of properly selected system (liposome and nanoparticles) should be narrow in the submicron (1µm) region, including colloidal particles[16][24]

a) Effects of ingredients on product quality:

Parameters determine the particle size of lipid nanoparticles, e.g. formulation constitutions (surfactant mix, lipid properties, and combination drugs), manufacturing processes, and environmental conditions. (Example: time, temperature, pressure, number of cycles, components, sanitization, and lyophilization)[8].

b) Influence of lipids:

Using hot homogenization, the mean particle size of the SLN dispersion increased with a higher degree of lipid fusion. However, other important parameters of lipid-dependent nanoparticle formation, for example, degree of lipid crystallinity, lipid hydrophilicity affecting self-emulsifying properties, and lipid crystal shape, (and hence the surface area). In addition, the content increased by more than 510%, resulting in large particles (including nanoparticles) and in most circumstances, particle size dispersion is important[13].

c) Effects of emulsifiers:

The lipid particle size is heavily influenced by the concentration of the surfactant mixture. Generally, when the proportion of high surfactant/lipid is, smaller particle size is observed. The decrease in the surfactant concentration increases size of the particle during storage. Surfactants reduce surface tension at particle interfaces, causing particle to break apart and increase surface area[3][16].

III. CHARACTERIZATION OF SOLID LIPID NANOPARTICLES:

a) Analytical characterization of SLNs:

Quality control requires correct and accurate identification of the characteristics of the SLN. However, the characterization of solid lipid nanoparticles is challenging due to the colloidal particle size and delivery method. Grain size, size distribution kinetics (zeta potential), crystallinity and lipid variability (polymorphism), the presence of additional colloidal structures (liposome, supercoiling, fluxes, drug nanoparticles), treatment dispersion of time, drug content, in vitro drug release, and surface morphology are all important parameters to consider when evaluating SLNs [16][13].

➤ **Particle size determination:**

Nanoparticle systems have essential properties such as particle size and distribution. They determine biodistribution, biological fate, and controllability of nanoparticle-based drug delivery systems. In addition, drug loading, drug release, and nanoparticle stability can also be monitored. Many studies have confirmed that submicron-sized nanoparticles have a medication delivery device, it has numerous benefits over nanoparticles[28][3][29].

➤ **Electron microscopy:**

Nanoparticles and their physical properties can be observed directly using scanning electron microscopy and transmission electron microscopy. Transmission electron microscopy has a lesser detection limit than other methods, thus it's important to understand the effect of vacuum on particles and the statistically tiny sample size. Photon correlation spectroscopy or dynamic light scattering is now the speedy and most frequent method for determining particle size. To measure the particle diameter, photon correlation spectroscopy requires knowledge of the medium's viscosity and relies on Brownian motion and light scattering properties. Cyclosporine-containing lipid nanoparticles were obtained by emulsion diffusion technique, and the particle size evaluation was used to determine physicochemical stability. The size variation was found to be larger in solid lipid nanoparticle, and the particle size increased with time in all batches. This impact may be due to the possibility of drug elimination due to partial rearrangement of lipids[3][23][7].

➤ **Dynamic light scattering (DLS):**

Dynamic light scattering, also known as semi elastic light scattering, captures changes in scattered light intensity over a microsecond time scale. The interference of light scattered by individual particles in Brownian motion causes this change, which is quantified by computing the autocorrelation function. The association decay constant related to the diffusion coefficient fits exponentially or combines or modifies it with this function. The rapidity of analysis, lack of calibration, and sensitivity to ultrafine particle are all advantages of this approach[30][5][16]. The most successful technologies for traditional particle size measurements are photon correlation spectroscopy (PCS) and laser diffraction (LD). The colter method is widely used to measure SLN particle size because it is difficult to evaluate small nanoparticles and requires electrolytes that can

destabilize colloidal dispersions. PCS (also known as variable light scattering) detects changes in scattered light intensity induced by particle mobility. This method can detect particles as small as a few nanometers in size and as large as 3 micrometers in diameter. This means that PCS is a good tool for the characterization of nanoparticles, but it cannot detect larger particles. This can be visualized using LD measurement. This method is based on particle radii (e.g., Fraunhofer spectroscopy). Smaller particles produce stronger scattering at high angles than larger particles. The obvious advantage of LD is the small nanometer to the millimeter size range [30][5][16].

➤ **Degree of crystallization:**

It can be measured by X-ray powder diffraction. The existence or absence of the first object is determined by the geometric scattering of radiation by the crystal plane inside the solid, thus estimating the degree of crystallinity. DSC can be used to detecting the nature and characterization of crystallinity in nanoparticles using measuring glass temperature and point molten and their associated enthalpies, which is slightly different from its application in bulk material [3][16][31].

➤ **Drug incorporation and loading capacity**[32][12]:

Solid lipid nanoparticles were discovered with lipids (triglycerides, steroids, fatty acids, waxes, and so on), emulsifier chemistry (anion, cationic, non-ionic), and production technique.

➤ **The following elements influence a drug's lipid loading capacity**[3][32][33]:

- a. Molten lipid solubility.
- b. Solubility of the active substance soluble in molten lipids.
- c. The solid lipid matrix's physical and chemical structure.
- d. Lipid compound polymorphic state

A sufficiently high solubility of the medication in the molten lipid is required to induce a suitable loading capacity. In general, solubility decreases with the cooling of the molten and may be lower in solid lipids. A solvent may be added to increase the solubility of the molten lipid; additionally, drug solubility is increased when mono and diglycerides are present in the lipid matrix. Because lipids are highly crystalline particles with a perfect network leading to drug ejection, their chemistry is also crucial.

IV. ESTIMATION OF THE INCORPORATED DRUG

a) **Acquisition efficacy**[1][21][12]:

This is important in LNS because it affects the release of drug molecules. The amount of drug encapsulated per unit weight of nanoparticle was estimated after removing the bound drug from the SLN formulation. Ultracentrifugation, filtration centrifugation, and/or gel permeation chromatography can all be used to get these results.

b) **Centrifugation filtration:**

With traditional centrifugation processes, ultra-free or ultra-sort filters are utilized. Centrifugation can be used to determine the degree of encapsulation. filtration/ultracentrifugation of the SLN suspension, determination of the amount of drug remaining in the supernatant, or by dissolving the precipitate in a solvent. appropriate and subsequent analysis[34][3][35].

c) **Drug Release Principles**[3][32][12]:

The following are the general principles of drug release from lipid nanoparticles:

- The drug release and drug distribution coefficient have an inverse relationship.
- Drug release is increased due to the bigger surface area created by lower nanometer particle sizes.
- If the drug is equally disseminated in the lipid matrix, slow drug release can be achieved. The type of SLN and drug entrapment model will determine this.
- The lipid crystallinity behavior and high drug mobility help to allow rapid drug release. The degree of crystallization and the mobility of the medication have an inverse connection.
- Fast release is aided by a large surface area, a high diffusion coefficient due to small molecule size, low matrix viscosity, and a short drug diffusion distance.

V. STORAGE STABILITY OF SLN

[12][33]:

Observing changes in zeta potential, particle size, drug content, morphology, shape, and viscosity over time can be used to assess the physical properties of SLN during long-term storage. External factors like light and temperature appear to play a role in long-term stability. To maintain physical stability, the zeta potential should normally be greater than 60 mV for dispersion.

- 4°C – most favorable storage temperature.

- 20°C - Does not clump or loss of drug during long-term storage.
- 50°C – Particle size increased rapidly.

VI. IN VITRO AND EX VIVO METHODS FOR THE EVALUATION OF DRUG RELEASE FROM THE SLNS[5][36]:

For SLN, a significant range of medicines have been investigated, including hydrophilic compounds. The following are some of the techniques used to investigate drug release in vitro:

- Proliferating cells coexist using synthetic or biological membranes
- Diffusion process for dialysis bags.
- Dialysis bag procedure in reverse
- Centrifuge ultrafiltration or shaking followed by ultracentrifugation

VII. DRUG RELEASE IN VITRO[3]:

a) Dialysis tubing:

A dialysis tube can be used for in vitro medication release. Fill a sealed dialysis tube with the solid lipid nanoparticle dispersion. At room temperature, the dialysis bag is dialyzed against an acceptable solvent medium; samples are obtained from the dissolving media at appropriate time intervals, centrifuged, and tested for drug content using appropriate analytical procedures[37][3][38].

b) Reverse dialysis:

Several tiny dialysis bags containing 1ml of dissolving medium are inserted into the SLN dispersion in this procedure. The SLN is then placed in the medium[3][37]

VIII. ADMINISTRATION ROUTE OF SLN:

1. Oral administration
2. Parenteral administration
3. Rectal administration
4. Respiratory administration
5. Nasal administration
6. Topical administration
7. Ocular administration

i. Oral administration:

The controlled release SLNs behavior allows bypassing the encapsulated medications' stomach and intestinal breakdown, as well as their probable absorption and transport through the intestinal mucosa. The stability of colloidal carriers in gastrointestinal fluids, on the other hand, is

critical in predicting their suitability for oral administration [3][39].

ii. Parenteral administration:

Peptide and protein preparations are widely available in the market for parenteral administration. Due to enzymatic degradation in the gastrointestinal tract, traditional oral delivery is not viable. The drug's negative effects are reduced with parenteral administration, including enhanced bioavailability. This system is particularly suitable for drug targeting [32][37].

iii. Rectal administration:

When immediate pharmacological effect is desired, parenteral or rectal delivery may be preferable. This route of administration is used in children due to its ease of administration[16].

iv. Respiratory administration:

Nebulization of SLN containing anti-tuberculosis, anti-asthma, and-passive cancer drugs has been observed to improve to better regulate pulmonary action, increase medication absorption and reduce dosage frequency [32][40].

v. Nasal administration:

The nasal route of administration is recommended because it allows for quick absorption and initiation of medication activity, avoiding gastrointestinal drug degradation and inadequate transport between epithelial cell layers[3][37].

vi. Topical administration:

In addition to the properties of a colloidal carrier system, SLN is a colloidal carrier system of great interest for use on the skin due to its various desired effects on the skin. Because it is made up of non-irritating and non-toxic lipids, it is especially good for damaged or inflamed skin [3][41][36].

vii. Ocular administration:

The compatibility and mucoadhesive qualities of SLN effective implementation contact with the ocular mucosa and extend the drug's residence duration in the cornea, allowing it to target ophthalmic drugs more effectively[33].

IX. APPLICATIONS OF SLNS

[42][8][38][16][28]:

A. SLN as gene vector carrier:

Cationic solid lipid nanoparticles have proven themselves well over the past few decades.

Through ionic interactions, it can directly attach to DNA and disrupt gene transition. Gene vectors can be assembled using SLNs. SLN carries genetic material/peptides like as DNA, plasmid DNA, and other nucleic acid cationic solid lipid nanoparticles are promising non-viral gene delivery vehicles appropriate for systemic usage, according to numerous recent investigations. The aptitude of cationic SLNs to plasmid DNA (pDNA) condensing and transfer it into neuroblastoma cells was examined in relation to their design.

B. SLNs as a solid tumor targeted carrier:

Among the most difficult aspects of drug distribution is getting pharmaceuticals to where they're needed in the body while avoiding side effects in organs that aren't afflicted. The non-restrictive toxicity of chemotherapy medicines hinders them from reaching their full therapeutic potential. Topical or targeted medicine administration increases local medicine concentration and gives a more detailed description treatment strategy. Specific nanoparticles serve as tools for implementing strategy. SLS has been suggested for use as a medication carrier in the treatment of neoplasia. Tumor targeting is achieved with SLNs contain with drugs such as camptothecin, methotrexate, and paclitaxel.

C. SLN in antitubercular chemotherapy:

A significant lung infection caused by Mycobacterium TB is another noteworthy like as SLN-based medication delivery of antimicrobials to the lungs for tuberculosis treatment. Anti-tuberculosis drugs, like as the SLN system containing rifampicin, isoniazid, and pyrazinamide, have reduced dosing frequency and improved patient compliance. To prepare solid lipid nanoparticles containing an anti-tuberculosis drug were prepared using solvent diffusion technology.

D. SLNs for topical use:

Corticosteroids are drugs that are often used to treat skin diseases like eczema and psoriasis. Topical SLN products show great potential in treating skin conditions by targeting corticosteroids at skin conditions while reducing systemic drug absorption. Topical medicine offers the advantage of administering the medication directly to the afflicted area. Topical therapies offer the benefit of direct delivery of medicine to the point of action when applied to the afflicted area. SLNs are used for topical applications of various drugs such as flurbiprofen, isotretinoin, and vitamin A. Lipid nanoparticles containing isotretinoin have

been developed for topical drug delivery. Preparation of topical SLN gels containing flurbiprofen has the a possible benefit of supplying the medication delivered straight to the point of action, as a result, tissue concentrations are higher.

E. SLN as cosmetics:

Cosmeceuticals are emerging as a target for this carrier. Support systems such as SLN and NLC (Nanostructured Lipid Support) have been designed to meet production requirements such as quality, scalability and low cost, simple technology, verification, etc. SLN is used as an active carrier in the manufacture of sunscreens, as well as in molecular sunscreens and UV blockers. Many properties of SLN have been reported to be useful for skin application in cosmetics. For example, occlusive properties, promote skin hydration, control release, increase skin penetration and prevent systemic absorption. The first two cosmetic products with lipid nanoparticles were introduced in 2005, and there are now over thirty cosmetic preparations with lipid nanoparticles on the market.

X. CONCLUSION

SLNs as a carrier of colloidal drugs combine the advantages of polymeric nanoparticle liposome and fat emulsion.

Many studies on Solid lipid nanoparticles as carrier systems have simplified the approach the solid lipid nanoparticles are minor systems with a complex matrix of lipid composition and microstructure of internal particles that can potentially colloidal drug carriers and pharmacologically complex active ingredients or molecules such as peptides hormones, proteins, genes, deoxyribonucleic acid, ribonucleic acid and viral vectors for targeting to achieve their respective benefits.

Other than particle size determination, proper characterization of complex surfactant/lipid dispersions necessitates the use of many analytical approaches.

In summary, solid lipid nanoparticle is a complicated system with clear merits and demerits compared to other colloidal systems. In the scientific community, new dimensions and meanings are still coming together, especially in nanoscale systems to make this system an industrially viable and commercially stable technology in the field of SLN technology. In vitro and in vivo research are needed to better

understand the structure and/or dynamics of solid lipid nanoparticles in a molecular location.

REFERENCES:

- [1] S. Mukherjee, S. Ray, R.S. Thakur, Solid lipid nanoparticles: A modern formulation approach in drug delivery system, *Indian J. Pharm. Sci.* (2009). <https://doi.org/10.4103/0250-474X.57282>.
- [2] N. Jamshidi, M.M. Cohen, The Clinical Efficacy and Safety of Tulsi in Humans: A Systematic Review of the Literature, Evidence-Based Complement. *Altern. Med.* (2017). <https://doi.org/10.1155/2017/9217567>.
- [3] P. Ekambaram, A. Abdul, H. Sathali, K. Priyanka, SOLID LIPID NANOPARTICLES: A REVIEW, *Sci. Revs. Chem. Commun.* 2 (2012) 80–102.
- [4] K.W. Kang, M.K. Chun, O. Kim, R.K. Subedi, S.G. Ahn, J.H. Yoon, H.K. Choi, Doxorubicin-loaded solid lipid nanoparticles to overcome multidrug resistance in cancer therapy, *Nanomedicine.* 6 (2010) 210–213. <https://doi.org/10.1016/J.NANO.2009.12.006>.
- [5] F.Q. Hu, Y. Hong, H. Yuan, Preparation and characterization of solid lipid nanoparticles containing peptide, *Int. J. Pharm.* 273 (2004) 29–35. <https://doi.org/10.1016/J.IJPHARM.2003.12.016>.
- [6] D. Pandurangan, P. Bodagala, V. Palanirajan, S. Govindaraj, Formulation and evaluation of voriconazole ophthalmic solid lipid nanoparticles in situ gel, *Int. J. Pharm. Investig.* 6 (2016) 56. <https://doi.org/10.4103/2230-973X.176488>.
- [7] G. Abdelbary, R.H. Fahmy, Diazepam-loaded solid lipid nanoparticles: design and characterization, *AAPS PharmSciTech.* 10 (2009) 211–219. <https://doi.org/10.1208/S12249-009-9197-2>.
- [8] R.H. Müller, K. Mäder, S. Gohla, Solid lipid nanoparticles (SLN) for controlled drug delivery - A review of the state of the art, *Eur. J. Pharm. Biopharm.* (2000). [https://doi.org/10.1016/S0939-6411\(00\)00087-4](https://doi.org/10.1016/S0939-6411(00)00087-4).
- [9] R. Article, M.K. Sarangi, S. Padhi, SOLID LIPID NANOPARTICLES-A REVIEW, (2016).
- [10] Ramteke KH, Joshi SA, Dhole SN, Solid Lipid Nanoparticle: A Review, *IOSR J. Pharm.* 2 (n.d.) 34–44.
- [11] I.P. Kaur, R. Bhandari, S. Bhandari, V. Kakkar, Potential of solid lipid nanoparticles in brain targeting, *J. Control. Release.* 127 (2008) 97–109. <https://doi.org/10.1016/J.JCONREL.2007.12.018>.
- [12] A. Zur Mühlen, C. Schwarz, W. Mehnert, Solid lipid nanoparticles (SLN) for controlled drug delivery--drug release and release mechanism, *Eur. J. Pharm. Biopharm.* 45 (1998) 149–155. [https://doi.org/10.1016/S0939-6411\(97\)00150-1](https://doi.org/10.1016/S0939-6411(97)00150-1).
- [13] P.P. Reddy, A MODERN REVIEW ON SOLID LIPID NANOPARTICLES AS NOVEL CONTROLLED DRUG DELIVERY SYSTEM, *Int. J. Res. Pharm. Nano Sci.* 3 (2014) 313–325.
- [14] O.T.P. Kim, M.D. Le, H.X. Trinh, H. V. Nong, In silico studies for the interaction of tumor necrosis factor-alpha (TNF- α) with different saponins from Vietnamese ginseng (*Panax vietnamsis*), *Biophys. Physicobiology.* (2016). https://doi.org/10.2142/biophysico.13.0_173.
- [15] A. Garud, D. Singh, N. Garud, Solid Lipid Nanoparticles (SLN): Method, Characterization and Applications, *Int. Curr. Pharm. J.* (2012). <https://doi.org/10.3329/icpj.v1i11.12065>.
- [16] V. Teja, V. Chowdary, Y. Raju, A glimpse on solid lipid nanoparticles as drug delivery systems, *J. Glob. Trends Pharm. Sci.* 5 (2014) 1649–1657.
- [17] M. Trotta, F. Debernardi, O. Caputo, Preparation of solid lipid nanoparticles by a solvent emulsification-diffusion technique, *Int. J. Pharm.* 257 (2003) 153–160. [https://doi.org/10.1016/S0378-5173\(03\)00135-2](https://doi.org/10.1016/S0378-5173(03)00135-2).
- [18] R H Muller, M. Radtke, S.A. Wissing, Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations, *Adv. Drug Deliv. Rev.* 54 (2002) 131–155.
- [19] Gassco MR., Date of Patent: METHOD FOR PRODUCING SOLID LIPID MICROSPHERES HAVING ANARROWSIZE, United State Pat. (1993).
- [20] M. Stuchlík, S. Zák, Lipid-based vehicle for oral drug delivery., *Biomed. Pap. Med. Fac. Univ. Palacky. Olomouc. Czech. Repub.* 145 (2001) 17–26. <https://doi.org/10.5507/BP.2001.008>.

- [21] Y.J. Chen, R.X. Jin, Y.Q. Zhou, J. Zeng, H. Zhang, Q.R. Feng, Preparation of solid lipid nanoparticles loaded with Xionggui powder-supercritical carbon dioxide fluid extraction and their evaluation in vitro release, *Zhongguo Zhongyao Zazhi*. 31 (2006) 376–379.
- [22] A. Bargoni, R. Cavalli, O. Caputo, A. Fundarò, M.R. Gasco, G.P. Zara, Solid Lipid Nanoparticles in Lymph and Plasma After Duodenal Administration to Rats, *Pharm. Res.* 1998 155. 15 (1998) 745–750. <https://doi.org/10.1023/A:1011975120776>.
- [23] V.A. Duong, T.T.L. Nguyen, H.J. Maeng, Preparation of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers for Drug Delivery and the Effects of Preparation Parameters of Solvent Injection Method, *Molecules*. 25 (2020). <https://doi.org/10.3390/MOLECULES25204781>.
- [24] T.B.A.R. on solid L.N.R.J.P. and T. 2012 D. Thulasi Ram, Subhashis Debnath, M. Niranjan Babu, T. Chakradhar Nath, (PDF) A review on solid lipid nanoparticles, (n.d.).
- [25] K. Mäder, Solid lipid nanoparticles as drug carriers, *Nanoparticulates as Drug Carriers*. (2006) 187–212. https://doi.org/10.1142/9781860949074_0009.
- [26] S. Sonali, I. Yogita, G. Sharda, C. Amit, A. Shital, Solid Lipid Nanoparticles: A Modern Formulation Approach in Drug Delivery System, *Int. J. Creat. Res. Thoughts*. 9 (2021) 2320–2882.
- [27] S. Meraj Sultana, A. Seetha Devi, home page: www.ajrcps.com Syed Meraj Sultana and Alla Seetha Devi, *Asian J. Res. Chem. Pharm. Sci. J.* 7 (2019) 263–277.
- [28] R. Pandey, S. Sharma, G.K. Khuller, Oral solid lipid nanoparticle-based antitubercular chemotherapy, *Tuberculosis (Edinb)*. 85 (2005) 415–420. <https://doi.org/10.1016/J.TUBE.2005.08.009>.
- [29] K. Sawant, S. Dodiya, Recent Advances and Patents on Solid Lipid Nanoparticles, *Recent Pat. Drug Deliv. Formul.* 2 (2008) 120–135. <https://doi.org/10.2174/187221108784534081>.
- [30] R.K. Subedi, K.W. Kang, H.K. Choi, Preparation and characterization of solid lipid nanoparticles loaded with doxorubicin, *Eur. J. Pharm. Sci.* 37 (2009) 508–513. <https://doi.org/10.1016/J.EJPS.2009.04.008>.
- [31] R. Paliwal, S.R. Paliwal, R. Kenwat, B. Das Kurmi, M.K. Sahu, Solid lipid nanoparticles: a review on recent perspectives and patents, *Expert Opin. Ther. Pat.* 30 (2020) 179–194. <https://doi.org/10.1080/13543776.2020.1720649>.
- [32] M. Üner, G. Yener, Importance of solid lipid nanoparticles (SLN) in various administration routes and future perspectives, *Int. J. Nanomedicine*. 2 (2007) 289.
- [33] W. Mehnert, K. Mäder, Solid lipid nanoparticles: Production, characterization and applications, *Adv. Drug Deliv. Rev.* 47 (2001) 165–196. [https://doi.org/10.1016/S0169-409X\(01\)00105-3](https://doi.org/10.1016/S0169-409X(01)00105-3).
- [34] R.M. Barbosa, C.M.G. Da Silva, T.S. Bella, D.R. De Araújo, P.D. Marcato, N. Durán, E. De Paula, Cytotoxicity of solid lipid nanoparticles and nanostructured lipid carriers containing the local anesthetic dibucaine designed for topical application, *J. Phys. Conf. Ser.* 429 (2013). <https://doi.org/10.1088/1742-6596/429/1/012035>.
- [35] N.A. Al Haj, R. Abdullah, S. Ibrahim, A. Bustamam, Tamoxifen Drug Loading Solid Lipid Nanoparticles Prepared by Hot High Pressure Homogenization Techniques, *Am. J. Pharmacol. Toxicol.* 3 (2008) 219–224. <https://doi.org/10.3844/AJPTSP.2008.219.224>.
- [36] K. Soni, B. Kaur Kukereja, M. Kapur, K. Kohli, Lipid Nanoparticles: Future of Oral Drug Delivery and their Current Trends and Regulatory Issues, Available Online *Int. J. Curr. Pharm. Rev. Res.* 7 (2015) 1–18.
- [37] A. Lippacher, R.H. Müller, K. Mäder, Preparation of semisolid drug carriers for topical application based on solid lipid nanoparticles, *Int. J. Pharm.* 214 (2001) 9–12. [https://doi.org/10.1016/S0378-5173\(00\)00623-2](https://doi.org/10.1016/S0378-5173(00)00623-2).
- [38] S. Sultana, S. Mohammed, As. Begum, REVIEW OF SOLID LIPID NANOPARTICLES, *Int. J. Res. Trends Innov.* 5 (2020) 88.
- [39] A. Bakthavachalam, P.N. Remya, N. Damodharan, Review on solid lipid nanoparticles, *Res. J. Pharm. Technol.* 13 (2020) 4430. <https://doi.org/10.5958/0974-360X.2020.00783.0>.
- [40] C.S. Maia, W. Mehnert, M. Schäfer-Korting, Solid lipid nanoparticles as drug carriers for



- topical glucocorticoids, *Int. J. Pharm.* 196 (2000) 165–167.
[https://doi.org/10.1016/S0378-5173\(99\)00413-5](https://doi.org/10.1016/S0378-5173(99)00413-5).
- [41] S.P. Vyas, R.K. Khar, Targeted & controlled drug delivery : novel carrier systems, 1st ed., CBS Publishers & Distributors, New Delhi India, 2004.
- [42] K. Ruckmani, M. Sivakumar, P.A. Ganeshkumar, Methotrexate loaded solid lipid nanoparticles (SLN) for effective treatment of carcinoma, *J. Nanosci. Nanotechnol.* 6 (2006) 2991–2995.
<https://doi.org/10.1166/JNN.2006.457>.