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REVIEW ON FORMULATION AND EVALUATION OF SOLID LIPID NANOPARTICLES

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ABSTRACT

Significance Solid lipid nanoparticles (SLN) are a novel drug delivery system that has attracted increasing interest and have been used to deliver many types of drugs since their introduction in the 1990s. SLNs have been paid attention in the field because of its special properties such as good bio-compatibility, controlled releasing and more stable. The abstract briefly covers areas of the SLN formulation, focusing on factors such as lipid composition, surfactants and approaches used for the preparation influencing particle size, drug loading etc. We summarize the influence of these parameters on the pharmacokinetics and therapeutic potential of SLN-incorporated drugs. The review also discusses the different techniques used for characterizing SLNs in relation to their function as one of the quality tests imposed on this type of product symbols use script. To sum up, this review will help to accumulate the current state-of-art regarding SLNs on how they will be attained or manufactured along with its characterization and perspective uses in pharmaceutical research. A literature review of existing research serves as a primary resource for investigators and clinicians looking to negotiate the complex reality of SLN-based drug delivery systems. A meticulous review of this paper will certainly benefit the scientists engaged in SLN-based drug delivery systems.

KEYWORDS: Solid lipid nanoparticles, Methods of preparation, Evaluation, Route of administration, Application.

INTRODUCTION

A Lipid Nanoparticle is a spherical particle of an average diameter that ranges from 10 to over 1000 nanometers in size. SLN have solid lipid core matrix that able to solubilize lipophilic molecules. Surfactant stabilizes the lipid core. The choice of emulsifier is related to the administration routes, and it should be more restricted for paraenteral administrations. In this context lipid means triglycerides, digylcerides, monoglycerides and fatty acids along with it includes steroids and waxes also. All classes emulsifiers were tried to stabilize the lipid dispersion. When combined, the emulsifiers could perhaps prevent particle agglomeration more effectively.[1]

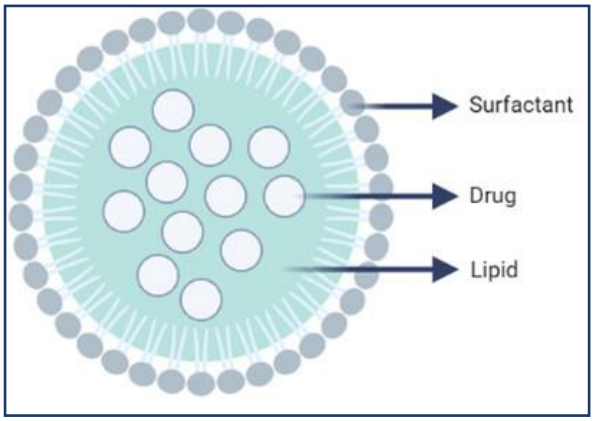

Figure 1: Structure of SLNs.

TYPES OF SOLID LIPID NANOPARTICLES

SLNs can be divided into 3 basic types on the basis of drug loading;

1. Homogeneous matrix
2. Drug-enriched shell
3. Drug-enriched core

Homogeneous matrix

Solid lipid nanoparticles SLNs with homogeneous matrix have uniform component distributions within these nanoscale drug delivery systems. In order to form NDLs, three essential components are required such as solid lipids themselves (medication/ active ingredients), a stabilizing surfactant and an optional co-surfactant. Homogeneity can be achieved only through proper formulation and processing strategies like high-pressure homogenization, ultrasonication which is important for uniform drug loading, release rate and stability. This guarantees controlled drug release functionality, and also helps to avoid problems with crystallization or phase separation.

Drug-enriched shell

Drug-enriched shell solid lipid nanoparticles are a type of nanoscale drug delivery system in which the drug or active component is primarily concentrated in the SLNs' surface layer or outer shell. The medication can be released gradually from the outer layer while the inner core contains additional lipid or other components which enables precise control over drug release kinetics. This method is helpful for applications needing targeted or sustained drug release and can improve the therapeutic efficacy of the encapsulated drug.

Drug-enriched core

The drug/active is present in the central or inner core of SLNs, within a definite particle area known as Drug-enriched Core. This design allows for a slow and controlled drug release since the drugs need to diffuse through the lipid matrix before they can be released. The lipid core can stabilize and protect the drug from being degraded. It is ideal for protecting sensitive drugs or extended drug release.[2]

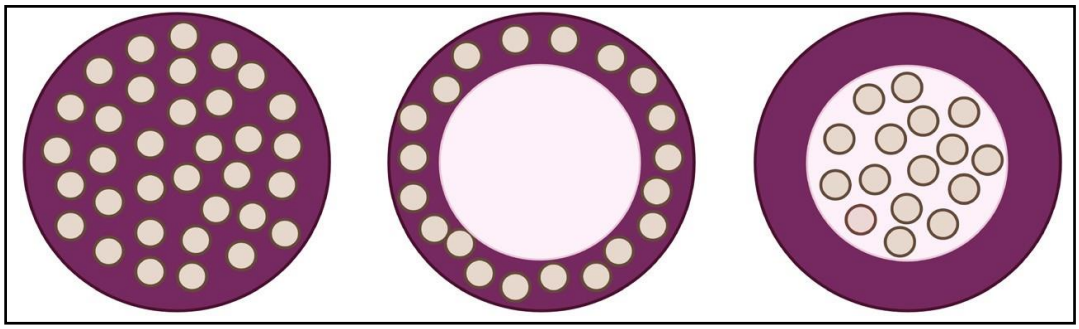

Figure 2: Illustration of drug incorporation model of SLN: Homogenous matrix of solid solution(left); Drug-enriched shell(middle); and Drug-enriched core(right).

ADVANTAGES[3]

Enhanced Drug Stability: Compared to conventional formulations, the solid lipid matrix improves stability and shelf life by shielding medications from degradation.

Enhanced Bioavailability: By improving drug absorption via oral, topical, and parenteral administration, SLNs can raise bioavailability and improve therapeutic efficacy.

Controlled Release: SLNs enable controlled and sustained drug release, allowing for reduced dosing frequencies and maintaining therapeutic levels over an extended period.

Biocompatibility and Safety: The risk of side effects is reduced because solid lipids used in SLNs are typically non-toxic and biocompatible.

Targeted Drug Delivery: By adding ligands, antibodies or peptides to the surface of SLNs, one can actively target particular cells or tissues, lessen side effects, and enhance treatment results.

Ease of Manufacturing: Since they can be prepared in a variety of ways, SLNs are reasonably simple to produce in large quantities.

LIMITATION

The flawless crystalline structure of SLN has several drawbacks as well, including a low drug loading efficiency and the potential for drug expulsion due to crystallization during storage.

1. Lipid dispersions have high water content.
2. Limited transdermal medication delivery.
3. Hydrophilic drug loading capacity is constrained.
4. Polymorphic change.
5. Increase in particle size while being storage.
6. Lipid dispersion gelation.
7. The toxicity of lipid Nanoparticle on retinol cells has not yet been thoroughly investigated.

KEY CONSIDERATIONS IN DESIGNING SLNs

Essential ingredients like lipids (matrix materials), emulsifiers, co-emulsifiers and water may be added to the formulation of Solid Lipid Nanoparticles (SLNs) in order to improve stability and accomplish targeted drug delivery.

Selection of lipid

The selection of lipid materials for the development of oral pharmaceutical dosage forms has been the subject of recent reviews. It is essential that lipid matrices have particular characteristics when creating solid lipid nanoparticles (SLNs) for intravenous (iv) delivery.[4]

Biocompatibility and Biodegradability: Lipid materials must demonstrate biocompatibility to ensure the absence of adverse effects upon IV administration. Additionally, biodegradability is crucial for the eventual breakdown of lipid nanoparticles within the body.

Stability: Ensuring stability is paramount to prevent degradation during storage and administration, safeguarding the Integrity of drug-loaded nanoparticles and maintaining a consistent drug release profile.[5]

Sufficient Loading Capacity: The lipid matrix should possess the capacity to encapsulate an adequate amount of the drug, guaranteeing the achievement of therapeutic concentrations.

Controlled Release: The lipid material needs to facilitate controlled and sustained release of the encapsulated drug, a key factor in achieving prolonged therapeutic effects and minimizing side effects.

Sterilizability: Lipid materials intended for IV administration should be amenable to sterilization methods, such as filtration or heat sterilization, to ensure product safety.

Particle Size Control: Precise control over particle size is essential for SLNs to behave optimally in the bloodstream. Smaller particle sizes are generally preferred to minimize interactions with the vascular system and enhance drug delivery to target tissues.

Surface Charge: SLNs with a neutral or slightly negative surface charge are preferred to minimize non-specific interactions with blood components, influencing their stability and biological compatibility.

Ease of Scale-Up and Manufacturing: Chosen lipid materials should facilitate scalable manufacturing processes, enabling the production of large quantities of SLNs with consistent quality.

Targeted Drug Delivery: If targeted drug delivery is a goal, lipid matrices should be compatible with surface modification techniques, such as ligand conjugation, to enhance the nanoparticles targeting capabilities.

Clinical Acceptance: Lipid materials with a history of safe use in pharmaceuticals are favored, streaming the regulatory approval process.

Loading capacity and intended use are important factors to take into account when selecting a drug carrier system. Complex glycerides, such as hard fats, melt at body temperature, making them inappropriate for applications requiring controlled release. Longer hydrocarbon chains make glycerides more lipophilic, which increases the solubility of lipophilic drugs in lipid melts containing longer fatty acid chains. The degree of crystallinity is one of the factors that must be taken into account when choosing lipids for the formulation of solid lipid nanoparticles (SLNs).[7]

Selection of emulsifier

For solid lipid nanoparticles (SLNs), the choice of emulsifier needs to meet a number of important requirements in order to guarantee peak performance. In addition to being non-toxic and compatible with other excipients, the emulsifier should be able to cover the surface of the SLNs and produce the desired particle size with a small amount of input. Furthermore, the fate of the emulsifier in vivo is taken into account. The poloxamer series, for example, has the capacity to give SLNs long circulating characteristics, which hinder uptake by the reticulo-endothelial system (RES) and enable passive targeting. However, polysorbate 80-coated SLNs exhibit enhanced medication delivery to the brain. The literature makes clear that the emulsifier type and quantity, preparation technique, and sterilization procedure such as autoclaving can all affect the stability and size of the particles. To sufficiently cover the surface of the nanoparticles, the right amounts of emulsifier are essential. An increase in particle size and particle aggregation may result from insufficient amounts. On the other hand, surfactant-related toxic effects, burst release seen in SLN release studies, and a decline in entrapment efficiency can all be avoided by avoiding excess emulsifier. Trotta and colleagues examined how emulsifiers affected the size of solid lipid nanoparticles (SLNs). Trotta were able to create solid lipid nanoparticles (SLNs) by using glyceryl monostearate in conjunction with a variety of emulsifiers.[8]

Selection of co-emulsifier

Different from conventional emulsifiers, phospholipids added to the formulation of solid lipid nanoparticles (SLNs) display unique properties. They do not form highly dynamic micelles nor are they soluble in the continuous phase. Excess phospholipid molecules have a tendency to group together and form tiny, primarily unilamellar vesicles during the homogenization process. When these phospholipid molecules are attached to vesicles, their mobility is restricted. Thus, when solid lipids recrystallize, they are unable to quickly cover recently formed interfaces. Phospholipid molecules low mobility increases the possibility of an abrupt emulsifier shortage on the particle surface, which can cause particle aggregation and a rise in the size of SLN particle. Co-emulsifiers like tyloxapol a nonionic polymer and an ionic glycocholate are used to solve this problem. These emulsifiers that dissolve in water have the capacity to form micelles. Interestingly, compared to vesicles, polymer molecules can diffuse to the particle surface more quickly. Micelles are extremely dynamic colloidal structures that serve as storage units. However, because of the potential for toxicity, it is advised against using surfactants that distribute quickly, such as sodium lauryl sulphate. Co-emulsifier

selection must be done carefully in order to guarantee the stability and security of SLN formulations.[9]

Solubility studies

Understanding the drug's affinity for the nanoparticle matrix and determining the ideal drug-to-lipid ratio are critical steps in determining the solubility of drugs in lipids or lipid combination. Solubility studies are a common part of studying solid lipids, and they are typically performed by heating the lipids to a temperature that is 10°C above their melting point. Small doses of the medication are added gradually throughout the procedure until lipid saturation is achieved. When there is an excess of solid medication that lasts longer than eight hours, saturation is recognized. This technique helps to design nanoparticle formulations with improved stability and drug-loading capacities by offering insightful information about how drugs and lipids interact.[10]

METHODS OF PREPARATION OF SLN

Solid Lipid Nanoparticle can be prepared by different methods.

1. HIGH SHEAR HOMOGENIZATION

Solid lipid nanodispersion was prepared by adopting first high shear homogenization. User-Agent Matching and IP Address Targeting: These are the most common techniques used to detect fake traffic. Yet, addition of microparticles changes the quality of the dispersion. Melt emulsification to get SLN was by high-speed homogenized method. The lipids were trimyristin and tripalmitin, a mixture of mono-, di-, and triglycerides, Witepsol W35, Witepsol H35 with glycerolphosphate, or poloxamer 188 as steric stabilizers at a concentration of 0.5% w/w. The optimum SLN quality was obtained at varying working conditions in Witepsol® W35 dispersions: 8 minutes of stirring at 20,000 rpm, coupled with an additional cooling phase of 10 minutes, before standardizing with a mixing speed of 5000 rpm to reach room temperature. Under those conditions with mixtures with Dynasan 116, the optimal mixing conditions were mixing for 10 min at 25,000 rpm, cooling the batch in cold water to about 16°, then re-homogenization in up to 5 min at ca speed 12 or above before feeding.[11] At the higher stirring rate, further improvement in the polydispersity index is observed, but it has no significant effect on particle size.

a) Hot homogenization

Hot homogenization occurs at a temperature above the melting point of the lipids. The emulsion mixing takes place in quite a similar manner. First, a pre-emulsion is prepared by simply blending melted lipid with aqueous emulsifier of matching temperature by high shear mixer such as silversion-type homogenizer. The quality of the pre-emulsion greatly influences the quality of the final product; therefore, droplets in the range of a few micrometers are best obtained. High pressure homogenization of the pre-emulsion takes place above the melting point of the lipids. Higher temperatures are generally associated with smaller particle sizes, as a result of the lower viscosity of the lipid phase, but may also accelerate degradation of the drug and carrier. In general, less than more passes, 3-5, usually produce better products. The high-pressure processing virtually leads to an increase of the sample temperature by 10°c at 500 bar.[12] Usually, 3-5 cycles of homogenization at 500-1500 bar are enough. However, increasing the homogenization process increases the size of particles, which might occur due to the coalescence of the particles because of the high kinetic energy.

b) Cold homogenization

Homogenization is performed in the cold state of a solid lipid, and hence it is comparable to milling a suspension under higher pressure. Effective temperature control has to be performed in order to keep the solid state of the lipid during homogenization. Cold homogenization was in turn developed to counter several problems of the hot homogenization technique. These include higher temperature leads to more rapid degradation of the drug, eventual loss of the drug in water due to its mixing and indefinite transformation of the fat form due to the complicated crystallization step of the nanoemulsion; hence, different kinds of transformation can take place or very viscous melts. As explained, the initial step of preparing with this technique involves dissolution or mixing of the drug in the melted fat, whereas cooling of the melt of the drug with the aid of dry ice or liquid nitrogen assists in distributing the drug uniformly in the fat; afterward, grinding with a ball or mortar crushes the resultant solid lipid containing the drug into smaller particles. 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, cold homogenized samples generally

have larger particle sizes and a wider range of size compared to hot homogenization. Lipid/drug mix in the first step to melt a homogeneous approach to reduce the heat input on the sample—however, heating still occurs.[13]

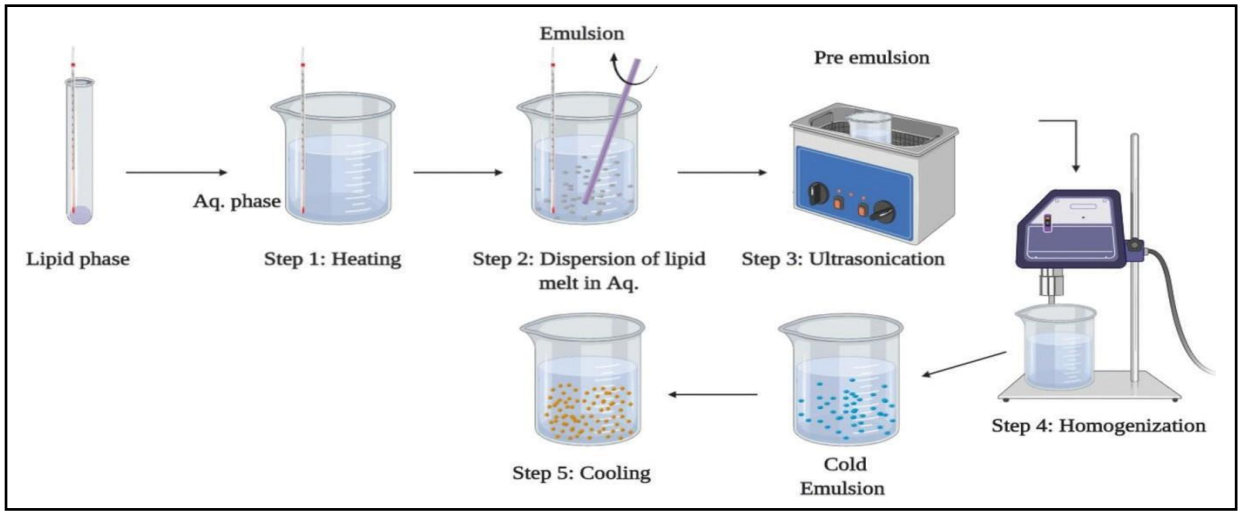

Figure 3: Hot Homogenization Technique.

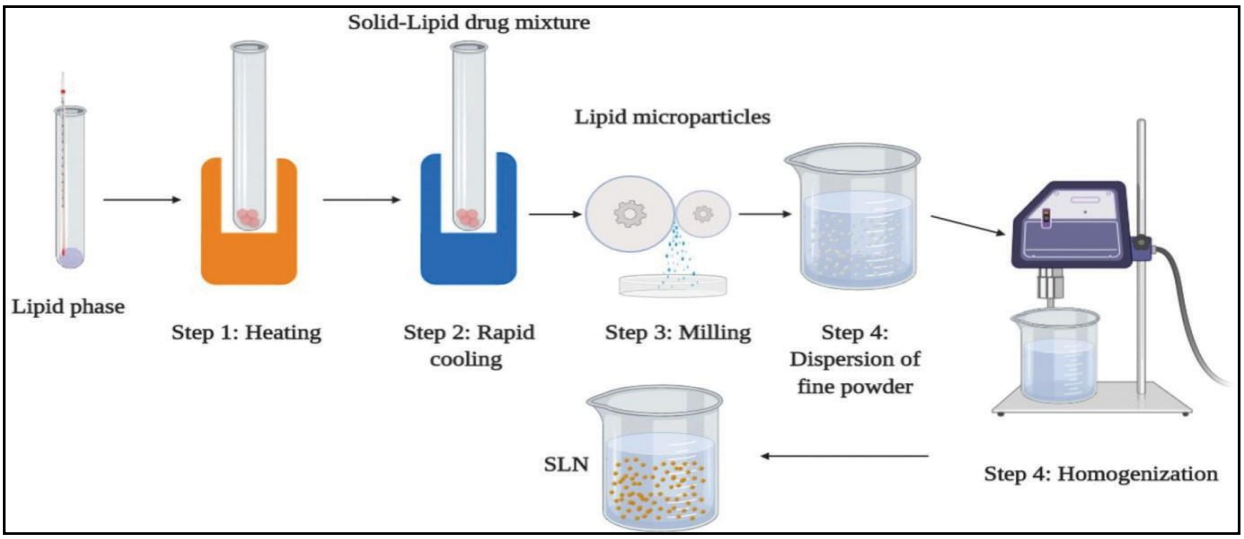

Figure 4: Cold Homogenization Technique.

2. ULTRASONICATION OR HIGH SPEED HOMOGENIZATION

SLN were also prepared by rapid mixing or applying ultrasound. One of the major advantages is that the involved equipment is available in practically every laboratory. The major drawback is that this preparation technique yields particles of different size, including larger particles. This may lead to physical instability such as particle growth during storage. Furthermore, there is a risk of metal contamination caused by the ultrasound, which is a severe problem concerning this technique. Thus, for the preparation of stable formulation,

different research groups have studied that high speed stirring along with ultrasonication is applied together, which is also carried out at high temperature.[14]

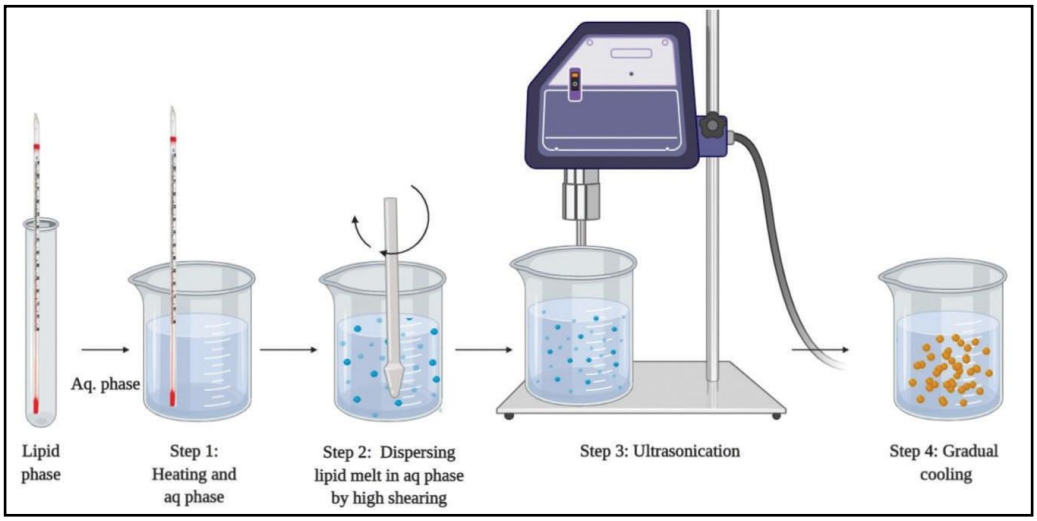

Figure 5: High shear homogenization or ultrasonication technique.

3. SOLVENT EMULSIFICATION OR EVAPORATION

This technique involves the dissolution of lipophilic material and hydrophobic drug in water immiscible organic solvents such as cyclohexane, toluene, and chloroform. The mixture is then emulsified in an aqueous phase through the use of high-speed homogenization. Immediately, the coarse emulsion is made to flow through a microfluidizer. Organic solvent is evaporated using a rotary evaporator with mechanical agitation at room temperature and reduced pressure. The main mastery of this technique is bypassing the thermal stress. Therefore, now there is possibility for the incorporation of highly thermo-labile drugs. The clear cut disadvantage is use of an organic solvent which may react with drug molecules.[15]

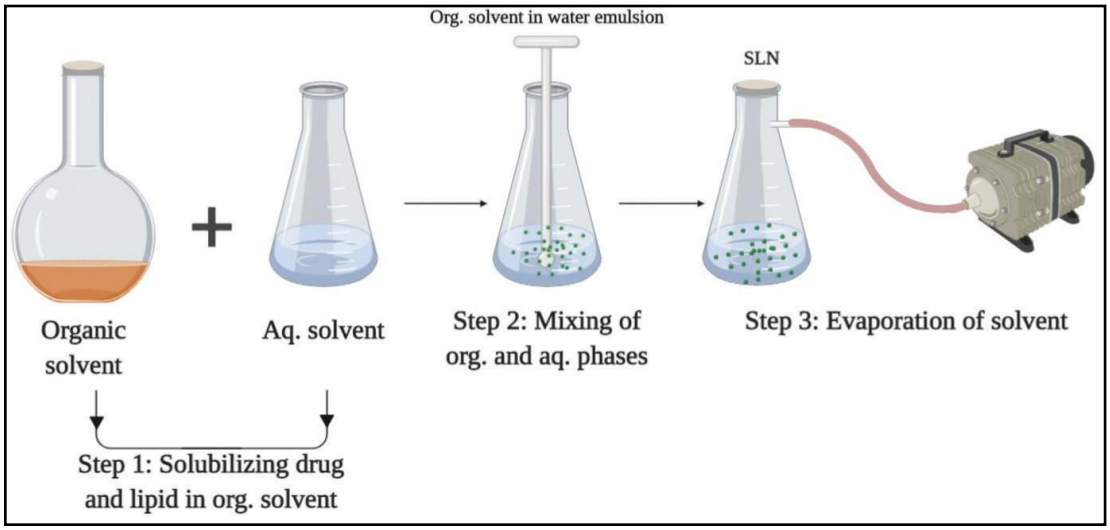

Figure 6: Solvent emulsification-evaporation technique.

4. SUPERCRITICAL FLUID TECHNIQUE [ScF]

This is comparatively an advanced technique of SLNs preparation. The supercritical fluid has some exclusive features, which can be changed by slight variation in the applied pressure. In this process, no organic solvents are used at all.[16] With an increase in pressure, its density as well as solvent capability increases, but flow rate remains the same. ScF is a substance above its pressure and critical temperature. The properties of the fluid under these conditions would be having: a density near that of a liquid, viscosity comparable to gases, diffusing more compared to most liquids in other words, between a liquid and a gas and which results in high mass-transfer rates. The techniques that can be employed include RESS- rapid expansion of supercritical solutions, supercritical antisolvent process, and PCA-precipitation with a compressed antisolvent process. There is also the generation of particles from gas-saturated solutions or suspensions and supercritical extraction from emulsions. For one to use the RESS technology, the drug in question should be well-soluble in ScCO2, That is the solvent. In this operation, the supercritical fluid is allowed to expand swiftly through a nozzle to transform the solute into micro or nanoparticles. The particle is controlled by three main controlling factors and the growth of the particles happens very fast. In an expansion chamber, a very diluted solution does not have much time available for growing the particles. According to griseofulvin pure powder was obtained using a cosolvent like methanol; it enhanced the solubility of the drug in ScCO2 by about 28 times. Griseofulvin nanoparticles in the size range 50−250 nm were prepared using a simple capillary nozzle. In PCA, the mist of the drug solution and compressed carbon dioxide is introduced into the chamber. The solution becomes over-saturated and small crystals are formed. A supercritical fluid that is a poor solvent for the drug is selected and introduced. The drug is mixed with the solvent. This solvent should be/miscible with the supercritical fluid. The supercritical fluids take all the solvent and then, when the drug solution is added to the supersaturated solution, the drug solution gets supersaturated. The drug forms fine crystals.[17] The main advantage of this technique is that the particles are obtained in the form of a dry powder instead of as a suspension.

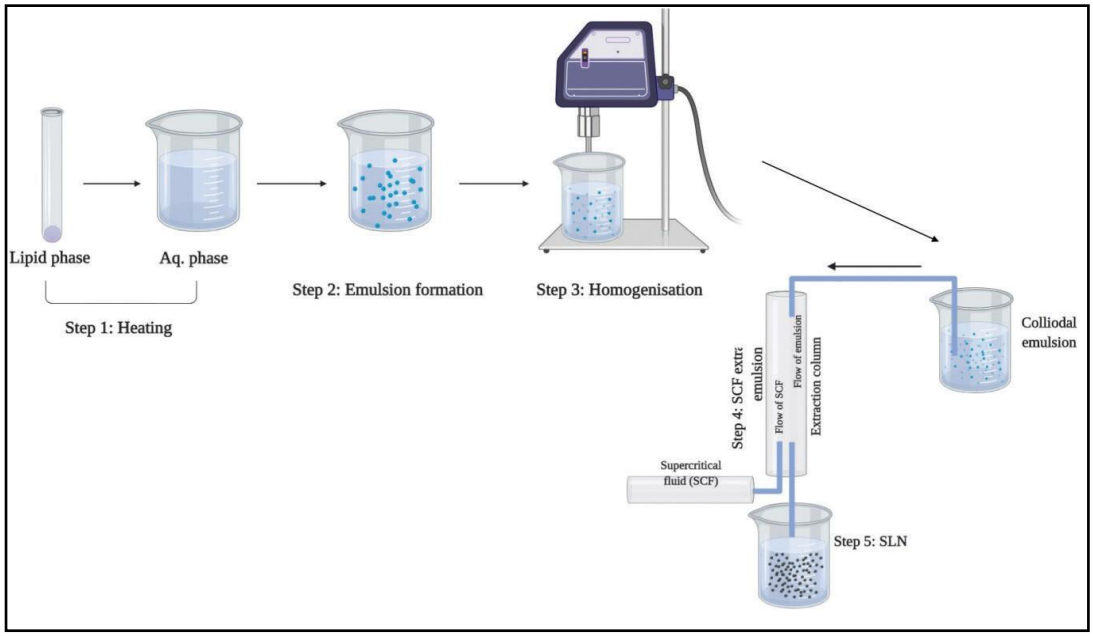

Figure 7: Supercritical Fluid Technique.

5. MICROEMULSION

The techniques of SLN preparation developed by Gasco and co-workers are based on the principle of dilution of microemulsions. They are prepared simply by stirring an optically transparent mixture normally at 65-70° made up of a low melting fatty acid (stearic acid), an emulsifier (polysorbate 20, polysorbate 60, soy phosphatidylcholine, and sodium taurodeoxycholate), co-emulsifiers (sodium monooctylphosphate) and water. The hot microemulsion is dispersed in cold water (2-3°) under stirring. Typical volume ratios of hot microemulsion to cold water range from 1:25 to 1:50. The microemulsion composition itself will critically determine the dilution process. As it was mentioned in the literature the droplet structure is already contained in the microemulsion and thus no energy is needed to achieve particle sizes below the micron range. Concerning the similarities of the production procedure of polymer nanoparticles described by French scientists, different mechanisms may be considered. Fessi produced polymer particles by dilution of polymer solutions in water.The particle size is critically determined by the velocity of the distribution processes. This indicates that nanoparticles were obtained only with solvents which distribute very rapidly into the aqueous phase, such as acetone, and larger particle sizes were obtained with more lipophilic solvents. The hydrophilic co-solvents of the microemulsion might play a similar role in the formation of the lipid nanoparticle as the acetone for the formation of polymer nanoparticle.[18]

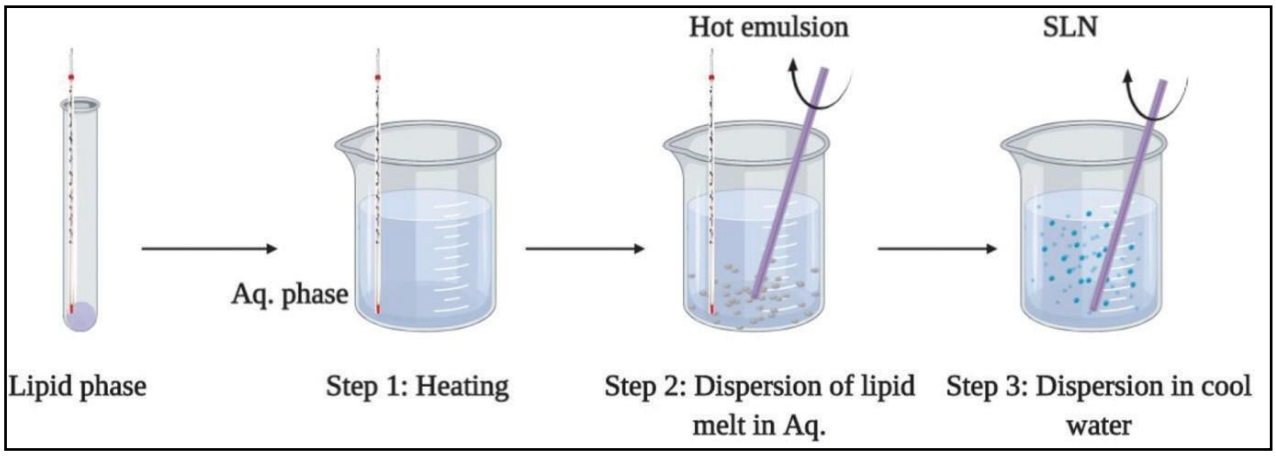

Figure 8: Microemulsion Technique.

6. SPRAY DRYING METHOD

A more economic and non-lyophilization method involves lipids having a melting point of >70°C. The best results were obtained when 1% SLN in a water solution of trehalose or a mixture of ethanol and water containing 20% trehalose was employed. Addition of carbohydrates to it, along with low content of the lipid, keeps the size of the colloidal particle constant throughout the process of spray drying. This results in the ethanol-water mixture being in favor over water alone in reducing the melting of lipids because they tend to form smaller, uniform crystals at much lower inlet temperatures.[19]

7. DOUBLE EMULSION METHOD

To prepare warm w/o/w double microemulsions, two different methods are available. In the first method, an aqueous solution containing medicine is added to a melted mixture of lipid, surfactant, and co-surfactant at a temperature slightly above the melting point of the lipid to develop a clear system. In the second method, a developed w/o microemulsion is mixed with water, surfactant and co-surfactant to form a clear w/o/w system. Indeed, SLNs can be prepared by mixing hot micro double emulsions in cold water and washing the dispersion media through an ultra-filtering system. Multiple emulsions are basically unstable due to internal aqueous droplet coalescence inside the oil phase, coalescence of internal oil droplets, and rupture of layers on the surface of the internal droplets.[20]

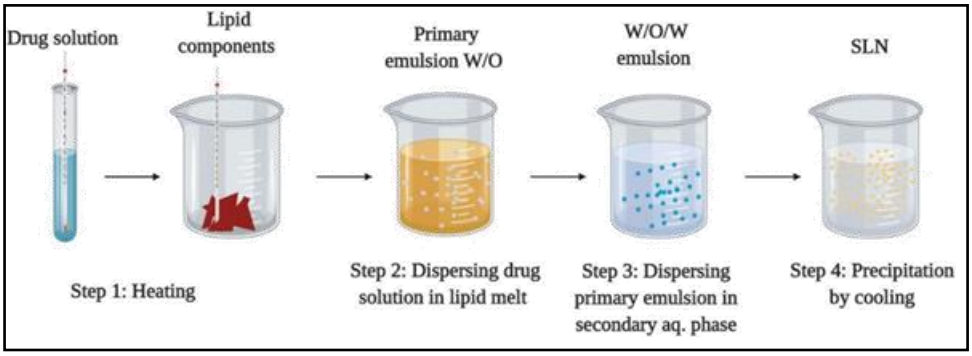

Figure 9: Double Emulsio Technique.

EVALUATION STUDIES

PARTICLE SIZE

The size of the particles and polydispersity index of SLN was determined by using Zeta sizer by dynamic. Light scattering Nano ZS - Malvern instruments, UK: Measurements were done in six replicates and values were measured as mean ±standard deviation (SD).[21]

SCANNING ELECTRON MICROSCOPY

Colloidal dispersion of SLNs was deposited on a glass cover slip which was previously adhered to carbon. Tape attached to a metallic stub. It was then air dried and further metalized either using gold coating by a vacuum coater. This sample was later analyzed by SEM.[22]

POLYDISPERSABILITY INDEX AND ZETA POTENTIAL

The average diameter (Z-AVE), polydispersity index(PI) and zeta potential of Drug Formulation was determined by photon Correlation spectroscopy (PCS) at room temperature. Nanosuspension was added to the sample dispersion unit (deionised water) and stirred at 2000 rpm with magnet in order to reduce the inter-particulate aggregation and laser obscuration range was maintained between 10-20%. The samples were well diluted with deionized water and placed in an electrophoretic cell. After the experiment was carried out in triplicates, the average particle size was determined. The Mean Zeta-potential was calculated from the electrophoretic mobility.[23]

DRUG CONTENT

The prepared SLN formulation, 1 ml of Nano-suspension, was dissolved in the 10 ml of 6.8 pH Phosphate buffer solution and ethanolic solution. The quantity of the drug was determined by UV spectrophotometer. Placebo the formulation prepared to drug-loaded SLN is used as blank form**.**

DRUG CONTENT= (Test absorbance / standard absorbance) x 100

DRUG ENTRAPMENT EFFICIENCY

Entrapment efficiency of the compound was determined by measuring the concentration of drug in the dispersion medium. The SLN suspension was ultra centrifuged at 4000 RPM for 30 minutes at 4◦ C temperature by using remi cooling centrifuge to separate the free drug. The amount of free drug was determined in the clear supernatant by UV spectrophotometer against blank at nano-meter.The analysis was performed in triplicate. Drug entrapment efficiency was calculated using the following Equation.

EE = (Amount of drug in SLN/ Amount of drug added) X 100

INVITRO DRUG RELEASE STUDIES FROM SLNs

The in-vitro release studies of drug loaded solid lipid nanoparticles were carried out by using Modified Franz diffusion cell. Dialysis membrane having pore size 2.4 nm with molecular weight cut off 10,000 daltons was used. Membrane was soaked in double distilled water for 12 hours before mounting in Franz diffusion cell. Drug loaded 2 mL of SLN dispersion equivalent to 4 mg was applied to the donor compartment. And the receptor compartment was filled with 12 ml of dialysis medium of 6.8 phosphate buffer. Samples (100 µL) were withdrawn from receiver compartment through side tube at regular time intervals and the same was replaced with fresh dialysis medium maintained at same temperature. In the similar way pure drug equivalent to 4mg was also added to the 2ml of distilled water and carried out in-vitro release studies.[24]

ROUTE OF ADMINISTRATION

Solid lipid nanoparticles can be administered via oral, parenteral, topical, intranasal, ophthalmic, and Pulmonary.

Oral administration

Solid Lipid Nanoparticles represent a promising novel drug delivery system for oral administration due to their various advantages regarding patient compliance, simplicity, and cost. Drugs formulated in nanoparticles of lipids upon oral administration have several advantages including enhanced drug solubilization in the GI tract, protection of labile drugs, potential controlled release characteristics, prolong residence times and possibility of selective drug delivery. Furthermore, nanoparticles are taken up through lymphatic flow, enhancing bioavailability and prolongs their half-life. This is especially helpful in the case of

drugs that are metabolized by the liver in the first pass. Lipid nanoparticles are very effective in the cases where the drug has harmful byproducts. The possibility of Solid Lipid Nanoparticles(SLNs) for the oral delivery of various drugs and natural products to treat various diseases has been a recent concern of the researchers. Therapies of diseases such as cancer, central nervous system disorders, cardiovascular, Among them are infections, diabetes, and osteoporosis.[25]

Parenteral administration

For those bioactive pharmacological agents characterized by poor bioavailability and limited Therapeutic index values, parenteral administration is the most efficient mode of administration.This is particularly the case for drugs recommended for unconscious patients. In response the novel technological advances in the delivery of parenteral drugs, sophisticated systems have been produced that allow for slow or controlled release of parenteral drugs. Drug targeting has also become viable. The oral route of administration remains the general method of protein and peptide drug administration require frequent replacement because of their high susceptibility to enzymatic degradation. Of interest, parenteral SLNs with controlled drug release mechanism have emerged as potential therapeutic entities. These formulations overcome problems of poor patient compliance and the need for frequent administration aside from offering controlled medication release. Rapid clearance by the reticuloendothelial system is the major drawback to their intravenous administration. This problem can be minimized through surface modification with materials such as Pluronic F68 or polyethylene glycol.[26]

Topical administration

Solid lipid nanoparticles (SLNs) offer a novel approach for topical drug delivery with the potential use in dermatology due to their advantages. As suspensions of lipophilic colloidal carriers, SLNs constitute a unique tool for controlled dermal drug delivery. Larger surface area and smaller particle size of nanoparticles constitutes for easy absorption as a medication and bioavailability. In addition to that, compared with lipid-poor liposomes, a slew of lipophilic medications are more soluble in the excipient used for solidification and surfactant portions of SLNs (lipid-rich) than water. This may offer optimum distribution into desired skin layers due to their ability to maximize partitioning into physiological barriers including stratum corneum. Moreover, SLNs are biocompatible and stable enough for topical administration. In addition, SLNs can be used for sustained release delaying how often they

need to be applied and improving the efficacy of treatment. Since the SLNs can hold both hydrophobic and normal medicines, these are effective in extensive kinds of dermatological problems. Overall, topical SLN delivery are promising for better efficiency of dermatological therapeutics and patient compliance.[27]

Intranasal delivery

An alternative oral and non-invasive route of medical product delivery is intranasal administration. Helps in reducing the degradation of sensitive drugs such as peptides and protein into digestive system, resulting quick absorption leading fast onset time of action. It further addresses limitations with transport of compounds across epithelial cells. This is a possible non-invasive method of drug delivery through the nose. Intranasal solid lipid nanoparticles (SLNs) are new and appealing for drug delivery. Made up of biocompatible lipids, solid lipid nanoparticles offer a stable and controllable substrate to encapsulate various therapeutic drugs. SLNs get quickly distributed into the systemic circulation via nasal mucosa with extensive surface area and rich vascular network upon intranasal delivery. This method is highly advantageous for medications with low bioavailability or are susceptible to enzymatic degradation in the GI system. In addition, the nasal route is non-invasive and patient-friendly which could potentially enhance compliance over traditional administration modalities. Solid lipid nanoparticles have unique physicochemical properties that can potentiate solubility, sustained release and bioavailability of various drugs. These properties are never found together, including their nanoparticle sizes and high surface area. In general, the solid lipid nanoparticles in intra-nasal delivery is a promising technology for enhancing drug bioavailability and for site-specific therapy of various pharmacotherapeutics.[28]

Ocular administration

In addition, the application of solid lipid nanoparticles into ocular delivery systems had been widely concerned as it aimed to circumvent some drawbacks linked with conventional ocular drug administration. One of the biggest hurdles for ocular formulation is rapid drug clearance upon administering. SLNs overcome this limitation due to their lipid matrix and nano-size range causing potential improved corneal permeation and extended drug delivery. This novel approach enhances bioavailability, potentially diminishing the need for multiple dosing; and it could be a way of enhancing patient compliance. Furthermore, SLNs are biocompatible which lowers the risk of ocular irritation. Intraocular administration of solid lipid

nanoparticles for an extended period might be able to improve both the precision and efficiency of ocular medicine delivery.[29]

APPLICATION

Solid lipid Nanoparticles possesses a better stability and ease of upgradability to production scale as compared to liposomes. This property may be very important for many modes of targeting. SLNs form the basis of colloidal drug delivery systems, which are biodegradable and capable of being stored for at least one year. They can deliver drugs to the liver in vivo and in vitro to cells which are actively phagocytic. There are several potential applications of SLNs, some of which are given below.[30]

a) SLNs as gene vector carrier

SLN provide another delivery vehicle in the gene vector formulation. In a single work, the gene delivery performance of SLN gene vector was improved through an HIV-1 HAT peptide (TAT 2) entering into this SLNs genes by which gene transfer were optimized. Several recent publications disclose more SLNs harboring genetic/peptide cargoes like DNA279,280 plasmid DNA or other nucleic acids. These liquid nanophases were composed of water and a water miscible organic solvent in which the lipid and DNA resided, but removal of the organic solvent yielded stable nano-sized (70–100 nm) particles containing an equal amount lipidselated by Helbery J. Lucking brewery nucleic acid as determined after analysis by DLS. It's called genospheres. By insertion of a targeted antibody-lipo polymer conjugated in the particle.

b) SLNs as cosmeceuticals

SLNs have been applied to 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. Better localization of vitamin A in upper layers of skin with glyceryl behenate SLNs has been achieved as compared with conventional formulations.

c) SLNs for potential agriculture application

Essential oil extracted from Artemisia arboreseens when incorporated in SLN, were able to reduce the rapid evaporation compared with emulsions and the systems have been used in

agriculture as a suitable carrier of ecologically safe pesticides. The SLN were prepared here by using compritol 888 ATO as lipid and poloxamer 188 or Miranol Ultra C32 as surfactant.

d) SLNs as a targeted carrier for anticancer drug to solid tumours

SLNs have been reported to be useful as drug carriers to treat neoplasms. Tamoxifen, an anticancer drug incorporated in SLN to prolong release of drug after IV administration in breast cancer and to enhance the permeability and retention effect. Tumour targeting has been achieved with SLNs loaded with drugs like methotrexate and camptothecin.

e) SLNs in breast cancer and lymph node metastases

The local injections of Doxorubicin Mitoxantrone-loaded SLN were prepared to reduce its toxicity and enhance the safety and bioavailability of drugs. The efficacy of doxorubicin (Dox) has been reported to be enhanced by incorporation in SLNs. Materials and Methods In the technique, the Dox complexed with soybean-oil-based anionic polymer was dispersed along with a lipid in water for the formation of Dox-loaded solid lipid nanoparticles. The system enhances its efficacy and reduces the cells of breast cancer.

f) Oral SLNs in antitubercular chemotherapy

Antitubercular drugs such as rifampicin, isonizide, pyrazinamide-loaded SLN systems were able to decrease the dosing frequency and improve patient compliance. By using the emulsion solvent diffusion technique this antitubercular drug loaded solid lipid nanoparticles were prepared. The nebulization in animal by incorporating the above drug in SLN also reported for improving the bioavailability of the drug.

g) Stealth nanoparticles

These represent a novel and unique drug-delivery system; they evade rapid elimination by the immune system. In theory, such particles can target distinct cells. Studies with antibody-labelled stealth lipobodies have resulted in improved delivery to target tissue in accessible sites. Stealth SLNs have been successfully studied by animal experimentations using marker molecules and drugs.

h) Adjuvant to vaccines

Adjuvants are used in vaccine preparation to enhance the immune response. Polymer vaccines were more stable against heat inactivation than aluminum hydroxide adjuvanted and fluid vaccines. In SLNs, the lipid components, being in the solid state, degrade more slowly,

thus providing a longer lasting exposure to the immune system. Degradation can be still slowed down using sterically stabilizing surfactants which hinder the anchoring of enzyme complexes. Advantages of use of SLNs compared to traditional.

Advantages of adjuvants are their biodegradation and their good tolerability by the body. Almeida et al tried to incorporate lysozyme, a model peptide, in SLNs. The contact between lysozyme and most SLNs excipients appear not to damage the protein molecules. The lysozyme molecule remained intact through out the process, without loosing its activity. This was confirmed by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE).[31]

CONCLUSION

SLNs are currently under great interest in research due to their unique properties and advantages compared with traditional dosage forms. The unique features of SLNs, including enhanced stability and bioavailability, together with the ability to deliver drugs that may be hydrophilic or hydrophobic, put SLNs among the hot topics in the pharmaceutical arena. In this regard, enhanced attention has been given to the possibilities of solid lipid nanoparticles for surpassing a number of difficulties characterizing conventional drug delivery systems with the purpose of enabling innovative and superior therapeutic options.

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