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UNVEILING THE PROMISE OF SOLID LIPID NANOPARTICLES: A COMPREHENSIVE REVIEW

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ABSTRACT
Solid Lipid Nanoparticles (SLNs) represent a versatile and promising platform in the field of nanotechnology-enabled drug delivery systems. Their unique characteristics, including biocompatibility, controlled release properties, and ease of surface modification, have garnered significant interest in pharmaceutical and biomedical research. This comprehensive review aims to provide a detailed overview of the current state-of-the-art in SLN technology, focusing on their formulation strategies, physicochemical properties, drug loading capacities, and applications in various therapeutic areas. Emphasis is placed on elucidating the underlying mechanisms governing SLN synthesis and optimization, along with highlighting recent advances and future prospects in this rapidly evolving field. Additionally, challenges such as stability issues, scale-up considerations, and regulatory hurdles are addressed, offering insights into overcoming barriers to the widespread adoption of SLNs in clinical practice. Overall, this review endeavours to consolidate existing knowledge and stimulate further research efforts toward harnessing the full potential of SLNs as innovative carriers for enhanced drug delivery and therapeutic efficacy.

KEYWORDS: Solid lipid nanoparticles; Methods of preparation; Nanostructured lipid carriers (NLCs).

1. INTRODUCTION

Solid lipid nanoparticles (SLNs) are introduced as a carrier system for in effectively water dissolvable medication and corrective dynamic medication. Colloidal particles ranging in size between 10 and 1000 nm are known as nanoparticles. They are incorporated from manufactured characteristic polymers and suited to advance medication conveyance and lessen lethality.[1] They have developed as a variable substitute to liposomes as medication carrier. They are fabricated from manufactured/characteristic polymers and are preferably suited to improve sedate conveyance and diminish lethality.[2] SLN offer interesting properties, for example, small size, huge surface zone, high medication stacking and the communication of stages at the interface, and are appealing for their potential to enhance the execution of pharmaceuticals.[3] Solid lipid nanoparticles (SLN) are aqueous colloidal dispersions, the matrix of which comprises of Solid biodegradable lipids. SLNs consolidate the favorable circumstances and maintain a strategic distance from the downsides of a few colloidal carriers of its class, for example, physical stability, assurance of fused labile medications from protection, of incorporated labile drugs from degradation, controlled release, excellent tolerability SLN formulations for various application routes (parenteral, oral, dermal, visual, pulmonar, rectal) have been developed and thoroughly characterized in-vitro and in-vivo. Solid lipid nanoparticles are one of the novel potential colloidal transporter system as option materials to polymers which is in distinguishable to oil in water emulsion for parenteral nourishment, however the fluid lipid of the emulsion has been supplanted by a Solid lipid nanopartical on Figure 1.

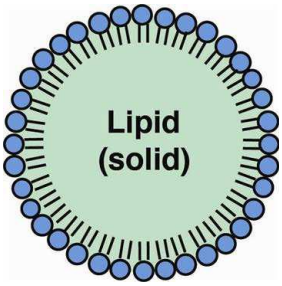

Fig. 1: Solid Lipid Nanoparticles (SLN)

1.1 Solid Lipid Nanoparticles

SLNs (Figure 2) were introduced in the late 20th century. They have been used to replace traditional drug carriers such as emulsions, liposomes, microemulsions, and other

polymer-containing formulations. Solid lipid nanoparticles were first developed for oral administration.[4] They are not without the problem of lipid toxicity and industrialization. It is a nano-sized drug contained in lipid that remains solid at room/body temperature. They can be produced in small sizes from 50 nm to 500 nm. Their size increases their surface area, causing them to exhibit more drug. They provide the potential for diffusion of chemicals and nutrients. Additionally, solid lipid nanoparticles produce less toxicity than other methods due to their biocompatibility.[5]

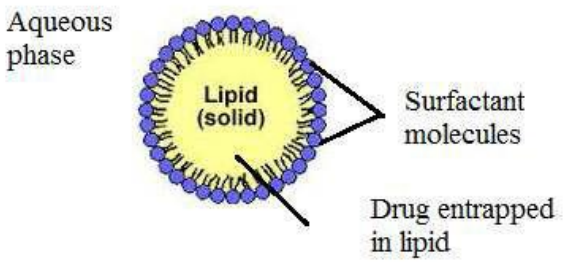

Fig. 2: Schematic diagram of solid lipid nanoparticles showing the drug entrapment in Lipid matrix stabilized by aqueous surfactant phase.

Solid lipid nanoparticles prepared from biodegradable lipids offer many advantages such as controlled release, high drug loading, low toxicity, and ease of mass production. Commonly used materials are solid lipids, surfactants and pure water. Lipids include fatty acids, triglycerides, waxes and steroids.[6] Nanostructured lipid carriers (NLC), a modified form of solid lipid nanoparticles in which drugs in liquid form are incorporated into a lipid matrix, are also popular for brain-targeted drug delivery.[7] Kinetic studies of the release of solid lipid nanoparticles show pseudo-zero order due to the slow release of the solid matrix drug from voids embedded in the lipid matrix. The ability to load more drugs into SLNs makes them suitable for development even in the pharmaceutical industry without the need for special materials. No organic solvent is required for the preparation of SLNs and they are made in the lipophilic drug delivery system.[8] Changing the characteristic structure of by coating hydrophilic molecules on the surface of solid lipid nanoparticles increases the plasma distribution and bioavailability of drugs.[9]

Advantages of Solid Lipid Nanoparticles[10,11]

1. Extended release for targeted tissue in therapy.
2. No plasma drug fluctuation.
3. High drug loading ability.
4. Flexibility to entrap both the hydrophilic and lipophilic drug molecules.
5. No acute or chronic toxicity
6. No use of organic solvent and avoid solvent toxicity.
7. Use of biodegradable lipids makes it biocompatible.
8. Improved formulation stability.
9. Suitable for production at huge scale.

Disadvantages of Solid Lipid Nanoparticles

1. Limited drug loading for hydrophilic drug due low lipid solubility of that drugs.
2. High content of aqueous phase in dispersion.
3. Sometimes drug exclusion due to change in crystalline behaviour of drug during storage.

The ability of a SLNs formulation regarding drug entrapment depends on factors given below

- Solubilisation behaviour of drug in melted lipid.
- Structure of the lipid matrix.
- Crystalline tendency of lipid in matrix.

1.2 Modified Forms of SLNs

1.2.1 Nanostructured lipid carriers (NLCs)

NLCs emerged after the turn of the 21st century in search of a new and better book for SLNs. Nano-lipid carriers consist of a lipid matrix that has the ability to disperse drugs in aqueous media and remain stable at room and body temperatures. A novel approach to lipid Nano carriers has been shown to overcome the challenges of solid lipid nanoparticles regarding loading capacity, drug transfer, and physical stability. The ways to create both files are similar.[12]

1.2.2 Lipid drug conjugates (LDCs)

The incorporation of hydrophilic drugs into the lipid matrix is always difficult in the case of solid lipid nanoparticles due to the solubility behaviour of the lipid materials used in their preparation. In this method, the drug is modified with lipids to increase its lipophilicity and facilitate its incorporation into the lipid matrix. This modification facilitates the encapsulation of highly active pharmaceutical ingredients in a solid lipid matrix.[13]

1.2.3 Lipid-polymer hybrid nanoparticles (LPNs)

LPNs are a form of internal synthesis using lipids and polyethylene glycol. They show properties of polymeric nanoparticles and liposomes regarding physical stability and biocompatibility.[14] LPN has been shown to have the ability to absorb lipophilic drugs with high loading capacity. It provides high drug delivery to the target area with sufficient plasma concentrations.[15-16]

1.3 General Excipients used in SLNs Formulation

Conventional materials used to prepare solid lipid nanoparticles (SLNs) are lipids that have a melting point and solidify at room temperature and body temperature. Surfactants participate in the emulsification using pure water to disperse the liquid phase. Some examples of tools used in these categories are given below.[17]

- **Lipids:** Triglycerides (mono, di, tri), Imwitor, Fatty acids, Steroids and Waxes etc.
- **Surfactants:** Free fatty acid salts (soaps), Fatty acid sulphonates (SLS), Ethoxylated compound

(propylene glycol), Short chain starches (polygluconates), Lecithin etc.

- **Stabilizers**: Poloxamer 407 (POL), Pluronic F-127 (PLU), Poly vinyl alcohol (PVA) etc.
- **Cryoprotectants**: Trehalose, Mannitol, Sucrose, DMSO, etc.

1.4 Method of Production for Solid Lipid Nanoparticles (SLNs)

1.4.1 High-pressure homogenization technique

HPH is a technique in which the oil/water coarse emulsion obtained after hot homogenization is reconstituted at high pressure above the melting point of the lipid to convert the lipid-rich drug emulsion into a nanoemulsion. Here, the high homogenization rate increases the temperature of the sample by approximately 10 °C at 5 x 10 Pa. In severe cases, 3-5 homogenization cycles at 5 × 10 Pa to 5 × 10 Pa are sufficient to achieve a good pressure. lipids in the nanometer range.[18, 19]

1.4.1.1. Hot homogenization technique

Hot homogenization is a sample homogenization technique that takes place at a temperature higher than the melting point of the lipids used. In this method, lipids are first absorbed into the soluble and easily soluble lipophilic compounds in the lipids. Another phase containing pure water mixed with surfactant is prepared and heated to seal the lipid phase. The molten phase was dispersed in the hot water mixture of surfactants, which was intelligently stirred and stirred under high pressure to form the initial o/w emulsion.[20] This type of emulsion concentrate has small particle size. This emulsion is further mixed at high pressure above the temperature of the lipid water to convert the lipid-rich drug emulsion into a nanoemulsion. This hot nanoemulsion is kept aside to cool to room temperature, where the lipids solidify at room temperature and are mixed, allowing filtration through a filter to obtain lipid nanoparticles.[21-25]

Advantages

1. High temperature reduces the viscosity and leads to smaller particles size.
2. Suitable for large scale industrial production.
3. High temperature exposure is short, hence no degradation of heat liable drugs.
4. No use of organic solvent in this method.

Disadvantages

1. Not suitable to encapsulate water soluble drugs
2. High temperature may cause degradation of lipid or drug
3. In-vitro burst release sometimes observed due to drug portioning in water phase
4. Lipid crystallization is retarded due to high temperature
5. High pressure homogenization may lead to aggregation of particles due to high kinetic energy

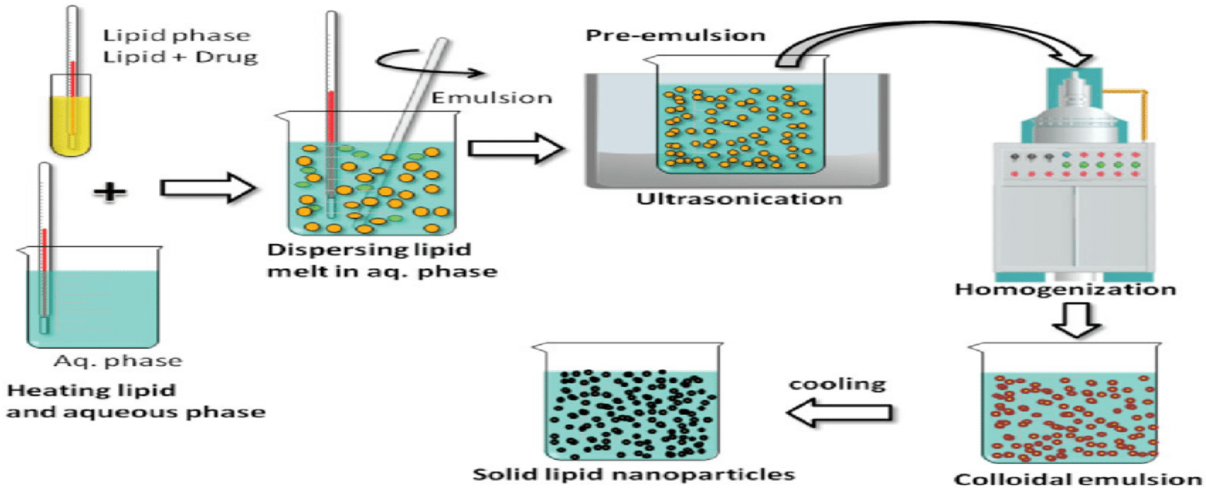

Fig. 3: Preparation of SLN by Hot homogenization technique.

1.4.1.2 Cold homogenization technique

The cold homogenization technique used to prepare solid lipid nanoparticles has the advantage of overcoming the problems associated with hot homogenization methods. The hot homogenization method causes degradation of thermolabile drugs, migration of unwanted lipids during reconstitution, and reduction of the drug in the aqueous phase. The first step in cold homogenization was the same as in hot homogenization. In this method, lipid with a boiling point of is hydrolyzed and the drug is dispersed in the lipid. The lipid-carrying phase is frozen to solidity using dry ice or liquid nitrogen. The dropped medicine contained large solid particles. Addition of these particles was done using a mill up to 50 m (100 in). The surfactant was dispersed in the liquid phase and the powder was dispersed in the surfactant mixture. The mixture was synthesized under high pressure at room temperature or below room temperature to obtain solid lipid nanoparticles.[26, 27]

Advantages
1. Lipid and drug degradation due to high temperature is avoided
2. Suitable for heat liable drugs
3. Melting of lipid is reduced and prevent the portioning of hydrophilic drug into aqueous phase

Disadvantages
1. Particle and poly dispersity index are higher than hot homogenization process
2. Thermal exposure of drug is reduced but not completely removed
3. Method is expensive and require special provisions like liquid nitrogen or dry ice
4. Milling is not appropriate method for reducing the particles size in nanometre range

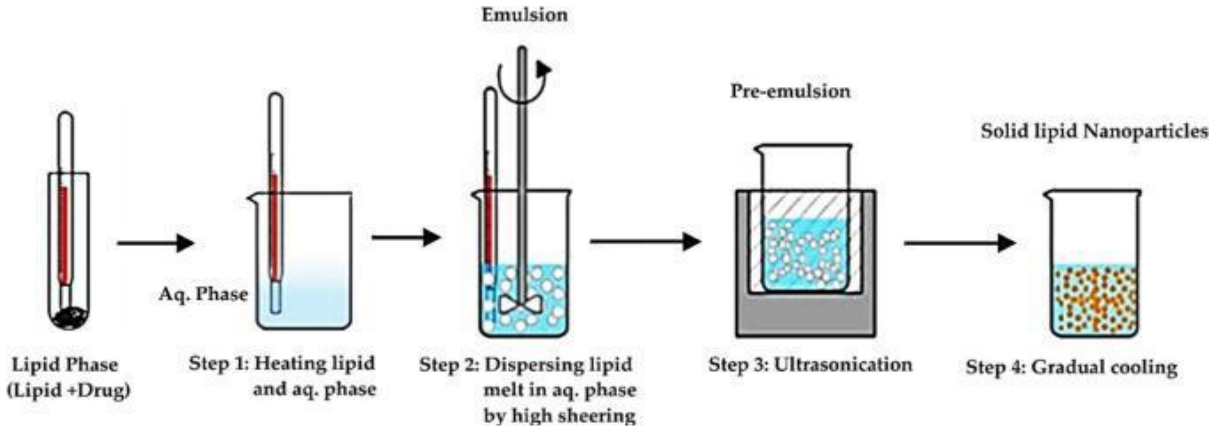

Fig. 4: Preparation of SLN by Cold homogenization technique.

The skin plays an important role in the transdermal drug delivery system. The skin of an average adult body covers a surface area of approximately 2 sq. m. and receives about one third of the blood circulating through the body and serves as a permeability barrier against the transdermal absorption of various chemical and The skin plays an important role in the transdermal drug delivery system. The skin of an average adult body covers a surface area of approximately 2 sq. m. and receives about one third of the blood circulating through the body and serves as a permeability barrier against the transdermal absorption of various chemical and The skin plays an important role in the transdermal drug delivery system. The skin of an average adult body covers a surface area of approximately 2 sq. m. and receives about one third of the blood circulating through the body and serves as a permeability barrier against the transdermal absorption of various chemical and The skin plays an important role in the transdermal drug delivery system. The skin of an average adult body covers a surface area of approximately 2 sq. m. and receives about one third of the blood circulating through the body and serves as a permeability barrier against the transdermal absorption of various chemical and The skin plays an important role in the transdermal drug delivery system. The skin of an average adult body covers a surface area of approximately 2 sq. m. and receives about one third of the blood circulating through the body and serves as a permeability barrier against the transdermal absorption of various chemical.

1.4.3 High shear homogenization (Ultra sonication) technique

Solid lipid nanoparticles are also prepared using the ultrasonication method. During rapid ultrasound of the distribution of drugs in vital organs according to lipid pores.[28-31]

Advantages
1. This method is convenient to use.
2. There is no use of organic solvent.
3. High shear enhances the formulation temperature may degrade the lipid or drug.

Disadvantages
1. Use of filtration is required for removal of impurities if any
2. Particle obtained are larger in size in micrometre range
3. Physical stability is poor due to larger size

1.4.3 Solvent emulsification-evaporation technique

This method is widely used in the synthesis of solid lipid nanoparticles. This technique facilitates the creation of a lipid phase in a drug that disperses the drug into pure lipids. Emulsification of lipids is facilitated by surfactants in the aqueous phase. Emulsification of the two phases is carried out using a machine operating at a speed of 1000 rpm. The organic phase is removed by suction under high pressure at room temperature. Lipid nanoparticles separated by precipitation.[32-35]

Advantages
1. Small particle size is produced
2. Suitable to encapsulate heat-sensitive drugs
3. Temperature-caused degradation is avoided

Disadvantages

1. Organic solvent may lead to toxicity in the final product.
2. Loss of solvent due tom evaporation.

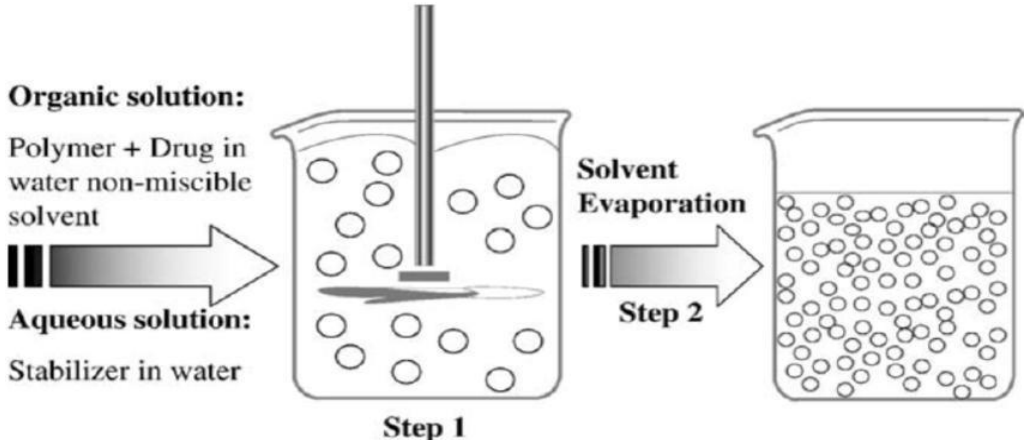

Fig.5: Preparation of SLN by Solvent evaporation technique.

1.4.4 Solvent in water diffusion technique

The distinguishing feature of diffusion techniques compared to direct ventilation is the selection of results for the process. While it is selected to be processed by transferring layers of volatile organic solvents, the water is not clear enough in the diffusion method. This technique is used for both liquid and organic phases.[36]

Advantages

1. Water miscible solvent reduces the toxicity
2. Less size particles are obtained
3. Method is simple and easy to conduct
4. Also suitable for heat sensitive drugs

Disadvantages

1. Drug diffusion in water phase lead to reduction in drug loading
2. Toxicity is reduced but not removed completely due to use of organic solvent
3. Drug dispersion in lipid matrix is essential therefore suitable for lipophilic drugs
4. Use of freeze drying require sophisticated instruments

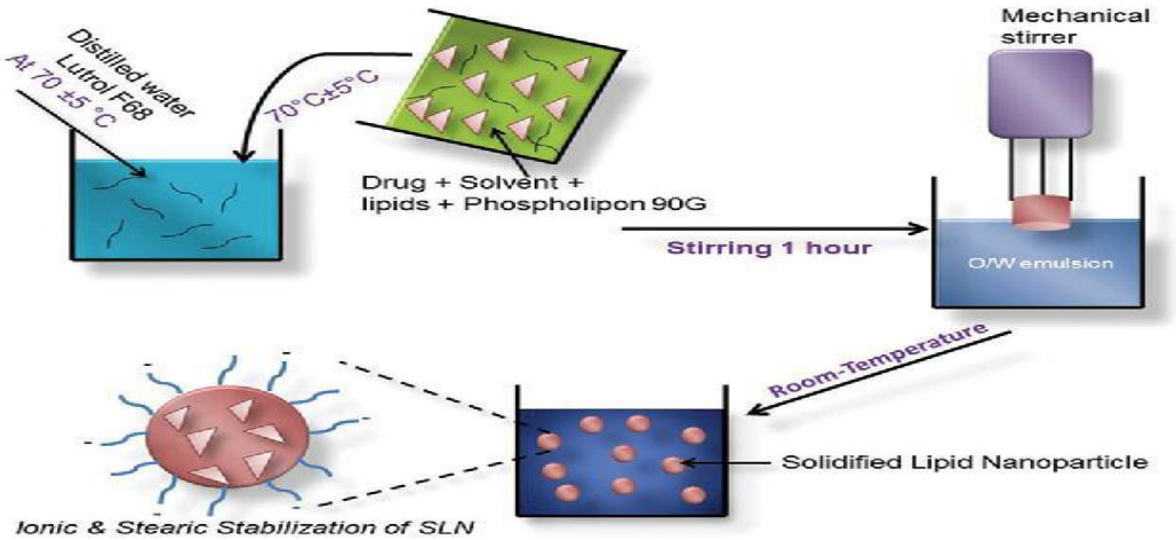

Fig.6: Preparation of SLN by Solvent Diffusion Technique.

1.4.5 Microemulsion technique

The concept of microemulsion formation was a unique evolution in NDDS research. In this method, the drug is separated into water and oil phase depending on the distribution coefficient of the drug. The reduction of lipids in this method leads to a lower coverage in the final form compared to the homogenization technique.[37]

1.4.5.1 Hot microemulsion induced SLNs

This is another microemulsion method in which the emulsion is made by dispersing dissolved lipids in a

liquid phase at a temperature between 60 and 80 °C. Using this method, lipid droplets in the nanometer range are produced after washing and filtering.[38-39]

Advantages

1. Emulsion obtained shows thermodynamic stability
2. No excess energy is required for the formulation
3. Rapid lipid crystallization takes place due to high temperature

Disadvantages

1. The concentration of nano droplets formed are less
2. Highly sensitive to stability during storage
3. High labour cost is involved

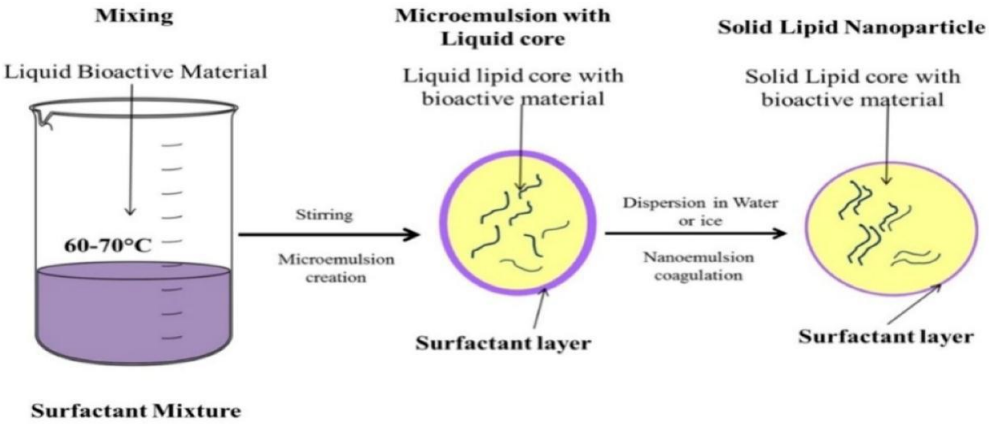

Fig.7: Preparation of SLN by Microemulsion Technique.

1.4.5.2 Double emulsion technique

This technique involves the formation of o/w/o type emulsion. Firstly, the hydrophilic drug is dissolved into purified water to prepare the primary emulsion. The aqueous phase is then dispersed into melted lipid phase, and with the help of a surfactant, the immiscible phases are emulsified to create the primary emulsion. The primary emulsion is then dispersed into an aqueous phase containing surfactant to produce a double emulsion. The process involves solvent evaporation, where the drug is entrapped in the lipid matrix after the solvent is removed.[40]

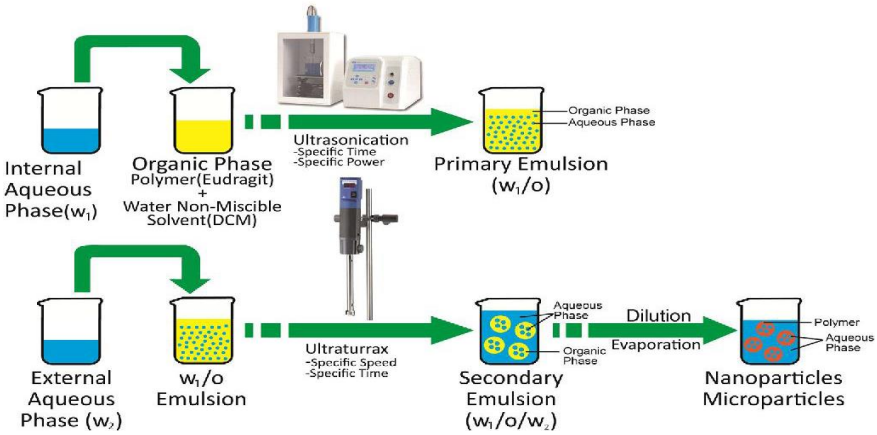

Fig. 8: Preparation of SLN by Double emulsion technique.

1.4.5.3 Reverse micelle-double emulsion technique

The double emulsion technique provided micrometer size and low drug loading. It is caused by the transition of chemicals into the outer liquid phase during emulsification. These problems have motivated researchers to develop two-phase micelle technology. In this method, mixed micelles containing phosphatidylcholine cholate are prepared and the drug is incorporated into the lipid matrix by inhalation. Stabilizers are used to provide adequate stability to nanodroplets using o/w/o emulsions.[41-42]

Advantages

1. The lipid content is decreased
2. Ability to encapsulate therapeutic and nutritional compounds in aqueous phase
3. Incompatible components can be easily separated

Disadvantages
1. High yield of the product is obtained

1.4.6 Melting dispersion method

In this way, lipids melt at temperatures above their melting points. The drug is dispersed in dissolved lipids to prepare the oil phase. The liquid phase is prepared by dissolving the surfactant in pure water, and the liquid phase is heated to mix and disperse the oil. Dispersion of the oil phase occurs slowly and continuously throughout the liquid phase. The mixture is cooled to room temperature to obtain the expected SLNs. Finally, excess solvent is removed by solvent emulsification.[43-44]

Advantages
2 This is reproducible method foe development of SLNs
3 Size distribution is uniform

Disadvantages
1. The final product may have toxicity as organic solvent is utilized
2. Thermos sensitive drugs could not be processed

1.4.7 Solvent injection method

This technique involves precipitating solid lipid nanoparticles from an aqueous organic phase. The process starts by melting the lipid and converting it into a dispersion with a water-miscible organic solvent. A hydrophilic surfactant is then dissolved in purified water to create an aqueous phase. Next, the organic lipid phase is rapidly injected into a miscible phase containing water, with regular agitation. The organic solvent mixes with the water and the drug-loaded lipid matrix separates to form lipid nanoparticles. The resulting nanoparticles are then filtered to separate them and the surfactant present in the formulation provides stabilization for the developed nanoparticles.[46-47]

Advantages
1. Non-toxic organic solvent is used
2. Easy and fast process
3. No use of specific equipment
4. Uniform size distribution with small size
5. Temperature induced loss of drug is avoided

Disadvantages
1. Additional operation of filtration is required
2. Toxicity is not completely removed

1.4.8 Precipitation method

In this method, the organic solvent facilitates the dispersion of lipids and emulsifies them in the aqueous phase in the presence of the emulsifier under continuous active. Because of the constant stirring, the temperature of the dispersion rises, and the volatility of the solvent makes it better for it to dissolve. As a result of the evaporation of organic solvents, it is dissolved in liquid in which precipitates and come out in the form of solid liquid nanoparticles. Finally, these nanoparticles are washed with water.[48]

Advantages
1. Ease of preparation
2. No use of specific equipment
3. Suitable for heat sensitive drugs

Disadvantages
1. Huge size particles formed
2. Solvent toxicity problem
3. Not compatible for large scale production

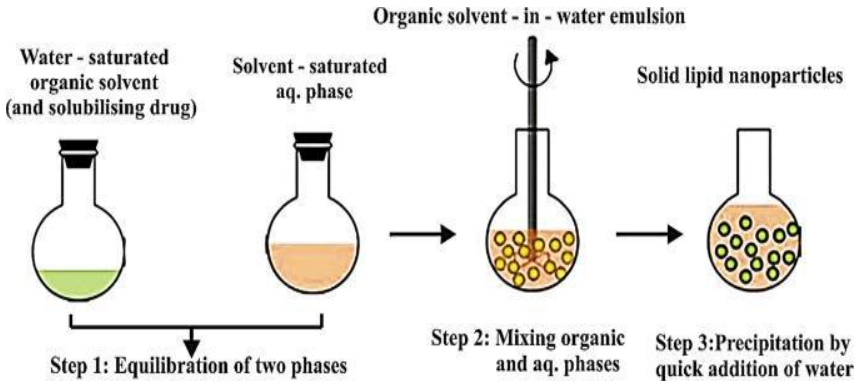

Fig.9: Preparation of SLN by precipitation technique.

1.4.9 Complex coacervation technique

A stable polymer solution is obtained by dissolving the polymer in water when heated, then the mixture becomes stable at room temperature. Lipids are dispersed in the polymer solution and the mixture is heated to a temperature where the surfactant starts to form micelles and turns into a clear solution. A hot water solution is mixed with the drug. The pH inducer for the acidic range is mixed dropwise in the lipid dispersion of the drug to achieve the desired pH. The prepared suspension was cooled to room temperature and isolated SLN.[49-50]

Advantages
1. Solvent free method
2. High temperature is avoided
3. Suitable for thermolabile drugs
4. No need of sophisticated equipment

Disadvantages
1. Difficult to produce at large scale
2. Toxicity is observed in product

1.4.10 Phase inversion technique

This method was developed in 1969 using polyethoxylate as a non-ionic surfactant. Solid lipid nanoparticles were grown at different temperatures followed by precipitation due to inversion. Non-ionic surfactants exhibit similar interactions with both phases, and this interaction is controlled by temperature. At a temperature where the surfactant is in contact with two phases, it is dispersed and dissolved because the interfacial tension is very low. Medicines are emulsified in Lid dispersion and are continuously strong and active. When the temperature suddenly drops, the lipid immediately begins to solidify and break down into lipid nanoparticles.[51-52]

Advantages
1. Easy and steps of preparation are less
2. No complex equipment is required

Disadvantages
1. Difficult to execute at large scale
2. Large particle size
3. Not good for heat liable drugs

1.4.11 Membrane emulsification method

The new method is used to produce solid lipid nanoparticles using micro reactors. This method is also called gas exchange method. In this way, the lipid dissolved in the dispersion medium can pass through the membrane and form small droplets. A lipid dispersed in a solvent mixed with water is absorbed into the medium. The liquid phase simultaneously acts as an outer coating. The two parts combine and cause the water to spread from the outside. This brings the lipids into a supersaturated state and they begin to degrade as lipid nanoparticles.[53]

Advantages
1. Large-scale production is possible
2. Smaller size of particles with good uniformity
3. Have the ability for mass transfer easily

Disadvantages
1. High temperature makes it not suitable for heat-sensitive drugs
2. The final product may be toxic
3. High pressure is involved

1.4.12 Supercritical fluid technology

Supercritical fluid method is an advanced technology for the production of solid lipid nanoparticles. A substance is called a supercritical fluid if its temperature and pressure are higher than the critical point. The most important point is the parallel phase, where the two phases can exist at the same time. Carbon dioxide is considered to be the best solvent for this process. Carbon dioxide is a safe, non-oxidizing solvent, easily reaching 31°C at 75 bar. is also non-flammable and globally friendly. This method requires a number of changes such as the size of the supercritical method, better method of dispersion ,and the ability to divide water into emulsions.[54]

Advantages
1. Solvent is not required
2. Particles formed in a single step
3. Frequent process
4. Smaller size distribution
5. Uniform size particles
6. Dry particles are formed & show high stability
7. Suitable for heat-sensitive drugs

Disadvantages
1. The choice of solvent is limited, only carbon dioxide is a choice
2. Limited solubilisation
3. Large-scale production is not possible
4. Expensive than other methods

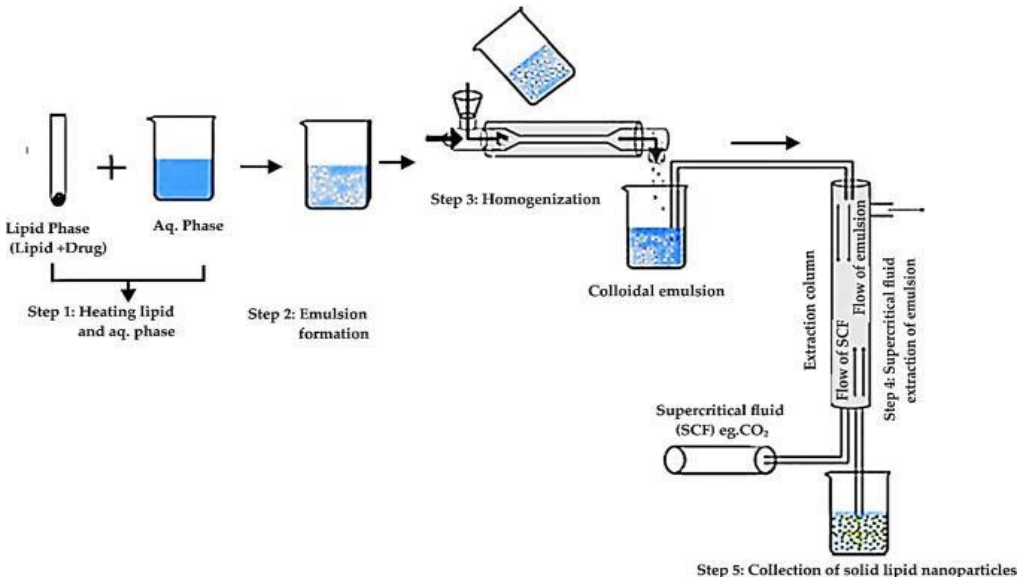

Fig.10: Preparation of SLN by Supercritical fluid technology.

1.5 Characterization of Solid Lipid Nanoparticles (SLNs)

The characterization of Solid Lipid Nanoparticles (SLNs) is a genuine challenge due to the small size of particles and the complexity of the system. Several essential parameters need to be assessed for SLNs, such as particle size, zeta potential (measure delivery energy), level of crystallinity and lipid alteration (polymorphism), conjunction of extra colloidal structures (micelles, liposome, supercooled, softens, drug nanoparticles), time size of circulation procedures, in vitro drug release, and surface morphology.[55] Therefore, several parameters must be considered during the characterization process.

1.5.1 Particle Size and Zeta Potential

There are several techniques available to determine the size of nanoparticles, such as photon-correlation spectroscopy (PCS), transmission electron microscopy (TEM), scanning electron microscopy (SEM), SEM combined with energy dispersive X-ray spectrometry, scanned probe microscopy, and Fraunhofer diffraction. Among them, PCS and electron microscopy techniques are the most widely used. SEM and TEM are highly useful in determining the shape and morphology of lipid nanoparticles and also allow for the determination of particle size and distribution. An advanced technique used for nanoparticle characterization is atomic force microscopy (AFM).[56] This is a tool that helps to visualize the original shape and surface properties of particles without any alteration. The system uses a drive to move the examining tip over the surface, resulting in a spatial resolution of up to 0.01μm. Another method that can be used is the laser diffraction procedure, which is suitable for particles in the sub-micrometre range. The calculations are based on the refractive index of the scattering medium, water (1.33), and the lipid particles.[57] The size of the particles depends on the constituents of the lattice, as well as the type and amount of emulsifying agents and lipids used. It has been reported that an increase in the amount of emulsifier decreases the mean width of the mass. The size and structure of the combined drug also affect the average diameter of the SLNs.[58] Photon correlation spectroscopy (PCS), also known as dynamic light scattering, is a technique that measures the variation of the intensity of scattered light caused by particle movement. This method provides a size range from 3 nanometres to 3 microns,[59,60]

1.5.2 Determination of Incorporated Drugs

The quantity of medication present in solid lipid nanoparticles is determined by separating the free medication and solid lipids from the liquid medium using techniques such as ultracentrifugation, centrifugation filtration, or gel penetration chromatography. Alternatively, the drug substance can be determined directly by extracting the drug with a suitable solvent under optimal conditions and analysing the resulting product in SLNs. Models have been proposed to describe the localization of drug molecules in SLNs.[61] The enhanced shell model describes drugs specifically positioned at the interface, either by rapid solidification of the network lipid or by efficient competition of the drug for the interface. Drugs dispersed by such a model may exhibit a successful burst effect during drug release. The homogeneous framework model is characterized by drugs dispersed evenly throughout the matrix, like a solid solution. The advanced core model is characterized by drug selectivity located at the core of the solid lipid nanoparticles, perhaps due to more rapid solidification of the drug relative to the matrix material. The advanced core model would be useful to develop a film-controlled release pattern. Although the chemical stability and the release kinetics of drugs are largely related to the confinement of drugs within the aggregates, more research is still needed to validate these models.

1.5.3 In-vitro Drug Release Studies

In-vitro drug release studies are mainly useful for quality control and to predict in-vivo behavior. The release profile of a drug can be conducted with or without dialysis tubing. In dialysis, the solid lipid nanoparticles (SLNs) dispersion is placed in prewashed dialysis tubing, which is then sealed and dialyzed against the dissolution medium at a constant temperature with continuous mixing. Samples are taken at different times, centrifuged, and measured for drug content. Impose and Benita (1990) have reported another method that avoids the confinement of the colloidal drug carrier in a dialysis sac and relies on reverse dialysis. However, this method is not sensitive enough to describe the rapid drug release rate from colloidal carrier.[62]

1.5.4 Storage Stability

The stability of solid lipid nanoparticles (SLNs) during prolonged storage can be determined by monitoring changes in particle size, drug content, appearance, and viscosity. This can also be achieved through thin-layer chromatography.[63,64] External factors such as temperature and light are crucial for long-term stability. The zeta potential of the particles should remain above -60mV to ensure physical stability. 4°C is the most suitable storage temperature, while storage at 20°C did not result in any loss of drug-loaded SLNs. However, at 50°C, a rapid increase in particle size was observed.

1.6 Evaluation of Solid Lipid Nanoparticles[65,66]

1.6.1 Electron Microscopy of Solid Lipid Nanoparticles

Solid lipid nanoparticles were visualized through transmission electron microscopy. The SLN samples were diluted by a factor of ten and then placed on a gold plate for mounting. After that, the mounted plates were dried and examined under a transmission electron microscope without the use of any staining agents. To visualize the SLN, the transmission electron microscope was equipped with a CCD camera and a sensitive imaging system.[67]

1.6.2 Zeta potential of Solid Lipid Nanoparticles

Zeta potential values of SLN were measured using a Zetasizer. Samples were diluted with deionized water to obtain 50 and 200 Kcps for the measurements. Samples were placed in the cell holder and zeta potential was measured directly.[68,69]

1.6.3 Particle Size and PDI of Solid Lipid Nanoparticles

The Zetasizer DTS (Malvern Instrument, UK) was used to measure the typical particle size and polydispersity of SLN samples. The SLN scatterings specimens were diluted with deionized water. The results for the typical particle size and polydispersity were obtained using an instrumental-based computational system.[70]

1.6.4. Encapsulation Efficiency of Solid Lipid Nanoparticles

Solid lipid nanoparticles were used to measure the level of testosterone, which was represented as epitomized productivity (EE). The nanoparticles were placed in a dialysis tube and dialyzed using 30 millilitres of 30% v/v PEG 400 in a phosphate buffer solution (pH-6) as a dialyzing medium.[71] The dialysis of the nanoparticles was carried out for two hours. After that, 100 milligrams of the dialyzed nanoparticles were taken from the dialysis pack and dissolved to determine the drug content using high-performance liquid chromatography (HPLC) at 254 nm on a Shimadzu instrument from Japan. The samples were suitably diluted and filtered through a Millipore membrane filter (0.2 μm).

1.6.5. Viscosity of Solid Lipid Nanoparticles

The viscosity of solid lipid nanoparticles containing testosterone was measured using a Brookfield viscometer (DV-E viscometer, Brookfield, USA) with a shaft number 63 at 30 rpm in the surrounding ambient. The viscometer's shaft speed was set to number 63, and the maximum torque was measured before observing the viscosity. The viscosity of solid lipid nanoparticles containing testosterone was measured directly from the viscometer's digital display.[72]

1.6.6 In Vitro Release Study of Solid Lipid Nanoparticles

The Solid lipid nanoparticles, a substance used for in vitro drug discharge, were extracted using a locally made Franz dispersion sort cell. The study was conducted at a temperature of 30±2°C. The receptor compartment of the dissemination cell contained a 30 ml solution of 30% v/v PEG 400 in a phosphate cradle (pH-6). The solution was continuously stirred by a magnetic stirrer at 50 r/m. A dialysis membrane with a molecular weight cut off of 12 KD was used as discharge hindrance between the receptor and donor compartments. The membrane was previously soaked in refined water and then treated with a 30% v/v PEG 400 solution. At intervals of one hour over an 8-hour period, 5 ml samples were withdrawn through the sampling port of the cell. The same amount of 30% v/v PEG 400 solution was immediately replaced each time. The collected samples were diluted and analyzed by HPLC at 254 nm.

CONCLUSIONS AND FUTURE RESEARCH

Solid lipid nanoparticles (SLNs) can be used as a delivery system for active compounds. These compounds are often lipophilic but can also be hydrophilic and can be encapsulated using methods like double emulsion w/o/w or by using emulsifiers. Success in SLN fabrication depends on several factors, including the choice of the fabrication method, the type of lipid matrices used, and the selection of surfactants or emulsifiers. The process used to prepare the SLNs is also essential. SLN fabrication has been successful in coating various active compounds such as drugs, minerals, and polar and non-polar antioxidant compounds. However, to produce more stable SLNs and have high entrapment efficiency, researchers need to carry out several material and process combinations.

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