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Review Article

EXPLORING SOLID LIPID NANOPARTICLES AS VERSATILE NANOCARRIERS: A REVIEW ON DESIGN, EVALUATION, AND APPLICATIONS

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ABSTRACT

Solid Lipid Nanoparticles (SLNs) represent an advanced nanocarrier system developed as an alternative to conventional colloidal delivery platforms such as emulsions, liposomes, and polymeric nanoparticles. They offer enhanced biocompatibility, controlled drug release, improved stability of labile compounds, and the ability to encapsulate poorly water-soluble drugs. SLNs consist of a solid lipid core stabilized by surfactants, ensuring protection of the incorporated drug and improved bioavailability. Various preparation methods including high-pressure homogenization, ultrasonication, solvent emulsification evaporation, microemulsion techniques, and supercritical fluid processing enable the production of nanosized dispersions with defined physicochemical attributes. Comprehensive characterization involving particle size analysis, zeta potential, morphology, crystallinity, and drug loading is essential to ensure product performance, stability, and therapeutic efficacy. SLNs have shown promising applications across several administration routes, including oral, parenteral, transdermal, and topical delivery, demonstrating their potential as versatile carriers for both hydrophilic and lipophilic drugs. This review outlines the principles, preparation methods, characterization techniques, and current applications of SLNs, emphasizing their growing significance in modern drug delivery systems.

Keywords: Solid Lipid Nanoparticles (SLNs), Nanotechnology, High-pressure homogenization, Particle size; Drug delivery systems, Lipid-based carriers, Zeta potential, Controlled release, Bioavailability enhancement, Nanocarriers.

INTRODUCTION

The field of Novel Drug Delivery System is emerging at an exponential rate with the deep understanding gained in diversified fields of Biotechnology, Biomedical Engineering and Nanotechnology (Nadkar and Lokhande, 2010). Many of the recent formulation approaches utilize Nanotechnology that is the preparation of Nanosized structures containing the API (Loxley, 2009). Nanotechnology, as defined by the National Nanotechnology Initiative (NNI), is the study and use of structures roughly in the size range of 1 to 100 nm. The overall goal of nanotechnology is the same as that of medicine: to diagnose as accurately and early as possible and to treat as effectively as possible without any side effects using controlled and targeted drug delivery approach (Mishra *et al.*, 2010). Some of the important Drug Delivery System developed using Nanotechnology principles are Nanoparticles, Solid Lipid Nanoparticles, Nanosuspension, Nanoemulsion, Nanocrystals

(Maravajhala *et al*., 2011). In this article the main focus is on Solid Lipid Nanoparticles (SLNs). SLNs introduced in 1991 represent an alternative and better carrier system to traditional colloidal carriers such as emulsions, liposomes and polymeric micro and nanoparticles (Ekambaram *et al*., 2012).

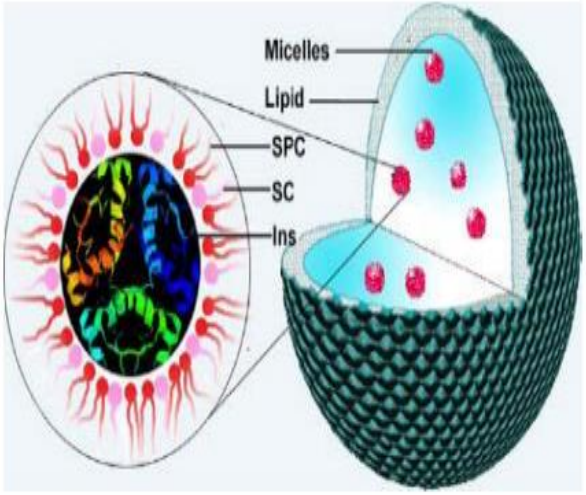

Figure 1: Shows structure of Solid Lipid Nanoparticles

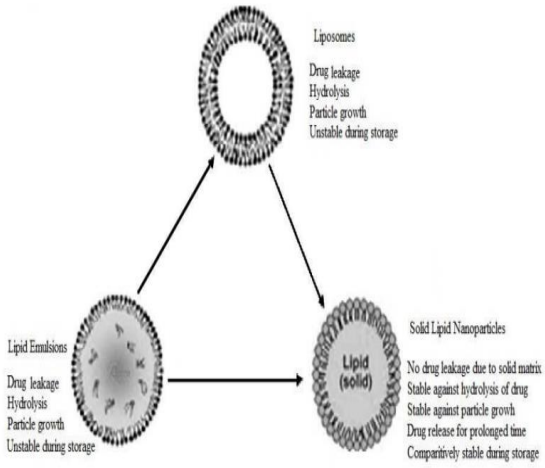

Figure 2: Shows a diagrammatic representation on SLN over emulsions and liposome (Ekambaram *et al*., 2012)

SLNs are colloidal carrier system composed of a high melting point lipid as a solid core coated by aqueous surfactant and the drugs used are of BCS Class II and IV (Loxley, 2009). In SLNs as compared to other colloidal carriers liquid lipid is replaced by solid lipid. The use of solid lipid as a matrix material for drug delivery is well known from lipid pellets for oral drug delivery (eg. Mucosolvan retard capsules) (Muller *et al*., 2000). The term lipid in a broad sense includes triglycerides, partial glycerides, fatty acids, hard fats & waxes. A clear advantage of SLN is the fact that the lipid matrix is made from physiological lipids which decreases the danger of acute and chronic toxicity (Mandawgade and Patravale, 2008). The use of solid lipid instead of liquid lipid is beneficial as it has been shown to increase control over the release kinetics of encapsulated compounds and to improve the stability of incorporated chemically-sensitive lipophilic ingredients.

These potentially beneficial effects are because of a number of physicochemical characteristics associated with the physical state of the lipid phase. Firstly, the mobility of reactive agents in a solid matrix is lower than in a liquid matrix and so the rate of chemical degradation reactions may be retarded. Secondly, micro phase separations of the active ingredients and carrier lipid within individual liquid particles can be controlled, thereby preventing the accumulation of active compounds at the surface of lipid particles where chemical degradation reactions often occur. Thirdly, the absorption of poorly absorbed bioactive compounds has been shown to be increased after incorporation into solid lipid nanoparticles. As a result of various research works it has also been shown that the use of a solid matrix instead of a liquid matrix can slow down lipid digestion thereby allowing for a more sustained release of the encapsulated compound.

Other major excipients of SLNs are surfactants of aqueous type. They mainly act as emulsifier to form o/w type emulsion and stabilizer for SLNs dispersion and their choice depends on mainly the route of administration. They are generally made up of a solid hydrophobic core containing the drug dissolved or dispersed (Helgason *et al*., 2009). SLNs are mainly prepared by high pressure homogenization or micro emulsification. SLNs prepared by any technique are in dispersion form which on long term storage results in instability mainly because of hydrolysis reactions so to increase their stability they can be converted into solid dry reconstituable powders through lyophilisation and a cheap and easy variant to lyophilisation is spray drying technique (Sinha *et al*., 2010).

Advantages of SLN

- Use of biodegradable physiological lipids which decreases the danger of acute and chronic toxicity and avoidance of organic solvents in production method.
- Improved bioavailability of poor water soluble molecules.
- Site specific delivery of drugs, enhanced drug penetration into the skin via dermal application.
- Possibility of controlled drug release and drug targeting.
- Protection of chemically labile agents from degradation in the gut and sensitive molecules from outer environment (Yadav *et al*., 2013).
- SLNs have better stability compared to liposomes.
- Enhance the bioavailability of entrapped bioactive and chemical production of labile incorporated compound (Ramteke *et al*., 2012).
- High concentration of functional compound achieved.
- Lyophilization possible (Kakadia and Conway, 2014).

Preparation of SLN

High-pressure homogenization

High-pressure homogenization (HPH) has been used as a reliable technique for the preparation of SLN. Several manufacturers produce homogenizers of diverse sizes at a reasonable cost. The particles of the submicron range are obtained at elevated shear stress and cavitation compulsion. Nanoemulsions for parenteral nutrition are produced by HPH. HPH pushes the liquid at high pressures (100–2,000 bar) through a narrow space (range of few microns). The fluid moves faster over a short distance with high velocity. With homogenization, even the high lipid concentration could be transformed into nanodispersions (Wolfgang and Karsten, 2001). Hot and cold homogenization techniques are the means for the manufacturing of SLN. A preparatory step involves in both the cases. Lipid matrix used in this process is extracted from the physiological lipids which reduce the risk of acute and chronic toxicity.

Hot homogenization

Temperatures higher than the melting point of the lipid are selected for this process and can subsequently be considered as the homogenization of an emulsion. An aqueous surfactant is used for the combination of lipid and drug at the same temperature. A device for high shear mixing is used to prepare a hot pre-emulsion, resulting in an emulsion of oil in water type. Then, the product is left for

cooling, and this leads to the initiation of crystals of lipid and then the formation of SLNs. For the production of perfect SLNs, 3–5 cycles of homogenization at a pressure of 500–1,500 bar are necessary (Akanksha *et al*., 2012). One should always be aware that there is a rise in temperature with HPH. With the rise in the number of cycles or the pressure, there is a growth in the particle size. This is due to attractive forces between the particles which are due to the energy of moving the particles (Siekmann and Westesen, 1994). Finally, cooling of the nanoemulsion to room temperature is done, where the recrystallization of lipids occurs and this leads to the formation of nanoparticles.

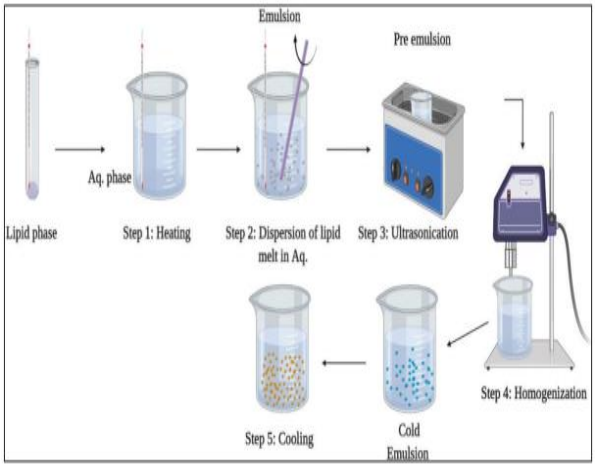

Figure 3: Hot homogenization

Cold homogenization

This technique has been developed to combat the problems of hot homogenization such as faster deterioration due to high temperatures, loss of drug during homogenization into the aqueous phase, and undetermined polymorphic transformations of the lipid due to the complexity of crystallization.

The first elementary step is indistinguishable as in the hot homogenization technique which includes the solubilization of drug in the lipid melt. The successive steps are altered; the drug-containing melt is refrigerated speedily with the aid of solid carbon dioxide or liquid nitrogen for attaining a homogenous drug distribution lipid matrix. The solid is then levigated into a fine dust by using a ball mill. Typical dust size attained is in the range of 50–100 µm. In the chilled aqueous surfactant, the fine dust particles are dispersed. Now, the dispersion is subjected to HPH to initiate the SLN production. However, compared to a hot homogenization technique, greater particle sizes and wider size distribution are typical of the cold homogenized product (Mehnert and Mader, 2001).

Cold homogenization lessens the heat vulnerability, but it is not completely avoided due to the softening of lipid mixture in the opening step.

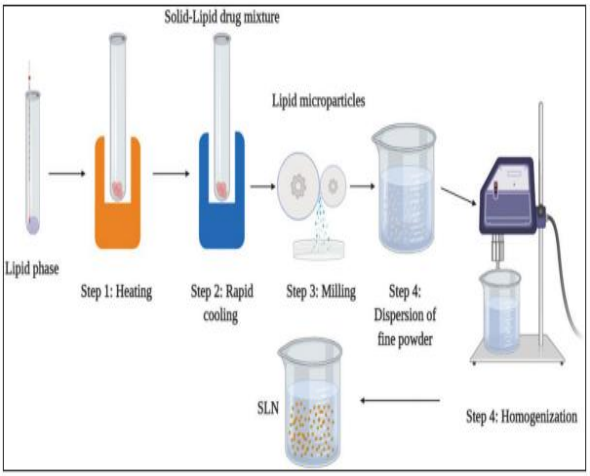

Figure 4: Cold homogenization

Ultrasonication

SLN was also produced by high-speed stirring or sonication (Eldem *et al*., 1991). The impedimenta used for this method is prevalent in every single laboratory. The main drawback of this technique is wider particle size distribution ranging into micrometer range which is the main cause for physical instability. Particle gain on storage and potential metal decay are acute problems in

this method. After many studies and intense research, it was proved that high-speed stirring and ultrasonication, when operated combinedly at high temperatures, yield a steady formulation (Eldem *et al*., 1991).

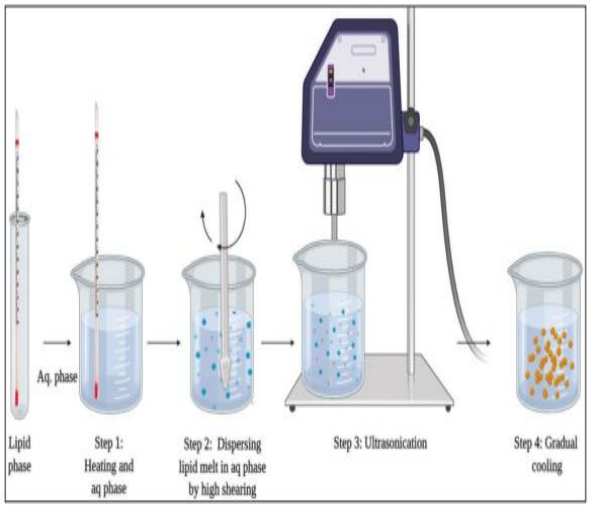

Figure 5: High shear homogenization or ultrasonication technique

Solvent emulsification evaporation

In this method, the lipophilic material and hydrophobic drug are dissolved in water-immiscible organic solvents such as cyclohexane, toluene, and chloroform. Now, by using a highspeed homogenization, the mixture is emulsified in an aqueous phase. The coarse emulsion is instantly allowed to flow through a microfluidizer.

A rotary evaporator with mechanical agitation at room temperature and decreased pressure is used to evaporate the organic solvent (Ramteke *et al*., 2012). The main mastery of this technique is bypassing the thermal stress. Therefore, now, there is a possibility for the incorporation of highly thermolabile drugs. The clear-cut disadvantage is the use of an organic solvent which may react with drug molecules (Sjostrom and Bergenstahl, 1992).

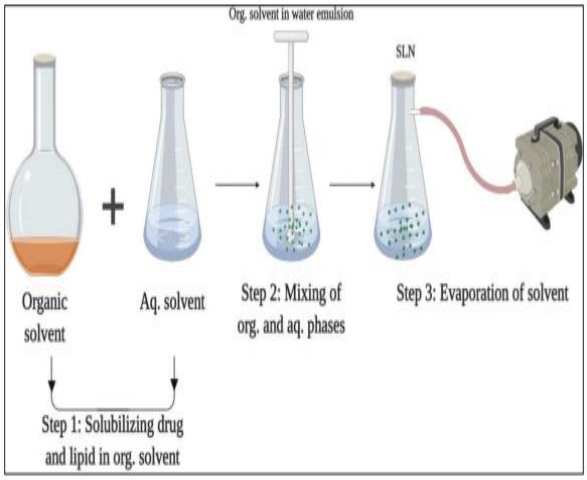

Figure 6: Solvent emulsification-evaporation technique

Supercritical fluid (ScF)

This is a comparatively advanced technique for the manufacturing of SLNs. The supercritical fluid has distinct thermophysical properties which can be finely adjusted by minute modifications in the pressure. It is solvent-free processing (Chen *et al*., 2006; Kaiser *et al*., 2001). With the elevation in pressure, the density and capability of fluid to liquefy compounds enhance, whereas the velocity remains the same. ScF is a substance above its pressure and critical temperature. The fluid has special properties at these conditions: liquid-like density, gas-like viscosity, and larger diffusivities than those of typical liquid (intermediate to that of a liquid and a gas), giving rise to its higher mass-transfer rate. Various techniques such as rapid expansion of supercritical solutions (RESS), supercritical antisolvent process and precipitation with a compressed antisolvent process (PCA), particles from gas-saturated solutions/suspensions, and supercritical extraction from emulsions can be used.

The high solubility of the drug in ScCO2 (solvent) is required for carrying out RESS technology.

In this process, the supercritical fluid is quickly enlarged via a nozzle to convert the solute as micro- or nanoparticles. There are three major factors which regulate the particle, and the particle growth is a short residence time, not much time available for particle growth and maximum dilution of the particles in the expansion chamber (Garces *et al*., 2018). Pure powder griseofulvin has been acquired using a cosolvent such as methanol which improves the drug solubility in ScCO2 for about 28 folds. The usage of a simple capillary nozzle, griseofulvin NPs in the range of 50−250 nm has been derived (Thakur and Gupta, 2005).

In the PCA technique, an atomized drug solution along with compressed carbon dioxide is introduced into the chamber. After the solution gets supersaturated, fine crystals precipitate out. A supercritical fluid with poor drug solubility is selected and used. The drug is dissolved in the solvent. This solvent should be miscible with the supercritical fluid. The supercritical fluids pull out all the solvent, and then, the drug solution becomes supersaturated after introducing the drug solution into the supersaturated solution. The drug precipitates as fine crystals (Alessi *et al*., 2012).

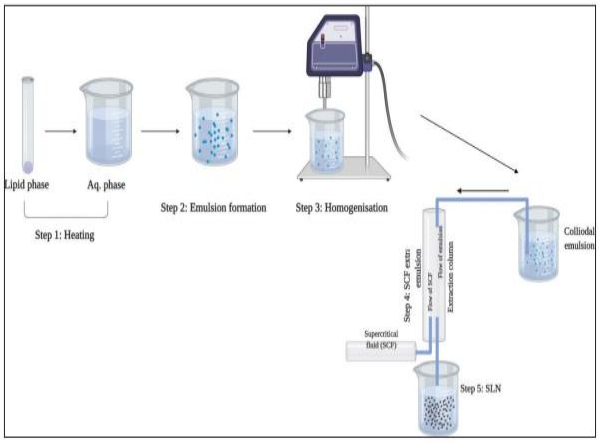

Figure 7: Supercritical fluid technique

Microemulsion

SLN preparations were developed by Gasco and coworkers on the basis of reducing the concentration of microemulsions (Akanksha *et al*., 2012). These microemulsions are biphasic units consisting of external and internal mediums. Combination consists of a low melting fatty acid (e.g., stearic acid), an emulsifier (e.g., polysorbate 20, polysorbate 60, and soy phosphatidylcholine), coemulsifiers (e.g., butanol and sodium mono cetyl phosphate), and water. In the cold water (2°C–3°C), the hot microemulsion is diffused. Based on the combination of microemulsion, the dilution process can be fixed. In this method, there is no extra energy consumed for attaining the submicron size (Gasco, 1997; Ramteke *et al*., 2012). The main criteria for the production of nanoparticles are that they can be produced only with certain solvents which rapidly distribute into the aqueous phase, whereas more lipophilic solvents are utilized for obtaining the large particle sizes. The main advantage of this method is low mechanical energy input which is sufficient.

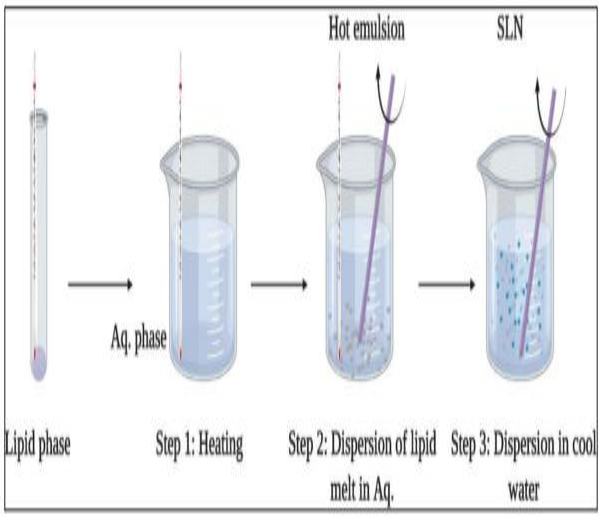

Figure 8: Microemulsion technique

Spray drying

It is another procedure to lyophilization for the modification of an aqueous dispersion into a drug. It is an economical method when compared to lyophilization. There is a chance of particle gathering due to the elevated temperature, shear forces, and incomplete melting of the particle (Jawahar *et al*., 2012). Freitas *et al*. (1998) recommended that the lipids with a boiling point higher than 70°C should be selected for spray drying. The best result was procured by spray drying with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol–water mixtures (10/90 v/v).

Double emulsion

This method is used for the preparation of hydrophilicloaded SLNs based on solvent emulsification evaporation. First, the drug is dissolved in aqueous-based solutions and then dissolved in a liquid melt. A stabilizer is used for the stabilization of the primary emulsion (He *et al*., 2015). This primary emulsifier is dispersed in the aqueous phase composed of hydrophilic emulsifier.

Now, the double emulsion is blended and then separated by sifting. Poly (lactic-co-glycolic acid) (PLGA) is vital for the primary w/o emulsion emulsification process. It is observed that with the increase in the concentration of PLGA, there is an enhancement in loading capacity, w/o emulsion stability, and the encapsulation efficiency. PLGA has no impact on the SLN particle size, and with the increase in the concentration of PLGA, there is a significant decline in the zeta potential.

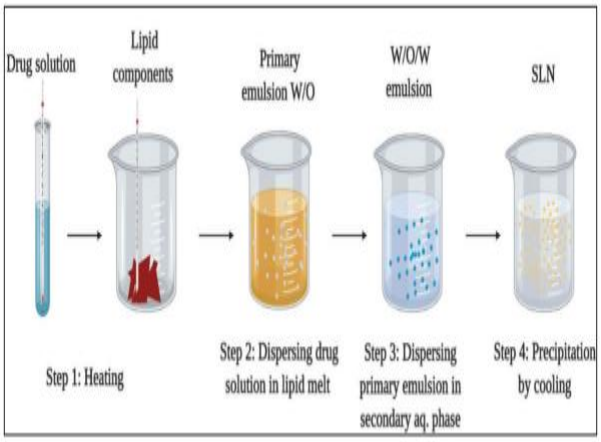

Figure 9: Double emulsion technique

Instrumental techniques for SLN production

The IKA Ultra-Turrax T 18 rotorstator homogenizer17

The lipid (lauric acid, stearic acid, trilaurin, or tristearin) was maintained at ~ 75 °C and allowed to melt completely. Separately, double distilled water was heated to 75 °C. Typically, surfactants were added to the water under magnetic stirring and allowed to equilibrate at 75 °C. Next, the water – surfactant solution was added to the melted lipid and once again allowed to equilibrate at 75 °C. If desired to create the emulsion (i.e., no spontaneous emulsification as in the case of micro emulsions), external mechanical energy then was added in the form of an IKA Ultra-Turrax T 18 rotor-stator homogenizer. The Ultra-Turrax T 18 homogenizer, equipped with the 19 mm dispersing tool, has a speed range of 6,000 – 30,000 rpm and an operational volume range of 10 – 2000 ml. The homogenizer motor produces 160 W of power. The homogenizer only was operated in a batch set-up.

The discontinuous Micron LAB 4018

Laboratory scale production of SLN and Disso Cubes is performed using a piston-gap homogenizer (Micron LAB 40, APV

Homogenizer Gmbl-1, Lubeek, Germany). Minimum batch size is 20 mL, maximum size is 40 mL. Pressure applied ranges from 100 bars to a maximum of 1500 bar. The aqueous dispersion is pressed by a piston through a small homogenization gap that is approximately 25 urns (at a pressure of 500 bars). The process is discontinuous, i.e., the system needs to be dismantled and the dispersion poured back into the central cylinder for the next homogenization cycle. It is more time consuming but the machine has the big advantage of an extremely low sample volume. This is of high interest for compounds that are expensive or of limited availability, but is very time consuming when performing a screening for optimized production parameters and optimized composition of the nanosuspension formulation. For example, screening of four production pressures (e.g., 100, 500, 1000, and 1500 bar) up to two homogenization cycles requires 40 homogenization steps. It gets even more complicated when different surfactants and surfactant mixtures at different concentrations in a nanosuspension need to be checked regarding optimized physical stability of the produced nanosuspension. For screening purposes, a continuous Micron LAB 40 is much more suitable.

The continuous LAB 4020

The continuous LAB 40 has a feeding vessel and a product vessel of a typical size of 0.5 L. It is only necessary to switch two tubes before running the next homogenization cycle. Product samples for size analysis can be drawn directly from the vessels between the homogenization cycles. This speeds up the screening procedure enormously but requires a sample volume of at least 200 mL. This minimum volume of suspension cannot he accepted in the case of very expensive drugs, e.g., paclitaxel (normal price for 1 g is approximately lO.000,-$ US). On the other hand the continuous LAB 40 provides the possibility of producing lab scale batches of up to 0.5—I L (to fit larger vessels to the systems).

The Micron LAB 6022

The Micron LAB 60 is a homogenizer for continuous production with a production capacity of 60 L/h. It consists of two pumps yielding a product flow with minimized fluctuations in homogenization pressure. The dispersion is subsequently passed through two homogenization valves: a first main homogenization valve, and a second valve that creates a certain reverse pressure and is also in charge of redispersing coalesced droplets or aggregates in the case of solid suspensions. As a general rule, the homogenization pressure of the second valve should be about one-tenth of the pressure used in the first valve. The Micron LAB 60 was modified according to the needs of a Good Manufacturing Practices (GMP) production. The production unit with the LAB 60 requires a batch size of approximately 2 L (approximately 2 kg). It is not possible to run such a low volume in the discontinuous production mode because of the relatively large dead volume of the machine (0.5 L) About 25% of the suspension would remain in the machine without being homogenized prior to the next homogenization cycle. From this it is more sensible to run the unit in a continuous circulating mode, with the product feed back after having passed the homogenization tower directly to the feeding vessel.

Characterization of SLN Quality and Structure

Adequate and proper characterization of the SLNs is necessary for its quality control. However, characterization of SLN is a serious challenge due to the colloidal size of the particles and the complexity and dynamic nature of the delivery system. The important parameters which need to be evaluated for the SLNs are, particle size, size distribution kinetics (zeta potential), degree of crystallinity and lipid modification (polymorphism), coexistence of additional colloidal structures (micelles, liposome, super cooled, melts, drug nanoparticles), time scale of distribution processes, drug content, in vitro drug release and surface morphology.

The particle size/size-distribution may be studied using photon correlation spectroscopy (PCS), transmission electron microscopy (TEM), scanning electron microscopy (SEM), atomic force microscopy (AFM), scanning tunneling microscopy (STM), or freeze fracture electron microscopy (FFEM).

Measurement of particle size and zeta potential

Photon correlation spectroscopy (PCS) and laser diffraction (LD) are the most powerful techniques for routine measurements of particle size. The Coulter method is rarely used to measure SLN particle size because of difficulties in the assessment of small nanoparticle and the need of electrolytes which may destabilize colloidal dispersions. PCS (also known dynamic light scattering) measures the fluctuation of the intensity of the scattered light which is caused by the particle movement. This method covers a size range from a few nanometers to about 3 microns. This means that PCS is a good tool to characterize nanoparticles, but it is not able to detect larger microparticles. They can be visualized by means of LD measurements. This method is based on the dependence of the diffraction angle on the particle radius (Fraunhofer spectra). Smaller particles cause more intense scattering at high angles compared to the larger ones. A clear advantage of LD is the coverage of a broad size range from the nanometer to the lower millimeter range. The development of polarization intensity differential scattering (PIDS) technology greatly enhanced the sensitivity of LD to smaller particles. However, despite this progress, it is highly recommended to use PCS and LD simultaneously. It should be kept in mind that both methods do not ‘measure’ particle size. Rather, they detect light scattering effects which are used to calculate particle size. For example, uncertainties may result from non–spherical particle shapes. Platelet structures commonly occur during lipid crystallization and have also been suggested in the SLN. Further, difficulties may arise both in PCS and LD measurements for samples which contain several populations of different size. Therefore, additional techniques might be useful. For example, light microscopy is recommended, although it is not sensitive to the nanometer size range. It gives a fast indication of the presence and character of microparticles (microparticles of unit form or microparticles consisting of aggregates of smaller particles). Electron microscopy provides, in contrast to PCS and LD, direct information on the particle shape. However, the investigator should pay special attention to possible artifacts which may be caused by the sample preparation. For example, solvent

removal may cause modifications which will influence the particle shape. Zeta potential is an important product characteristic of SLNs since its high value is expected to lead to deaggregation of particles in the absence of other complicating factors such as steric stabilizers or hydrophilic surface appendages. It is usually measured by zetameter (Meyer and Heinzelmann, 1992).

Dynamic light scattering (DLS)

DLS, also known as PCS or quasi-elastic light scattering (QELS) records the variation in the intensity of scattered light on the microsecond time scale. This variation results from interference of light scattered by individual particles under the influence of Brownian motion, and is quantified by compilation of an autocorrelation function. This function is fit to an exponential, or some combination or modification thereof, with the corresponding decay constant(s) being related to the diffusion coefficient(s). Using standard assumptions of spherical size, low concentration, and known viscosity of the suspending medium, particle size is calculated from this coefficient. The advantages of the method are the speed of analysis, lack of required calibration, and sensitivity to submicrometer particles (Meyer and Heinzelmann, 1992).

Static light scattering/Fraunhofer diffraction

Static light scattering (SLS) is an ensemble method in which the pattern of light scattered from a solution of particles is collected and fit to fundamental electromagnetic equations in which size is the primary variable. The method is fast and rugged, but requires more cleanliness than DLS, and advance knowledge of the particles' optical qualities.

Acoustic methods

Another ensemble approach, acoustic spectroscopy, measures the attenuation of sound waves as a means of determining size through the fitting of physically relevant equations. In addition, the oscillating electric field generated by the movement of charged particles under the influence of acoustic energy can be detected to provide information on surface charge.

Nuclear magnetic resonance (NMR)

NMR can be used to determine both the size and the qualitative nature of nanoparticles. The selectivity afforded by chemical shift complements the sensitivity to molecular mobility to provide information on the physicochemical status of components within the nanoparticle.

Electron microscopy

SEM and TEM provide a way to directly observe nanoparticles, physical characterization of nanoparticles with the former method being better for morphological examination. TEM has a smaller size limit of detection, is a good validation for other methods, and affords structural required, and one must be cognizant of the statistically small sample size and the effect that vacuum can have on the particles (Meyer and Heinzelmann, 1992).

Atomic force microscopy (AFM)

In this technique, a probe tip with atomic scale sharpness is rastered across a sample to produce a topological map based on the forces at play between the tip and the surface. The probe can be dragged across the sample (contact mode), or allowed to hover just above (noncontact mode), with the exact nature of the particular force employed serving to distinguish among the

subtechniques. That ultrahigh resolution is obtainable with this approach, which along with the ability to map a sample according to properties in addition to size, e.g., colloidal attraction or resistance to deformation, makes AFM a valuable tool (Drake *et al*., 1989).

X-ray diffraction (powder X-ray diffraction) and differential scanning calorimetry (DSC)

The geometric scattering of radiation from crystal planes within a solid allow the presence or absence of the former to be determined thus permitting the degree of crystallinity to be assessed. Another method that is a little different from its implementation with bulk materials, DSC can be used to determine the nature and speciation of crystallinity within nanoparticles through the measurement of glass and melting point temperatures and their associated enthalpies (Drake *et al*., 1989).

Applications of SLN

Per oral administration

Per oral administration forms of SLN may include aqueous dispersions or SLN loaded traditional dos-age forms, e.g. tablets, pellets or capsules. The microclimate of the stomach favors particle aggregation due to the acidity and high ionic strength. It can be expected, that food will have a large impact on SLN performance. The plasma levels and body distribution were determined after administration of CA–SLN suspension versus a CA solution (CA-SOL). Two plasma peaks were observed after administration of CA–SLN. The first peak was attributed to the presence of free drug; the second peak can be attributed to controlled release or potential gut uptake of SLN. These two peaks were also found in the total CA concentration–time profiles of all measured organs. It was also found that the incorporation into SLN protected CA from hydrolysis. The conclusion from this study was that SLN are a promising sustained release system for CA and other lipophilic drugs after oral administration. Increased bioavailability and prolonged plasma levels have been described after per oral administration of cyclosporine containing lipid nanodispersions to animals (Ekambaram *et al*., 2012).

Parenteral administration

SLN have been administered intravenously to animals. Pharmacokinetic studies of doxorubicin incorporated into SLN showed higher blood levels in comparison to a commercial drug solution after i.v. injection in rats. Concerning the body distribution, SLN were found to cause higher drug concentrations in lung, spleen and brain, while the solution led to a distribution more into liver and kidneys. Parenteral application is a very wide field for SLN. Subcutaneous injection of drug loaded SLN can be employed for commercial aspect, e.g., erythropoietin (EPO), interferon-β. Other routes are intraperitonial and also intra-articular. Intraperitoneal application of drug-loaded SLN will prolong the release because of the application area. In addition, incorporation of the drug into SLN might reduce irritancy compared to injecting drug micro particles (Ekambaram *et al*., 2012).

Transdermal application

The smallest particle sizes are observed for SLN dispersions with low lipid content (up to 5%). Both the low concentration of the dispersed lipid and the low viscosity are disadvantageous for dermal ad-ministration. In most cases, the incorporation of the SLN

dispersion in an ointment or gel is necessary in order to achieve a formulation which can be administered to the skin. The incorporation step implies a further reduction of the lipid content. An increase of the solid lipid content of the SLN dispersion results in semisolid, gel-like systems, which might be acceptable for direct application on the skin (Bhaskar *et al*., 2009).

Topical application

Regarding the regularity aspect, topical application is relatively unproblematic. The major advantages for topical products are the protective properties of SLN for chemically labile drugs against degradation and the occlusion effect due to film formation on the skin. Especially in the area of cosmetics there are many compounds such as retinol or vitamin C which cannot be incorporated because of the lack of chemical stability. Incorporation of retinol is only possible when applying certain protective measures during production (e.g. noble gasing) and using special packing materials (e.g. aluminium) (Lippacher *et al*., 2001).

Ophthalmic administration

Many investigations have been made to use nanoparticles for prolonged release of drugs to the eye. The basic problem of ophthalmologic formulation is the fast removal from the eye, which implies clearance of the applied drug through the nose. It could be shown for nanoparticles that an increased adhesiveness is available leading to higher drug levels at desired site of action. However, the basic problem was that the nanoparticles are of limited toxicological acceptance. It was shown by Gasco that SLN have a prolonged retention time at the eye. This was confirmed by using radiolabiled formulations and γ-scintigraphy. The lipids of SLN are easy to metabolize and open a new ways for ophthalmological drug delivery without impairing vision (Araujo *et al*., 2009).

Pulmonary administration

A very interesting application appears to be the pulmonary administration of SLN. SLN powders cannot be administered to the lung because the particle size is too small and they will be exhaled. A very simple approach is the aerosolization of aqueous SLN dispersions. The important point is that the SLN should not aggregate during the aerosolization. The aerosol droplets were collected by collision of aerosol with a glass wall of a beaker. This basically demonstrates that SLN are suitable for lung delivery. After localization into the bronchial tube and in the alveoli, the drug can be released in a controlled way from the lipid particles (Ekambaram *et al*., 2012).

CONCLUSION

Solid lipid nanoparticles (SLNs) have emerged as a promising class of lipid-based nanocarriers capable of overcoming the limitations associated with conventional drug delivery systems. Their unique advantages including biocompatibility, controlled and sustained release, enhanced drug stability, and improved bioavailability make them suitable for a wide range of therapeutic applications. The review highlights that the formulation of SLNs is strongly influenced by factors such as lipid selection, surfactant concentration, production technique, and processing parameters, all of which play critical roles in determining particle size, entrapment efficiency, drug loading, and stability. Modern characterization tools further enable a deeper understanding of SLN behavior,

ensuring quality, reproducibility, and regulatory compliance.

Despite significant progress, challenges such as limited drug loading, potential polymorphic transitions, and scale-up complexities remain to be fully addressed. Continued advancements in formulation optimization, surface engineering, and hybrid nanocarrier systems are expected to expand the clinical and industrial potential of SLNs. SLNs represent a versatile and efficient platform for next-generation drug delivery, offering immense promise for targeted therapy, enhanced patient compliance, and improved therapeutic outcomes.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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