Current Status of Solid Lipid Nanoparticles: A Review

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Abstract

Most of the active pharmaceutical ingredients (APIs) under development are poorly water soluble and have poor bioavailability. Nanotechnology is an approach to overcome the challenges of conventional drug delivery systems. Solid Lipid nanoparticles show interesting features concerning therapeutic purposes. The main advantage is that they are prepared with physiologically well-tolerated lipids. Solid Lipid Nanoparticles (SLNs) as novel lipid based nanocarriers with size range between 10 to 1000nm. SLNs were introduced to overcome problems of polymeric nanoparticles. By putting forward physiological safe lipids in place of polymers to prepare lipid nanoparticles, a novel formulation technique came into light. An approach undertaken here is to focus on various production methods for preparation of SLNs, wide pharmaceutical applications of SLNs in drug delivery are explored.

Keywords: Solid lipid nanoparticles; Colloidal delivery system; Homogenization; Phospholipids; Hydrophilic; Lipophilic

Introduction

Targeted delivery system is one of the most challenging research areas in pharmaceutical sciences. By developing colloidal delivery systems such as liposomes, micelles and nanoparticles, new challenge have opened for improving drug delivery [1].

Compared to many other materials used as drug carriers, in particular to polymers, lipids are regarded as a more physiological option and a high biocompatibility is expected [2]. From all the different types, Solid lipid nanoparticles are at the forefront of the rapidly developing field of nanotechnology with several potential applications in drug delivery, clinical medicine and research as well as in other varied sciences. Solid lipid nanoparticles (SLN) introduced in 1991 represent an alternative carrier system to tradition colloidal carriers [3]. In system consists of spherical solid lipid particles in the nanometer ranges, which are dispersed in water or in aqueous surfactant solution. It is identical to an oil-in-water emulsion for parenteral nutrition but the liquid lipid (oil) of the emulsion has been replaced by a solid lipid, i.e. yielding Solid Lipid Nanoparticles. Different production methods which are suitable for large scale production and applications of solid lipid nanoparticles are described [4]. Nanoparticles made from solid lipids are attracting major attention as novel colloidal drug carrier for intravenous applications as they have been proposed as an alternative particulate carrier system [5]. Basically, SLNs are made of a solid lipid core with a monolayer phospholipid shell. The solid state of the nanoparticulate matrix provides protection to chemically labile drugs and prolongation of drug release [3]. The solid core contains the drug dissolved or dispersed in the solid high melting fat matrix. The hydrophobic chains of phospholipids are embedded in the fat matrix. They have potential to carry lipophilic or hydrophilic drugs or diagnostics [6] (Figure 1).

Figure 1: Metabolomics Process in Phytomedicine.

SLN encompasses the advantages of polymeric nanoparticles, fat emulsion and liposomes but simultaneously avoid some of their disadvantages. They have many advantages such as good biocompatibility, non toxic, stable against coalescence, drug leakage, hydrolysis, biodegradable, physically table and good carrier for lipophilic drugs. There are major difference between lipid emulsion and liposomes. The basic structure of a lipid emulsion is a neutral lipophilic oil core surrounded by monolayer of amphiphilic lipid [4]. Nanosized drug delivery systems have been developed to overcome the following problems...
a) Low or highly variables drug concentrations after per oral administration due to poor absorption, rapid metabolism and elimination.

b) Poor drug solubility which includes iv injections of aqueous drug solutions

c) Drug distribution to other tissue combined with high toxicity. (eg: Cancer drugs) [1].

Advantages of SLN

a) The shelf-life stability of SLNs can be very good. Lipids can be chosen that do not hydrolyze in aqueous suspension [7].
b) Easy to manufacture than bipolymeric nanoparticles.
c) SLNs have better stability and ease of upgradability to production scale as compared to liposome.
d) Controlled release kinetics [3].
e) Most of the materials for preparing SLNs are low cost with ease of scale-up for industrial production [2].
f) SLNs can be enhancing the bioavailability of entrapped bioactive.
g) Chemical protection of labile incorporated compound.
h) Large scale production possible.
i) Lyophilization possible.
j) Site specific delivery of drugs, enhanced drug penetration into the skin via dermal application

Disadvantage of SLN

a) Poor drug loading capacity.
b) Relatively high water content of the dispersions (70-99.9%).
c) Drug expulsion after polymeric transition during storage.
d) The low capacity to load hydrophilic drugs due to partitioning effects during the production process.
e) Need to remove too much water in tablet / pellet production [1].

Principle of Drug Release from SLN

a) Higher surface territory because of little molecule measure in nanometer extent gives higher medication discharge.
b) Slow medication discharge can be accomplished when the medication is homogenously scattered in the lipid framework. It depends on sort and medication entanglement model of SLN.
c) Fast initial drug release in the first 5min in the drug enriched shell model as a result of the outer layer of particle due to larger surface area of drug depositon on the particle surface.
d) The burst release is reduced with increasing particle size and prolonged release could be obtained when the particles are sufficiently large, i.e., lipid macromolecules.
e) The type of surfactant and its concentration, which will interact with the outer shell and affect its structure, should be noted as the outer factor which is important, because a low surfactant concentration leads to a minimal burst and prolonged drug release.
f) The particle size affect drug release rate directly depends on various parameters such as composition of SLN formulation (such as surfactant, lipid, drug) production method and conditions (such as production time, equipment, sterilization and lyophilisation [5,6].

Formulation of SLN

General ingredients include solid lipid(s), emulsifier(s) and water. The term lipid is used here in a broader sense and includes triglycerides (e.g. tristearin), partial glycerides (e.g. Imwitor), fatty acids (e.g. stearic acid), and steroids (e.g. cholesterol) and waxes (e.g. cetyl palmitate). All classes of emulsifiers (with respect to charge and molecular weight) have been used to stabilize the lipid dispersion. It has been found that the combination of emulsifiers might prevent particle agglomeration more efficiently [9,10].

Method of Preparation - High Pressure Homogenization

High pressure homogenization (HPH) has emerged as a reliable and powerful technique for the preparation of SLN. High pressure homogenizers push a liquid with high pressure (100-2000 bar) through a narrow gap. The fluid accelerates on a very short distance to very high velocity (over 1000km/h). Very high shear stress and cavitation forces disrupt the particles down to the submicron range. Typical lipid contents are in the range 5-10% and represent no problem to the homogenizer. Even higher lipid concentrations (up to 40%) have been homogenized to lipid nanodispersions [9].

Hot homogenization

Hot homogenization is generally carried out at temperatures above the melting point of the lipid. A pre-emulsion of the drug loaded lipid melt and the aqueous emulsifier phase (same temperature) is obtained by high shear mixing device. The resultant product is hot o/w emulsion and the cooling of this emulsion leads to crystallization of the lipid and the formation of SLNs. Generally, 3-5 homogenization cycles at a pressure of 500-1500 bar are used [8]. Mangesh Bhalekar, prepared Darunavir solid lipid Nanoparticles by using hot homogenisation method technique Freeze-dried SLN further characterized using SEM, DSC.
and PXRD analysis revealed complete entrapment of the drug and amorphous nature of the SLN. In vitro release studies in 0.1N HCl and 6.8 pH buffer demonstrated 84 and 80% release at the end of 12h. The apparent permeability of the SLN across rat intestine was found to be $24 \times 10^{-6}$ at 37 °C at the end of 30min while at 4 °C the same was found to be $5.6 \times 10^{-6}$ prompting involvement of endocytic processes in the uptake of SLN. Accelerated stability studies revealed no prominent changes upon storage [11]. In another article the researcher prepared alendronate sodium-loaded SLN by using hot homogenization method. In result they found that High drug encapsulation efficiency (70-85%) was achieved by drug determination through derivatization with o-phthalaldehyde. The physical stability of drug-loaded SLNs in aqueous dispersions was assessed in terms of size and drug leakage during two weeks. Scanning electron microscopy images showed spherical particles in the nanometer range confirming the obtained data from size analyzer. Several cytotoxicity studies including MTT, DAPI staining and DNA fragmentation assays as well as flow cytometry analysis confirmed the low toxicity of alendronate-loaded SLNs [12].

Gamze Güney formulated ascorbic acid loaded solid lipid nanoparticles by using hot homogenisation method. The obtained SLN formulations were characterized by Nano Zetasizer ZS and HPLC with the particle size being less than 250nm. AA-SLNs exhibited sustained release and high entrapment efficiency. According to MTT test results, AA-SLNs showed high cytotoxic activity compared to the free AA against H-Ras 5RP7 cells without damaging NIH/3T3 control cells [13].

- Cold homogenization
- Cold homogenization is carried out with the solid lipid containing drug and therefore called as milling of a suspension. Cold homogenization has been developed to prevent:
  - Temperature induced drug degradation.
  - Partitioning of hydrophilic drug from lipid phase to aqueous phase.
  - Complexity of the crystallization step of the nanoemulsion leading to several modifications and/or super cooled melts [9] (Figure 2).

**Figure 2:** Hot and Cold High Pressure Homogenization Technique in the Production of SLN/NLC [14].

**Ultrasonication / High Speed homogenization**

Ultrasonication or high speed homogenization is another method for the production of SLNs. The advantage of this method is that the equipment used is commonly available at lab scale [8]. Disadvantage is like it distributes larger particle size ranging between micrometer range lead to physical instability like particle growth upon storage and also metal contamination due to ultrasonication [14,15]. YiFan Luo prepared vinpocetine’s solid lipid Nanoparticles by using ultrasonic-solvent emulsification technique. The mean particle size and droplet size distribution, drug loading capacity, drug entrapment efficiency (E. E%), zeta potential, and long-term physical stability of the SLNs were investigated in detail respectively. Drug release from two sorts of VIN-SLN was studied using a dialysis bag method. A pharmacokinetic study was conducted in male rats after oral administration of 10mgkg-1 VIN in different formulations, it was found that the relative bioavailability of VIN in SLNs was significantly increased compared with that of the VIN solution. The absorption mechanism of the SLN formulations was also discussed. These results indicated that VIN absorption is enhanced significantly by employing SLN formulations [16].

**Solvent Emulsification-Evaporation Method**

In solvent emulsification-evaporation method, the lipophilic material and hydrophobic drug were dissolved in a water
immiscible organic solvent (e.g. cyclohexane, dichloromethane, toluene, chloroform) and then that is emulsified in an aqueous phase using high speed homogenizer. To improve the efficiency of fine emulsification, the coarse emulsion was immediately passed through the microfluidizer. Thereafter, the organic solvent was evaporated by mechanical stirring at room temperature and reduced pressure (e.g. rotary evaporator) leaving lipid precipitates of SLNs [4]. The big advantage of this method is the avoidance of any thermal stress, which makes it appropriate for the incorporation of highly thermo labile drugs. A clear disadvantage is the use of organic solvent which may interact with drug molecules and limited the solubility of the lipid in the organic solvent [17]. Deepthi Soma, prepared irbesartan solid lipid Nanoparticles using glyceryl monostearate by solvent emulsification method followed by probe sonication. Formulation was then further evaluated for the pharmacokinetic studies in Wistar rats. Irbesartan-loaded SLN of particle size 523.7nm and 73.8% entrapment efficiency showed good bioavailability in Wistar rats and also showed optimum stability in the studies. The SLN prepared using glyceryl monostearate by solvent emulsification method leads to improve bioavailability of the drug [18] (Figure 3).

Supercritical Fluid Method

The supercritical fluid has unique thermo-physical properties which can be finely tuned by small changes in the pressure. As the pressure raises the density and the ability of the fluid to dissolve compounds increases while the viscosity remains relevantly constant. Accordingly under high pressure and appropriate temperature in the supercritical range the fluid can act as an alternative to organic solvents and dissolve different APIs and lipids [14]. Super critical carbon dioxide has a tendency to dissolve the lipophilic drugs, by combination with ultrasonication technique it can be used to prepare SLNs. Xionggui loaded SLNs have been prepared by using super critical carbon dioxide fluid extraction and ultrasonication [19].

Microemulsion Based Method

Gasco et al. (1997) developed SLNs based on the dilution of microemulsions [8]. This method is based on the dilution of microemulsions. As micro-emulsions are two-phase systems composed of an inner and outer phase (e.g. o/w microemulsions). They are made by stirring an optically transparent mixture at 65-70 °C, which typically composed of a low melting fatty acid (e.g. stearic acid), an emulsifier (e.g. polysorbate 20), co-emulsifiers (e.g. butanol) and water. The hot microemulsion is dispersed in cold water (2-3 °C) under stirring [4]. According to De Labouret et al. [20] the particle size is critically determined by the velocity of the distribution processes. Nanoparticles were produced only with solvents which distribute very rapidly into the aqueous phase (acetone), while larger particle sizes were obtained with more lipophilic solvents (Figure 4).

Spray Drying Method

Spray drying method is a cheaper method than lyophilization. This method causes particle aggregation due to high temperature, shear forces and partial melting of the particle [21]. Freitas C et al. [22] recommends the use of lipid with melting point >70 °C.
for spray drying, the best result by spray drying method was obtained with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol water mixtures (10/90 v/v) [21,22].

**Double Emulsion Method**

Novel method based on solvent emulsification evaporation has been used for preparation of hydrophilic loaded SLNs [8]. Drug (mainly hydrophilic drugs) was dissolved in aqueous solution, and then was emulsified in melted lipid. This primary emulsion was stabilized by adding stabilizer (e.g. gelatin, poloxamer-407). Then this stabilized primary emulsion was dispersed in aqueous phase containing hydrophilic emulsifier (e.g. PVA). Thereafter, the double emulsion was stirred and was isolated by filtration [4]. ShuYu Xie prepared hydrophilic protein-loaded SLN by w/o/w double emulsion and solvent evaporation techniques. The results showed that PLGA was essential for the primary w/o emulsification. In addition, the stability of the w/o emulsion, the encapsulation efficiency and loading capacity of the nanoparticles were enhanced with the increase of PLGA concentration. Furthermore, increasing PLGA concentration decreased zeta potential significantly but had no influence on particle size of the SLN. In vitro release study showed that PLGA significantly affected the initial burst release, i.e. the higher the content of PLGA, the lower the burst release [23].

**Membrane Contactor Method**

In this method membrane contactor was used to prepare SLNs, lipid was pressed at the temperature above the melting point of lipid through the membrane pores, water circulated beyond the pores flow with the produced droplets of melted lipid which was further cooled at room temperature [19]. The advantages of this process of SLN preparation using a membrane contactor are shown to be its facility of use, the control of the SLN size by an appropriate choice of process parameters and it’s scaling up ability [4]. The membrane contactor method is also used for the preparation of polymeric nanoparticles, by methods involving a polymerization of dispersed monomers (interfacial polymerization method) or a dispersion of preformed polymers (nano precipitation method) (Figure 5).

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**Solvent Injection Technique**

In this technique, the solid lipid was dissolved in water-miscible solvent (e.g. ethanol, acetone, isopropanol) or a water-miscible solvent mixture. Then this organic solvent mixture was slowly injected through an injection needle in to stirred aqueous phase with or without surfactant. Then the dispersion was filtered with a filter paper in order to remove any excess lipid [19]. The presence of surfactant within the aqueous phase helps to produce lipid droplets at the site of injection and stabilize the formed SLNs until solvent diffusion was complete by reducing the surface tension. Solvent injection lyophilization method was used to prepare cinnarizine SLNs, a lipophilic drug.

**Applications of SLN-SLN for Chemotherapy**

Cancer is characterized by the formation of abnormal tissues known as neoplasm. Developed basically due to change in the way cells proliferate and differentiate. Currently, cancer fighting drugs are toxic to both tumor and normal cells, thus the efficacy of chemotherapy is always limited by the side effects of the drug [24].

Use of nanotechnology in cancer biology has provided hope within scientific communities of developing novel cancer therapeutic strategies. Some nanoscale devices can be targets to the cancer cells. This increases the selectivity of the drugs toward the cancer cells and will reduce the toxicity for normal tissue. There are many reports describing potentials of lipid nanoparticles for parental delivery particularly for the treatment of cancer. Over the past couple of decades, a huge amount of detailed data have been amassed regarding the basic biological processes that become perturbed in cancer, such as disturbances in growth-factor binding, signal transduction, gene transcription control, cell-cycle checkpoints, apoptosis, and angiogenesis. These in turn have prompted the search for rational anticancer drugs and produced a record number of
novel compounds, currently being used in cancer treatment trials [25,26]. In another research tamoxifen citrate loaded nanoparticles were administered by intravenous injection in rats and the pharmacokinetic parameters were determined. The \( t_{1/2} \) and mean residence time of TC-loaded SLNs in plasma was about 3.5-folds (\( p < 0.001 \)) and 3-fold (\( p < 0.001 \)) higher, respectively than free tamoxifen, this indicates the potential of TC-loaded SLNs as a long circulatory system in blood. Thus the above mentioned solid lipid nanoparticles can be a beneficial system to deliver tamoxifen to cancer tissues through enhanced permeability and retention (EPR) effect [27].

**SLNs for Topical use**

Corticosteroids are therapeutic agents generally used in the treatment of skin diseases such as eczema or psoriasis. Topical SLN products show enormous prospective for treating dermatological conditions by targeting corticosteroids to dermal disease sites while decreasing systemic drug absorption. Topical application of the drugs at the pathological sites offers possible advantages of delivering the drug directly to the site of action [15]. SLNs used for topical application for various drug such as anticancer, vitamin-A, isotretinoin, flurbiprofen. Using glyceryl behenate, vitamine A-loaded nanoparticles can be prepared. This method is useful for the improvement of penetration with sustained release. The isotretinoin-loaded lipid nanoparticles were formulated for topical delivery of drug. Production of the flurbiprofen-loaded SLN gel for topical application offer a potential advantage of delivering the drug directly to the site of action, which will produce higher tissue concentrations [28-30]. Dermal delivery of Doxorubicin (Dox) would be an ideal way in maximising drug efficiency against skin cancer accompanying with minimising side effects [31].

**Oral SLN in Antitubercular Chemotherapy**

Antitubercular drugs such as rifampcin, isoniazide, pyrazinamide-loaded SLN systems were able to reduce the dosing frequency and improve patient compliance. Antitubercular drugs loaded SLNs were prepared using solvent diffusion technique [4].

**SLNS as Cosmeceuticals**

Cosmeceuticals is rising as the major application target of these carriers. Carrier systems like SLNs and NLC were formulated with a point of view to meet manufacturing needs like scale up, qualification and validation, simple technology, low cost etc [15]. The SLNs have been applied in the preparation of sunscreens and as an active carrier agent for molecular localization has been achieved for vitamin A in upper layers of skin with minimising side effects [31].

**SLNs as Gene Vector Carrier**

SLN can be used in the gene vector formulation. There are several recent reports of SLN carrying genetic/peptide materials such as DNA, plasmid DNA and other nucleic acids. The gene transfer was optimized by incorporation of a diametric HIV-1 HAT peptide into SLN gene vector. The lipid nuclic acid nanoparticles were prepared from a liquid nanophase containing water and a water miscible organic solvent where both lipid and DNA are separately dissolved by removing the organic solvent, stable and homogeneously size lipid-nuclic acid nanoparticle (70-100nm) were formed. It’s called genspheres. It is targeted specific by insertion of an antibody-lyopo polymer conjugated in the particle [21].

**SLNs in Breast Cancer and Lymph Node Metastases**

Mitoxantrone-loaded SLN local injections were formulated to reduce the toxicity and improve the safety and bioavailability of drug efficacy of doxorubicin (Dox) has been reported to be enhanced by incorporation in SLNs. In the methodology the Dox was complexed with soybean -oil-based anionic polymer and dispersed together with a lipid in water to form Dox-loaded solid lipid nanoparticles. The system has enhanced its efficacy and reduced breast cancer cells [1,33].

**SLNs as a Targeted Carrier for Anticancer Drug to Solid Tumors**

SLNs have been reported to be useful as drug carriers to treat neoplasm's. Tumour targeting has been achieved with SLNs loaded with drugs like methotrexate and Camptothecin. Tamoxifen an anticancer drug is incorporated in SLN to prolong release of drug after iv [34].

**Stealth Nanoparticles**

These provide a novel and unique drug-delivery system they evade quick clearance by the immune system. Such nanoparticles can target specific cells. Stealth SLNs have been successfully tested in animal models with marker molecules and drugs. Antibody labelled stealth Lipobodies have shown increased delivery to the target tissue in accessible sites [35].

**Diabetes**

Diabetes mellitus is one of the most common metabolic diseases worldwide. Hyperglycemia caused by diabetes is a serious pathologic condition producing neurological and CV damage. Researchers focus considerable attention on SLNs as the carriers to protect peptides and proteins known for their sensitivity to various environmental factors such as pH, temperature, and ionic strength [36]. Zhang et al designed SLNs coated with stearic acid octaarginine as carriers for insulin. Octaarginine is a cell-penetrating peptide that can facilitate cellular uptake of some drugs [37]. The size and insulin encapsulation of the octaarginine-coated SLNs were 162nm and 77%, respectively. Octaarginine-coated and noncoated SLNs increased Caco-2 cell uptake by 2.3 times and 18.4 times, respectively. The SLNs containing octaarginine showed a significantly higher hypoglycemic effect (3-fold) in rats compared to noncoated SLNs. Oral delivery of insulin may significantly improve the quality of life of diabetes patients who routinely receive insulin by the subcutaneous route [38-40].
SLNs for Potential Agriculture Application

Essential oil extracted from *Artemisia arboresens* L 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 [41].

Infection

Infection can cause host tissues to react to organisms and the toxins they produce. Nanocarriers can be effective drug delivery systems for treating infections [42]. Among the different types of nanosystems, SLNs were widely applicable for carrying anti-infection drugs to treat bacterial, fungal, viral, and parasitic infection. Lopinavir is a human immunodeficiency virus (HIV) protease inhibitor used in antiretroviral therapy. SLNs can act as a feasible carrier for lopinavir because of P-glycoprotein efflux and first-pass metabolism. The lopinavir-loaded SLNs composed of stearic acid were stable at 4°C for 4 months based on particulate size and the release profile [43]. Higher oral bioavailability was obtained for SLNs (2.5-fold) in comparison with lopinavir solution because of higher lymphatic delivery. In another study, Compritol 888 ATO was used as the solid lipid for preparing lopinavir-loaded SLNs [44]. The drug release showed a delayed pattern both in 0.1N HCl (pH 1.2) and phosphate buffer (pH 6.8). The SLNs could bypass P-glycoprotein efflux to reach systemic circulation, leading to a 3.6- and 4.9-fold increase in bioavailability and Cmax compared to solution.

Evaluation of SLN

*in vitro* drug release

Dialysis tubing: *in vitro* drug release could be achieved using dialysis tubing. The solid lipid nanoparticle dispersion is placed in pre-washed dialysis tubing which can be hermetically sealed. The dialysis sac is then dialyzed against a suitable dissolution medium at room temperature, the samples are withdrawn from the dissolution medium at suitable intervals, centrifuged and analyzed for the drug content using a suitable analytical method.

Reverse dialysis: In this technique a number of small dialysis sacs containing 1 ml of dissolution medium are placed in SLN dispersion. The SLN’s are then displaced into the medium.

Franz diffusion cell: The SLN’s dispersion is placed in the donor chamber of Franz diffusion cell fitted with a cellophane membrane. The dispersion is then analyzed against a suitable dissolution medium; the samples are withdrawn from the dissolution medium at suitable intervals and analyzed for drug content using suitable methods like spectroscopy and HPLC methods [4,45].

Characterization of SLN’s

Particle size analysis and Zeta potential

Many techniques are available for particle size analysis and zeta potential like scanning electron microscopy (SEM), atomic force microscopy (AFM), scanning tunneling microscopy (STM) and photon correlation spectroscopy (PCS) [32]. Photon correlation spectroscopy (PCS) and laser diffraction (LD) are the most powerful techniques for determination of particle size. PCS (also known as dynamic light scattering) measures the fluctuation of the intensity of the scattered light, which is caused by particle movement [8].

Zeta potential

Zeta potential measurement can be carried out using zeta potential analyzer or zetameter. Zeta potential gives information about the magnitude of the electrostatic repulsion or attraction between particles in the aqueous suspension of SLN. Zeta potential can serve as an important parameter in the predictions for long term stability of the formulations. High values of zeta potential (e.g., more than +30 mV or less than -30 mV) can stabilize the colloidal suspension by electric repulsion. Electric repulsion generally results in less contact between the particles and less aggregation. For example colloidal systems that contain steric stabilizers can express good long term stability even in cases when zeta potential is as low as around 0 mV [14] (Figure 6).

![Figure 6: Influence of zeta potential on the repulsion/coalescence of particles [13].](image-url)
Electron microscopy

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) provide ways to directly observe nanoparticles. SEM is however better for morphological examination. TEM has a small size limit of detection. Transition electron microscopy and light microscopy both are based on same principle but one difference is that in light microscopy light is used instead of electron [8].

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) is a widely used technique that measures differences in the amount of heat required to increase the temperature of a sample compared to a reference. Differences in heat flow may be positive or negative and are presented as function of the temperature. At phase transition there are differences in the sample compared to the reference [14]. The rate of crystallinity using DSC is estimated by comparison of the melting enthalpy/g of the bulk material with the melting enthalpy/g of the dispersion [8,46].

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 [47].

X-ray diffraction

A useful technique to exclude aggregate of more than 1μm and substantial polymorphic β1 transition form to stable; thus help in characterizing the crystalline nature of the compound and determine the polymorphic shifts present [48]. X-ray diffraction (XRD) play a prominent role because they are able to provide structural information on the dispersed particles [49].

Entrapment efficiency

The entrapment efficiency of the drug is determined by measuring the concentration of free drug in the dispersion medium. Ultracentrifugation was carried out using Centrisart, which consist of filter membrane (molecular weight cutoff 20,000Da) at the base of the sample recovery chamber. The SLNs along with encapsulated drug remain in the outer chamber and aqueous phase moves into the sample recovery chamber. The amount of the drug present in the aqueous phase is determined by HPLC or UV spectrophotometer [50-52].

Conclusion and Future Perspective

SLN constitute an attractive colloidal drug carrier system due to successful incorporation of active compounds and their related benefits. The present review has focused on increasing awareness about nano technological field in drug delivery with the emergence of several promising approaches like solid lipid nanoparticles, nano structured lipid carriers, lipid drug conjugates etc. for improving medical therapeutics. SLNs have already been proven as good formulations in cosmeceuticals and other allied fields, they must occupy a considerable place in the pharmaceutical market. To exploit the broad applications of lipid based nanoparticulate formulations, it is essential that the pharmaceutical industries specialized in the development of new drug delivery systems should engage in novel formulation technology to promote their scale up and bring them onto the pharmacist’s shelves. SLN offer an economical and patient-friendly device for administration of drugs by various routes to maximize effectiveness while avoiding adverse effects on non-target tissues.

For more than 20 years of research the current and future applications of SLN seem well shaped. In parenteral formulations they will offer more possibilities for many drugs with poor aqueous solubility, short half-life and low chemical stability. Moreover SLN are likely to find more applications as targeted drug delivery systems which will “direct” the drug molecules to specific organs of interest and to reduce the systemic toxicity. Thus they can provide solutions for APIs that failed clinical tests due inappropriate tissue localization.

References

Modern Applications of Bioequivalence & Bioavailability


