IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

SOLID LIPID NANOPARTICLES: A REVIEW

Ms. P.A.Panmand [*1], Mrs.V. P. Thorat [2], Mr. Gourav Singh [3], Mr. Sourav Singh [4]

1. Indrayani Institute of Pharmaceutical Education and Research, Talegaon dabhade Pune, Maharashtra
2. SSP Shikshan Sanstha's Siddhi College of Pharmacy Chikhali, Pune, Maharashtra 411062
3. SSP Shikshan Sanstha's Siddhi College of Pharmacy Chikhali, Pune, Maharashtra 411062
4. SSP Shikshan Sanstha's Siddhi College of Pharmacy Chikhali, Pune, Maharashtra 411062

ABSTRACT

Solid lipid nanoparticles (SLN) have emerged as a next-generation drug delivery system with potential applications in pharmaceutical field, cosmetics, research, clinical medicine and other allied sciences. Recently, increasing attention has been focused on these SLN as colloidal drug carriers for incorporating hydrophilic or lipophilic drugs. Proteins and antigens intended for therapeutic purposes may be incorporated or adsorbed onto SLN, and further administered

By parenteral routes or be alternative routes such as oral, nasal and pulmonary. The obstacles associated with conventional chemotherapy may be partially overcome by encapsulating them as SLN. The present review focuses on the utility of SLN in terms of their advantages, disadvantages, method of preparation, characterization and applications.

***Key Words*:** Solid lipid nanoparticles, drug delivery, drug incorporation.

Introduction[1.2, 3]

The SLN is submicron colloidal carriers with the particle size range from 50 nm to 1000 nm.

Which are comprised of physiological lipids, dispersed in water or an aqueous surfactant solution. They are made up of solid hydrophobic core having a monolayer of phospholipids coating. The solidcore encloses the drug dissolved or dispersed in the solid high melting fat matrix as shown in Figure no 1. They are capable to carry both lipophilic and hydrophilic drugs

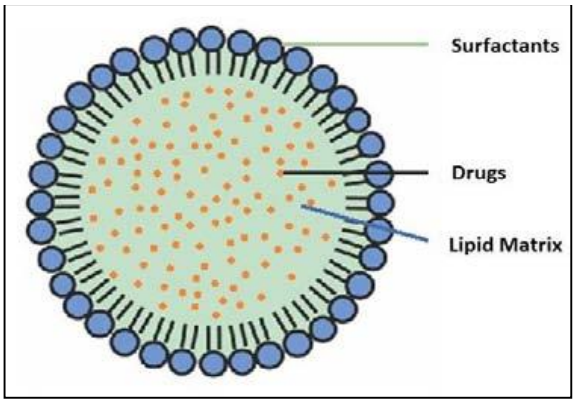


Figure no 1: Structure of solid lipid nanoparticle

Advantages of SLNs [13, 14]

- The use of biodegradable lipids reduces the possibilities of severe and prolonged toxicity.
- Enhancing the bioavailability of low water-soluble active constituents.
- Enhancing the stability of chemically labile drugs through protection from the external environment.
- SLNs have improved stability in comparison with other drug carriers as liposomes.
- The high entrapment efficiency of the active constituents.
- The possibility of lyophilisation.

Disadvantages of SLN [14,16, 17]

- The drug loading ability is poor.
- Water content in the dispersions is comparatively high (70-99.9%).
- The unpredictable tendency to gelation.
- The unpredicted dynamics of polymeric changes.
- Drug expulsion during storage after a polymeric transition.
- The possibility of particle growth.

Methods of preparation[18,19, 20]:

- High pressure homogenization
  - Hot homogenization
  - Cold homogenization
- Ultrasonication/high speed homogenization
- Solvent evaporation method
- Supercritical fluid method
- Microemulsion based method
- Spray drying method
- Double emulsion method
- Precipitation technique

- Film-ultrasound dispersion
- Membranecontactor technique
-

High pressure homogenization [5,6,7,8]

The most popular production technique is considered to be the High-Pressure Homogenization (HPH) which can be operating at low or high temperatures. It has been reported that HPH is the technique used for more than fifty years for the production of**.** Parenteral nutrition, such as Intralipid and Lipofundin .

Hot homogenization[9, 10]:

The first step in this process is the melting of the lipid and dissolving or dispersing of the drug in the lipid melt. Then dispersing this drug-loaded lipid melt in a hot surfactant solution. Premixing is carried out with the help of an ultrasonicator. Then this emulsion is passed through the high-pressure homogenizer, where the temperature should be kept above the lipid melting point. Finally, hot O/W nanoemulsion is cooled down to room temperature where the lipid recrystallizes and leads to the formation of nanoparticles

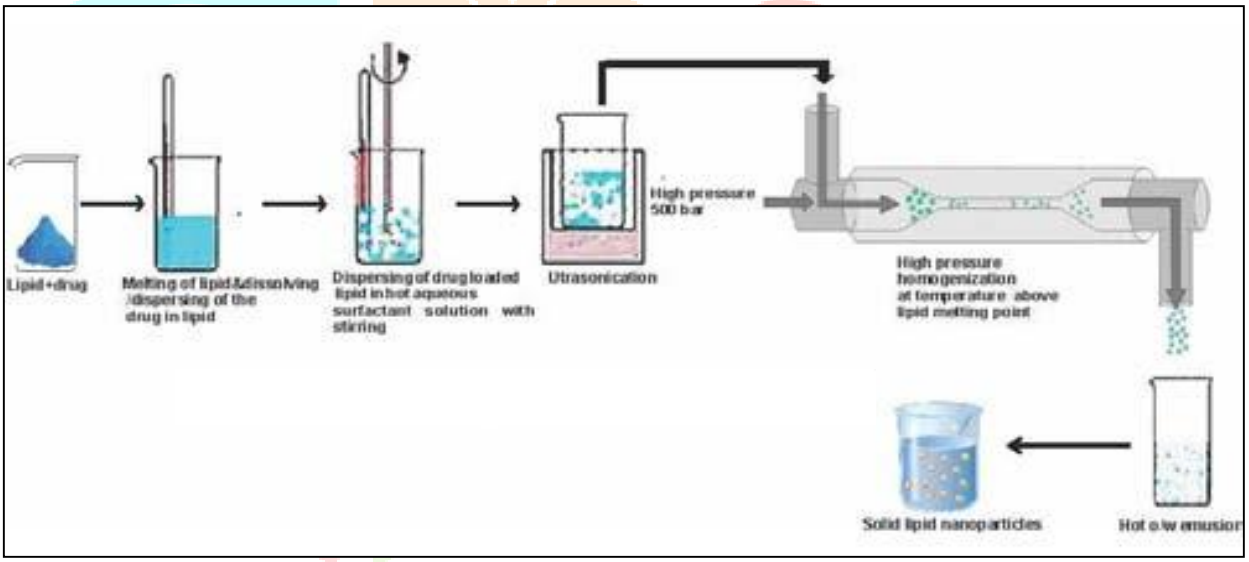


Figure no 2: Hot homogenization techniques

Cold homogenization[11, 12]:

The first step of this technique is the same as that of hot homogenization which includes dispersion or dissolving or solubilization of the drug in the melted lipid. Then the drug lipid mixture is rapidly solidified either with the help of liquid nitrogen or dry ice. The drug-loaded solid lipid is milled by using a roller mill or ball mill to a micron size range of 50-micron to 100 micron and further microparticles are dispersed in chilled emulsifier solution to obtain a pre-suspension (Figure 3). Then this pre-suspension is subjected to high-pressure homogenization at room or below room temperature, where the cavitation force is strong enough to break the microparticles to SLN.

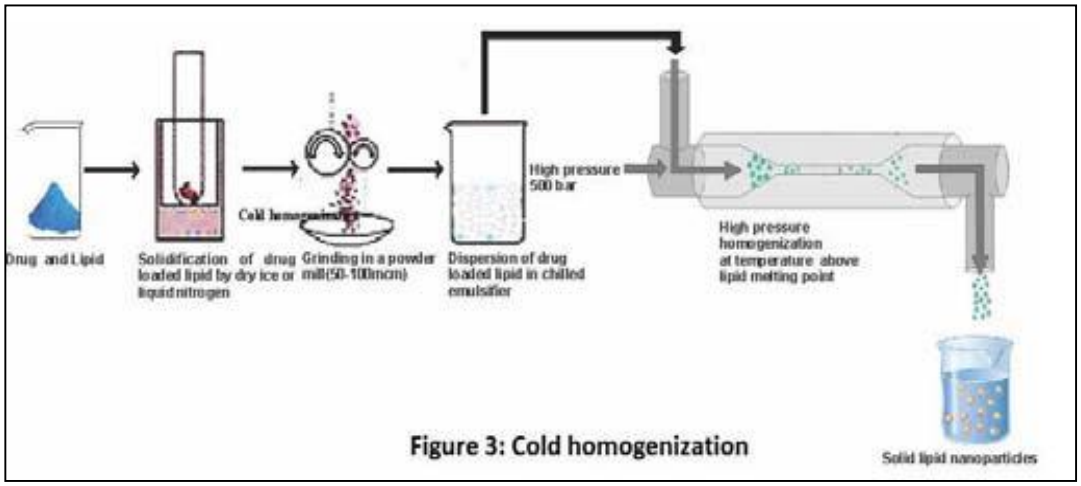


Figure no 3: Coldhomogenization techniques

Advantages[21-25]:

- Hot homogenization method is most suitable for hydrophobic or lipid derivate, direct incorporation of such drugs are easy in this method.
- This method is suitable for large scale-up.it was reported that this technique can be used to produce small particle diameter with a low poly dispensability index usually below 0.2
- HPH technique doesn't require any usage of toxic organic solvent.

Disadvantages[26, 27, 28]:

- When hot homogenization compares with cold homogenization, SLN developed by cold homogenization particle size and poly dispensability index is more.
- By using cold homogenization, we can only minimize the thermal contact of thedrug, but it does not completely avoid it because it also required the melting of the lipid/drug mixture in the first step of preparation.

Ultrasonication or high speed homogenization[29]:

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. However, this method suffers from problems such as broader size distribution ranging into micrometer range. Potential metal contaminations, physical instability like particle growth upon storage are other drawbacks associated with this technique

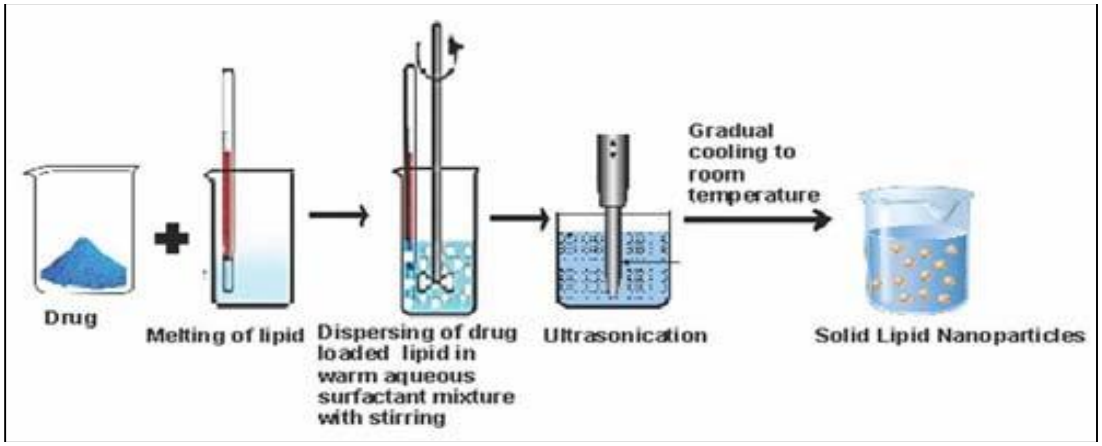


Figure no 4: Cold homogenization techniques

Solvent evaporation method[30]

In this method, the first step is lipids are dissolved in an organicsolvent(e.g.cyclohexane).Thelipidphaseisthenemulsifiedinanaqueousphasewhichcontainingdrugathigh-pressurehomogenization.Theorganicsolventwasremovedfromtheemulsion by evaporation under reduced pressure (40 mbar to 60mbar).Evaporationofsolventleadstoprecipitationofthelipidintheaqueousmediumyieldsdrug-loadednanoparticles (Figure no 5).

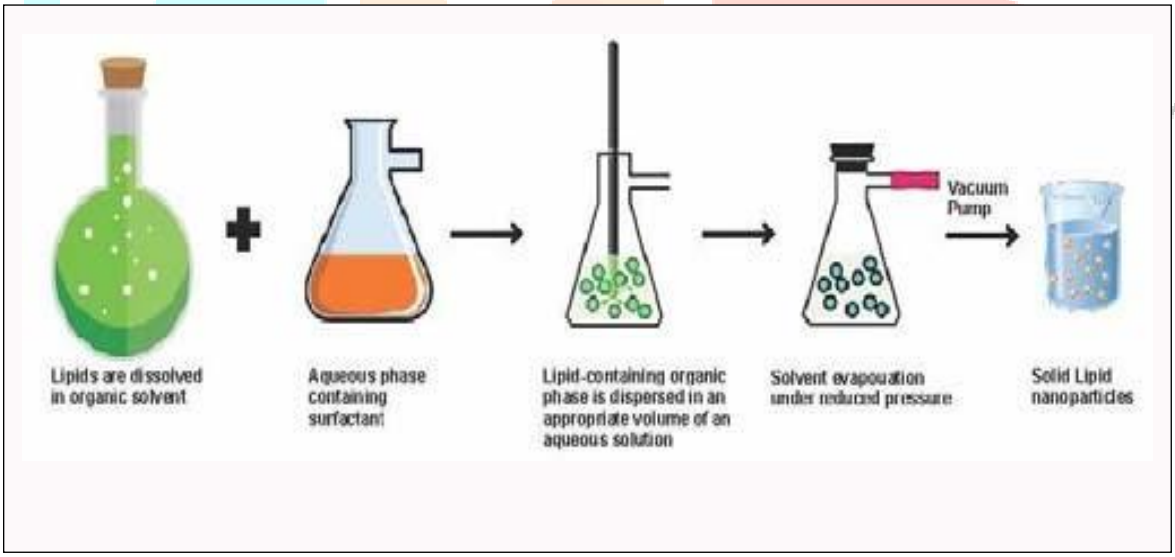


Figure no 5: Solvent evaporation techniques

Advantages: This method is easily scalable and a continuousprocess.

Disadvantage: Itisanextremelycost-effectiveprocessandinwhichpolydisperseddistributionsmayoccur.Toxicologicalproblemsarisingfromsolventresidues

Spray drying[31]

It is considered to be an alternative method to the lyophilization process. This recommends the use of lipid with a melting point more than 70ºC. It was reported that there are different approaches to produce drug-loaded SLN-based formulations by Spray Drying (SD).

In the first approach is that the drug-loaded SLN nanosuspension can be converted into a powder (Figure 6) in the second approach a suspension of drug-loaded SLN in a polymer solution yields SLN/ polymer composites, which can later dissolve to give free SLN; the

third one is a solution of lipid, drug, and polymer can be converted into SLN-loaded polymer particles in the SD step, and again the latter can be dissolved in an aqueous medium to free the SLN, and finally, a lipid/drug/polymer solution can be processed into a molecular

Dispersion composite, which then self-assembles into drug-loaded SLN when water is added.

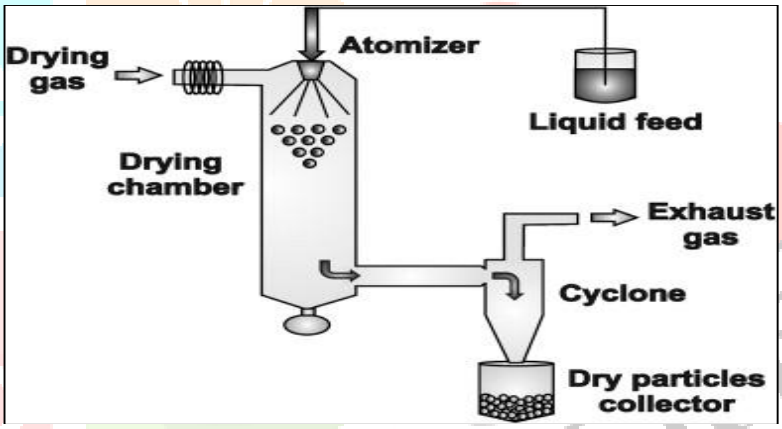
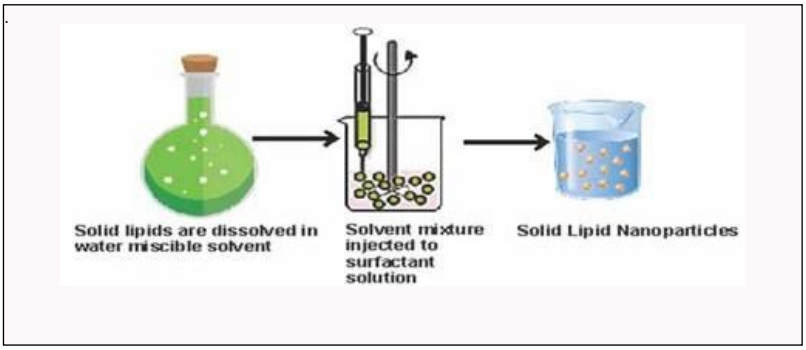


Figure no 6. : Spray drying techniques

Solvent-injection method[33]:

In solvent injection (or solvent displacement) method the lipid and the drug are dissolved in a water-miscible organic solvent (ethanol, acetone, isopropanol) and this solution is injected through a syringe needle in water under stirring: lipid precipitates as nanoparticles while contactingwater, encapsulating the drug. Particle size can be



influenced by lipid type, surfactant and solvent used, and from the viscosity of the outer phase.

Figure no 7: Solvent-injection method

Supercritical fluids[43-48]

It has been reported by numerous researchers that SupercriticalFluids (SCFs) based techniques have been effectively utilized inseveral fields such as the micronization extraction of natural matter,impregnationofmetalsordrugsinaerogels,membranesandscaffoldsproduction.SupercriticalAssistedInjectionina LiquidAntisolvent(SAILA)isaneffectivemethod,whichincludesinjectionofasolutionthatcontainssolidsolutedissolvedin anorganicsolventcontaining controlled quantities of SC-CO_2, in an antisolvent (e.g.:water)solution.Toobtainparticleprecipitation,thesoluteshouldbe such a way that it has to be soluble in the solvent, but not in theantisolventsimultaneously,thesolventandtheantisolventhavetobecompletelymiscible.SC-CO_2dissolvedinthesolutionsolvent-solute,decrease the mixture viscosity and surface tension that will favor theatomization in the antisolvent. A saturator that contains high surfacepacking's and ensures long residence times are used and a near-equilibrium solution between solute, solvent, and CO_2 is formed.Then,thisexpandedliquidsolutionissenttoathinwallinjectorand sprayed into the precipitation vessel containing the antisolventmixingofthetwofluidsproducesarapidsupersaturationandparticleprecipitation,consequently.

Advantages[46-49]: This process offers several advantages no thermaldegradation, use of nontoxic solvents, directly producing a stabilizedwatersuspensionanditprovidesgoodcontrolonparticlesizedistribution.

Film-ultrasounddispersion[42]

In this method the lipid, as well as the drug, were dissolved intosuitable organic solutions, then aqueous phase containing surfactantsolution is introduced to the lipid phase with continuous stirring andupon evaporation of the organic solutions, a lipid film is formed.Further, continue the stirring using the ultrasound with the probesolicitor finally, the SLN with tiny and poly dispersed particle size isformed.

Doubleemulsion method [32]

Inthedoubleemulsionmethod,thehydrophilicdrugisdissolvedin aqueous solution and then was emulsified in melted lipid. Thisprimary emulsion was stabilized by adding suitable stabilizers suchasgelatin,poloxamer-407.Thenthisstabilizedprimaryemulsionwasdispersed in an aqueous phase containing hydrophilic emulsifier likePVA. Further, the double emulsion was stirred and was isolated byfiltration(Figure8).

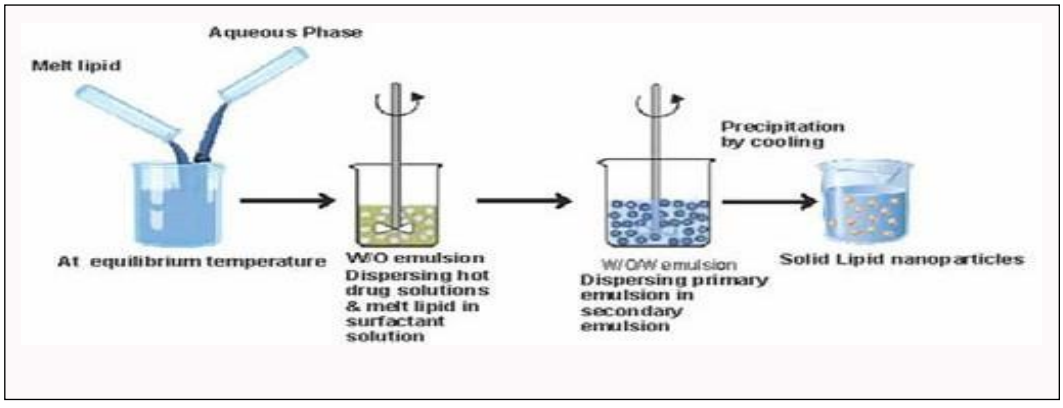


Figure no 8: Doubleemulsion method

9. Precipitation method

The glycerides are dissolved in an organic solvent (e.g. chloroform) and the solution will be emulsified in an aqueous phase. After evaporation of the organic solvent the lipid will be precipitated forming nanoparticles.

Membranecontactor technique[42, 50]

ItisanoveltechniquetopreparetheSLN.Inthistechniqueata temperature above the melting point of the lipid, it was pressedthrough the membrane pores to form small droplets. At the sametime,theaqueousphasewascirculatedtangentiallyinsidethemembrane module with constant stirring and also bows the dropletsbeing formed at the pore outlets. When it cools at room temperature,SLN is formed. In which both the phases were placed in the thermostated bath to maintain sufficient temperature and pressure at theliquidphasewascreatedbynitrogengas

Advantages: SLNpreparationusingamembranecontactoris shown to be its facility of use, the control of the SLN size by anappropriatechoiceofprocessparametersandit'sscalingupability.

Disadvantages: Themaindrawbacksofthismethodarepotentialmetal contaminations, physical instability like particle growth uponstorage.

Characterization of Solid Lipid Nanoparticles (SLNs):

The methods for the characterization should be perceptive to the key parameters of the performance of SLNs. Several parameters which have to be considered in characterization are as follows

1. **Particle size and Zeta Potential [11,12,13,14] :**

- Size of nanoparticles can be determined by several methods such as photon-correlation spectrometry (PCS), transmission electron microscopy (TEM), and scanning electron microscopy (SEM), SEM combined with energydispersive X-RAY spectrometry, scanned probe microscopy and fraunhofer diffraction.
- Among these, the most widely used techniques are PCS and electron microscopy methods.
- SEM and TEM are very useful in determining the shape and morphology of lipid nanoparticles and also allow determination of particle size and distribution.
- Another advanced microscopic technique used for characterization of nanoparticles is atomic force microscopy (AFM).
- This is a new tool to image the original unaltered shape and surface properties of the particles. In this technique, the force acting between the surface and probing tip results in a spatial resolution up to 0.01µm.
- Laser diffraction technique could also be used which is applicable for sub micrometer range particles and calculations are based on the refractive index of the dispersion medium water (1.33) and on the lipid particles.
- The particle size depends on the matrix constituents as well as on the type and amount of emulsifying agents and lipids. It has been reported that increase in amount of emulsifier decreases the mean diameter of the bulk.
- The size and structure of incorporated drug also affects average diameter of the SLNs. Photon correlation spectroscopy (PCS) is also known as dynamic light scattering. This method measures the fluctuation of the

intensity of the scattered light which is caused by particle movement and gives a size range from 3 nanometres to 3 microns.

- The PCS device consists of a light source, a temperature-controlled sample cell, and a photomultiplier for detection of the scattered light. Zeta potential is measure of the charge on the particles. It helps in designing particles with reduced reticuloendothelial uptake.
- In order to divert SLNs away from the RES, the surface of the particles should be hydrophilic and free from charge. Structure of the SLNs can be determined by nuclear magnetic resonance (NMR) technique after Mn+2 or Pr+3 ion complication.

2. Determination of Incorporated Drugs[16]:

- The amount of drug incorporated is determined after separation of the free drug and solid lipids from the aqueous medium and the separation carried out by ultracentrifugation, centrifugation filtration or gel permeation chromatography.
- Drug content can also be determined directly by extracting the drug with suitable solvent under optimum conditions and then analysis of resulted product in SLNs. Models have been proposed to describe the localization of drug molecules in SLNs.
- The enriched shell model is characterized by drug selectively locating at the interface, either by fast solidification of the matrix lipid or by successful competition of the drug for the interface.
- Drug dispersed by such a model might exhibit a successful burst effect during drug release. The homogeneous matrix model is characterized by drug dispersed evenly throughout the matrix, much like a solid solution.
- The enriched 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 enriched core model would be useful to produce a membrane controlled release pattern. Although the chemical stability and the release kinetics of drugs are largely related to localization of drugs within the aggregates, more research is still required to validate these models.

3. In-vitro Drug Release Studies[17]:

- In-vitro drug release studies are mainly useful for quality control as well as for the prediction of in-vivo kinetics. Release profile of drug can be conducted in dialysis tubing or without tubing.
- In dialysis, the SLNs dispersion is introduced into prewashed dialysis tubing, which is then hermetically sealed and then dialyzed against dissolution medium at constant temperature with constant stirring. Samples were taken at different times, centrifuged and assayed for drug content.
- Levy and Benita (1990) have reported a new technique which avoids the enclosure of the colloidal drug carrier in a dialysis sac and is based on reverse dialysis. This method is not sensitive enough to characterize rapid release rate of drug from colloidal carrier.

4. Storage stability[18, 19]:

The physical stability of the SLNs during prolonged storage can be determined by monitoring changes in particle size, drug content, appearance and viscosity. This can also be done by thin layer chromatography.

5. Crystallization tendency and polymorphic behaviour of SLNs[20, 21]:

- Special consideration must be given to crystallization of lipids because this is associated with drug incorporation and release rates.
- The solid state of the particles is of major importance, as it reduces the mobility of incorporated drugs and thus preventing drug leakage from the carrier.
- Basic techniques to establish the physic-chemical state of particles include thermal analysis and X-ray diffraction.
- In thermal analysis most commonly used techniques are differential thermal analysis (DTA) and differential scanning Calorimetry (DSC).

Applications of SLN [4, 26, 27]:

There are several potential applications of SLNs some of which are given below:

1. SLN as potential new adjuvant for Vaccines[4, 26, 27]:

- Adjutants are used in vaccination to enhance the immune response. The safer new subunit vaccines are less effective in immunization and therefore effective adjuvants are required.
- New developments in the adjuvant area are the emulsion systems. These are oil-in-water emulsions that degrade rapidly in the body.
- Being in the solid state, the lipid components of SLNs will be degraded more slowly providing a longer lasting exposure to the immune system.

2. Solid Lipid Nanoparticles in Cancer Chemotherapy[4, 26, 27]:

- From the last two decades several chemotherapeutic agents have been encapsulated in SLN and their in-vitro and in-vivo efficacy have been evaluated.
- Outcomes of these studies have been shown to improve the efficacy of chemotherapeutic drugs, simultaneously reduction in side effects associated with them.
- Improved stability of drugs, encapsulation of chemotherapeutic agents of diversified physicochemical properties, enhanced drug efficacy, improved pharmacokinetics and less in-vitro toxicity are the important features of SLN which make them a suitable carrier for delivering chemotherapeutic drugs.
- Several obstacles frequently encountered with anticancer compounds, such as normal tissue toxicity, poor specificity and stability and a high incidence of drug resistant tumor cells, are at least partially overcome by delivering the musing SLN.
- The rapid removal of colloidal particles by the macrophages of the RES is a major obstacle to targeting tissues elsewhere in the body, such as bone marrow and solid tumors.

3. SLN as Targeted Carrier for Anticancer drug to Solid Tumor [28-30, 31]:

- SLN have been to be useful as drug carriers.
- Tamoxifen is an anticancer drug incorporated in SLN to prolong the release of drug after IV administration in breast cancer.
- Tumor targeting has been achieved with SLN loaded with drugs like methotrexate and camptothecin.

4. SLN in breast cancer and lymph node metastases [31] :

Mitoxantrone SLN local injections were formulated to reduce the toxicity and improve the safety and bioavailability of the drug.

5. Solid Lipid Nanoparticles for delivering Peptides and Proteins [32] :

- Solid lipid particulate systems such as solid lipid nanoparticles (SLN), lipid microparticles (LM) andlipospheres have been sought as alternative carriers for therapeutic peptides, proteins and antigens.
- The research work developed in the area confirms that under optimized conditions they can be produced to incorporate hydrophobic or hydrophilic proteins and seem to fulfill the requirements for an optimum particulate carrier system.
- Proteins and antigens intended for therapeutic purposes may be incorporated or adsorbed onto SLN, and further administered by parenteral routes or by alternative routes such as oral, nasal and pulmonary.
- Formulation in SLN confers improved protein stability, avoids proteolysis degradation, as well as sustained release of the incorporated molecules.
- Important peptides such as cyclosporine A, insulin,calcitonin and somatostatin have been incorporated into solid lipid particles and are currently under investigation. Several local or systemic therapeutic applications may be foreseen, such as immunisation with protein antigens, infectious disease treatment, chronic diseases and cancer therapy.

6. Solid Lipid Nanoparticles for Targeted Brain Drug Delivery [22]:

- The extremely small particle size of solid lipid nanoparticles, which are less than 50 nm, might be beneficial with respect to drug targeting.
- Small carrier size generally favors reduced uptake by thereticuloendothelial system. Drug targeting might also be possible by surface modification of solid lipidnanoparticles. SLNs can improve the ability of the drug to penetrate through the blood-brain barrier and is promising drug targeting system for the treatment of central nervous system disorders.
- In a study to overcome the limited access of the drug 5-fluoro-2'-deoxyuridine (FUdR) to the brain, 3',5'-dioctanoyl-5-fluoro-2'deoxyuridine (DO-FUdR) was synthesized and incorporated into solid lipid nanoparticles (DOFUdR-SLN) .
- The state of the art on surfactant coated poly (alkylcyanoacrylate) nanoparticles specifically designed for brain targeting is given by emphasizing the transfer of this technology to solid lipid matrices.
- The potential advantages of the use of solid lipid nanoparticles over polymeric nanoparticles are accounted on the bases of a lower cytotoxicity, higher drug loading capacity, and best production scalability.
- Solid lipid nanoparticles physicochemical characteristics are also particularly regarded in order to address the critical issues related to the development of suitable brain targeting formulations.

6. **Solid Lipid Nanoparticles for Parasitic Diseases[4, 27, 34]:**

- Parasitic diseases (like malaria, leishmaniasis, tryanosomiasis) are one of the major problems around the globe.
- Ant parasitic chemotherapy is the only choice of treatment for these parasitic infections, the reason for this is that these infections do not elicit pronounced immune response hence effective vaccination may not be possible.
- Solid lipid nanoparticles (SLNs) and nanostructure lipid carriers (NLCs) represent a second generation of colloidal carriers and have emerged as an effective alternative to liposomes mainly due to their better stability profile, ease of scalability and commercialization and relative cost efficacy.
- Moreover, SLN and NLC due to their particulate nature and inherent structure exhibit good potential in the treatment of parasitic infections. Recent reports including our investigation have validated their utility at least to some extent.
- However, the need of hour is to undertake extensive investigations on SLN and NLC matrices in order to extend their versatility with respect to encapsulation ability and target ability and to arrive at a versatile, effective and economical approach for the delivery of anti-parasitic drugs.

7. **Solid Lipid Nanoparticles for Ultrasonic drug and Gene Delivery [4] :**

- Drug delivery research employing micelles and nanoparticles has wide application in ultrasonic drug and gene delivery in recent years of particular interest is the use of these nanovehicles that deliver high concentrations of cytotoxic drugs to diseased tissues selectively, thus reducing the agent's side effects on the rest of the body.
- Ultrasound, traditionally used in diagnostic medicine, is finding a place in drug delivery in connection with these nanoparticles.
- In addition to their non-invasive nature and the fact that they can be focused on targeted tissues, acoustic waves have been credited with releasing pharmacological agent’s from nanocarriers, as well as rendering cell membranes more permeable.
- Ultrasonic drug delivery from micelles usually employs polyether block copolymers and has been found effective in vivo for treating tumors.
- Ultrasound releases drug from micelles, most probably via shear stress and shock waves from the collapse of cavitation bubbles.
- Liquid emulsions and solid nanoparticles are used with ultrasound to deliver genes invitro and in vivo.
- The small packaging allows nanoparticles to extravagate into tumor tissues. Ultrasonic drug and gene delivery from nano carriers has tremendous potential because of the wide variety of drugs and genes that could be delivered to targeted tissues by fairly non-invasive means.

8. **SLN applications for improved delivery of antiretroviral drugs to the brain [27] :**

- Human immunodeficiency virus (HIV) can gain access to the central nervous system during the early course of primary infection.
- Once in the brain compartment the virus actively replicates to form an independent viral reservoir, resulting in debilitating neurological complications, latent infection and drug resistance.

- Current antiretroviral drugs (ARVs) often fail to effectively reduce the HIV viral load in the brain. This, in part, is due to the poor transport of many ARVs, in particular protease inhibitors, across the bloodbrainbarrier (BBB) and blood-cerebrospinal fluid barrier (BCSBF).
- Studies have shown that nanocarriers including polymeric nanoparticles, liposomes, solid lipid nanoparticles (SLN) and micelles can increase the local drug concentration gradients, facilitate drug transport into the brain via endocytotic pathways and inhibit the ATP-binding cassette (ABC) transporters expressed at the barrier sites.
- By delivering ARVs withnanocarriers, significant increase in the drug bioavailability to the brain is expected to be achieved. Recent studies show that the specificity and efficiency of ARVs delivery can be further enhanced by usingnanocarriers with specific brain targeting, cell penetrating ligands or ABC transporters inhibitors.
- Future research should focus on achieving brain delivery of ARVs in a safe, efficient, and yet cost-effective manner

9. SLN applied to the treatment of Malaria [27] :

- Despite the fact that we live in an era of advanced technology and innovation, infectious diseases, like malaria, continue to be one of the greatest health challenges worldwide.
- The main drawbacks of conventional malaria chemotherapy are the development of multiple drug resistance and the nonspecific targeting to intracellular parasites, resulting in high dose requirements and subsequent intolerable toxicity.
- Nanosized carriers have been receiving special attention with the aim of minimizing the side effects of drug therapy, such as poor bioavailability and the selectivity of drugs.
- Several nanosized delivery systems have already proved their effectiveness in animal models for the treatment and prophylaxis of malaria.
- A number of strategies to deliver antimalarials using nanocarriers and the mechanisms that facilitate their targeting to Plasmodium spp-infected cells are discussed in this review.
- Taking into account the peculiarities of malaria parasites, the focus is placed particularly on lipid-based (e.g., liposomes, solid lipid nanoparticles and nano and microemulsion) and polymer-based nanocarriers (Nanocapsules and nanospheres).

9. Targeted delivery of Solid Lipid Nanoparticles for the treatment of Lung Diseases [4]:

- Targeted delivery of drug molecules to organs or special sites is one of the most challenging research areas in pharmaceutical sciences.
- By developing colloidal delivery systems such as liposomes, micelles andnanoparticles a new frontier was opened for improving drug delivery.
- Nanoparticles with their special characteristics such as small particle size, large surface area and the capability of changing their surface properties have numerous advantages compared with other delivery systems.
- Targeted nanoparticle delivery to the lungs is an emerging area of interest.

10. Solid Lipid Nanoparticles in Tuberculosis Disease [4, 51] :

- SLN have longer stability and better encapsulation efficiency than liposomes and, as opposed to polymeric nanoparticles, the production process involves minimal amounts of organic solvents.
- SLN have been used to encapsulate Anti Tubercular Drugs (ATD) and were proved to be successful in experimental tuberculosis.
- Anti tubercular drugs such as rifampicin, isoniazid, and pyrazinamide SLN systems were able to decrease the dosing frequency and to improve patient compliance.
- ATD were co-incorporated into SLN to evaluate the potential of these carriers in tuberculosis chemotherapy via the oral route.
- The finding of this study suggested that SLN have great potential in the delivery of ATD by reducing frequency of doses and improving patient compliance by better management of tuberculosis.

11. Transfection Agent [37] :

- Cationic SLNs for gene transfer are formulated using the same cationic lipid as for liposomal transfection agents.
- The differences and similarities in the structure and performance between SLN and liposomes were investigated. PCS showed that the prepared SLNs were smaller in diameter than the corresponding liposomes while AFM supported the expected structural differences.
- DNA binding differed only marginally.
- Cationic lipid composition governs the in vitro transfect ion performance than the colloidal structure it is arranged in. Hence, cationic SLN extends the range of highly potent non-viral transfection agents by one with favorable and distinct technological properties.
- Combination of cationic SLN with the nuclear localization signal TAT2 increased transfection efficiency hundredfold.

12. SLN in Cosmetic and Dermatological preparations [66]:

- An area of big potential for SLN and with a short time-to market are topical products based on the SLN technology, that means pharmaceutical but also cosmetic formulations.
- SLN are considered as being the next generation of delivery system after liposome.
- Due to the lower risk of systemic side effects topical treatment of skin disease appears favorable, yet the stratum cornea counteracts the penetration of xenobiotics into viable skin.
- Particulate carrier systems may mean an option to improve dermal penetration. Since epidermal lipids are found in high amounts within the penetration barrier, lipid carriers attaching themselves to the skin surface and allowing lipid exchange between the outermost layers of the stratum corneum and the carrier appear promising.
- Besides liposomes, solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) have been studied intensively 40.

- Following the evaporation of water from the lipid nanodispersion applied to the skin surface, lipid particles form an adhesive layer occluding the skin surface.
- Then hydration of the stratum corneum may increase by which reducing corneocyte packing and widening of the inter-corneocytes gaps can facilitate drug penetration into deeper skin strata. Occlusive effects appear strongly related to particle size.
- Nanoparticles have turned out 15-fold more occlusive than microparticles, and particles smaller than 400 nm in a dispersion containing at least 35% lipid of high crystallinity has been most potent.

13. Solid lipid nanoparticles for lymphatic targeting [4]:

The solid lipid nanoparticles (SLN) were developed and evaluated for the lymphatic uptake after intraduodenal administration to rats.

14**. SLN for potential agriculture applications [14]:**

Essential oil extracted from Artemesia arboreseens L when incorporated into SLN, were able to reduce the rapid evaporation compared with emulsions and the systems have been used in agriculture as suitable carrier of safe pesticides.

References

1) Vyas SP, Khar RK. Targeted and Controlled Drug Delivery, novel carrier systems. 1st ed. CBS Publishers & Distributors, 2012.
2) Donald LW. Handbook of Pharmaceutical controlled release technology. 2nd ed. New York Marcel Dekker, 2005.
3) Mueller RH, Mehnert W, Lucks JS, Schwarz C, Zurmuhlen A, Weyhers H, et al. Solid Lipid Nanoparticles (SLN) an alternative colloidal carrier system for controlled drug delivery. Eur J Pharm Biopharm. 1995;62-9.
4) Schwarz, C., Mehnert, W., Lucks, J.S., Muller, R.H. (1994). Solid lipid nanoparticles (SLN) for controlled drug delivery I. Production, characterization and sterilization. J Control Release 30(1): 83-96.
5) J Kaur; G Singh; S Saini; AC Rana. *J. drug deliv. Ther.*, **2012**, 2(5), 146-150.
6) [21]C Pardeshi; P Rajput; V Belgamwar; A Tekade; G Patil; K Chaudhary; A Sonje. *Acta Pharm.*, **2012**, 62, 433– 472.
7) Rainer H. Muller, Karsten Mader and Sven Gohla, Eur. J. Pharm. Biopharm., 50(1), 161-177 (2000).
8) Wolfgang Mehnart and Karsten Mader, Adv. Drug. Deliv. Rev., 47, 165-196 (2001).
9) Houli Li, Xiaobin Zhao, Yukun Ma and Guangxi Zhai, Ling Bing Li and Hong Xiang, Lou. J. Cont. Release, 133, 238-244 (2009).
10) Melike Uner, Gulgun Yener, Int. J. Nanomedicine, 2(3), 289-300 (2007).
11) Annette Zur Mehlen, Cora Schwarz and Wolfgang Mehnart, Eur. J. Pharm. Biopharm., 45, 149-155 (1998).
12) Elena Ugazia, Roberta Cavalli and M. R. Gasco, Int. J. Pharm., 241, 341-344 (2002).
13) Indu Pal Kaur, Rohit Bhandari, Swati Bhandari and Kakkur. J. Cont. Rel., 127, 97-109 (2008).
14) Ghada Abdelbary and Rania H. Fahmy, AAPS Pharm. Sci. Tech., 10(1) (2009).
15) N. Al-Haj and A. Rasedee, Int. J. Pharmacol., 5(1), 90-93 (2009).

16) Dong Zhi Hou, Chang Sheng Xie, Kaijn Huang and Chang Hong Zhu, Biomaterials, 24, 1781-1785 (2003). Alessandro Bargoni, Roberto Cavalla, Otto Caputo and M. R Gasco, Pharm. Res., 15(5), 745-750 (1998). Milan Stuchlík and Stanislav Žák, Biomed, Papers, 145(2), 17-26 (2001).

17) C. Olbrich and R. H. Muller, Int. J. Pharm., 180, 31-39 (1999).

18) D. Schwarz, W. Mehnert, J. S. Lucks and R. H. Muller, J. Cont. Release, 30, 83-96 (1994).

19) Wei Liu, Meling Hu, Wehsuang Liu and Chengbin Xue, Huibi Xu, Int. J. Pharm., 364, 141-146 (2008). Sci. Revs. Chem. Commun.: 2(1), 2012 99

20) Qing Zhi Lu, Aihua Yu, Yanwei Xi and Houli Li, Zhimei Song, Jing Cui and Fengliang Cao, Guangxi Zhai, Int. J. Pharm., 372, 191 – 198 (2009).

21) Yi Fan Luo, DaWei Chen, Li Xiang Ren and Xiu Li Zhao, Jing Qin, J. Cont. Release, 114, 53–59 (2006).

22) Rishi Paliwal, Shivani Rai, Bhuvaneshwar Vaidya, Kapil Khatri, Amit K. Goyal, Neeraj Mishra, Abhinav Mehta and Suresh P. Vyas, PhD. Nanomedicine, Nanotechnology, Biology and Medicine, 5(2), (2009) pp. 184-191.

23) Zhenghong Xu, Lingli Chen, Wangwen Gu and Yu Gao, Liping Lin, Zhiwen Zhang and Yong Xi, Yaping Li, Biomaterials, 30, 226 (2009).

24) Rathapon Asasutjarit, Sven - Iver Lorenzen, Sunee Sirivichayakul and Kiat Ruxrungtham, Uracha Ruktanonchi and Garnpimol C. Ritthidej, Pharm. Res., 24(6), 1098 – 1107 (2007).

25) Carsten Rudolph, Ulrike Schillinger, Aurora Ortiz and Kerstin Tabatt, Christian Plank, Rainer H. Müller and Joseph Rosenecker, Pharm. Research, 21(9), 1662-1669 (2004).

26) Robhash Kusam Subedia, Keon Wook Kanga and Hoo-Kyun Choi, Eur. J. Pharm. Sci., 37(3-4), 508- 513 (2009).

27) Suresh Gande, Kopparam Manjunath, Vobalaboina Venkateswarlu and Vemula Satyanarayana, AAPS Pharm. Sci. Tech., 8(1), Article 24 (2007).

28) Nagi A. Alhaj, Rasedee Abdullah, Siddig Ibrahim and Ahmed Bustamenn, Amer. J. Pharmacology and Toxicology, 3(3), 219 – 224 (2008).

29) Michael D. Triplett, E. James, F. Rathman, J. Nanopart Res., 11, 601–614 (2009).

30) Yung-Chih Kuo and Hung-Hao Chen, Int. J. Pharm., 365, 206-213 (2009).

31) K. Vivek, Harivardhan Reddy and Ramachandra S. R. Murthy, AAPS Pharm. Sci. Tech., 8(4), Article 83 (2007).

32) S. Mukherjee, Subhabrata Ray and R. S. Thakur, Pak. J. Pharm. Sci., 22(2), 131-138 (2009).

33) E. Q. Hu, H. Yuan, H. H. Zhang and M. Fang, Int. J. Pharm., 239, 121-128 (2002).

34) Niladi Chattopadhyay, Jason Zastre, Ho-Lun Wong and Xiao Yu Wu, Reina Bendayan, Pharm. Research, 25(10), (2008).

35) Katja Jores, Annekathrin Haberland, Siegfried Wartewig and Karsten Mader, Wolfgang Mehnart, Pharm. Res., 22(11), 1887-1879 (2005).

36) Bin Lua, Su-Bin Xionga, Hong Yanga and Xiao-Dong Yina, Ruo- Bing Chaoa, Eur. J. Pharmaceutical Sci., 28(1-2), 86-95 (2006).

37) Meyer E Heinzelmann and Wiesendanger R. Springer Verlogg, 99-149 (1992).

38) Pallavi V. Pople and Kamalinder K. Singh, AAPS Pharm. Sci. Tech., 7(4), Article 91 (2006).

39) Lang Sc, Lu L. F, Cai Y and Zhu J. B, Liang BW and Yang CZ, J. Controlled Release, 59, 299-307 (1999).

40) Biswajit Basu, Kevin Garala, Ravi Bhalodia and Bhavik Joshi, Kuldeep Mehta, J. Pharm. Res., 3(1), 84-92 (2010).

41) Wolfgang Mehnert and Karsten Mader, Adv. Drug Delivery Rev., 47, 165-196 (2001).

42) Vivek Ranjan Sinha, Saurabh Srivastava and Honey Goel, Int. J. Adv. Pharm. Sci., 1, 212-238 (2010).

43) Melike Uner, Gulgun Yener, Int. J. Nanomedicine, 2(3), 289-300 (2007).

44) Antonio J. Almeida and Eliana Souto, Adv. Drug Delivery Rev., 59, 478-490 (2007).

45) Manisha Misra, P. Muthuprasanna and K. Surya Prabha, Int. J. Pharm. Tech. Res., 1(4), 1354-1365 (2009).

46) Malgorzata Smola, Thierry Vandamme and Adam Sokolowski, Int. J. Nanomedicine, 1-9 (2008).

47) Jessy Shaji and Vinay Jain, Int. J. Pharmacy and Pharm. Sci., 2(3), 8-17 (2010).

48) Biswajit Basu, Kevin Garala, Ravi Bhalodia and Bhavik Joshi, Kuldeep Mehta, J. Pharm. Res., 3(1), 84-92 (2008).

49) Suphiya Pareev and Sanjeeh K. Sahoo, Nanomedicine, Nanotechnology, Biology and Medicine, xx. xxx-xxx (2011).

50) S. Mukherjee, S. Ray and R. S. Thakur, Ind. J. Pharm. Sci., 349-358 (2009). 50. Hania Degobert, Adv. Drug Delivery Reviews, 1688-1713 (2006).

51) Sven Gohla, Eur. J. Pharm. Biopharm., 50, 161-177 (2000).

52) S. P. Vyas and R. K. Khar, Controlled Drug Delivery - Concepts and Advances, First Edition, Vallabh Prakashan (2002) pp. 38-50.

53) N. K. Jain, Controlled and Novel Drug Delivery, First Edition, CBS Publishers and Distributors, (1997) pp. 3-28.

54) Y. W. Chien, Novel Drug Delivery, 2nd Edition, (2005) pp. 1-5. 55. S. P. Vyas and R. K. Khar, Targeted Drug Delivery System, 112-146 (2000).

55) Joseph Robinson and Vincent H. L. Lee, Controlled Drug Delivery - Fundamentals and Applications, 2nd Edition, 4-33.

56) Shuyu Xie, Luyan Zhu, Zhao Dong and Yan Wang, Colloids and Surfaces B: Biointerfaces, 83, 382- 387 (2011).

57) Vinay Kumar V, AAPS Pharm. Sci. Tech., Feb, 42-49 (2010).

58) Maria Luisa Bondi, Antonina Azzolina and Melchiorre Cervello, Current Nanoscience, 5, 39-44 (2009).

59) Waree Tiyaboonchai, Watcharaphorn Tungpradit and Ponyupa Plianbangchang, Int. J. Pharm., 337, 299-306 (2007).

60) Ziyaur Rahman, Ahmed S. Zidan and Mansoor K. Khan, Eur. J. Pharm. Biopharm., 76, 127-137 (2010)

61) L. Harivardhan Reddy and R. S. R. Murthy, AAPS Pharm. Sci. Tech., 6(2), 24 (2005).

62) Ambikanandan Misra and Mayor Kalariya, Drug Delivery Technol., 4(8), (2004).

63) K. Vivek, Harivardhan Reddy and Ramachandra S.R. Murthy, AAPS Pharm. Sci. Tech., 8(4), 83 (2007).

64) Gande Suredh, Kopparam Manjunath, Vobalaboina Venkateswarlu and Vemula Styanarayana, AAPS Pharm. Sci. Tech., 8(1), 24 (2007).

65) T. Helgason, T. S. Awas, K. Kristbergsson and J. Weiss, J. Colloid, Interface Science, 334, 75-81 (2009).

66) Zaida Urban-morlan, Adriana Ganem- rondero and David Quintanar-guerrero, Int. J. Nanomedicine, 5, 611-620 (2010).