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Solid Lipid Nanoparticles: A Modern Formulation Approach in Drug Delivery System

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Abstract:

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. This review presents a broad treatment of solid lipid nanoparticles discussing their aims, production procedures, advantages, limitations and their possible remedies. The ability to incorporate drugs into Nanoparticle system offers a new prototype in drug delivery that could use for drug targeting. The preparation techniques for production of SLN are Novel and more efficient. Appropriate analytical techniques for the characterization of SLN. 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.

Keywords: solid lipid nanoparticles, methods of preparation, applications,, route of administration

Introduction:

Solid lipid nanoparticles (SLN) introduced in 1991 represent an alternative carrier system to tradition colloidal carriers such as - emulsions, liposomes and polymeric micro – and nanoparticles. Nanoparticle is a novel versatile drug delivery approach having targeted and site specific activity. Many of the recent formulation approaches utilize Nanotechnology that is the preparation of Nanosized structures containing the active pharmaceutical material. Nanoparticle is a nanosized particle having the size range of 1 to 1000 nm. They are incorporated from manufactured characteristic polymers and suited to advance medication conveyance and lessen lethality. They have developed as a variable substitute to liposomes as medication carrier. They are fabricated from manufactured/characteristic polymers and preferably suited to improve sedate conveyance and diminish lethality . SLN offer interesting properties, for example, little size, huge surface zone, high medication stacking and the communication of stages at the interface and are appealing for their potential to

enhance execution of pharmaceuticals. Solid lipid nanoparticles (SLN) are aqueous colloidal dispersions, the matrix of which comprises of Solid biodegradable lipids. SLNs consolidate the favorable circumstances and maintain a strategic distance from the down sides of a few colloidal carriers of its class, for example, physical stability, assurance of fused labile medications from protection, of incorporated labile drugs from degradation, controlled release, excellent tolerability SLN formulations for various application routes (parenteral, oral, dermal, visual, pulmonar, rectal) have been developed and thoroughly characterized in-vitro and in-vivo]. Solid lipid nanoparticles are one of the novel potential colloidal transporter system as option materials to polymers which is in distinguishable to oil in water emulsion for parenteral nourishment, however the fluid lipid of the emulsion has been supplanted by a Solid lipid nanopartical

Advantages of SLN

- Small estimate and generally contract measure dissemination which gives natural chances to siteparticular medication conveyance by SLNs
- Conventional emulsion producing techniques pertinent
- Can be stop dried to shape powdered detailing
- Controlled arrival of dynamic medication over a long stretch can be achieved
- Excellent biocompatibility Nanoscience and Nanotechnology Research
- Improve stability of pharmaceuticals
- Excellent reproducibility with a high-weight homogenization technique as the readiness methodology.
- High and enhanced drug content.
- The achievability of consolidating both hydrophilic and hydrophobicmedications.
- The transporter lipids are biodegradable and consequently protected. Avoidance of natural solvents. Enhanced bioavailability of inadequately water dissolvable atoms
- Avoidance of natural solvents underway strategies
- Feasible huge scale generation and cleansing.

Disadvantages of SLN

- Poor sedate stacking limit.
- Drug ejection after polymeric move amid capacity.
- Unpredictable gelation propensity.
- The low ability to stack hydrophilic medications because of apportioning impacts amid the generation procedure

Types of Nanoparticles

Nanoparticle is a nano sized particle is mainly divided by thirteen types,

1. Polymeric Nanoparticles,
2. Solid Lipid Nanoparticles
3. Nanosuspension
4. Polymeric Micelles
5. Ceramic Nanoparticles
6. Liposome
7. Dendrimers
8. Magnetic Nanoparticles

9. Nanoshells Coated With Gold
10. Nanowires
11. Nanopores
12. Quantum Dots
13. Ferrofluids

Aims of solid lipid nanoparticles

- Possibility of controlled drug release
- Increased drug stability.
- High drug pay load
- No bio-toxicity of the carrier.
- Avoidance of organic solvents.
- Incorporation of lipophilic and hydrophilic drugs.

Preparation of solid lipid nanoparticles

SLNs are prepared from lipid, emulsifier and water/solvent by using different methods and are discussed below.

Methods of preparation of solid lipid nanoparticles

1. High pressure homogenization

A. Hot homogenization

B. Cold homogenization

2. Ultrasonication/high speed homogenization

A. Probe ultrasonication

B. Bath ultrasonication

3. Solvent evaporation method

4. Solvent emulsification-diffusion method

5. Supercritical fluid method

6. Microemulsion based method

7. Spray drying method

8. Double emulsion method

9. Precipitation technique

10. Film-ultrasound dispersion

1. High pressure homogenization (HPH)

It is a reliable and powerful technique, which is used for the production of SLNs. High pressure homogenizers push a liquid with high pressure (100–2000 bar) through a narrow gap (in the range of a few microns). The fluid accelerates on a very short distance to very high velocity (over 1000 Km/h). Very high shear stress and cavitation forces disrupt the particles down to the submicron range. Generally 5-10% lipid content is used but up to 40% lipid content has also been investigated.

Two general approaches of HPH are hot homogenization and cold homogenization, work on the same concept of mixing the drug in bulk of lipid melt.

A. Hot homogenization :

Hot homogenization is carried out at temperatures above the melting point of thelipid and can therefore be regarded as the homogenization of an emulsion. A pre-emulsion of the drug loaded lipid melt and the aqueous emulsifierphase (same temperature) is obtained by high-shear mixing device. HPH of the pre-emulsion is carried out at temperatures above the melting point of the lipid. In general, higher temperatures result in lower particle sizes due to the decreased viscosity of the inner phase. However, high temperatures increase the degradation rate of the drug and the carrier. Increasing the homogenization pressure or the number of cycles often results in an increase of the particle size due to high kinetic energy of the particles.

B. Cold homogenization

Cold homogenization has been developed to overcome various problems associated with hot homogenization such as: Temperature-induced drug degradation, drug distribution into the aqueous phase during homogenization, Complexity of the crystallization step of the nanoemulsion leading to several modifications and/or super cooled melts. In this technique the drug containing lipid melt is cooled, the solid lipid ground to lipid microparticles and these lipid microparticles are dispersed in a cold surfactant solution yielding a pre-suspension. Then this pre-suspension is homogenized at or below room temperature, the gravitation force is strong enough to break the lipid.

Advantages

™Low capital cost.
™Demonstrated at lab scale.

Disadvantages

™Energy intensive process.
™Demonstrated at lab scale Biomolecule damage.
™Polydisperse distributions.
™Unproven scalability

2. Ultrasonication/high speed homogenization

SLNs are also prepared by ultrasonication or high speed homogenization techniques. For smaller particle size combination of both ultrasonication and high speed homogenization is required.

Advantages

™Reduced shear stress.

Disadvantages

™Potential metal contamination.
™Physical instability like particle growth upon storage.

3.Solvent evaluation method :

SLNs can also prepared by solvent evaporation method. The lipophilic material is dissolved in a water-immiscible organic solvent (e.g. cyclohexane) that is emulsified in an aqueous phase. Upon evaporation of the solvent, nanoparticles dispersion is formed by precipitation of the lipid in the aqueous medium by giving the nanoparticles of 25 nm mean size. The solution was emulsified in an aqueous phase by high pressure homogenization. The organic solvent was removed from the emulsion by evaporation underundereduced pressure (40–60 mbar).

Advantages

™Scalable.

™Mature technology.

™Continuous process.

™Commercially demonstrated.

Disadvantages

™Extremely energy intensive process.

™Polydisperse distributions.

™Biomolecule damage.

4. Solvent emulsification-diffusion method

The particles with average diameters of 30-100 nm can be obtained by this technique.Voidance of heat during the preparation is the most important advantage of this technique.

5.Supercritical fluid method

This is an alternative method of preparing SLNs by particlesfromgassaturatedsolutions(PGSS).

Advantages

- Avoid the use of solvents.
- Particles are obtained as a dry powder, instead of suspensions.
- Mild pressure and temperature conditions.
- Carbon dioxide solution is the good choice as a solvent for this method.

6. Microemulsion based method

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. SLN dispersion can be used as granulation fluid for transferring in to solid product (tablets, pellets) by granulation process, but in case of low particle content too much of water needs to be removed. High-temperature gradients facilitate rapid lipid crystallization and prevent aggregation. Due to the dilution step; achievable lipid contents are considerably lower compared with the HPH based formulations.

Advantages

™Low mechanical energy input.

™Theoretical stability.

Disadvantages

™Extremely sensitive to change.

™Labor intensive formulation work.

™Low nanoparticle concentrations.

7. Spray drying method

It is an alternative technique to the lyophilization process. This recommends the use of lipid with melting point more than 70oC. The best results were obtained with SLN concentration of 1% in a solution of trehalose in water or 20% trehalose in ethanol-water mixture.

8. Double emulsion method

Here the drug is encapsulated with a stabilizer to prevent the partitioning of drug in to external water phase during solvent evaporation in the external water phase of w/o/w double emulsion.

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 precipitatedforming nanoparticles.

10. Film-ultrasound dispersion

The lipid and the drug were put into suitable organic solutions, after decompression, rotation and evaporation of the organic solutions, a lipid film is formed, then the aqueous solution which includes the emulsions was added. Using the ultrasound with the probe to diffuser at last, the SLN with the little and uniform particle size is formed.

Secondary Production steps

Freeze drying

Lyophilization is a promising way to increase the chemical and physical stability over extended periods of time. Lyophilization had been required to achieve long term stability for a product containing hydrolysable drugs or a suitable product for per-oral administration. Transformation into the solid state would prevent the Oswald ripening and avoid hydrolytic reactions. In case of freeze drying of the product, all the lipid matrices used, form larger solid lipid nanoparticles with a wider size distribution due to presence of aggregates between the nanoparticles. The conditions of the freeze drying process and the removal of water promote the aggregation among SLNs. An adequate amount of cryoprotectant can protect the aggregation of solid lipid nanoparticles during the freeze drying process.

Sterilization

Sterilization of the nanoparticles is desirable for parenteral administration and autoclaving which is applicable to formulations containing heat-resistant drugs. Effect of sterilization on particle size have been investigated and it was found to cause a distinct increase in particle size.

Spray drying

Spray drying might be an alternative procedure to lyophilization in order to transform an aqueous SLN dispersion into a dry product. This method has been used scarcely for SLN formulation, although spray drying is cheaper as compared to lyophilization. The lipids with melting points at temperature >70°C had been recommended for spraydrying.

Influence of excipients :

Formulation variables in the product quality

Particle size

Alteration of the size significantly affects the physical stability, biofate of the lipid particles, and release rate of the loaded drug. Hence the size of the SLNs has to be controlled within reasonable range. Well formulated systems (liposomes, nanospheres and nanoparticles) should display a narrow particle size distribution in the submicron size range (as having size below 1μm), according to the definition of colloidal particles. Influence of the ingredients on product quality The particle size of lipid nanoparticles is affected by various parameters such as composition of the formulation (such as surfactant/ surfactant mixture, properties of the lipid and the drug incorporated), production methods and conditions (such as time, temperature, pressure, cycle number, equipment, sterilization and lyophilization). Large particle size is obtained at lower processingtemperature. The hot homogenization technique gives a smaller particle size, generally below 500 nm, and a narrow particle size distribution as compared to cold homogenization. Mean particle size as well as polydispersity index (PI) values are reported to be reduced at increasing homogenization pressure up to 1500 bar and number of cycles (3-7 cycles).

Influence of the lipids

Using the hot homogenization, it has been found that the averageparticle size of SLN dispersions is increasing with higher melting lipids. However, other critical parameters for nanoparticle formation will be different for the different lipids. The examples include the velocity of lipid crystallization, the lipid hydrophilicity (influence on self-emulsifying properties and the shape of the lipid crystals (and therefore the surface area). Further, increasing the lipid content over 5-10% resulted in larger particles (including microparticles) and broader particle size distribution in most cases.

Influence of the emulsifiers

The concentration of the surfactant/surfactant mixture strongly affects the particle size of the lipid nanoparticles. In general, smaller particle sizes were observed when a higher surfactant/lipid ratio was chosen. The decrease in surfactant concentration resulted in increase of particle size during storage. Surfactants decrease the surface tension between the interface of the particles causing portioning of the particles and thereby increasing the surface area.

Drug incorporation models of SLN

Factors affecting loading capacity of a drug in lipid are:

1. Solubility of drug in lipid melt.
2. Miscibility of drug melt and lipid melt.
3. Chemical and physical structure of solid matrix lipid.
4. Polymorphic state of lipid material.

Solid solution model:

1. Drug is molecularly dispersed in lipid matrix when SLN is prepared by cold homogenization.
2. Drug-enriched shell model.
3. A solid lipid core forms upon recrystalization temperature of the lipid is reached.
4. Drug-enriched core model.
5. Cooling the nanoemulsion leads to a super saturation of the drug which is dissolved in the lipid melt leads to recrystalization of the lipid.

CHARACTERIZATION OF SOLID LIPID NANOPARTICLES

1. **PhotonCorrelation Spectroscopy (PCS)**
   It is an established method which is based on dynamic scattering of laser light due to Brownian motion of particles in solution/suspension. This method is suitable for the measurement of particles in the range of 3 nm to 3 mm.The PCS device consists of laser source, a sample cell (temperature controlled) and a detector.Photomultiplier is used as detector to detect the scattered light. The PCS diameter is based on the intensity of the light scattering from the particles.
2. **Electron Microscopy**Electron Microscopy methods such as Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are used to measure the overall shape and morphology of lipid nanoparticles. It permits the determination of particle size and distributions.SEM uses electrons transmitted from the surface of the sample while TEM uses electrons transmitted through the sample.
3. **Atomic Force Microscopy (AFM)**
   It is an advanced microscopic technique which is applied as a new tool to image the original unchanged shape and surface properties of the particles. AFM measures the force acting between surface of the sample and the tip of the probe, when the probe is kept in close proximity to the sample which results in a spatial resolution of up to 0.01 nm for imaging.
4. **Determination of Incorporated Drug**
   Amount of drug incorporated in SLNs influences the release characteristics hence it is very important to measure the amount of incorporated drug. The amount of drug encapsulated per unit wt. of nanoparticles is determined after separation of the free drug and solid lipids from the aqueous medium and this separation can be done by ultracentrifugation, centrifugation filtration or gel permeation chromatography. The drug can be assayed by standard analytical technique such as spectrophotometer, a spectroflurophotometry, HPLC or liquid scintillation counting.
5. **In vitro drug release**
   Dialysis tubing
   In vitro drug release could be achieved using dialysis tubing. The solid lipid nanoparticle dispersionis placed in pre washed dialysis tubing which can be hermetically sealed. The dialysis sac then dialyzedagainst a suitable dissolution medium at room temperature; the samples are withdrawn from the dissolutionmedium at suitable intervals, centrifuged and analyzed for the drug content using a suitable analyticalmethod.
   Reverse dialysis
   In this technique a number of small dialysis sacs containing 1 mL of dissolution medium are placedin SLN dispersion. The SLN's are then displaced into the medium.
6. **Rheology**Rheological measurements of formulations can perform by Brookfield Viscometer, using a suitable spindle number. The viscosity depends on the dispersed lipid content. As the lipid content increases, the flow becomes non-Newtonian from Newtonian.
   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.

7. **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.

8. **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.

Route of drug administration

Interactions of the SLN with the biological surroundings including: distribution processes (adsorption of biological material on the particle surface and desorption of SLN components into to biological surroundings) and enzymatic processes. Various administration routes are: **.**

1.Parenteral administration Peptide and proteins drugs are usually available for parenteral use in the market. Since their conventional oral administration is not possible due to enzymatic degradation in GI tract. Parenteralapplication of SLN reduces the possible side effects of drug incorporated with the increased bioavailability. These systems are very suitable for drug targeting.

2.Oral administration

Controlled release behavior of SLNs is reported to enable the bypass of gastric and intestinal degradation of the encapsulated drug, and their possible uptake and transport through the intestinal mucosa. However, the assessment of the stability of colloidal carriers in GI fluids is essential in order to predict their suitability for oral administration.

3.Rectal administration

When rapid pharmacological effect is required, in some circumstances, parenteral or rectal administration is preferred. This route is used for pediatric patients due to easy application.

4. Nasal administration

Nasal route is preferred due to its fast absorption and rapid onset of drug action also avoiding degradation of labile drugs in the GIT and insufficient transport across epithelial cell layers.

5. Respiratory delivery

Nebulisation of solid lipid particles carrying anti-tubercular drugs, anti-asthmatic drugs and anti- cancer was observed to be successful in improving drug bioavailability and reducing the dosing frequency for better management of pulmonary action.

6. Ocular administration

Biocompatibility and muco-adhesive properties of SLN improve their interaction with ocular mucosa and prolong corneal residence time of the drug, with the aim of ocular drug targeting.

7. Topical administration

SLN are very attractive colloidal carrier systems for skin applications due to their various desirable effects on skin besides the characteristics of a colloidal carrier system. They are well suited for use on damaged or inflamed skin because they are based on non-irritant and non-toxic lipids.

APPLICATIONS

Oral SLNs in ant tubercular chemotherapy

Ant tubercular drugs such as rifampicin, isonizide, pyrazinamide-loaded SLN systems,were able to decrease the dosing frequency andimprove patient compliance . By using theemulsion solvent diffusion technique this antitubercular drug loaded solid lipidnanoparticles are prepared.

SLNs for topical use

SLNs used for topical application for various drugsuch as anticancer , vitamin-A ,isotretinoin, flurbiprofen .Using glyceryl behenate, vitamineA-loaded nanoparticles can be prepared. Thismethod is useful for the improvement ofpenetration with sustained release. Theisotretinoin-loaded lipid nanoparticles wereformulated for topical delivery of drug.Productionof the flurbiprofen-loaded SLN gel for topicalapplication offer a potential advantage ofdelivering the drug directly to the site of action,which will produce higher tissue concentrations.

SLNS as Cosmeceutical

The SLNs have been applied in the preparationof sunscreens and as an active carrier agent formolecular sunscreens and UV blockers. SLNand NLCs have proved to be controlled releaseinnovative occlusive topicals. Better localizationhas been achieved for vitamin A in upper layersof skin with glyceryl behenate SLNs compared toconventional formulations .

SLNs as gene vector carrier

SLN can be used in the gene vectorformulation. There are several recent reports ofSLN carryinggenetic/peptide materials such asDNA, plasmid DNA and other nucleic acids . The gene transfer was optimized byincorporation of a diametric HIV-1 HAT peptide(TAT 2) into SLN gene vector. The lipid nuclicacid nanoparticles were prepared from a liquidnanophase containing water and a watermiscible organic solvent where both lipid andDNA are separately dissolved by removing theorganic solvent, stable and homogeneously sizedlipid-nuclic acid nanoparticle (70-100 nm) wereformed. It's called genospheres. It istargetedspecific by insertion of an antibody-lipo polymerconjugated in the particle.

SLNs in breast cancer and lymph node metastases

Mitoxantrone-loaded SLN local injections wereformulated to reduce the toxicity and improve thesafetyand bioavailability of drug . Efficacy ofdoxorubicin (Dox) has been reported to beenhanced by incorporation in SLNs.In themethodology the Dox was complexed withsoybean-oil-based anionic polymer anddispersed together with a lipid in water to formDox-loaded solid lipid nanoparticles. The systemhas enhanced its efficacy and reduced breastcancer cells.

SLNs as a targeted carrier for anticancer drugto solid tumors

SLNs have been reported to be useful as drugcarriers to treat neoplasm's . Tumour targetinghas been achieved with SLNs loaded with drugs like methotrexateand Camptothecin. Tamoxifen ananticancer drug is incorporated inSLN to prolong release of drug after

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 thetarget tissue in accessible sites .

SLNs for potential agriculture application

Essential oil extracted from Artemisiaarboreseens L when incorporated in SLN, wereable to reduce the rapid evaporation comparedwith emulsions and the systems have been usedin agriculture as a suitable carrier of ecologicallysafe pesticides.

CONCLUSION

SLN as colloidal drug carrier combines the advantage of polymeric nanoparticles, fat emulsions and liposome; due to various advantages, including feasibility of incorporation of lipophilic and hydrophilic drugs, improved physical stability, low cost, ease of scale-up, and manufacturing. SLNs are prepared by various advanced techniques. The site specific and sustained release effect of drug can better achieved by using SLNs.Nanoparticles have been used extensively for applications in drug discovery, drug delivery, and diagnostics and for many others in medical field. They are relatively novel drug delivery systems, having received primary attention from the early 1990s and future holds great promise for its systematic investigation and exploitation. We can expect many patented dosage forms in the form of SLNs in the futures

REFERENCES-

1. Nadkar S, Lokhande C. Current Trends in Novel Drug DeliveryAn OTC Perspective. Pharma Times 2010; 42 Suppl 4 :17-23.

2 . Loxley A. Solid Lipid Nanoparticles for the Delivery of Pharmaceutical Actives. Drug Delivery Technology2009; 9 Suppl 8 :32.

3 . Mishra B, Patel BB, Tiwari S. Colloidal nanocarriers: a review on formulation technology, types and applications toward targeted drug delivery. Nanomedicine: NMB2010; 6 Supply 1 :

-4. Maravajhala V, Papishetty S, Bandlapalli S. Nanotechnology in Development of Drug Delivery System. International Journal of Pharmaceutical Science and Research2011; 3 Suppl 1 :84-96.

5. Ekambaram P, Sathali AH, Priyanka K. Solid Lipid Nanoparticles: A Review. Scientific Reviews and Chemical. Communication2012; 2 Suppl 1 :80-102.

6. Muller RH, Mader K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery -a review of the state of the art. European Journal of Pharmaceutics and Biopharmaceutics2000; 50 :161-177.

7 . Mandawgade SD, Patravale VB. Development of SLNs from natural lipids: Application to topical delivery of tretinoin. International Journal of Pharmaceutics2008; 363 :132-138.

8. Helgason T, Awad TS, Kristbergsson K, McClements DJ, Weiss J. Effect of surfactant surface coverage on formation of solid lipid nanoparticles (SLN). Journal of Colloid and Interface Science2009; 334 :177-161.

9.Pal K, Bhandari R, Bhandari S, Kakkur L. Potential of solid lipid nanoparticles in brain targeting. J Cont Rel 2008; 127:97-109.

10.Sailaja A, Amareshwar P, Chakravarty P. Formulation of solid lipid nanoparticles and their applications. CPR 2011; 1(2):197-203.

11.Li HL, Zhao XB, Ma YK, Zhai GX. Enhancement of gastrointestinal absorption of quercetin by solid lipid nanoparticles. J Control Release 2009; 133:238-44.

12. Luo YF, Chen DW, Ren LX, Zhao XL. Solid lipid nanoparticles for enhancing vinpocetine's oral bioavailability. J Control Release 2006; 114:53-59. [84]Rahman SMH, Telny TC, Ravi TK, Kuppusamy S. Role of surfactant and pH in dissolution of curcumin. Ind J Pharm Sci 2009; 71:139-42.

13. Schwarz C. Mehnert W. Freeze-drying of drug free and drug loaded solid lipid nanoparticles. Int J Pharm 1997; 157:171-79.

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

15. Y. W. Chien, Novel Drug Delivery, 2nd Edition, (2005) pp. 1-5.

16.S. P. Vyas and R. K. Khar, Targeted Drug Delivery System, 112-146 (2000).

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

18.. Shuyu Xie, Luyan Zhu, Zhao Dong and Yan Wang, Colloids and Surfaces B: Biointerfaces, 83, 382387 (2011).

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

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

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

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

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

24.. Nagi A. ALHaj, Rasedee Abdullah, Siddig Ibrahim and Ahmad Bustamam, Amer. J. Pharmacol. Toxicol., 3(3), 219-224 (2008).

25s. Franscesco Lai, Sylvia A. Wissing and Anna M. Fadda, AAPS Pharm. Sci. Tech., 7(1), 2 (2006). 65. Alaa Eldeen B. Yassin, Md Khalid Anwer and Ibrahim A. Alsarra, Int. J. Medical Sci., 7(6), 398-408 (2010).