Indian Journal of Novel Drug Delivery

IJNDD

An Official Publication of Karnataka Education and Scientific Society

Review Article

Solid lipid nanoparticles: Potential applications

JS MULLA*[1], IM KHAZI [2], VG JAMAKANDI[1]

[1]Department of Pharmaceutics, K.L.E.University's College of Pharmacy, Hubli, INDIA

[2]Department of PG Studies in Chemistry, Karnatak University, Dharwad, INDIA

ARTICLE DETAILS

Article history:
Received on 9 August 2010
Modified on 2 September 2010
Accepted on 8 September 2010

Keywords:
Solid lipid nanoparticles
Administration routes
Controlled release
Targeted drug delivery

ABSTRACT

In the middle of the 1990s, the attention of different research groups has focused on alternative nanoparticles made from solid lipids by name solid lipid nanoparticles (SLN or lipospheres or nanospheres). The SLN combine the advantages (e.g. physical stability, protection of incorporated labile drugs from degradation, controlled release, excellent tolerability) of other traditional colloidal systems, such as emulsions, liposomes and polymeric microparticles and nanoparticles; while at the same time minimizing the associated problems. SLN formulations for various application routes (parenteral, oral, dermal, ocular, pulmonar, rectal) have been developed and thoroughly characterized *in vitro* and *in vivo.* Recently, solid lipid nanoparticles (SLN) have been widely studied as a next-generation delivery system in pharmaceuticals and cosmetics. This paper reviews the applications of lipid based carrier systems, SLN.

INTRODUCTION

In recent years it has become more and more evident that the development of new drugs alone is not sufficient to ensure progress in drug therapy. Exciting experimental data obtained *in vitro* are very often followed by disappointing results *in vivo*. Most important reasons for the therapy failure include insufficient drug concentration, poor drug solubility and high fluctuation of plasma levels due to unpredictable bioavailability after peroral administration. Looking for drug carrier formulations increasing the bioavailability and consisting of well tolerated excipients, the Solid Lipid Nanoparticles (SLNs) are alternative drug carrier systems. Solid lipid nanoparticles (SLN, also referred to as lipospheres or solid lipid nanospheres) are a relatively new class of drug carrier. They are particles of submicron size (50 to 1000 nm) made from lipids that remain in a solid state at room temperature and body temperature [1-15].

Over the last decades, colloidal drug delivery systems and especially nanoparticles have received great attention. Nanoparticles can be administered via different routes of administration such as parenteral, oral, intraocular, transdermal or pulmonary inhalation. Aerosol therapy using particulate drug carrier systems is becoming a popular method to deliver therapeutic or diagnostic compounds either locally or systemically as shown by the development of inhalable insulin.

Author for Correspondence:
Email: jameelahmed5@rediffmail.com

Studies have shown that solid lipid nanoparticles (SLN) 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. Several nanosized delivery systems have already proved their effectiveness in animal models for the treatment and prophylaxis of malaria. Topical application of drugs to the eye is the most popular and well-accepted route of administration for the treatment of various eye disorders. The bioavailability of ophthalmic drugs is, however, very poor due to efficient protective mechanisms of the eye. Blinking, baseline and reflex lachrymation, and drainage remove rapidly foreign substances, including drugs, from the surface of the eye. Moreover, the anatomy, physiology and barrier function of the cornea compromise the rapid absorption of drugs. Numerous strategies were developed to increase the bioavailability of ophthalmic drugs by prolonging the contact time between the preparation, and therefore the drug, and the corneal/conjunctival epithelium.

Tuberculosis (TB) is the second most deadly infectious disease. Despite potentially curative pharmacotherapies being available for over 50 years, the length of the treatment and the pill burden can hamper patient lifestyle. Thus, low compliance and adherence to administration schedules remain the main reasons for therapeutic failure and contribute to the development of multi-drug-resistant (MDR) strains. Nanotechnologies appear as one of the most promising approaches for the development of more effective and compliant medicines. The great interest in mucosal vaccine delivery arises from the fact that mucosal surfaces represent the major site of entry for many pathogens. Among other mucosal

sites, nasal delivery is especially attractive for immunization, as the nasal epithelium is characterized by relatively high permeability, low enzymatic activity and by the presence of an important number of immunocompetent cells. Use of nanocarriers provides a suitable way for the nasal delivery of antigenic molecules. Parenteral formulations, particularly intravascular ones, offer a unique opportunity for direct access to the bloodstream and rapid onset of drug action as well as targeting to specific organ and tissue sites. Nanoemulsions, nanosuspensions and polymeric phospholipid micelles constitute novel parenteral formulations of approved drugs or new chemical entities [16-30].

Recently, solid lipid nanoparticles (SLN) have been widely studied as a next-generation delivery system in pharmaceuticals and cosmetics [31, 32]. This paper intends to describe the wide applications of lipid based carrier systems, SLN.

Administration routes and in vivo fate

SLN are administered by several routes. The *in vivo* fate of the SLN particles will depend mainly on the following parameters:

(a) Administration route
(b) Interactions of the SLN with the biological surroundings including:

(b1) distribution processes (adsorption of biological material on the particle surface and desorption of SLN components into the biological surrounding)

(b2) enzymatic processes (e.g. lipid degradation by lipases and esterases)

SLN are composed of physiological or physiologically related lipids or waxes. Therefore, pathways for transportation and metabolism are present in the body which may contribute to a large extent to the *in vivo* fate of the carrier. Probably the most important enzymes of SLN degradation are lipases, which are present in various organs and tissues. Lipases split the ester linkage and form partial glycerides or glycerol and free fatty acids. Most lipases require activation by an oil /water interface, which opens the catalytic center (lid opening) [33-35]. *In vitro* experiments indicate that solid lipid nanoparticles show different degradation velocities by the lipolytic enzyme pancreatic lipase as a function of their composition (lipid matrix, stabilizing surfactant) [36-38].

Peroral administration

Peroral administration forms of SLN may include aqueous dispersions or SLN loaded traditional dosage forms, e.g. tablets, pellets or capsules. The microclimate of the stomach favors particle aggregation due to the acidity and high ionic strength [39]. Oral administration of SLN is possible as aqueous dispersion or alternatively after transform into a traditional dosage form, i.e. tablets, pellets, capsules or powders in sachets. For the production of tablets the aqueous SLN dispersion can be used instead of a granulation liquid in the granulation process. Alternatively SLN can be transferred to a powder (e.g. by spray-drying) and added to the tabletting powder mixture. For the production of pellets the SLN dispersion can be used as wetting agent in the extrusion process [17].

Parenteral administration

SLN have been administered intravenously to animals. Pharmacokinetic studies of doxorubicin incorporated into SLN showed higher blood levels in comparison to a commercial drug solution after i.v. injection in rats. Concerning the body distribution, SLN were found to cause higher drug concentrations in lung, spleen and brain, while the solution led to a distribution more into liver and kidneys [40].

SLN in cosmetic and dermatological preparations

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 liposomes [41].
Due to the lower risk of systemic side effects topical treatment of skin disease appears favourable, yet the stratum corneum 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 **[42].**

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 which by 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 **[43-45].**

SLN as potential new adjuvant for vaccines

Adjuvants 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 [41].

Solid lipid nanoparticles in cancer chemotherapy:

The prospect of improved cancer chemotherapy using solid lipid nanoparticles (SLN) as a drug delivery system is promising. Several obstacles frequently encountered with anticancer compounds, such as normal tissue toxicity, poor specificity and stability and a high incidence of drugresistant tumor cells, are at least partially overcome by delivering them using SLN. The emergence of the newer forms of SLN such as polymer lipid hybrid nanoparticles, nanostructured lipid carriers and long-circulating SLN may further expand the role of this versatile drug carrier in cancer treatment. This review focuses on the current use of SLN for the

encapsulation and delivery of cytotoxic anticancer compounds. It also discusses more recent trends in the use of SLN as vehicles for delivery of chemosensitizers and cytotoxic therapeutic molecules. It is anticipated that, in the near future, SLN will be further improved to deliver anticancer compounds in a more efficient, specific and safer manner **[46].**

Solid lipid nanoparticles for delivering peptides and proteins

Solid lipid particulate systems such as solid lipid nanoparticles (SLN), lipid microparticles (LM) and lipospheres 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 fulfil 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 proteolytic 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 [47].

Solid lipid nanoparticles for targeted brain drug delivery

The state of the art on surfactant coated poly (alkyl cyanoacrylate) nanoparticles specifically designed for brain targeting is given by emphasizing the transfer of this technology to solid lipid matrices. The available literature on solid lipid nanoparticles and related carriers for brain drug targeting is revised as well. 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. A critical consideration on the potential application of such technology as related to the current status of brain drug development is also given [48].

Solid lipid nanoparticles for parasitic diseases

Solid lipid nanoparticles (SLNs) and nanostructured 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 targetability and to arrive at a versatile, effective and economical approach for the delivery of anti-parasitic drugs [49].

Solid lipid nanoparticles for ultrasonic drug and gene delivery

Drug delivery research employing micelles and nanoparticles has expanded 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 agents 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 *in vitro* and *in vivo.* The small packaging allows nanoparticles to extravasate into tumor tissues. Ultrasonic drug and gene delivery from nanocarriers has tremendous potential because of the wide variety of drugs and genes that could be delivered to targeted tissues by fairly non-invasive means [50].

SLN applications for improved delivery of antiretroviral drugs to the brain

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 blood-brain barrier (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 with nanocarriers, 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 using nanocarriers 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 [51].

SLN applied to the treatment of malaria

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 non-specific 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 microemulsions) and polymer-based nanocarriers (nanocapsules and nanospheres) [52].

Targeted delivery of solid lipid nanoparticles for the treatment of lung diseases

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 and nanoparticles 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 [53].

Solid lipid nanoparticles in tuberculosis disease

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. RIF, INH and PYZ were incorporated into oral SLN produced by an emulsion/solvent diffusion method. Encapsulation efficiency was 51, 45 and 41%, respectively. A single dose administered orally in mice resulted in drug concentrations detectable after 3 h and for up to 8 days [54-56].

Solid lipid nanoparticles for lymphatic targeting

The solid lipid nanoparticles (SLN) were developed and evaluated for the lymphatic uptake after intraduodenal administration to rats [11, 57, 58].

CONCLUSION

In conclusion, solid lipid nanoparticles play an important role as novel carrier with potential applications. To guarantee a broad application of a carrier system it is highly desirable that companies specialized in drug delivery systems engage themselves in the new technology. Drug delivery companies develop pharmaceutical solutions adapted to the needs of many different pharmaceutical companies, that means the technology will spread to many companies and not only be localized inside one company using this new technology just limited to their own drugs

REFERENCES:

[1] Wretlind A. Development of fat emulsions. J Parenter Enter Nutr. 1981; 5: 230–5.

[2] Collins-Gold L. Feichtinger N. Warnheim T. Are lipid emulsions the drug delivery solution? Mod Drug Discov. 2000; 3 (3): 44–8.

[3] Bangham AD, Horne RW. Negative staining of phospholipids and their structural modification by surface-active agents as observed in the electron microscope. J Mol Biol. 1964; 8: 660–8.

[4] Allemann E, Gurny R, Doelker E. Drug loaded nanoparticles-preparation methods and drug targeting issues. Eur J Pharm Biopharm. 1993; 39: 173–91.

[5] Smith A, Hunneyball IM. Evaluation of polylactid as a biodegradable drug delivery system for parenteral administration. Int J Pharm.1986; 30: 215–30.

[6] Siekmann B, Westesen K. Sub-micron sized parenteral carrier systems based on solid lipids. Pharm Pharmacol Lett. 1992;1:123–6.

[7] Gasco MR. Method for producing solid lipid microspheres having a narrow size distribution. 1993;US Patent No. 5250236.

[8] Schwarz C, Mehnert W, Lucks JS, Muller RH. Solid lipid nanoparticles (SLN) for controlled drug delivery: I. Production, characterization and sterilization. J Control Release.1994; 30: 83–96.

[9] Westesen K, Siekmann B, Koch MHJ. Investigations on the physical state of lipid nanoparticles by synchroton radiation X-ray diffraction. Int J Pharm. 1993; 93: 189–99.

[10] Cavalli R, Marengo E, Rodriguez L, Gasco MR. Effects of some experimental factors on the production process of solid lipid nanoparticles. Eur J Pharm Biopharm. 1996; 43(2): 110–5.

[11] Muller RH, Mehnert W, Lucks JS, Schwarz C, Muhlen A, Weyhers H, Freitas C, Ruhl D. Solid lipid nanoparticles (SLN)-an alternative colloidal carrier system for controlled drug delivery. Eur J Pharm Biopharm. 1995; 41(1): 62–9.

[12] Bunjes H, Westesen K, Koch MHJ. Crystallization tendency and polymorphic transitions in triglyceride nanoparticles. Int J Pharm. 1996; 129: 159–73.

[13] Gasco MR. Solid lipid nanospheres from warm microemulsions. Pharm Technol Eur. 1997; 9(11): 52–8.

[14] Heiati H, Phillips NC, Tawashi R. Evidence for phospholipid bilayer formation in solid lipid nanoparticles formulated with phospholipid and triglyceride. Pharm Res. 1996; 13(9): 1406-10.

[15] De Vringer T, De Ronde HAG. Preparation and structure of a water-in-oil cream containing lipid nanoparticles. J Pharm Sci. 1995; 84(4): 466–72.

[16] Sjostrom B, Kaplun A, Talmon Y, Cabane B. Structure of nanoparticles prepared from oil-in-water emulsions. Pharm Res. 1995; 12(1): 39–48.

[17] Pinto JF, Muller RH. Pellets as carriers of solid lipid nanoparticles (SLNk) for oral administration of drugs. Pharmazie. 1999; 54: 506–9.

[18] Dingler A. Blum RP, Niehus H, Gohla S, Muller RH. Solid lipid nanoparticles (SLNs/Lipopearls)—a pharmaceutical and cosmetic carrier for the application of vitamin E in dermal products. J Microencapsul. 1999; 16(6): 751–67.
[19] Demirel M. Yazan Y, Muller RH, Kilic F, Bozan B. Formulation and *in vitro– in vivo* evaluation of piribedil solid lipid particles. J Microencapsul. 2001; 18(3): 359–71.
[20] Wissing SA, Muller RH. Solid lipid nanoparticles as carrier for sunscreens: *in vitro* release and *in vivo* skin penetration. J Control Release. 2002; 81: 225–33.
[21] Cavalli R, Caputo O, Gasco MR. Solid lipospheres of doxorubicin and idarubicin. Int J Pharm. 1993; 89: R9–R12.
[22] Morel S, Gasco MR, Cavalli R. Incorporation in lipospheres of [D-Trp-6]LHRH. Int J Pharm. 1994; 105: R1– R3.
[23] Cavalli R. Morel S, Gasco MR, Chetoni P, Saettone MF. Preparation and evaluation *in vitro* of colloidal lipospheres containing pilocarpine as ion pair. Int J Pharm. 1995; 117: 243–6.
[24] Cavalli R, Peira E, Caputo O, Gasco MR. Solid lipid nanoparticles as carriers of hydrocortisone and progesterone complexes with ß-cyclodextrins. Int J Pharm. 1999; 182: 59–69.
[25] Cavalli R, Zara GP, Caputo O, Bargoni A, Fundaro A, Gasco MR. Transmucosal transport of tobramycin incorporated in SLN after duodenal administration to rats: Part I. A pharmacokinetic study. Pharm Res. 2000; 42(6): 541-5.
[26] Cavalli R, Gasco MR, Chetoni P, Burgalassi S, Saettone MF. Solid lipid nanoparticles (SLN) as ocular delivery system for tobramycin. Int J Pharm. 2002; 238: 241–5.
[27] Jenning V, Schafer-Korting M, Gohla S. Vitamin A-loaded solid lipid nanoparticles for topical use: drug release properties. J Control Release. 2000; 66: 115–26.
[28] Videira MA, Almeida AJ, Botelho MF, Santos AC, Gomes C, De Lima JJP. Lymphatic uptake of radiolabelled solid lipid nanoparticles administered by the pulmonary route. Eur J Nucl Med. 1999; 26(9): 1168.
[29] Yang S, Zhu J, Lu Y, Liang B, Yang C. Body distribution of camptothecin solid lipid nanoparticles after oral administration. Pharm Res. 1999; 16(5): 751–7.
[30] Sznitowska M, Gajewska M, Janicki S, Radwanska A, Lukowski G. Bioavailability of diazepam from aqueous-organic solution, submicron emulsion and solid lipid nanoparticles after rectal administration to rabbits. Eur J Pharm Biopharm. 2001; 52: 159–63.
[31] Wissing SA, Muller RH. The influence of the crystallinity of lipid nanoparticles in their occlusive properties. Int J Pharm. 2002; 242: 377–9.
[32] Wissing SA, Muller RH. Cosmetic applications for solid lipid nanoparticles (SLN). Int J Pharm. 2003; 254: 65–8.
[33] Borgstrom B. Importance of phospholipids, pancreatic phospholipase A2, and fatty acid for the digestion of dietary fat. Gastroenterology. 1980; 78: 954–62.
[34] Borgstrom B, Donner J. The polar interactions between pancreatic lipase, colipase and the triglyceride substrate. FEBS Lett. 1977; 83: 23–6.
[35] Scow RO, Olivecorona T. Effect of albumin products formed from chylomicron triacyl-glycerol by lipoprotein lipase *in vitro*, Biochem Biophys Acta.1977; 487: 472–86.
[36] Olbrich C, Muller RH. Enzymatic degradation of SLN-effect of surfactant and surfactant mixtures. Int J Pharm. 1999; 180: 31–9.
[37] Muller RH, Olbrich C. Solid lipid nanoparticles: phagocytic uptake, in vitro cytotoxicity and *in vitro* biodegradation, 2nd communication. Pharm Ind. 1999; 61: 564–9.
[38] Muller RH, Ruhl D, Runge SA. Biodegradation of solid lipid nanoparticles as a function of lipase incubation time. Int J Pharm. 1996; 144: 115–21.
[39] Mehnert W, Mader K. Solid lipid nanoparticles Production, characterization and applications. Adv Drug Del Rev. 2001; 47:165–196
[40] Zara GP, Cavalli R, Fundaro A. Bargoni A, Caputo O, Gasco MR. Pharmacokinetics of doxorubicin incorporated in solid lipid nanospheres (SLN). Pharm Res. 1999; 44: 281–6.
[41] Muller RH, Mader K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery-a review of the state of the art. Eur J Pharm Biopharm. 2000; 50: 161-77
[42] Schafer-Korting M, Mehnert W, Hans-Christian K. Lipid nanoparticles for improved topical application of drugs for skin diseases. Adv Drug Del Rev. 2007; 59: 427–43
[43] Zhai H, Maibach HI. Effects of skin occlusion on percutaneous absorption: an overview. Skin Pharmacol Appl Skin Physiol. 2001; 14: 1–10.
[44] Cevc G. Lipid vesicles and other colloids as drug carriers on the skin. Adv Drug Deliv Rev. 2004; 56: 675–711.
[45] Wissing SA, Muller RH. Solid lipid nanoparticles (SLN)-a novel carrier for UV blockers. Pharmazie. 2001; 56: 783–6.
[46] Wong HL, Bendayan R, Rauth AM, Li Y, Yu WX. Chemotherapy with anticancer drugs encapsulated in solid lipid nanoparticles. Adv Drug Del Rev. 2007; 59: 491–504
[47] António J. Almeida, Eliana Souto. Solid lipid nanoparticles as a drug delivery system for peptides and proteins. Adv Drug Del Rev. 2007; 59: 478–90
[48] Blasi P, Giovagnoli S, Schoubben A, Ricci M, Rossi C. Solid lipid nanoparticles for targeted brain drug delivery. Adv Drug Del Rev. 2007; 59: 454–77
[49] Date AA, Joshi MD, Patravale VB. Parasitic diseases: Liposomes and polymeric nanoparticles versus lipid nanoparticles. Adv Drug Del Rev. 2007; 59: 505-21
[50] Husseini GA, Pitt WG. Micelles and nanoparticles for ultrasonic drug and gene delivery Adv Drug Del Rev. 2008; 60: 1137–52
[51] Wong HL, Chattopadhyay N, Yu WX, Bendayan R. Nanotechnology applications for improved delivery of antiretroviral drugs to the brain. Adv Drug Del Rev. 2010; 62: 503–17
[52] Santos-Magalhães NS, Furtado Mosqueira VC. Nanotechnology applied to the treatment of malaria. Adv Drug Del Rev. 2010; 62: 560–75

[53] Azarmi S, Roa WH, Löbenberg R. Targeted delivery of nanoparticles for the treatment of lung diseases. Adv Drug Del Rev. 2008; 60: 863–75

[54] Sosnik A, Carcaboso ÁM, Glisoni RJ, Moretton MA, Chiappetta DA. New old challenges in tuberculosis: Potentially effective nanotechnologies in drug delivery. Adv Drug Del Rev. 2010; 62: 547–59

[55] Pandey R, Sharma S, Khuller GK. Oral solid lipid nanoparticle-based antitubercular chemotherapy. Tuberculosis. 2005; 85: 415–20.

[56] Sharma A, Sharma S, Khuller GK. Lectin-functionalized poly (lactide-coglycolide) nanoparticles as oral/aerosolized antitubercular drug carriers for treatment of tuberculosis. J Antimicrobial Chemoherapy. 2004; 54(4): 761-6

[57] Bargoni A, Cavalli R, Caputo O, Fundaro A, Gasco MR, Zera GP. Solid lipid nanoparticles in lymph and plasma after duodenal administration to rats. Pharm Res. 1998; 15:745–750.

[58] Nishioka Y, Yoshino H. Lymphatic targeting with nanoparticulate system. Adv Drug Del Rev. 2001; 47: 55–6