Review Article

Lipid Nanoparticles (SLNs and NLCs): Wide Range of Application from Cosmetics to Cancer Chemotherapy

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ABSTRACT: The present review compiles the applications of lipid nanoparticles mainly solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for the delivery of pharmaceutical actives. The attempts to overcome the low solubility and bioavailability of some drugs by their incorporation into lipid nanocarriers have been summarized. A special focus of this review is on different routes of administration of SLNs and NLCs which begins from oral route especially for administration of anticancers, parentral route for drug targeting, pulmonary and topical route for administration of antimicrobial, anti-proliferative and anti inflammatory agents, ophthalmic application to finally cosmetic application of lipid nanocarriers.
Key words: SLNs, NLCs, drug targeting, pulmonary application, topical application.

INTRODUCTION:

Solid lipid nanoparticles (SLN), prepared from a lipid matrix that is solid at body and room temperature, stabilized by suitable surfactants and having size from 50 to 1000 nm (Ghalandarlaki *et al.*, 2014), they were developed at the beginning of the 1990s as an alternative carrier system to emulsions, liposomes and polymeric nanoparticles and since then they have received great and still increasing attention in pharmaceutical technology research (Bhalekar *et al*., 2009). SLNs are valuable in many aspects such as (Kaur and Singh, 2014, Doktorovova *et al.*, 2014): (i) use of organic solvents can be avoided to produce SLNs, (ii) have negligible toxicity, (iii) lipophilic compounds can be effortlessly encapsulated, (iv) bioavailability of highly lipophilic molecules can be increased via lymphatic uptake, (v) degradation of chemical/moisture/light/oxidation of sensitive molecules can be prevented by their incorporation in the nanoparticle matrix, (vi) sustained drug release from the nanoparticle matrix is possible due to solid nature of the matrix leading to prolonged drug release and minimization of the adverse side effects of the encapsulated drug molecule, (vii) penetration through skin or mucus barrier is possible due to nano size. (Das *et al.,* 2012, Rostami *et al*., 2014). Nanostructured lipid carriers (NLC), i.e. nanoparticles composed of a mixture of a solid and a liquid lipid which lipid matrix is solid at room and body temperature, NLCs are the second generation of lipid nanoparticles. NLC show a higher loading capacity when compared to SLN by conceiving a less arranged solid lipid matrix, i.e. by mixing a fluid lipid with the solid lipid, a higher element drug stacking can be obtained. Thus, the NLC have an extended drug stacking capacity in evaluation to SLN and the probability of drug expulsion throughout storage is less. (Selvamuthukumar and Velmurugan, 2012).

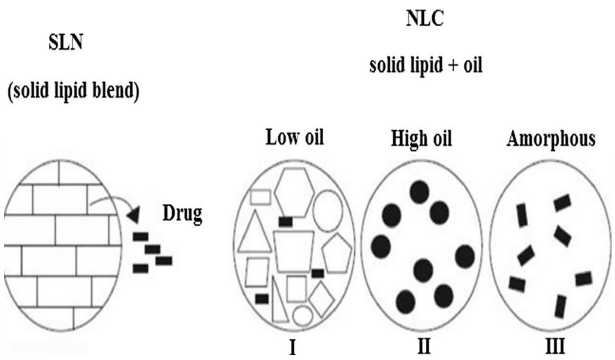

Figure 1: SLN with high crystallinity and Different types of NLC. I – Highly imperfect matrix, II – Multiple O/F/W type, III – non-crystalline amorphous NLC. (Selvamuthukumar and Velmurugan, 2012).

Lipid nanoparticles (SLNs and NLCs) showed bioavailability enhancement,controlled drug delivery of entrapped drugs via modification of dissolution rate and improvement of tissue distribution and targeting of drugs. They have been reported in various application routes (Üner and Yener, 2007):

- Parenteral for drug targeting (intravenously, intramuscularly or subcutaneously),
- Oral,
- Pulmonary application,
- Opthalmic,
- Topical (in cosmetics and dermatological preparations).

Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLCs) in various administration routes

- Oral administration of SLNs and NLCs

Drugs owing poor solubility and bioavailability after oral administration can be formulated as SLN and NLC

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to overcome these problems. After intake the lipid matrices composed of triglycerides are normally digested by pancreatic lipases into mono- and di-glycerides. The monoglycerides could form micelles and mixed micelles (with bile salts) that still contain the drug. Then these lipids may perform absorption along with the drug by means of chylomicron formation mainly into the lymphatic system. This transportation surrounds the liver and minimizes the first pass effect. Lymphatic uptake can be affected by particle size as smaller size results in higher uptake (Svilenov and Tzachev, 2014).

Several drugs (hydrophobic and hydrophilic) such as Apomorphine, α-Asarone, Carvedilol, Clozapine, Digoxin, Insulin and Praziquantel have been incorporated in the SLN and/or NLC formulations for oral administration. In most cases, the aim was to improve oral bioavailability either by increasing GI absorption or by bypassing the first-pass metabolism. (Das and Chaudhury, 2011).

Oral administration of anticancer agents is preferred by patients for its convenience and potential for outpatient treatment. In addition, oral administration facilitates prolonged exposure to a cytotoxic agent. (Calixto *et al*., 2014)

Holpuch *et al* (Holpuch *et al*., 2010.) tested a SLN formulation as a local oral cancer chemoprevention strategy and found that the penetration and subsequent internalization of nanoparticles within proliferating basal layer cells demonstrates the feasibility of nanoparticle formulations for local delivery and the stabilization of oral chemopreventive compounds.

Aditya *et al* (Aditya *et al*., 2013) made curcumin and genistein co-loaded NLCs based on oleic acid, lecithin, Tween®80 and glycerol monostearate. These NLCs were found to be promising vehicles for the oral delivery of poorly bioaccessible molecules such as curcumin and genistein. Chinsriwongkul *et al* (Chinsriwongkul *et al*., 2012) and Liu *et al* (Liu *et al*., 2011) researched NLCs loaded with the anticancer drugs all-trans retinoic acid (ATRA) and DTX respectively. NLCs based on oleic acid enhanced the entrapment efficiency of the drug in the NLCs; however, all drug-loaded NLCs had prolonged release in addition to being more cytotoxic than the free drug . (Calixto *et al*., 2014)

- Drug targeting using SLNs and NLCs via parentral adminstration

Targeting drug delivery is one of the most important fields of nanomedicine. The absence of selective targeting to the tumor usually results in low antitumor activity and severe side effects. Therefore, an active tumor-targeting delivery system of chemotherapeutic drugs is urgently needed (Yang *et al*., 2013). One of the most important strategies is the use of biodegradable nanoparticles in drug delivery, such as SLNs and NLCs as drug carriers. Due to their potential to encapsulate drugs, they are able to transport drugs to different parts of the body. Targeting may be achieved by one of the following ways (Rostami *et al*., 2014):

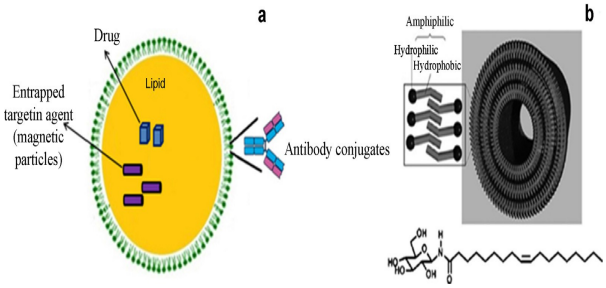

Fig. 2. The schematic figure of SLN targeting systems (a) and solid lipid nanotubes used as a pH sensitive drug delivery system (b) (Rostami *et al*., 2014)

- Antibody mediated targeted drug delivery

The drug may be incorporated into the core or located on the surface of lipidic nanoparticle and directs it via a targeting antibody to the desired site of action for various diagnostic and therapeutic applications (Rostami *et al*., 2014)

- Nanoparticle -magnetic targeting drug delivery

Magnetic drug targeting is the main application of iron oxide nanoparticles. In an external magnetic field they are able to deliver particles to the desired target area (Alexiou *et al*., 2005) and fix them there while the drug is released to make a local effect (Liu *et al*., 2011). By integrating magnetic heating elements into solid lipid nanoparticles, release control and treatment enhancement has been achieved. The heating is performed around 45–55°C (Jordan *et al*., 1999) which cause melting of the solid lipid matrices and the encapsulated drug molecules released out of the nanoparticles. Meanwhile, the temperature rising, also described as hyperthermia (Jordan *et al*., 1999), could potentially stimulate the immune response for non-specific immunotherapy of certain diseases. By precisely controlling the concentration and distribution of a drug inside the body, potential side effects and required drug dosage could be significantly reduced. (Rostami *et al*., 2014)

- pH sensitive nanoparticles

pH sensitive carriers are another option for targeted drug delivery which were used by Kashanian and coworkers. They prepared aqueous dispersions of lipid nanoparticles using a modified, pH-sensitive derivative of phosphatidyl ethanolamine for pH-sensitive nanoparticles preparation. SLNs were prepared using polysorbate 80 as the surfactant and tripalmitin glyceride and N-glutarylphosphatidyl ethanolamine as the lipid components. The SLNs prepared in this study were able to control the release of triamcinolone acetonide under acidic condition (Kashanian *et al*., 2011).

- Cationic solid lipid nanoparticles in drug delivery

It was firstly reported by Olbrich *et al*. (Olbrich *et al* 2001) that the cationic SLNs could efficiently bind and transfect plasmid DNA. Also, Liu *et al*. (Liu *et al*. 2010) prepared N3-O-toluyl-fluorouracil loaded cationic solid lipid nanoparticles (N3-O-toluyl-fluorouracil-SLNs) which enhance the GI absorption of N3-O-toluyl-fluorouracil by oral administration.

- Pulmonary application

For the pulmonary application, lipid nanoparticles have several advantages (Fig. 3). SLN and NLC have good tolerability in the airways, their biodegradable lipid content resulting in non-toxic, often even endogenous degradation products [Pilcer and Amighi, 2010]. In addition, nanoparticles can be easily entrapped into particles or aerosolized into droplets with aerodynamically suitable properties due to their size, which lead to sufficient deep lung deposition of the drug. Moreover, SLNs and NLCs adhere to the mucosal surface of the lung for longer time compared to larger particles [Ponchel *et al*., 1997, Jacobs and Muller, 2002, Lenaerts *et al*., 1990]. All these advantages lead to sustained and enhanced therapeutic effects and therefore result in a longer dosing interval and better patient compliance [Patlolla, *et al*., 2010]. This can play an important role in treatment for chronic diseases since many of the existing inhalation formulations have to be applied at least twice a day due to the relatively short duration of the drug in the lung [Pilcer and Amighi, 2010].

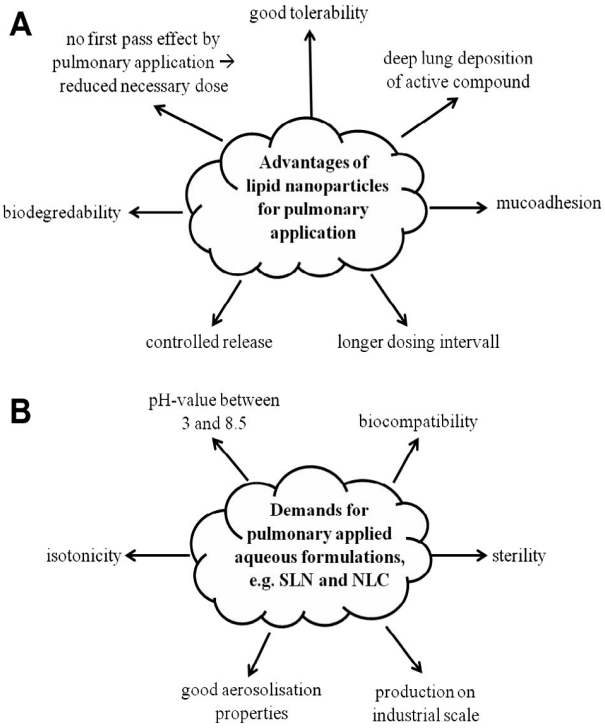

Fig. 3.A) Advantages of lipid nanoparticles for pulmonary application and B) formulation challenges for lipid nanoparticles and other aqueous formulations for pulmonary application. (Weber *et al*., 2014)

Lipid nanoparticles must meet certain requirements to be suitable for pulmonary application. First of all, they could be sterilized by one of the following methods: autoclaving, gamma ray irradiation and sterile filtration, if the particle size is smaller than 200 nm [Mukherjee *et al*., 2009]. Secondly, controlling the pH value and the osmolarity of the formulation for inhalation. A lipid nanoparticle formulation can be isotonized by adding ionic and nonionic (glycerol or carbohydrates) isotonization agents. If necessary, the pH value of SLN or NLC formulations can be adjusted to neutrality using acids, bases , buffers with low ion concentrations or buffers composed of peptizers [Weber *et al*., 2014]. Good biocompatibility is also an important criteria. Tolerability of SLNs and NLCs can be achieved by using biodegradable and biocompatible lipids and surfactants/stabilizers. For example of solid lipids used: Cetylpalmitate [Rudolph *et al*., 2004] Compritol 888 ATO [Hu *et al*., 2010] and Glycerol monostearate [Zhang *et al*., 2011, Li *et al*., 2010] Liquid lipids (Oils): Oleic acid [Pardeike *et al*., 2011], Miglyol 812 [Patlolla *et al*., 2010] and Castor oil [Weber, *et al*., 2012.], and Surfactants: Poloxamer 188 [Li *et al*., 2010, Zhang *et al*., 2011], Polysorbate 20 [Pardeike *et al*., 2011,Weber, *et al*., 2012], Polysorbate 80 [Rudolph *et al*., 2004, Videira *et al*., 2012] and Polyvinyl alcohol [Pandey and Khuller, 2005]. Finally, it is necessary that the generated aerosols SLN or NLC formulation show good aerodynamic properties for sufficient deposition in the desired airway regions. The aerodynamic size distribution of an aerosol is recognized to be in the range of 0.5–10 µm. However, the optimal aerodynamic size is related to the desired site of deposition and therefore varies depending on the therapeutic approach [Capstick and Glifton, 2012].

Lipid nanoparticles are investigated as a possibility to improve therapy of these severe pulmonary diseases. Jafaar-Maalej *et al*. [Jaafar-Maalej *et al*., 2011] developed SLN and NLC loaded with beclomethasone dipropionate they observed a sustained release with a cumulative released amount of 20% beclomethasone from SLN and 77% from NLC, respectively, after 16 days was demonstrated in vitro. Another glucocorticoid i.e., dexamethasone, was incorporated into NLC by Weber *et al*. [Weber, *et al*., 2012.]. This formulation was successfully adjusted to isotonicity and then sterilized. The developed NLC showed good stability during jet stream nebulization.

- Nanoparticles for topical administration

SLN and NLC for the topical application to the skin are made of lipids such as glycerol palmito stearate, glycerol behenate, or the wax cetylpalmitate. For NLC, liquid lipids such as oleic acid or medium chain triglycerides (Miglyol® 812) are added. Nanodispersions formulated by 5 to 40% of lipid. The higher concentrated preparations are of semisolid appearance and are cosmetically adequate as they are. According to the mode and concentration of the lipid, 0.5 to 5% surfactant such as Poloxamer 188, lecithin, Polysorbate 80, TegoCare® 450, Tyloxapol, Miranol® Ultra C32 have to be added to stabilize the particles (Korting *et al*., 2007). To facilitate dermal application, liquid dispersions which are obtained when the lipid content is low (10%) can be incorporated into a gel or cream base which does not induce aggregation or dissolution of nanoparticles [Wissing and Muller, 2001].

Lipid nanoparticles offer many advantages over suspended particles which are: increased drug chemical stability, high occlusion, film formation, improved skin hydration and controlled drug release (Fig. 3) (Pardeike *et al*., 2009).

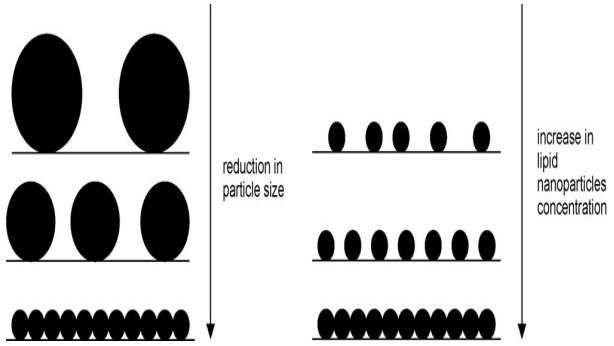

Fig. 4: The occlusion factor of lipid nanoparticles depends on various factors: at identical lipid content, reducing the particle size leads to an increase in particle number, the film becomes denser (left) and therefore the occlusion factor increases. At a given particle size, increasing the lipid concentration increases particle number and density of the film (right) which also leads to a higher occlusion factor (Pardeike *et al*., 2009).

Therefore drug classes as anti-inflammatory drugs, antimicrobial drugs and anti-proliferative agents could be successfully incorporated in lipid nanocarriers to be administered topically:

- Anti-inflammatory drugs

Anti-inflammatory drugs represent a broad range of molecules, many with potential for topical delivery. Reports on nanoparticle delivered drugs with anti-inflammatory properties for topical use. These drugs can be divided into steroids, e.g. corticosterone[Jensen *et al*., 2010], and nonsteroidal anti-inflammatory drugs (NSAIDs), e.g. naproxen[Puglia *et al*.,2008].

- **Antimicrobial agents**

The most prominent topical antimicrobial in consumer products is nanoparticle formulated imidazole and silver. Silver nanoparticles possesses antimicrobial properties and the mechanism by which silver functions as a disinfectant is not yet fully understood, but may be related to silver ion induced metabolic inhibition. (Prow *et al*., 2011)

- **Anti-proliferative agents**

Hyperproliferative skin disease is not limited to cancer, but also precancerous lesions. It can also be caused by inappropriate inflammatory responses. Several anti-cancer and anti-proliferation drugs have been delivered with nanoparticles, including 5-aminolevulinic acid (ALA), 5-fluorouracil (5FU), paclitaxel, podophyllotoxin, and Realgar [Prow *et al*., 2011).

- **Nanotechnology in cosmetics**

The use of nanotechnology has found applications in the field of cosmetics by taking the name of nanocosmetics. Solid lipid nanoparticles have been found to improve the penetration of active compounds into the stratum corneum and could be used to control delivery of cosmetic agents over a prolonged period of time and in vivo studies have shown that an SLN-containing formulation is more efficient in skin hydration than a placebo.[Raj *et al*., 2012] It was also found by Sanad *et al* (Sanad *et al*., 2010) that when SLNs was loaded with 0.5% oxybenzone (a molecular sunscreen), SPF values became about 6 fold higher when compared to that of 0.5% oxybenzone suspension. The amount of oxybenzone could be reduced while maintaining the protection level. Moreover, anti-photoageing drugs and antioxidants as tretinoin derivatives, isotretinoin, retinol, and vitamin A palmitate, have also been delivered to skin with SLN (Prow *et al*., 2011).

NLCs are interesting for formulations where higher concentrations of cosmetic actives are required. Compared to SLNs, the loading capacity can be improved when creating the imperfect matrix structure of NLCs, for example for retinol from 1.0% to 5.0% (Saupe *et al*., 2005). The loading capacity of NLCs depends also on the miscibility of the active in the lipid selected for their production. It can range from about 4% (e.g. ferulic acid), 25% (e.g. tocopherol), or even up to 50% and more, in case of well lipid miscible lipophilic actives (e.g. tocopherol and coenzyme Q10) (Müller *et al*.,2007). 'Super-loaded' NLCs were developed having a sunscreen loading of 70%. This was achieved by using the liquid sunscreen as oil component in the NLCs formulation (Souto and Muller, 2008). The first marketed NLCs products were cosmetics, employing these particles for coenzyme Q10 delivery to the skin for anti-ageing purposes. Topical application of aqueous NLCs dispersions is known to create a mono-layered lipid film onto the skin, which avoids water evaporation, and thus increases the skin's moisture and hydration (Doktorovova *et al*., 2009).

- Applications of nanoparticles in ophthalmology

SLNs and NLCs are the modern nanocarriers having the benefit of delivering ocular drugs to precise target sites and hold promise to modernize the therapy of many eye diseases. Existence of several barriers in the eye which consist of superficial barriers include the ocular surface epithelium and the tear film, and internal barriers consist of the blood-aqueous and blood-retina barriers may hindered direct and systemic drug access to the specific site of action. Topical application is the favored route for the majority of drugs, even when the goal tissues are at the posterior part of the eye where intraocular injections are now the most frequent route of administration. Many problems related to drug bioavailability, together with side effects and repeated painful treatments to reach therapeutic drug levels were achieved upon using direct administration by any of these two routes. Incidentally, the advantages of using nanoparticles include better topical route of large, poorly water-soluble molecules such as glucocorticoid drugs or cyclosporine for immune-related, vision-threatening diseases. Other massive and unstable molecules, for example nucleic acids, delivered using nanoparticles suggest better outcome for gene transfer therapy in harsh retinal diseases. Also, in the case of brimonidine (standard treatment for glaucoma) or corticosteroids (treatment for a severe intraocular inflammatory process), nanoparticle-mediated drug delivery increases the contact time of the administered drug with its target tissue. In addition, nanocarriers permit indomethacin (non-steroidal antiinflammatory drug) to reach inner eye structures using the transmucosal route. Finally, nanoparticles permit the opportunity of targeted delivery to reach exact types of

cancer, for example melanoma, leaving normal cells unharmed. (Zou *et al*., 2013, Diebold and Calonge 2010).

Conclusion: In this review, NPs applications through different routes of administration were introduced. Nanoparticulate drug delivery was one of the most promising technologies to overcome poor stability in physiological medium and delivering them across biological barriers. Lipid nanoparticles, even applied as dispersion or as a dry powder formulation, can enhance the bioavailability of an encapsulated drug and improve and prolong therapeutic effects.

REFERENCES:

Aditya, N.; Shim, M.; Lee, I.; Lee, Y.; Im, M.H.; Ko, S. (2013). Curcumin and genisteinco loaded nanostructured lipid carriers: In vitro digestion and antiprostate cancer activity. J Agric Food Chem., 61(8):1878–1883.

Alexiou, C.; Jurgons, R.; Schmid, R.; Hilpert, A.; Bergemann, C.; Parak, F.; Iro, H.; (2005). In vitro and in vivo investigations of targeted chemotherapy with magneticnanoparticles. J. Magn. Magn. Mater., 293 (1): 389–393.

Bhalekar, M.R.; Pokharkar, V.; Madgulkar, A.; Patil, N.; Patil, N. (2009). Preparation and Evaluation of Miconazole Nitrate-loaded solid lipid nanoparticles for Topical Delivery. AAPS PharmSciTech, 10:289-296.

Calixto, G.; Bernegossi, J.; Santos, B. F.; Chorilli, M. (2014). Nanotechnology-based drug delivery systems for treatment of oral cancer: a review Int. J. of Nanomed., 9: 3719–3735

Capstick, T.G.; Clifton, I.J. (2012). Inhaler technique and training in people withchronic obstructive pulmonary disease and asthma, Expert Rev. Respir. Med. 6: 91–101.

Chinsriwongkul, A.; Chareanputtakhun, P.; Ngawhirunpat, T. (2012). Nanostructured lipid carriers (NLC) for parenteral delivery of an anticancer drug. AAPS Pharm Sci Tech., 13(1):150–158.

Das, S. and Chaudhury, A. (2011). Recent Advances in Lipid Nanoparticle Formulations with Solid Matrix for Oral Drug Delivery, AAPS PharmSciTech, 12 (1): 1-9

Das, S.; Ng , W. K.; Tan, R. B.H. (2012). Are nanostructured lipid carriers (NLCs) better than solid lipid nanoparticles (SLNs): Development, characterizations and comparative evaluations of clotrimazole-loaded SLNs and NLCs. Eur J. of Pharm Sci, 47:139–151

Diebold, Y. and Calonge, M. (2010). Applications of nanoparticles in ophthalmology. Progress in Retinal and Eye Research, 29: 596-609.

Doktorovova, S.; Souto, E.B. (2009). Nanostructured lipid carrier-based hydrogel formulations for drug delivery: A comprehensive review, Expert Opin. Drug Deliv. 6: 165-176

Doktorovovaa, S; Soutob, E. B.; Silva A. M. (2014). Nanotoxicology applied to solid lipid nanoparticles and nanostructuredlipid carriers – A systematic review of in vitro data. European Journal of Pharmaceutics and Biopharmaceutics, 87: 1–18

Ghalandarlaki, N.; Alizadeh, A. M. and Esfahani, S. A. (2014). Nanotechnology-Applied Curcumin for Different Diseases Therapy, Biomedical Research International, Article ID 394264, 23 pageshttp://dx.doi.org/10.1155/2014/394264

Holpuch, A.S.; Hummel G.J.; Tong M. (2010). Nanoparticles for local drug delivery to the oral mucosa: proof of principle studies. Pharm Res., 27(7):1224–1236.

Hu, L.; Jia, Y.; Ding, W. (2010). Preparation and characterization of solid lipid nanoparticles loaded with epirubicin for pulmonary delivery, Pharmazie, 65: 585–587.

Jaafar-Maalej, C.; Andrieu, V.; Elaissari, A.; Fessi, H. (2011). Beclomethasone-loadedlipidicnanocarriers for pulmonary drug delivery: preparation, characterization and in vitro drug release, J. Nanosci. Nanotechnol. 11: 1841–1851.

Jacobs, C.; Müller, R.H. (2002). Production and characterization of a budesonide nanosuspension for pulmonary administration, Pharm. Res., 19: 189– 194.

Jensen, L.B.; Magnussson, E.; Gunnarsson, L.; Vermehren, C.; Nielsen, H.M.; Petersson, K. (2010). Corticosteroid solubility and lipid polarity control release from solidlipid nanoparticles. Int. J. Pharm., 390: 53–60.

Jordan, A.; Scholz, R.; Wust, P.; FaKhling, H.; Felix, R. (1999). Magnetic fluid hyper-thermia (MFH): cancer treatment with AC magnetic field induced excitation of biocompatible superparamagnetic nanoparticles. J. Magn. Magn. Mater., 201(1–3): 413–419.

Kashanian, S.; Azandaryani, A.H.; Derakhshande, K. (2011). New surface-modified solid lipid nanoparticles using N-glutaryl phosphatidyl ethanolamine as the outer shell. Int. J.Nanomed., 6 (1): 1–9.

Kaur , I. P. and Singh, H.(2014). Nanostructured drug delivery for better management of tuberculosis. J. Controlled Release 184: 36–50.

Korting , M. S.; Mehnert , W.; Korting, H.C. (2007). Lipid nanoparticles for improved topical application ofdrugs for skin diseases, Adv. Drug Delivery Rev.59: 427–443.

Lenaerts, V.; Couvreur, L.; Grislain, L.; Maincent, P. (1990). Nanoparticles as agastroadhesive drug delivery system, in: V. Lenaerts, R. Gurny (Eds.),Bioadhesive Drug Delivery Systems, CRC Press, Boca Raton, , pp. 93–108.

Li, Y.Z.; Sun, X.; Gong, T.; Liu, J.; Zuo, J.; Zhang, Z.R. (2010). Inhalable microparticles ascarriers for pulmonary delivery of thymopentin-loaded solid lipidnanoparticles, Pharm. Res. 27: 1977–1986.

Liu, D.; Liu, C.; Zou, W.; Zhang, N. (2010). Enhanced gastrointestinal absorption ofN3-O-toluylfluorouracil by cationic solid lipid nanoparticles. J. Nanopart. Res.12 (1): 975–984.

Liu, D.; Liu, Z; Wang, L; Zhang C.; Zhang, N. (2011). Nanostructured lipid carriers as novel carrier for parenteral delivery of docetaxel. Colloids Surf B Biointerfaces., 85(2):262–269.

Mukherjee, S.; Ray, S. and Thakur, R. S. (2009). Solid Lipid Nanoparticles: A Modern Formulation Approach in Drug Delivery System, Indian J Pharm Sci., 71(4): 349–358.

Müller, R.H.; Petersen, R.D.; Hommoss, A.; Pardeike, J. (2007). Nanostructured lipid carriers (NLC) in cosmetic dermal products, Adv. Drug Deliv. Rev. 59: 522–530.

Olbrich, C.; Bakowsky, U.; Lehr, C.M.; Müller, R.H.; Kneuer, C. (2001). Cationicsolid–lipid nanoparticles can efficiently bind and transfect plasmid DNA. J. Controlled Release 77 (3): 345–355.

Pandey, R.; Khuller, G.K. (2005). Solid lipid particle-based inhalable sustained drugdelivery system against experimental tuberculosis, Tuberculosis 85: 227–234.

Pardeike, J.; Hommoss, A.; Muller, R.H. (2009). Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. Int. J. Pharm., 366: 170–184.

Pardeike, J.; Weber, S.; Haber, T.; Wagner, J.; Zarfl, H.P; Plank, H.; Zimmer, A. (2011). Development of an Itraconazole-loaded nanostructured lipid carrier (NLC) formulation for pulmonary application, Int. J. Pharm. 419: 329–338.

Patlolla, R.R.; Chougule, M.; Patel, A.R.; Jackson, T.; Tata, P.N.; Singh, M. (2010). Formulation, characterization and pulmonary deposition of nebulized celecoxib encapsulated nanostructured lipid carriers, J. Controlled Release, 144: 233–241.

Pilcer, G. ; Amighi, K. (2010). Formulation strategy and use of excipients in pulmonary drug delivery, Int. J. Pharm. 392: 1–19.

Ponchel, G.; Montisci, M.-J.; Dembri, A.; Durrer, C.; Duchene, D. (1997). Mucoadhesion of colloidal particulate systems in the gastro-intestinal tract, Eur. J. Pharm. Biopharm., 44: 25–31.

Prow, T. W.; Grice , J. E.; Lin, L. L.; Faye, R.; Butler, M.; Elisabeth, W. B.; Wurm , M.T.; Yoong, C.; Robertson, T. A.; Soyer, H. P.; Roberts., M. S. (2011). Nanoparticles and microparticles for skin drug delivery, Adv. Drug Delivery Rev. 63: 470–491

Puglia, C.; Blasi, P.; Rizza, L.; Schoubben, A.; Bonina, F.; Rossi, C.; Ricci, M. (2008). Lipid nanoparticles for prolonged topical delivery: an in vitro and in vivo investigation, Int. J. Pharm. 357: 295–304.

Raj, S.; Jose, S.; Sumod, U. S.; Sabitha, M. (2012). Nanotechnology in cosmetics: Opportunities and challenges. J. Pharm. Pharmacol. Bio. Sci., 4:186-93

Rostamia, E.; Kashanianb, S.; Azandaryanic, A. H.; Faramarzia, H.; Dolatabadie, J. E. N.; Omidfar, K. (2014). Drug targeting using solid lipid nanoparticles, Chem. Phys. Lipids, 181: 56–61

Rudolph, C.; Schillinger, U.; Ortiz, A.; Tabatt, K.; Plank, C.; Müller, R.H.; Rosenecker, J. (2004). Application of Novel Solid Lipid Nanoparticle (SLN)-gene vector formulations based on a dimeric HIV-1 TAT-peptide in vitro and in vivo, Pharm. Res., 21: 1662–1669.

Sanad, R. A.; Abdel Malak, N. S.; El-Bayoomy, T. S.; Badawi, A. A. (2010). Preparation and characterization of oxybenzone-loadedsolid lipid nanoparticles (SLNs) with enhanced safety and sunscreening efficacy: SPF and UVA-PF. Drug Discoveries & Therapeutics, 4(6):472-483.

Saupe, A.; Wissing, S.A.; Lenk, A.; Schmidt, C.; Müller, R.H. (2005). Solid lipid nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC) – Structural investigations on two different carrier systems, Bio-Med. Mater. Eng. 15: 393–402.

Selvamuthukumar S. and Velmurugan, R. (2012). Nanostructured Lipid Carriers: A potential drug carrier for cancer chemotherapy, Lip Health and Dis, 11:159-166

Souto, E.B.; Muller, R.H. (2008). Cosmetic features and applications of lipid nanoparticles (SLN®, NLC®), Int. J. Cos. Sci., 30 157–165.

Svilenov, H.; Tzachev, C. (2014). Solid Lipid Nanoparticles – A Promising Drug Delivery System, Nanomedicine, 3: 219-223

Üner M. and Yener G. (2007). Importance of solid lipid nanoparticles (SLN) in various administration routes and future Perspectives, Int J of Nanomed, 2(3): 289–300

Videira, M.; Almeida, A.J.; Fabra, A. (2012). Preclinical evaluation of a pulmonary delivered paclitaxel-loaded lipid nanocarrier antitumor effect, Nanomed. Nanotechnol. Biol. Med. 8: 1208–1215.

Weber, S.; Bauer, B.; Zimmer, A.; Pardeike, J. (2012). Dexamethasone-loaded NLC: astable carrier system for pulmonary application by jet stream nebulisation, in: 8th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Istanbul,.

Weber, S.; Zimmer , A.; Pardeike, J. (2014). Solid Lipid Nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC)for pulmonary application: A review of the state of the art, Eur. J. Pharm and Biopharm, 86: 7–22

Wissing, S.A.; Müller, R.H. (2001). Solid lipid nanoparticles (SLN)—a novelcarrier for UV blockers, Pharmazie 56: 783–786.

Yang , X.; Li , Y.; Li , M.; Zhang , L.; Feng , L. (2013). Na Zhang Hyaluronic acid-coated nanostructured lipid carriers for targeting paclitaxel to cancer. Cancer Letters, 334: 338–345

Zhang, P.-R.; Tu, Y.-F.; Wang, S.; Wang, Y.-H.; Xie, Y.; Li, M.; Jin, Y.-G. (2011). Preperation and characterization of budesonide-loaded solid lipid nanoparticles for pulmonary delivery, J. Chin. Pharm. Sci., 20: 390–396.

Zou, H. Y.; Hao, J.; Shuangwang, Zheng, Y.; Zhang, W. S. (2013). Nanoparticles in the ocular drug delivery. Int j ophth, 6 (3): 126-133.

الدهون النانوية (SLNs وNLCs): مجموعة واسعة من التطبيقات من مستحضرات التجميل إلى العلاج الكيميائي للسرطان

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هذا الاستعراض يجمع تطبيقات الجسيمات ذات النانوية الدهون الصلبة (SLN)، وحاملات الدهون ذات البنية النانومترية (NLC) لتوزيع الأصول الصيدلانية. تم تلخيص محاولات التغلب على انخفاض الذوبان والاتاحة الحيوية لبعض الأدوية عن طريق إدماجها في حاملات الدهون. وهناك تركيز خاص في هذا الاستعراض على طرق مختلفة لتعاطي SLNs و NLCsالذي يبدأ من التعاطي عن طريق الفم ، لاستهداف مضادات السرطان، والطرق الوريديه للعقارات المستهدفة التوزيع والطريق الرئوي، والطريق الموضعي لتعاطي مضادات الميكروبات، وكمضادات للالتهابات ، والتطبيق الرمدي و أخيرا التطبيق في مستحضرات التجميل.