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Review Article

Nanostructured Lipid Carrier System for the Treatment for Skin Disease-A Review

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Abstract

Nanostructured lipid carrier is a novel delivery system that has shown great potential as an excellent carrier system. Skin disease treatment usually employs topical and systemic delivery with topical delivery being more preferred. The limitations of topical therapy are its lack of adherence to the application site and larger particle size of drug which makes it difficult for drugs to penetrate through the layers of skin. In Nanostructured lipid carrier formulations the drugs are in Nano range that are encapsulate in a lipid core which helps achieve localized and slow release over time. The advantage of loading drugs on nanostructured lipid carrier in terms of efficacy and formulation aspect is discussed in this review with the help of current research literary papers.

INTRODUCTION

Skin disease is one of the most common types of disease that affects human beings. Though rarely fatal these diseases not just hurts physically, its presence makes individuals disturb emotionally, isolated, lack in self-esteem and discomfort. With an average surface area of 1.6-2m^2 and constituting about 15% of total body weight of an adult human, skin is considered as one of the largest organ of the body. It functions as a barrier and protects the underlying muscles, bones, ligaments and internal organs [1,2].

LAYERS OF SKIN

Skin can be divided into three layers:

Epidermis

The foremost barrier for external environment prevents pathogens from entering into the skin and causing infection [2]. Its cellular components includes a) keratinocytes- also known as basal cells since they are present on the basal layer of the skin and functions as a barrier for the environmental damage; b) melanocytes- melanin producing cells located in the stratum basale of skin and uvea of the eye; c) Langerhans cells- functions as antigen presenting cells; d) merkel cells- oval receptor cells that are associated with the sense of touch discrimination of shape and texture [2,3].

The epidermis consists of 4 sublayers: i) stratum corneum- the outermost layer composed mostly of corneocytes (non- living keratinocytes). It consists of dense network of keratin which makes it the toughest layer to penetrate for topical drug delivery; ii) stratum lucidum- is translucent under microscope and is a clear layer of dead keratinocytes cells; iii) stratum granulosum- consists of keratinocytes that have migrated from lower layer and appear granular; iv) stratum spinosum- or "pickle cell" layer. Keratinization begins in this sub layer. The basal layer or stratum basale consists of proliferating or non-proliferating keratinocytes. This layer also consists melanocytes, Langerhans cell and merkel cells [2-4].

Dermis

Dermis is present below the epidermis layer and is thick, fibrous and elastic imparting flexibility and strength to the skin [3], consist of sweat, oil glands, nerve ending, hair follicles, blood and lymph vessels. It maintains and repairs the skin [4].

Hypodermis

Hypodermis is the lowermost layer of the skin consisting of loose connective tissue, elastic fibres and cells such as fibroblasts, macrophages and adipocytes. It functions as energy reserve and insulator [4] (Figure 1 and Table 1).

New improvements are being developed for the proper delivery of the medications for the treatment of skin diseases [16]. As we know that only developing new therapies is not enough for the drugs to work appropriately, the therapies may look very efficient theoretically and while conducting in vitro studies but the dosage regimen when applied may show different result in vivo. Various approaches can be made to enhance the efficiency

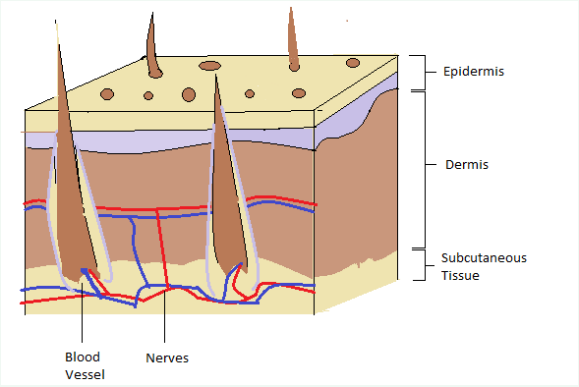

Figure 1 Electrospun nanofibers membrane of poly-ε-caprolactone visualization after 21 days of human Osteoblasts culture (Cells visualization in blue (nucleus /DAPI) and PLL^{FITC} labelled nanofibers in green): colonization and proliferation of osteoblasts into the nanofibers membrane.

of the very drug used in those therapies either by increasing its solubility in the body or absorption at the site by using different techniques [17].

One of such approach can be development of suitable carriers for the drug. Nanostructured lipid carrier (NLC) is a novel technology that can be used for the treatment of skin diseases. Numerous researches are on-going for developing drug loaded NLC delivery for the treatment of skin disorders. Commonly systemic and topical medications are used as a treatment method, systemic delivery have higher potential of adverse effects compared to systemic delivery. Patients are more complaint and satisfied with topical delivery. Carrier system for the drugs that makes it more soluble and absorbable is being studied like lipid nanoparticles where the drugs are dissolved in lipids. Lipid nanoparticles have shown promising results and progress are being made in this novel drug delivery system [17,18].

NANOSTRUCTURED LIPID CARRIER

Lipid nanoparticles are colloidal carriers which have shown a high potential as a suitable drug carrier because of their potential to increase solubility and improve bioavailability of poorly water soluble or lipophilic drugs and extensive research have been conducted on it in the recent years [17]. It can be mainly divided into solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC). Prior to this, various other lipid carriers like liposomes, micro and nanoemulsions, nanocapsules, nanosponges and polymeric nanoparticles were used for the effective delivery of poorly soluble drugs which had its own drawbacks such as rapid degradation by the pH and enzymes present in the GIT, stability problems during storage, organic solvent residues, toxicity from polymers, etc. Then SLN were developed as an alternate carrier scheme to liposomes, emulsions and polymeric nanoparticles. The difference between SLN and NLC is that in SLN only solid lipid is used in which the drug is incorporated whereas in NLC the drug is incorporated in solid and liquid lipid mix which may give better sustained release characteristic to the formulation [19-22].

Many research conducted have found that drugs are more soluble in fluids lipid than in solid lipids. NLC is the second generation in lipid based nanoparticles and is reported to be better when compared to SLN [23,24].

Limitations of SLN

- low drug load capacity
- Drug leakage/ expulsion during storage
- Unpredictable gelation tendency
- High water content of SLN dispersion
- Tendency for particle size growth
- Payload of hydrophilic drug is low

NLC formulation utilizes liquid lipids along with solid lipids that make it advantageous over SLN. But stability issues are still a point of concern for NLC formulators [25].

COMPONENTS

Solid lipids

Compounds with high melting point i.e. higher than 40 °C are used as solid lipid. It should be biodegradable and must be accepted by GRAS (generally recognized as safe) [26].

Eg: beeswax, tristearin, carnauba wax, percifac, stearic acid, cholesterol, apifil, cutina CP; cetyl palmitate

Liquid lipids

The liquid lipids used are digestable oils from natural sources. It must have well tolerated GRAS status and also accepted for human use [26].

Eg: cetiol V, miglyol, castor oil, oleic acid, davana oil, palm oil, olive oil.

Emulsifying agent

Emulsifying agents are also called surfactants which lower the interfacial tension between two immiscible liquids or components. When used in small amount it enhances colloidal activity by decreasing rate of aggregation. Hydrophilic surfactants are mostly used. PEG added to the formulation prevents the uptake by reticuloendothelial system (RES) which results in the increase the circulation time of the drug. It should be biocompatible, cost effective, capable of being sterilized before application and non-irritating. Lipophilic or ampiphillic emulsifiers are used for the fabrication of NLCs [25].

Eg: miranol ultra, tween 80, poloxamer.

UV blockers

Added to prevent the damages caused by UV rays, lowering the risk of skin cancer.

Eg: avobenzone- absorbs UV-A radiation

Aqueous medium

Purified water is used.

To select the appropriate solid lipid, liquid lipid screening tests are carried out and the lipids in which the drug is most soluble is

Table 1: Table shows the Common skin diseases, causative agents, affected site and treatment.

SN	Disease	Cause	Affected site	Symptoms	Treatment	Ref.
1	Scabies	Mites under skin	Anywhere on the body except face	Itching, red papules	Malathion or 5% permethrin lotion	[8,9]
2	Psoriasis	Immune- mediated hyperproliferation disorder, chronic inflammatory dermatitis	Plaque psoriasis (elbows, knee & sacrum); palmopustular (palms, soles); Flexural (auxillae, submammary)	Thick red rash covered with silvery scales	Topical- corticosteroids, vitamin D analogues, Tar based preparations, dithranol Systemic- methotrexate, immunosuppressant, retinoids	[10]
3	Acne vulgaris	Chronic inflammation of pilosebaceous apparatus	Areas rich in sebaceous glands such as face, shoulders and trunk	Open comedones (dilated pore with a plug of keratin) or closed comedones (small cream coloured papules- whiteheads)	Benzoyl peroxide cream, tretinoin, antibiotics (tetracyclin, erythromycin, trimethoprim), anti androgen, retinoids, steroids, non drug therapies (excision, cryotherapy)	[11, 12, 13]
4	Cold sores	Herpes simplex virus fever, triggered by stress, sun or menstruation	mouth or nose	Small, painful, fluid filled blisters	Antiviral pills or creams	
5	Vitiligo	Autoimmune disease associated with pernicious anemia, thyroid disease and Addison's disease	Hands, wrist, face and genitalia	Macules of pigment loss on the skin, in some cases hair may be depigmented	Potent topical steroids and uv phototherapy	[14]
6	Melasma	Pregnancy	Cheeks, nose, forehead and chin	Tan or brown patches	Prescription creams and over the counter products	[15]

Table 2: Screening tests carried out and the lipids in which the drug is most soluble is selected.

Ingredient	Materials
Solid lipid	Glyceryl behenate (compritol 888 ATO); glyceryl palmitostearate (percirol ATO 5); dynasan; fatty acid (eg: stearic acid); triglyceride (tristearin); steroids (cholesterol); waxes (cetyl palmitate)
Liquid lipid	Medium chain triglycerides (miglyol 812); paraffin pil; 2- octyl dodecanol; propylene glycol dicaprylocaprate (labrafac); isopropyl myristate and squalene; palm oil Fatty acids: oleic acid; linoleic acid, decanoic acid
Hydrophilic emulsifier	Pluronic F68 (poloxamer 188); Pluronic F127 (poloxamer 407); polysorbate 20; polysorbate 40; polysorbate 80; polyvinyl alcohol; Solutol HS15; trehalose; sodium deoxycholate; sodium glycocholate; sodium oleate; polyglycerol methyl glucose distearate
Lipophilic emulsifier	Myverol 18-04K; span 20; Span 40; Span 60
Amphiphilic emulsifier	Egg lecithin; soya lecithin; phosphatidylcholines; phosphatidylethanolamines; Gelucire 50/13

selected. The selected lipids must be mixed in appropriate ratio to prepare stable NLC and for that purpose binary lipid phase selection is also done in which different ratios of selected solid lipid and liquid lipid are mixed and the best ratio is selected for preparing NLC [23,26] (Table 2)

In Gaba B et al., different solid lipids and liquid lipids were screened and from the results obtained the drug was found to be most soluble in glyceryl monostearate and labrasol. The selected lipids at 6:4 ratio when stirred at 200 rpm at 85 °C for one hour gave appropriate binary lipid phase [25]. Kelidari HR, et al., reported that increase in oleic acid (liquid lipid) concentration increased the entrapment efficiency. While particles size shows no significant affect due to lipid concentration as reported by Souza LG, et al. [28].

PREPARATION

There are many techniques used for the preparation of nanostructured lipid carriers. The most commonly used techniques are high pressure homogenization, solvent emulsification method, supercritical fluid extraction of emulsion, ultrasonication or high speed homogenization and spray drying. The selection of method employed depends upon the drug, its solubility and stability, route of administration, etc [20,26,27].

High pressure homogenization technique

HPH technology has been widely popular and dependable technique for the production of lipid nanoparticles. It can also be used for large scale production of lipid nanocarriers. In this technique the fluids are pushed through a narrow gap of few micro ranges by high pressure (100- 200 bars). This reduces the particles size to submicron range. There are two homogenization processes developed i.e, hot and cold process. In both the process, prior to the application of homogenization the active pharmaceutical component is dissolved or dispersed in the melted lipids [27-30].

Hot homogenization process

The drug and the melted lipids is dispersed in the aqueous solution of same temperature containing emulsifier with the application of continual stirring using mixing device forming pre-emulsion which is then subjected to homogenization [31].

Cold homogenization technique

The process is similar to that of hot homogenization where the drug is mixed in the melted lipid and subsequently the mix is subjected to rapid cooling using liquid nitrogen or ice. This process has been developed to control the limitations with hot homogenization process like accelerated degradation due to elevated temperature of the lipid mix since cold homogenization reduces the duration of thermal exposure [32].

Gaba B, et al., reported that terbinafine loaded NLC prepared by high pressure homogenization method in which glyceryl monostearate, labrasol and pluronic F 127 used as solid lipid, liquid lipid and surfactant showed reduced fungal burden, better release profile and permeation when compared with marketed formulation [25].

Microemulsion technique

The microemulsion is prepared at a temperature above the melting point of the lipids. The lipids are heated at a temperature above its melting point and a combination of water, co-surfactant(s) and the surfactant is heated to the same temperature as the lipids and added to the lipid melt with mild stirring. Then the microemulsion is dispersed in cold aqueous medium consisting of water under mild stirring. This dispersion in cold aqueous medium leads to rapid recrystallization of the oil droplets [33-35].

Solvent emulsification-evaporation technique

The hydrophobic drug and lipophilic material were dissolved in organic solvent and is further mixed with an aqueous phase using high speed homogenizer then the resultant coarse emulsion was immediately passed through the microfluidizer. Upon evaporation of the organic solvent by continuous stirring lipids precipitates from the aqueous medium to form nanoparticles dispersion. No thermal stress is applied which makes this method suitable for heat sensitive drugs. Particle size is determined by the concentration of lipid in organic phase; smaller the lipid load (5%) smaller will be particle size [36].

High shear homogenization or ultrasonication technique

Drug is mixed with the lipid phase heated and simultaneously the aqueous surfactant solution is heated to the same temperature. Then the heated aqueous phase is poured into the lipid mixture using magnetic stirrer forming pre emulsion. Ultrasonication was applied to the pre emulsion using probe sonicator with water bath (at 0 °C). After ultrasonication the product is passed through 0.45 μm to remove impurities. The disadvantage of this process is the use of high amount of surfactant also it has stability issues associated with the inappropriate particle size distribution. But this process can easily be taken as the most attainable one since the instruments used are relatively more available in labs than compared to hot and cold homogenization [20].

Pinto MF, et al., reported that methotrexate loaded NLC using high shear homogenization combined with ultrasonication where witepsol S51, oleic acid and polysorbate 60 or 80 were used as solid lipid, liquid lipid and surfactant. The particle sizes obtained were below 300 nm which is suitable for topical delivery. Also the in vitro skin permeation studies showed higher skin penetration with methotrexate loaded NLC when compared with free drug formulation [37,41].

Melting dispersion method

In melting method, drug, solid lipid and an organic solvent is melted together and water phase is heated to the same temperature separately. The solid lipid melt containing drug is subsequently added to water phase followed by high speed stirring for few hours. The resulting mixture is cooled down to room temperature to yield nanoparticles [38].

Spray drying

In spray drying technique, hot gas is applied to liquid or viscous liquid to produce dry powder, though it is expensive it is considered cost effective method when compared to lyophilisation- another technique used for product having stability issues. It is a method of preference for thermo sensitive products as the products are exposed to elevated temperature for every short period of time. Lipid with melting point greater than 70 °C are suitable, lower than that makes them unsuitable as the high shear force and temperature makes them to aggregate.

LYOPHILLIZATION

Lyphillization follows the principle of sublimation where the water changes directly from the solid state (ice) to the gaseous state without passing through the liquid state. This procedure is done to preserve the product from chemical and physical degradation. Cryoprotectants such as mannitol, trehalose, sorbitol, glucose, sucrose are added to the product to protect it from high stress generated during lyophilisation process. It does not change the molecular structure of the product and is the most reliable drying process [24].

Tilmicosin was loaded in lipid nanoparticles including solid lipid nanoparticles, liquid lipid nanoparticles and lipid core nanocapsules. The tilmicosin NLC suspension was prepared by hot homogenization technique using compritol 888 ATO, sesame oil and poloxamer 407 and tween 80. The NLC prepared was lyophilized using mannitol as cryoprotectant. The lyophilized products showed better stability over long period of storage [39].

Many research have been done to showcase the potential of NLC using different preparation methods. Drugs have shown increase in their efficiency when loaded in NLC. V.M. Ghate et al., In a research conducted on tretinoin loaded NLC for topical delivery, formulations were made using microemulsion technique and hot probe sonication technique. Stearic acid, oleic acid and tween 80 & span 60 were used as solid lipid, liquid lipid and surfactant respectively. The results obtained from the two preparation techniques showed that the particle size of the NLC prepared by microemulsion technique was found greater (2156 nm approximately with PDI value 0.891) than the ones prepared by probe sonication technique (762 nm with

PDI value 0.483). The release profile of both the techniques showed less percentage of drug release when compared with the commercially available tretinoin gel which is a desirable for topical preparation and indicates prolonged release of drug can be achieved. Also tretinoin loaded NLC gel showed no irritation after 7 days of repeated application which marketed gel showed irritation within 3 days of application.

CONCLUSION

Nanaostructured lipid carriers have great advantage over other lipid nanoparticles and have better loading capacity. Lipid carriers show good potential to deliver the drugs in effective manner and can be considered as a progress in the treatment of skin disease. The drugs are more soluble in these lipid system and delivery of drug over prolong period of time can be achieved which is one of the desirable property of topical delivery. Also the particle size of drug is small in NLC and topical penetration is found to be more. Though lipid carriers are advantageous and seem to be safe their potential for toxicity over a long period of usage time must be checked. From all the information gathered from recent relevant literature it can be concluded that NLC is an excellent carrier system for the delivery of drugs for treatment of skin disease.

REFERENCES

1. Iizuka H. Epidermal turnover time. J Dermatol Sci. 1994; 8: 215-217.
2. Tripathi KD. Essentials of medical pharmacology. Ind J Pharmacol. 1994; 26: 166.
3. Waugh A, Ross GA, Anatomy W. Physiology: In Health and Illness. 10th edn. Churchill Livinstone: Elsevier. 2006; 293-295.
4. Tortora GJ, Derrickson BH. Principles of anatomy and physiology. John Wiley & Sons. 2008.
5. Johnstone CC, Farley A, Hendry C. The physiological basics of wound healing. Nurs Stand. 2005; 19: 59-65.
6. Mohan H. Textbook of pathology. New Delhi: Jaypee brothers medical publishers. 2005.
7. James WD, Berger TG, Elston DM. Andrews' Diseases of the Skin: Clinical Dermatology, 11th edn. Philadelphia: Saunders Elsevier. 2011.
8. Mounsey KE, McCarthy JS. Treatment and control of scabies. Current opinion in infectious diseases. 2013; 26: 133-139.
9. Hengge UR, Currie BJ, Jäger G, Lupi O, Schwartz RA. Scabies: a ubiquitous neglected skin disease. Lancet Infect Dis. 2006; 6: 769-779.
10. Feldman SR, Horn EJ, Balkrishnan R, Basra MK, Finlay AY, McCoy D, et al. Council IP. Psoriasis: improving adherence to topical therapy. J Am Acad Dermatol. 2008; 59: 1009-1016.
11. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. The Lancet. 2012; 379: 361-372.
12. Leyden JJ. A review of the use of combination therapies for the treatment of acne vulgaris. J Am Acad Dermatol. 2003; 49: S200-210.
13. Haider A, Shaw JC. Treatment of acne vulgaris. Jama. 2004; 292: 726-735.
14. Cui J, Shen LY, Wang GC. Role of hair follicles in the repigmentation of vitiligo. J Invest Dermatol. 1991; 97: 410-416.
15. Piamphongsant T. Treatment of melasma: a review with personal experience. Int J Dermatol. 1998; 37: 897-903.
16. Ferreira M, Silva E, Barreiros L, Segundo MA, Costa Lima SA, Reis S. Methotrexate loaded lipid nanoparticles for topical management of skin- related diseases: Design, characterization and skin permeation potential. Int J Pharm. 2016; 14-21.
17. Khan S, Baboota S, Ali J, Khan S, Narang RS, Narang JK. Nanostructured lipid carriers: an emerging platform for improving oral bioavailability of lipophilic drugs. Int J Pharm Invest. 2015; 5: 182.
18. Mishra B, Patel BB, Tiwari S. Colloidal nanocarriers: a review on formulation technology, types and applications toward targeted drug delivery. Nanomedicine. 2010; 6: 9-24.
19. Müller RH, Souto EB, Radtke M. Nanostructured Lipid Carriers: A Novel Generation of Solid Lipid Drug Carriers Pharm Techn Europe. 2005; 17: 45-50.
20. Naseri N, Valizadeh H, Zakeri-Milani P. Solid lipid nanoparticles and nanostructured lipid carriers: structure, preparation and application. Advanced pharmaceutical bulletin. 2015; 5: 305.
21. Severino P, Andreani T, Macedo AS, Fangueiro JF, Santana MH, Silva AM, et al. Current State of-Art and New Trends on Lipid Nanoparticles (SLN and NLC) for Oral Drug Delivery. J Drug Deliv. 2012; 2012: 750891.
22. Puglia C, Bonina F. Lipid nanoparticles as novel delivery systems for cosmetics and dermal pharmaceuticals. Expert Opin Drug Deliv. 2012; 9: 429-441.
23. Katouzian I, Esfanjani AF, Jafari SM, Akhavan S. Formulation and application of a new generation of lipid nano-carriers for the food bioactive ingredients. Trends Food Sci Technol. 2017; 68: 14-25.
24. Kaur S, Nautyal U, Singh R, Singh S, Devi A. Nanostructure Lipid Carrier (NLC): the new generation of lipid nanoparticles. Asian Pac J Health Sci. 2015; 2: 76-93.
25. Gaba B, Fazil M, Khan S, Ali A, Baboota S, Ali J. Nanostructured lipid carrier system for topical delivery of terbinafine hydrochloride. Bulletin Faculty of Pharmacy, Cairo University. 2015; 53: 147-159.
26. Jenning V, Thünemann AF, Gohla SH. Characterisation of a novel solid lipid nanoparticle carrier system based on binary mixtures of liquid and solid lipids. Int J Pharm. 2000; 199: 167-177.
27. Uner M. Preparation, characterization and physicochemical properties of Solid Lipid Nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC): Their benefits as colloidal drug carrier systems. Pharmazie. 2006; 61: 375-386.
28. Souza LG, Silva EJ, Martins AL, Mota MF, Braga RC, Lima EM, et al. Development of topotecan loaded lipid nanoparticles for chemical stabilization and prolonged release. Eur J Pharm Biopharm. 2011; 70: 189-196.
29. Hu FQ, Jiang SP, Du YZ, Yuan H, Ye YQ, Zeng S. Preparation and characterization of stearic acid nanostructured lipid carriers by solvent diffusion method in an aqueous system. Colloid Surf B Biointerfaces. 2005; 45: 167-173.
30. 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.
31. Liedtke S, Wissing S, Muller RH, Mader K. Influence of high pressure homogenisation equipment on nanodispersions characteristics. Int J Pharm. 2000; 196: 183-185.
32. Lippacher A, Muller RH, Mader K. Preparation of semisolid drug carriers for topical application based on solid lipid nanoparticles. Int J Pharm. 2001; 214: 9-12.
33. Gasco MR. Solid lipid nanospheres from warm micro-emulsions. Pharm Technol Eur. 1997; 9: 52-58.

34. Boltri L, Canal T, Esposito PA, Carli F. Lipid nanoparticles: evaluation of some critical formulation parameters. Proc Int Symp Control Release Bioact Mater. 1993; 20: 346-347.

35. Dianrui Zhang, Tianwei Tan, Lei Gao. Preparation of oridonin-loaded solid lipid nanoparticles and studies on them *in vitro* and *in vivo*. Nanotechnol. 2006; 17: 5821.

36. Pinto MF, Moura CC, Nunes C, Segundo MA, Lima SA, Reis S. A new topical formulation for psoriasis: development of methotrexate-loaded nanostructured lipid carriers. Int J Pharm. 2014; 477: 519-526.

37. Reithmeier H, Hermann J, Gopferich A. Lipid microparticles as a parenteral controlled release device for peptides. J Control Release. 2001; 73: 339-350.

38. Al-Qushawi A, Rassouli A, Atyabi F, Peighambari SM, Esfandyari-Manesh M, Shams GR, et al. Preparation and Characterization of Three Tilmicosin-loaded Lipid Nanoparticles: Physicochemical Properties and in-vitro Antibacterial Activities. IJPR. 2016; 15: 663.

39. Ghate VM, Lewis SA, Prabhu P, Dubey A, Patel N. Nanostructured lipid carriers for the topical delivery of tretinoin. Eur J Pharm Biopharm. 2016; 108: 253-261.

40. Gupta M, Vyas SP. Development, characterization and *in vivo* assessment of effective lepidic nanoparticles for dermal delivery of fluconazole against cutaneous candidiasis. Chem Phys Lipids. 2012; 165: 454-461.

41. Agrawal Y, Petkar KC, Sawant KK. Development, evaluation and clinical studies of Acitretin loaded nanostructured lipid carriers for topical treatment of psoriasis. Int J Pharm. 2010; 401: 93-102.

42. Allemann E, Gurny R, Doelker E. Drug-loaded nanoparticles: preparation methods and drug targeting issues. Eur J Pharm Biopharm. 1993; 39: 173-191.

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