IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
August 2016 Vol.:7, Issue:1

Solid Lipid Nanoparticles: A Potential Carrier for Transdermal Drug Delivery

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Madhulika Pradhan[1]

[1] *Rungta College of Pharmaceutical Sciences and Research, Kohka, Kurud Road, Bhilai, Chhattisgarh 490024, India.*

Submission: 10 August 2016
Accepted: 15 August 2016
Published: 25 August 2016

www.ijppr.humanjournals.com

Keywords: Transdermal delivery, solid lipid nanoparticles, delivery systems and skin barrier

ABSTRACT

Transdermal delivery constitutes one of the most important routes for novel drug delivery system. Significant resistant nature of skin is the main trouble for successful drug delivery to deep skin layers for systemic absorption. Several approaches including physical, chemical and novel formulation techniques have been explored for safe and effective drug delivery across the skin barrier. Among them, potential lipid-based carrier solid lipid nanoparticles have gained a unique position for transdermal delivery of drugs due to the presence of high amount of epidermal lipids as the chief component of the penetration barrier of the skin. Skin-carrier interaction involves attachment of these carriers to skin with a view to permit the exchange of lipid between the outermost layers of the stratum corneum. This review specifically focuses on the hurdles of transdermal drug delivery, the need of novel carriers for transdermal delivery with special emphasis on role of solid lipid nanoparticles suggesting this lipid carrier a potential moiety for drug delivery through the skin.

1. INTRODUCTION

Transdermal delivery constitutes one of the most important routes for the novel delivery system. Transdermal route is emerging as an extensively accepted route of drug administration due to its ability to apply the drug to the site of action without rupturing the skin membrane (Sampath et al., 2010). Transdermal drug delivery system makes available the drugs through the skin portal to systemic circulation at a predetermined rate and maintains clinically the effective concentrations over a prolonged period of time.

The main merits of transdermal delivery are non-invasiveness, sustained release, self-administration, and enhancement of therapeutic efficacy and specificity to the target site (Liuzzi et al., 2016).

However targeted delivery of drug molecules to the skin is still a most challenging area of research in pharmaceutical development. The main hurdle in the way is barrier property of skin (Foldvari et al., 2010). It's notable barrier properties are due in large part to the stratum corneum, which represents the thin outer layer of the epidermis. In contrast to other tissues in the body, the stratum corneum consists of corneocytes (composed primarily of aggregated keratin filaments encased in a cornified envelope) that are surrounded by an extracellular milieu of lipids organized as multiple lamellar bilayers. These structured lipids avoid extreme loss of water from the body and likewise block access of most topically applied drugs, except those that are lipid-soluble and of low molecular weight. This posses a significant challenge to administering medications via the skin either for local cutaneous effects or as systemic therapy following their entry into superficial dermal capillaries (Gupta 2014, Manikandan et al., 2014).

Many approaches have been investigated to defeat this hurdle including physical methods of interruption and externally applied forces (e.g., iontophoresis, microneedles and phonophoresis), chemical disruption (e.g., permeation enhancers), novel formulations (e.g., nanoparticles , liposome etc), and a combination of these approaches (Charoenputtakun et al., 2015).

Among this, novel formulation based approach has become an important area of pharmaceutical research for transdermal drug delivery. Further lipid-based novel carriers present a unique position for transdermal drug delivery as lipids display exceptional properties in terms of safety,

biocompatibility, and physical stability. Numerous lipid based systems such as liposomes, transferosomes, niosomes, ethosomes, virosomes, phytosomes, cubosomes, solid lipid nanoparticles, nanostructured lipid carriers etc have been investigated successfully for transdermal delivery of drugs (Singh et al., 2015).

Solid Lipid Nanoparticles (SLNs) have materialized as an alternative to other novel delivery approaches as they present various advantages such as the feasibility of incorporation of lipophilic and hydrophilic drugs, improved physical stability, low cost compared to liposomes and ease of scale-up and manufacturing (Pradhan et al., 2013). Moreover, the potential of SLNs in epidermal targeting, follicular delivery, controlled drug delivery, increased skin hydration due to greater occlusivity and photostability improvement of active pharmaceutical ingredients has been very well established (Rawat et al., 2008, Sathali et al., 2012; Pradhan et al., 2013). Solid lipid nanoparticles are colloidal carrier systems composed of a high melting point lipid/s as a solid core coated by surfactants. The term lipid in a broader sense includes triglycerides, partial glycerides, fatty acids, hard fats and waxes. A clear advantage of SLNs is the fact that the lipid matrix is made from physiological lipids which decrease the danger of acute and chronic toxicity (Pradhan et al, 2015a).

Present review article focuses on the benefits and need of transdermal drug delivery system, hurdles in transdermal drug delivery and necessity of novel drug delivery carrier especially focusing on the solid lipid nanoparticles as an efficient carrier for drug delivery to the skin.

2. Benefits of transdermal drug delivery

Transdermal delivery offers various advantages over other routes such as hypodermic injections, which are painful, generate dangerous medical waste and pose the risk of disease transmission by needle re-use. Furthermore, as compared with the oral route, it is used when there is a significant first-pass effect of the liver that can prematurely metabolize drugs. In addition, transdermal systems are non-invasive and can be self-administered. They can provide prolonged drug release of about a week. (Prausnitz and Langer, 2008; Kogan and Garti, 2006).

Various other advantages of transdermal drug delivery have been discussed below:

- Avoids vagaries associated with gastrointestinal absorption due to pH, enzymatic activity, drug-food interactions etc.
- Substitutes oral administration when the route is unsuitable as in case of vomiting, diarrhea.
- Avoids hepatic "first pass" effect.
- Avoid the risks and inconveniences of parenteral therapy.
- Reduces daily dosing, thus, improving patient compliance.
- They also improve patient compliance and the systems are generally inexpensive.
- Offers controlled the release of the drug into the patient, it enables a steady blood-level profile, resulting in reduced systemic side effects and, sometimes, improved efficacy over other dosage forms.
- Extend the activity of drugs having short plasma half-life through the reservoir of drug present in the therapeutic delivery system and its controlled release characteristics.
- Rapid termination of drug effect by removal of drug application from the surface of the skin.
- Rapid identification of the medication in emergencies. (e.g. Non-responsive, unconscious, or comatose patient.) Elimination of the hazards and difficulties of I.V. infusions or I.M. injections.
- Enhance therapeutic efficacy, reduced side effects due to optimization of the blood concentration-time profile and elimination of pulse entry of drugs into the systemic circulation.
- Provide predictable activity over extended duration of time and ability to approximate zero-order kinetics
- Offers improved control of the drug concentrations with small therapeutic indices.
- Minimize inter and intra-patient variation.
- Provide suitability for self-administration.

3. Need of novel drug delivery system for drug delivery to skin

Field of pharmaceutical science has been mounting progressively over the time, and presently it has become precious in helping to keep us healthy and avert disease. In the past few decades, extensive interest has been focused on the development of transdermal delivery of drugs because

of a number of advantages offered by this route. Skin is the largest body organ covering a surface of about 2m and gaining about one-third of the blood circulating through the body. Topical drug delivery means the application of drug to skin for localized effect and in transdermal drug delivery system (TDDS) skin is used as a potential route for the delivery of systemic action of drugs (Rawat et al., 2016). TDDS offers a number of advantages like longer duration of action, flexibility in dosing, reduced side effects, uniform plasma levels, high patient compliance etc. But at the same time, it also bears some drawbacks like possibility of local irritation effect, erythema, itching, and most important is the low permeability of drugs in the stratum corneum. In addition stratum corneum behaves as a tough natural barrier (Manosroi *et al.,* 2012). This limits the route to transport drugs with a low octanol–water partition coefficient of 1 to 3, molecular weight of less than 500 Da and a melting point of less than 200 °C.

Nanotechnology has established a widespread exploration as the nanocarriers are able to fluidize the stratum corneum as a function of shape, size, surface charges, and hydrophilicity–lipophilicity balance, during drug delivery across the skin barrier (Wong 2016). Many physical, chemical and novel formulation techniques like iontophoresis, electroporation, sonophoresis, microneedle, magnetophoresis, thermophoresis, skin abrasion, use of penetration enhancers, pro-drugs, salt formation, liposome, transferosomes, niosomes, ethosomes, virosomes, phytosomes, cubosomes, solid lipid nanoparticles, nanostructured lipid carriers etc. has been investigated to evade this barrier (Barry 2001; Benson 2005, Singh et al., 2014).

Among this novel formulation, technique is most promising for drug delivery through the skin. These novel delivery carriers bear great potential for dermal delivery. The novel carriers can be broadly classified into polymer based and lipid-based delivery carriers. However, lipid-based novel carriers gain unique position, especially for drug delivery to skin as lipids, display exceptional properties in terms of safety, biocompatibility, physical stability, efficacy, economic constituents, ease of preparation, scale-up, better entrapment of lipid soluble drugs, prolonged drug release and flexibility of formulation (Pradhan et al., 2016).

Furthermore, epidermal lipids exist in great homology with synthetic lipid. Thus lipid-based carriers mean an alternative to assist dermal penetration. They attach themselves onto the skin surface; facilitate adhesiveness and permits lipid exchange between the lipid-based carriers and the outermost layers of skin (Kakadia and Conway 2015).

Till date numerous polymeric and lipid-based carriers including, liposome, transferosomes, niosomes, ethosomes, virosomes, phytosomes, cubosomes, solid lipid nanoparticles, nanostructured lipid carriers etc. have been used successfully for safe and effective transdermal delivery of drugs. Various novel carriers used for transdermal delivery of drug has been enlisted in **Table 1.**

Table 1: Various novel carriers used for transdermal delivery of drug

Delivery carrier	**Drug**	**Disease/Disorder**	**Remark**	**Reference**
Polymeric carriers				
Microsphere	Propranolol hydrochloride	Hypertension	Completely controlled drug release was observed	Thacharodi and Rao 1995
Polymeric nanoparticle	Rabeprazole	Ulcer	Enhanced skin permeability and controlled drug release was observed	Ahmed and El-Say 2014
	Betamethasone propionate	Skin inflammation	Prolonged drug release, enhanced stability and drug was observed.	Silva et al., 2015
Dendrimers	Indomethacin	Inflammation	Enhanced drug activity of developed system as compared to the pure drug suspension was reported.	Chauhan et al., 2003
Lipid based carriers				
Liposome	Propranolol hydrochloride	Hypertension	Increased drug concentration in skin with about 74 folds as compared to plain propanolol gel	Guan et al., 2015

Ethosome	Clotrimazole	Candidiasis	Enhanced drug permeation across skin	Rahul et al., 2012
	Psoralen	Psoriasis	Improved dermal and transdermal delivery of psoralen with increased biocompatibility	Zhang et al., 2014
	Methotrexate	Psoriasis	Enhanced skin permeation was observed	Dubey et al., 2007.
Transferosomes	Insulin	Diabetes	Prolonged hypoglycemic activity over 24 h after transdermal administration was observed	Malakar el al., 2012
	Pentoxifylline	Chronic occlusive arterial diseases	Enhanced bioavailability and sustained drug release was observed	Shuwaili et al., 2016
Solid lipid nano particles	Fluocinolone acetonide	Psoriasis	Enhanced skin permeation and prolonged drug release was observed	Pradhan et al., 2015a
	Naproxen	Inflammation	Increased concentration of naproxen in the skin layer with less systemic absorption was found.	Akbari et al.,, 20116
Nanostructured lipid carriers	Fluocinolone acetonide	Psoriasis	Enhanced skin permeation and prolonged drug release was observed	Pradhan et al., 2015b
	Lansoprazole	Gastric ulcer	Drug accumulation in the skin with continuous drug penetration drug concentration for at least 24 hours was reported	Lin and Duh 2016

4. Solid lipid nanoparticles for transdermal drug delivery

Solid Lipid Nanoparticles (SLNs), which were first mentioned in 1991, are colloidal carriers developed as an alternative system to the existing traditional carriers (emulsions, liposomes and polymeric nanoparticles). They are a new generation of submicron-sized lipid emulsions where the liquid lipid (oil) has been substituted by a solid lipid (Mehnert and Mäder, 2001).

They may increase the solubility and bioavailability of active pharmaceutical ingredients (API), guard these compounds from external objects such as light or oxygen thereby facilitating drug targeting (Müller *et al*., 2000). Other advantages include the simple and scalable manufacturing processes such as microemulsion technique, high-pressure homogenization, and ultrasonication, their non-toxicity and biocompatibility as SLNs are constituted from GRAS (generally recognized as safe) ingredient, ability to modify drug release at the site of action (Bunjes 2010)

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. Due to their unique size-dependent properties, lipid nanoparticles offer the possibility to develop new therapeutics. The ability to incorporate drugs into nano-carriers offers a new prototype in drug delivery that could be used for secondary and tertiary levels of drug targeting (Cavalli et al., 2000).

SLNs are composed of physiological lipid dispersed in an aqueous medium containing emulsifier exhibiting an average particle size in the nanometer range and epidermal lipids are found in great homology with synthetic lipid. SLNs mean an option to facilitate dermal penetration. In addition nano size range provides a high specific surface area for drug absorption through the skin thereby providing greater efficacy as a delivery system (Lauterbach and Müller-Goymann, 2015)

They are also able to attach themselves on to the skin surface, promoting adhesiveness and increasing hydration, even realizing lipid exchange between the lipid-based carriers and the outermost layers of skin. Several researchers have been carried out for safe and effective transdermal delivery of skin though solid lipid nanoparticles.

In this context **Verma *et al*., 2013** developed SLN of piroxicam for transdermal delivery of drug for the effective management of rheumatoid arthritis, osteoarthritis. They developed SLN using

solvent emulsification-diffusion method and performed *in vitro* release of piroxicam from SLNs in the phosphate buffer of ph 7.4. They reported a biphasic release pattern with an initial burst & prolonged release. Conclusively they demonstrated that piroxicam loaded SLNs based hydrogel formulation SLNs-C8H had the accumulative amount of piroxicam in skins & should a significant skin targeting effect.

Elnaggar *et al*., 2011 developed SLN of sildenafil citrate for transdermal permeation of drug for the effective management of erectile dysfunction. They developed SLNs using high-pressure homogenization method. They reported that SLNs have successfully improved stratum corneum transdermal permeation via human skin with promising implication for shorter onset & longer duration of drug action.

In another study **Praveen *et al.*, 2013** developed SLN for transdermal drug delivery for effective management of anti-inflammatory activity. They developed SLNs using melt emulsion sonication & low-temperature solidification method. Further, they performed in vitro drug release by using acetate synthetic membrane. Overall they concluded that it would be advantageous for controlled transdermal delivery of drug.

Akbari *et al.*, 2016 developed naproxen loaded solid lipid nanoparticles (Nap-SLNs) by the ultrasonication method to improve its skin permeation and examined the effect of Hydrophilic-lipophilic balance (HLB) changes on nanoparticles properties. They reported that the amount of naproxen noticed in the receptor chamber at all the sampling times for the reference formulation (naproxen solution containing all surfactants at pH 7.4) was higher as compared to Nap-SLN8 formulation. Further, Nap-SLN8 exhibited increased concentration of naproxen in the skin layer with less systemic absorption. The overall finding suggested that majority of drug in Nap-SLN8 retained in the skin which in turn reduces the side effect resulted from systemic drug absorption. In addition, enhanced concentration of the drug at the site was also observed.

Ghanbarzadeh *et al*., 2015 developed hydroquinone (HQ) loaded SLNs to overcome the problems associated with HQ such as drug instability due to rapid oxidation, insufficient skin penetration, and severe systemic side effects. These results indicated the better HQ localization in the skin and its lower systemic absorption. They suggested that, SLNs to be a promising drug carrier for dermal administration of HQ in the treatment of hyperpigmentation due to suitable

HQ loading value, enhanced stability against oxidation and suitable skin penetration in addition to reduced systemic absorption.

Apart from the above discussed findings, numerous researches which suggest SLNs to be a potential carrier for transdermal delivery have been presented in the Table 2.

Table 2: Various SLNs used in the transdermal delivery of drug

Drug	**Preparation method of SLNs**	**Diseases/Disorders**	**Remark**	**Reference**
Meloxicam	Microemulsion method	Pain and inflammation	Noticeable anti-inflammatory activity with excellent skin tolerability was achieved	Khurana *et al*., 2013
Safranal	Ultrasound and high-pressure homogenization (HPH) methods	Sunburn	Enhanced sunscreen and moisturizing activity was observed	Khameneh *et al.*, 2015
Grisofulvin	Hot micro-emulsion method	Fungal infection	Enhanced skin permeation was observed	Aggrawal and Gondi, 2013
Aconitine	Micro-emulsion method	Fever and pain	Enhanced drug permeability and reduce administration time was reported	Zhanng *et al*., 2015
Isotretinoin	Hot homogenization method	Psoriasis	Significantly improved skin targeting effect and good stability	Liu *et al.*, 2007
Quercetin	Homogenization and ultra-	Skin cancer	Enhanced permeation of drug loaded SLNs	Han *et al.*, 2014

	sonication method		as compared to quercetin dissolved in propylene glycol	
Terbinafine	Solvent-injection method	Candidiasis	Reduced fungal burden of Candida albicans in rats as compared to commercial product	Vaghasiya *et al.*, 2013
Acyclovir	High pressure homogenization method	Fungal infection	Two times more skin accumulation of drug loaded SLNs formulation than marketed acyclovir gel cream	Gide *et al.*, 2013
Halobetasol propionate	Solvent injection method	psoriasis	HP-SLN exhibited controlled drug release with enhanced skin targeting with no skin irritation.	Bikkad *et al.*, 2014
Clobetasol propionate	High-pressure homogenization	Psoriasis and other skin inflammation	Noticeable improvement in therapeutic response with1.9 fold improvement in inflammation and 1.2 fold improvement in itching against marketed formulation	Kalariya *et al*., 2005
Flucnazole	Solvent diffusion method	Cutaneous candidiasis	Enhanced dermal localization of drug was reported	Gupta *et al.*, 2013

5. CONCLUSION

The transdermal drug delivery system encourages drug absorption via the skin. This offers many advantages over conventional administration routes such as oral or intravenous administration for systemic and local drug delivery with easy administration. It is patient friendly and reduces the patient inconvenience caused by intravenous administration. In addition it minimizes drug loss from pass effect of the liver thereby delivering therapeutic drugs at a controlled rate. But natural barrier property of skin is main hurdle in development of transdermal drug delivery system. However overcoming the skin barrier, including the stratum corneum and epidermal layer, success could be achieved in this area. Though chemical and physical techniques already exist, they possess certain unavoidable limitations such as need high doses or high potency to exert efficiency which results in irritation, causes harm to skin and trim downs the skin barrier function. Consequently, a nanoparticle delivery system is gaining increased attention as a transdermal drug delivery carrier.

In this context solid lipid nanoparticles have materialized as a versatile novel approach transdermal delivery of drugs drug. SLNs link the merits of lipid emulsion and polymeric nanoparticle systems while overcoming the sequential and in vivo stability issues that discourage the conventional as well as polymeric nanoparticles drug delivery approaches. The potential of SLNs as resourceful carrier for dermal and transdermal delivery for the treatment of various diseases like hypertension, diabetes, gastric ulcer, psoriasi, candidiasis etc. have been reported by numerous researchers. Conclusively SLNs are very complex systems with clear advantages having great potential for drug delivery through skin. In future work needs to be done to understand the structure, dynamics and toxicity issues of SLN to explore its usefulness for in vivo point.

6. Acknowledgement

Authors are thankful to SERB-DST New Delhi, India for financial support and Chairman, Santosh Rungta Group of Institution for providing infrastructural facilities.

7. REFERENCES

1. Aggarwal N, Goindi S. Preparation and in vivo evaluation of solid lipid nanoparticles of griseofulvin for dermal use. J Biomed Nanotechnol. 2013;9(4):564-76.
2. Ahmed TA, El-Say KM. Development of alginate-reinforced chitosan nanoparticles utilizing W/O nano emulsification/internal crosslinking technique for transdermal delivery of rabeprazole. Life Sci. 2014;110(1):35-43.
3. Akbari J, Saeedi M, Morteza-Semnani K, Rostamkalaei SS, Asadi M, Asare-Addo K, Nokhodchi A. The design of naproxen solid lipid nanoparticles to target skin layers. Colloids Surf B Biointerfaces. 2016; 145:626-33.
4. Al Shuwaili AH, Rasool BK, Abdulrasool AA. Optimization of elastic transfersomes formulations for transdermal delivery of pentoxifylline. Eur J Pharm Biopharm. 2016; 102:101-14.
5. Barry BW. 2001. Novel mechanisms and devices to enable successful transdermal drug delivery. Eur J Pharm Sci. 14: 101– 114.
6. Benson HAE. 2005. Transdermal drug delivery: penetration enhancement techniques. Curr Drug Deliv. 2 : 23 – 33.
7. Bikkad ML, Nathani AH, Mandlik SK, Shrotriya SN, Ranpise NS, Halobetasol propionate-loaded solid lipid nanoparticles (SLN) for skin targeting by topical delivery. J Liposome Res. 2014; 24(2):113-23. Gupta M, Tiwari S, Vyas SP. Influence of various lipid core on characteristics of SLNs designed for topical delivery of fluconazole against cutaneous candidiasis.. Pharm Dev Technol. 2013;18(3):550-9.
8. Bunjes H. Lipid nanoparticles for the delivery of poorly water-soluble drugs. J. Pharm. Pharmacol. 2010;62: 1637–1645.
9. Cavalli R, Caputo O, Gasco MR. Preparation and characterization of solid lipid nanospheres containing paclitaxel.Eur. J. Pharm. Sci. 2000;10: 305–309.
10. Charoenputtakun P, Li SK, Ngawhirunpat T. Iontophoretic delivery of lipophilic and hydrophilic drugs from lipid nanoparticles across human skin. Int J Pharm. 2015;495(1):318-28.
11. Chauhan AS, Sridevi S, Chalasani KB, Jain AK, Jain SK, Jain NK, Diwan PV. Dendrimer-mediated transdermal delivery: enhanced bioavailability of indomethacin. J Control Release. 2003;90(3):335-43.
12. Dubey V, Mishra D, Dutta T, Nahar M, Saraf DK, Jain NK. Dermal and transdermal delivery of an anti-psoriatic agent via ethanolic liposomes. J Control Release. 2007;123(2):148-54. Epub 2007 Aug 16.
13. Foldvari M, Badea I, Wettig S, Baboolal D, Kumar P, Creagh AL, Haynes CA. Topical delivery of interferon alpha by biphasic vesicles: evidence for a novel nanopathway across the stratum corneum. Mol Pharm. 2010;7(3):751-62.
14. Ghanbarzadeh S, Hariri R, Kouhsoltani M, Shokri J, Javadzadeh Y, Hamishehkar H. Enhanced stability and dermal delivery of hydroquinone using solid lipid nanoparticles. Colloids Surf B Biointerfaces. 2015 1; 136:1004-10.
15. Gide PS, Gidwani SK, Kothule KU, Enhancement of transdermal penetration and bioavailability of poorly soluble acyclovir using solid lipid nanoparticles incorporated in gel cream. Indian J Pharm Sci. 2013;75(2):138-42.
16. Guan Y, Zuo T, Chang M, Zhang F, Wei T, Shao W1, Lin G. Propranolol hydrochloride-loaded liposomal gel for transdermal delivery: Characterization and in vivo evaluation. Int J Pharm. 2015; 487(1-2):135-41.
17. Gupta R. Transdermal drug delivery system,World J. Pharm. Pharm. Sci. 2014;3: 375–394.
18. Han SB, Kwon SS, Jeong YM, Yu ER, Park SN. Physical characterization and in vitro skin permeation of solid lipid nanoparticles for transdermal delivery of quercetin. Int J Cosmet Sci. 2014;36(6):588-97.
19. Kakadia PG, Conway BR. Lipid nanoparticles for dermal drug delivery. Curr Pharm Des. 2015;21(20):2823-9.
20. Kalariya M, Padhi BK, Chougule M, Misra A. Clobetasol propionate solid lipid nanoparticles cream for effective treatment of eczema: formulation and clinical implications. Indian J Exp Biol. 2005;43(3):233-40.
21. Khameneh B, Halimi V, Jaafari MR, Golmohammadzadeh S. Safranal-loaded solid lipid nanoparticles: evaluation of sunscreen and moisturizing potential for topical applications. Iran J Basic Med Sci. 2015;18(1):58-63.
22. Khurana S, Bedi PM, Jain NK. Preparation and evaluation of solid lipid nanoparticles based nanogel for dermal delivery of meloxicam. Chem Phys Lipids. 2013;175-176:65-72.

23. Kogan A, Garti N. Microemulsions as transdermal drug delivery vehicles. Adv. Colloid Interface Sci. 2006; 123:369–385.
24. Lauterbach A, Müller-Goymann CC. Applications and limitations of lipid nanoparticles in dermal and transdermal drug delivery via the follicular route. Eur J Pharm Biopharm. 2015;97(Pt A):152-63.
25. Lin WJ, Duh YS. Nanostructured lipid carriers for transdermal delivery of acid labile lansoprazole. Eur J Pharm Biopharm. 2016. Accepted manuscript. doi: 10.1016/j.ejpb.2016.07.015.
26. Liu J1, Hu W, Chen H, Ni Q, Xu H, Yang X. Isotretinoin-loaded solid lipid nanoparticles with skin targeting for topical delivery. Int J Pharm. 2007; 328(2):191-5.
27. Liuzzi R, Carciati A1, Guido S2, Caserta S. Transport efficiency in transdermal drug delivery: What is the role of fluid microstructure? Colloids Surf B Biointerfaces. 2016;139:294-305.
28. Maheshwari RG, Tekade RK, Sharma PA, Darwhekar G, Tyagi A, Patel RP, Jain DK. Ethosomes and ultradeformable liposomes for transdermal delivery of clotrimazole: A comparative assessment. Saudi Pharm J. 2012;20(2):161-70.
29. Malakar J, Sen SO, Nayak AK, Sen KK. Formulation, optimization and evaluation of transferosomal gel for transdermal insulin delivery. Saudi Pharm J. 2012;20(4):355-63.
30. Manikandan P, Nethaji R, Surenderan N, Babu G. A review on: transdermal drug delivery systems.Indo Am. J. Pharm. Res. 2014;4:1809–1824.
31. Manosroi A, Chankhampan C , Manosroi W, Manosroi J . 2012. Transdermal absorption enhancement of papain loaded in elastic niosomes incorporated in gel for scar treatment. Eur J Pharm Sci. 48: 474 – 483.
32. Mehnert W, Mäder K. Solid lipid nanoparticles – production, characterization and applications. Adv. Drug Deliv. Rev. 2001; 47: 165–196.
33. Müller RH, Mäder 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: 161–177.
34. Pradhan M, Singh D, Singh MR. Novel colloidal carriers for psoriasis: current issues, mechanistic insight and novel delivery approaches. J Control Release. 2013; 170(3):380-95.
35. Pradhan M, Singh D, Murthy SN, Singh MR. Design, characterization and skin permeating potential of Fluocinolone acetonide loaded nanostructured lipid carriers for topical treatment of psoriasis. Steroids. 2015; 101:56-63.
36. Pradhan M, Singh D, Singh MR. Development characterization and skin permeating potential of lipid based novel delivery system for topical treatment of psoriasis. Chem Phys Lipids. 2015; 186:9-16.
37. Pradhan M, Singh D, Singh MR. Influence of selected variables on fabrication of Triamcinolone acetonide loaded solid lipid nanoparticles for topical treatment of dermal disorders. Artif Cells Nanomed Biotechnol. 2016; 44(1):392-400.
38. Prausnitz MR, Langer R.Transdermal drug delivery. Nat.Biotechnol. 2008; 26:1261–1268.
39. Rawat M, Singh D, Saraf S, Saraf S. Lipid carriers: a versatile delivery vehicle for proteins and peptides. Yakugaku Zasshi. 2008; 128(2):269-80.
40. Sathali AH, Ekambaram P, Priyanka K. Solid lipid nanoparticles: a review. Sci. Revs. Chem. Commun. 2012;2: 80–102.
41. Silva CO, Rijo P, Molpeceres J, Figueiredo IV, Ascensão L, Fernandes AS, Roberto A, Reis CP. Polymeric nanoparticles modified with fatty acids encapsulating betamethasone for anti-inflammatory treatment. Int J Pharm. 2015;493(1-2):271-84.
42. Singh D, Dubey P, Pradhan M, Singh MR. Ceramic nanocarriers: versatile nanosystem for protein and peptide delivery. Expert Opin Drug Deliv. 2013;10(2):241-59.
43. Singh D, Pradhan M, Nag M, Singh MR.Vesicular system: Versatile carrier for transdermal delivery of bioactives. Artif Cells Nanomed Biotechnol. 2015;43(4):282-90.
44. Singh D, Pradhan M, Shrivastava S, Murthy SN, Singh MR, Chapter 11 - Skin autoimmune disorders: lipid biopolymers and colloidal delivery systems for topical delivery, Nanobiomaterials in Galenic Formulations and Cosmetics; 2016:257-296.

45. Thacharodi D, Rao KP. Development and in vitro evaluation of chitosan-based transdermal drug delivery systems for the controlled delivery of propranolol hydrochloride. Biomaterials. 1995;16(2):145-8.
46. Vaghasiya H, Kumar A, Sawant K. Development of solid lipid nanoparticles based controlled release system for topical delivery of terbinafine hydrochloride. Eur J Pharm Sci. 2013;49(2):311-22.
47. Wong T. Microwave technology enabled transdermal nanocarrier and drug delivery. Asian J. Pharm. Sci. 2016;11: 43–44.
48. Zhang YT, Han MQ, Shen LN, Zhao JH, Feng NP,.Solid Lipid Nanoparticles Formulated for Transdermal Aconitine Administration and Evaluated In Vitro and In Vivo. J Biomed Nanotechnol. 2015;11(2):351-61.
49. Zhang YT, Shen LN1, Wu ZH1, Zhao JH1, Feng NP. Comparison of ethosomes and liposomes for skin delivery of psoralen for psoriasis therapy. Int J Pharm. 2014;471(1-2):449-52.