WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 7, 388-400. Review Article ISSN 2277– 7105

A REVIEW ON NANOSTRUCTURED LIPID CARRIER BASED GEL FOR TOPICAL TREATMENT OF PSORIASIS

Sonali P. Derkar*, Dr. Shagufta A. Khan and Dr. Rajendra O. Ganjiwale

Department of Pharmaceutics, Institute of Pharmaceutical Education and Research, Borgaon (Meghe), Wardha-442001, Maharashtra, India.

Article Received on
07 April 2022,

Revised on 28 April 2022,
Accepted on 18 May 2022

DOI: 10.20959/wjpr20227-24284

***Corresponding Author**
Sonali P. Derkar
Department of Pharmaceutics, Institute of Pharmaceutical Education and Research, Borgaon (Meghe), Wardha-442001, Maharashtra, India.

ABSTRACT

Psoriasis is one of the common chronic immune mediated inflammatory, non-catching skin disease, having characteristic features like red patches on skin covered with thick silvery scales, small scaling spots (most commonly seen in children). The prevalent reported in various countries ranges between 0.09 and 11.43%, making psoriasis a global problem with at least 100 million individuals affected worldwide. Currently, there are many modern and alternative treatments strategies including systemic administration, phototherapy and ultraviolet radiation and biological treatment to treat psoriasis but none of them have been proven to provide complete relief to patients. Moreover, they are associated with certain side effects. In order to overcome the issues, Topical nanostructured lipid carrier based gel is a most suitable for treatment of psoriasis, as it make close contact with stratrum corneum and increase drug skin permeability and also help in controlled release of drug.

KEYWORDS: Psoriasis, Transdermal drug delivery system (TDDS), Nanostructured lipid carrier (NLC).

1. INTRODUCTION

Psoriasis is a chronic, inflammatory skin disease, characterized by raised, red scaly plaques.[1] This disease affects about 2-3% of the world-wide population, although it is more prevalent in American, Canadian, and European populations.[2] Psoriasis is also associated with several co-morbidities, suggesting that the underlying pathogenesis of the disease is more than "skin deep".[3] Psoriasis arises through chronic interactions between hyperproliferative

keratinocytes and infiltrating, activated immune cells. Initially, psoriasis was considered solely to be due to dysfunction of limiting keratinocyte proliferation.[4]

Psoriasis is clinically classified in 2 group: pustular and non-pustular lesions. Figure no.1

1) Non-pustular psoriasis

- Psoriasis vulgaris (early and late onset)
- Guttate psoriasis
- Erythrodermic psoriasis
- Palmoplantar psoriasis
- psoriatic arthritis (PsA)
- Inverse psoriasis

2) Pustular psoriasis

- Generalized pustular psoriasis (von Zumbusch type)
- Impetigo herpetiformis
- Localized pustular psoriasis

a. Palmoplantar pustular psoriasis (Barber type)

b. Acrodermatitis continua of Hallopeau.[5]

Psoriasis vulgaris is the most common form of psoriasis. Vulgaris is Latin for "common," so it means a common form of psoriasis. Plaque psoriasis is not contagious. Psoriasis vulgaris causes plaques, or scales. These are patches of inflamed, silvery skin that usually occur on the scalp, knees, face, hands, feet and outside of the elbow.[6,7]

Guttate psoriasis, from the Greek word gutta meaning a droplet, describes the acute onset of a myriad of small, 2–10 mm diameter lesions of psoriasis. Guttate psoriasis is a type of psoriasis that shows up on skin as red, scaly, small, teardrop-shaped spots. It doesn't normally leave a scar. It is usually found in child or young adult.[8]

Erythrodermic psoriasis is an uncommon, aggressive, inflammatory form of psoriasis. Symptoms include a peeling rash across the entire surface of the body. The rash can itch or burn intensely, and it spreads quickly.[9,10]

Palmoplantar psoriasis is a variant of psoriasis that affects the skin of the palms and soles. It features hyperkeratotic, pustular, or mixed morphologies.[11] Inverse psoriasis, sometimes called

hidden psoriasis or intertriginous psoriasis, is a form of psoriasis that affects skin folds. These are areas of body where skin rubs against skin.[12,13]

Generalized pustular psoriasis (GPP) is a severe form of a skin disorder called psoriasis. GPP and other forms of psoriasis are caused by abnormal inflammation. Inflammation is a normal immune system response to injury and foreign invaders (such as bacteria).[14] However, when inflammation is abnormal and uncontrolled, it can damage the body's tissues and organs. Individuals with GPP have repeated episodes in which large areas of skin become red and inflamed and develop small pus-filled blisters (pustules).[15]

The pathogenesis of psoriasis can be explained by dysregulation of immunological cell function as well as keratinocyte proliferation/differentiation. The epidermis is composed of a basal layer, spinous layer, granular layer and cornified layer. The transit time of keratinocytes from the basal layer to the spinous layer is reduced from approximately 13 days in the normal epidermis to only 48 h in psoriatic lesions.[16] It was also reported that the cell cycle was shortened from 311 h in normal lesions to 36 h in basal keratinocytes of psoriatic lesions, indicating substantial acceleration of keratinocyte proliferation in psoriatic lesions.[17]

Recently, the immunological pathomechanism has been clarified substantially. Whereas T-helper (Th)1 overactivation was thought to induce occurrence of psoriasis, it has been demonstrated that Th17 cells play a key role. Th17 development is maintained by interleukin (IL)-23 mainly produced by dendritic cells. Th17 cells produce various cytokines, including IL-17A, IL-17F and IL-22. IL-17A and IL22 induce not only keratinocyte proliferation, but also tumor necrosis factor (TNF)-a, chemokine (C-X-C motif) ligand (CXCL)1 and CXCL8 production. TNF-a accelerates the infiltration of inflammatory cells, including lymphocytes, monocytes and neutrophils, from the peripheral blood into skin with dendritic cell activation. In addition, antimicrobial peptides are overexpressed in psoriatic skin lesions, and the antimicrobial peptide, LL-37, activates dendritic cells, which leads to the development of inflammation.[18]

Two steps in the development of psoriasis: priming versus elicitation. The very first time a psoriasis patient experiences an outbreak of skin lesions can be considered the priming phase. Naïve T cells with autoimmune potential circulating through secondary lymphoid organs such as lymph nodes are activated by mature skin derived dendritic cells, clonally expanded and induced to upregulate adhesion molecules necessary for entrance into skin compartments.

Upon recognition of the lesional inciting (auto-) antigen presented by lesional dendritic cells in a TNF-a-rich environment T cells will be activated, proliferate and secrete T helper (TH)-1 cytokines.[19]

Elicitation or recall phase of psoriasis have a lower threshold and are triggered by events described above including physical stress leading to an activation of local T cells by skin derived antigen-presenting dendritic cells (intrinsic T-cell activation hypothesis). Local proliferation and expansion of T cells with consecutive secretion of TH-1 cytokines will again lead to downstream events including keratinocyte proliferation and an angiogenic tissue reaction. An alternative scenario involves selectin and integrin dependent recruitment of effector T cells along chemokines gradients into inflamed skin as predicted by the conventional immune surveillance concept (recirculation hypothesis). working hypothesis for the immunopathogenesis of psoriasis is provided in **Figure no.2.**[19]

Currently, there are many modern and alternative treatments strategies including systemic administration, phototherapy and ultraviolet radiation and biological treatment to treat psoriasis but none of them have been proven to provide complete relief to patients. Moreover, they are associated with certain side effects. In order to overcome the issues accompanied with these strategies, transdermal drug delivery systems have been utilized and found effective with negligible toxicity.[20]

TDDS has significantly influenced the delivery of various therapeutic agents, especially in pain management, hormonal therapy, and treatment of diseases of the cardiovascular and central nervous systems. TDDS does not involve passage through the gastrointestinal tract; therefore, there is no loss due to first-pass metabolism, and drugs can be delivered without interference from pH, enzymes, and intestinal bacteria.[21] In addition, TDDS can be used to control drug release according to usage restrictions, thereby contributing to the high persistence of this method. Most importantly, because TDDS is a non-invasive administration method and involves minimal pain and burden on the patient, drugs can be safely and conveniently administered to children or the elderly.[22]

In this review, we addressed the types of gels for dermal drug application.[23] (Table no 1). The gels can prove to be a beneficial vehicle for topical drug delivery or for the localized drug action on skin such as in case of sprains or acute musculoskeletal disorders. A gel is defined as a semisolid formulation, which exhibits an external solvent phase, is hydrophobic

or hydrophilic in nature, and is immobilized within the spaces available of a three-dimensional network structure.[23]

Gels have a broad range of applications in cosmetics, medicine, biomaterials and food technologies. Compared to creams and ointments, gels are mostly used because of their high-water content, permit a greater dissolution of drugs and facilitate migration of the drug through the vesicle. In addition, gels can hydrate the skin by retaining a significant amount of trans epidermal water and facilitate drug transport.[24]

Additionally, the topical treatment is the preferred route of administration for psoriasis as it provides targeted action at the site. Major challenge with conventional topical administration is poor drug penetration through psoriatic skin due to thickening, abnormal maturation of stratum corneum, lipid imbalance and deficiency of natural moisturizer. NLC loaded gel can overcome stratum corneum barrier of psoriatic skin and can prove vital for psoriatic therapy.[25,26] NLC cause occlusive effect which leads to increased skin hydration as nanosized lipid particles ensure close proximity with stratum corneum which increase the drug amount.[27,28]

Nanostructured lipid carriers (NLCs), as second generation of lipid nanoparticles to overcome the shortcomings of first generation i.e. SLNs. Biodegradable and compatible lipids (solid and liquid) and emulsifiers are used for the preparation of NLCs. Liquid lipids (oil) incorporation causes structural imperfections of solid lipids leading to a less ordered crystalline arrangement which avert drug leakage and furnish a high drug load.[29] In last few years, NLCs have gained attention of researchers as an alternative of SLNs, polymeric nanoparticles, emulsions, microparticles, liposomes etc. These nanocarriers possess the utility in delivery of hydrophilic as well as lipophilic drugs.[25] NLCs have emerged as a promising carrier system for the delivery of pharmaceuticals via oral, parenteral, ocular, pulmonary, topical, and transdermal route. Recently, NLCs are also being exploited in brain targeting, chemotherapy, gene therapy, food industry and delivery of cosmeceuticals and nutraceuticals.[30] Depend on the location of incorporated drug moieties in NLC, they can be categorized into three types[26,31], as shown in **Figure no:3.**

Preparation procedures of nanostructured lipid carriers (NLCs)[32,33]: hot homogenization, cold homogenization and microemulsion as shown in **Figure no:4.**

Advantages of NLCs over the conventional formulation[34,35]

- Prevent or minimize the drug expulsion during storage
- Control and targeted drug release
- Feasibilities of loading both lipophilic and hydrophilic drugs
- Use of biodegradable and biocompatible lipids
- Avoid organic solvents
- More affordable (less expensive than polymeric/surfactant based carriers
- Better physical stability
- Ease of preparation and scale-up
- Improve benefit/risk ratio
- Increase of skin hydration and elasticity
- Small size ensures close contact with the stratum corneum
- Enhanced stability of drugs

NLCs particles can make close contact with superficial junctions of SC and furrows between corneocyte islands, allowing superficial spreading of the active agents. Following the evaporation of water from the nano systems applied to the skin surface, particles form an adhesive layer occluding the skin. Hydration of SC thus increases to reduce corneocyte packing and widen inter-corneocyte gaps. Hydration also influences partitioning of the drug into SC. Intact nanoparticles sized above 100 nm are not considered to permeate the SC because of their dimensions and rigidity.[36]

Although the particles do not penetrate across SC, uptake of the components is to be expected. Since epidermal lipids are rich in SC, lipid nanoparticles attaching to the skin surface would allow lipid exchange between SC and the nanocarriers. Lipid nanoparticles have the potential to deliver drugs via the follicles. Furthermore, each follicle is associated with sebaceous glands, which release sebum, creating an environment enriched in lipids. This environment is beneficial for trapping of lipid nanoparticles. Sebum is a mixture of triglycerides, squalene and waxes. Some glyceride lipids present in NLCs may accelerate the entrance into the follicles/sebaceous glands. The possible mechanisms involved in skin permeation enhancement by NLCs are depicted in **Figure no. 5.** Various Antipsoriatic drugs loaded in Nanoparticles.[37,38] **(Table no. 2)**

Rapali V et.al[39] have formulated Curcumin loaded nanostructured lipid carriers for enhanced skin retained topical delivery. Hot emulsification probe sonication method was employed for the preparation of the Curcumin loaded NLC. Further, in-vitro and ex-vivo characterization was performed for designed NLC. Curcumin-NLC showed extended in-vitro release up to 48 hours, whereas free Curcumin showed 100% drug release within 4 hours. Ex vivo skin permeation studies revealed 3.24 fold improved permeation and skin retention in the case of Curcumin loaded NLC gel compared to free Curcumin gel.

Zhao Z et.al[40] have formulated and evaluated Corylin loaded nanostructured lipid carriers gel for topical treatment of uv-induced skin aging. Corylin-NLCs were prepared using emulsification and solvent evaporation method. Prepared formulation were optimized on UV irradiated mouse as the oxidative stress model to detect the therapeutic effect of Corylin loaded NLC gel. Result of study showed that Corylin-NLCs can significantly suppress the LDH release, decrease MDA content, increase in CAT, SOD, GSH-Px activity, increased the expression of Bcl-2/Bax protein and reduced the expression of cleaved caspase-3/caspase-3 protein on UVB induced HaCaT cells.

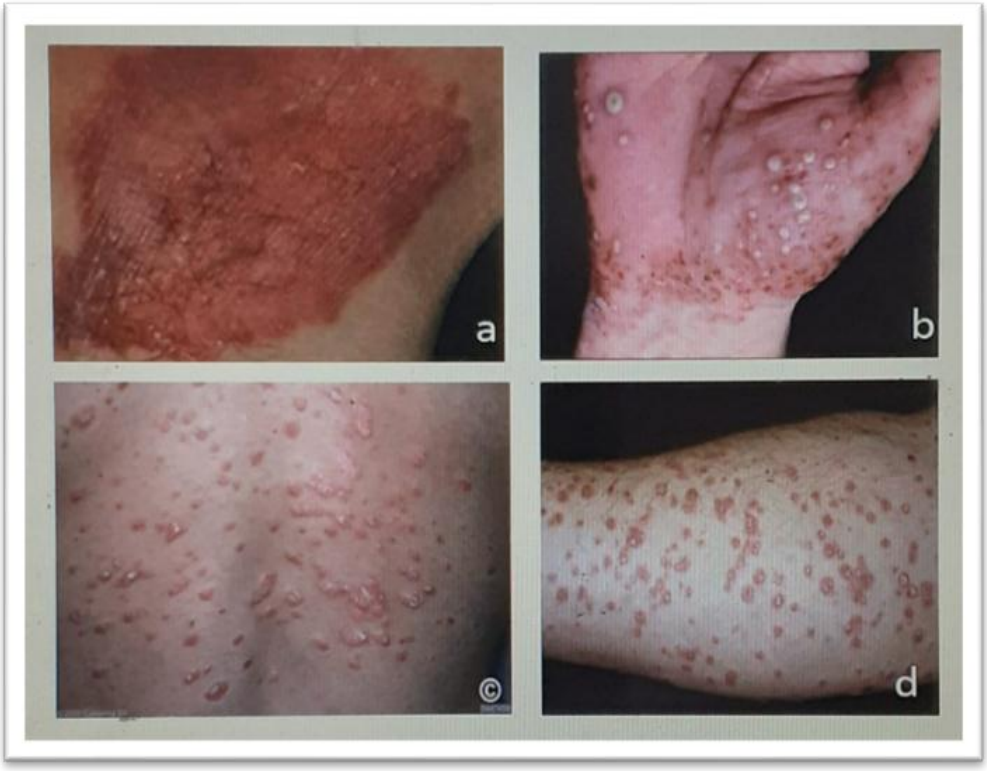

Figure no.1 a) Inverse psoriasis b) pustular psoriasis c) Guttate psoriasis d) plaque psoriasis.

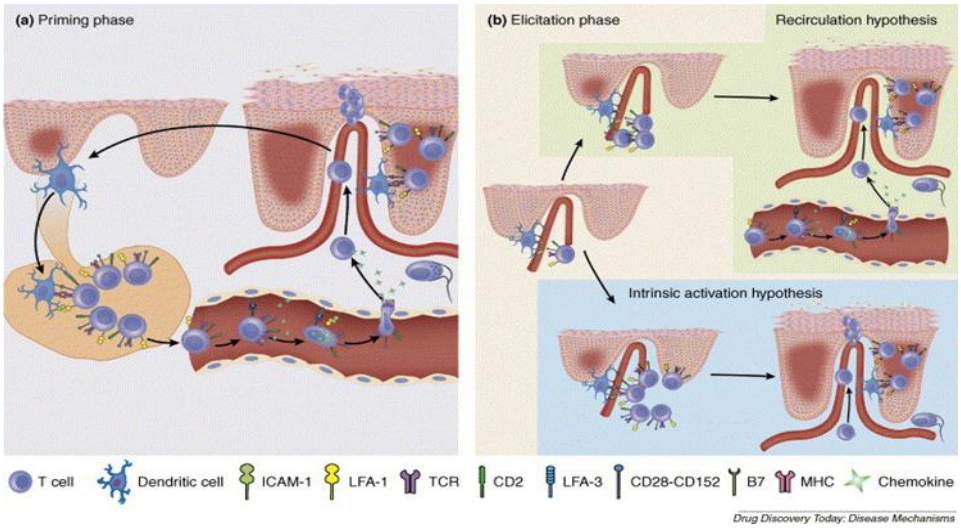

Figure no.2: Mechanism of psoriasis.

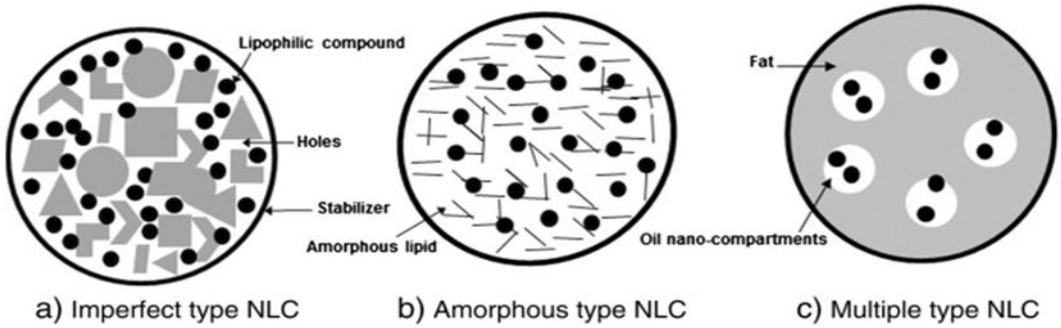

Figure no.3: Types of Nanostructured lipid carrier.

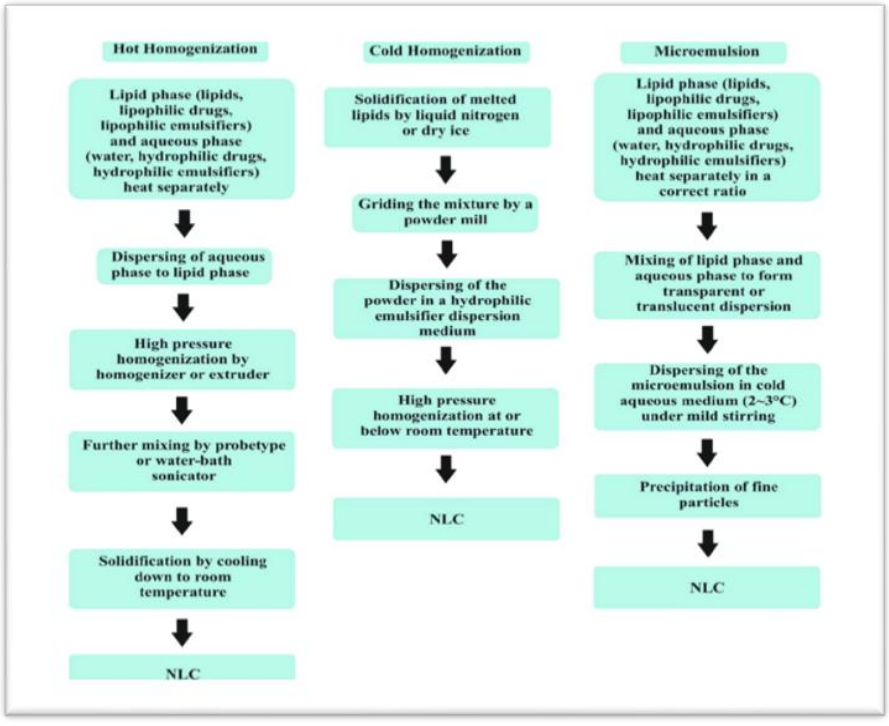

Figure no. 4. Preparation procedures of nanostructured lipid carriers (NLCs).

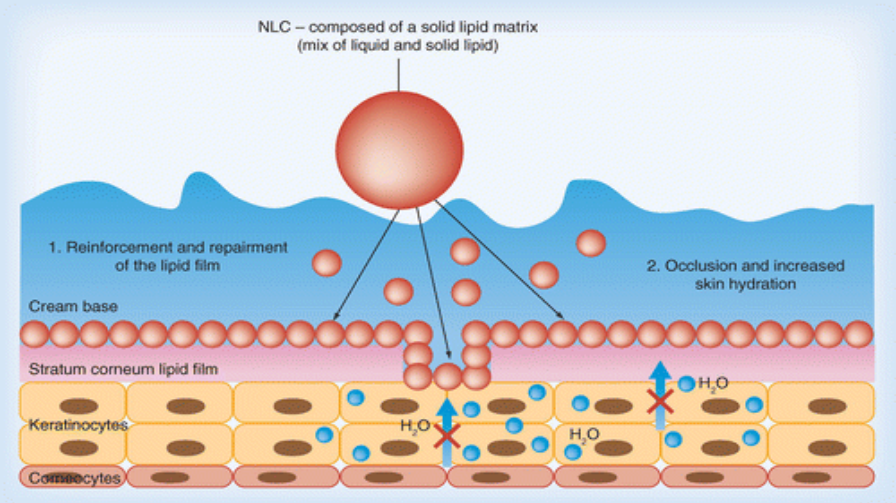

Figure no. 5: Mechanisms for skin permeation enhancement of drugs or active ingredients from nanostructured lipid carriers (NLCs).

Table no. 1: Gel Types and their distinguishing features and examples of commercial products.[50]

Gel type	Distinguishing features	Commercial product	Indication
Hydrogel	Water entrapped in a three-dimensional network by using a hydrophilic gelling agent	Atropro, Aurstat, Nimulid Transgel, Luofucon, Tegaderm, Skinintegrity, Maxgel	Atopic dermatitis Eczema Anti-inflammatory Skin care
Niosomal and Proniosomal gels	Liposomes consisting of a nonionic surfactant, which can be of a hydrogel or oleogel nature. A proniosomal gel is a hydrated form of niosomes.	Premiere Massage gel, Lancome niosome plus	Skin care Cosmetic antiaging
Emulgels	Consist of a hydrogel or oleogel with o/w or w/o emulsion and a surfactant	Voltaren, Voveran, Voltarol, Biogel, White glow, Topicane	Anti-inflammatory Skin care
Oleogels/ Organogels	Organic liquid entrapped in a threedimensional network by using an organogelator	Oleogel Plus, Gilugel, Phlojel Ultra, Eucerin, Circularom, Przondo, Lancamento	Skin Care Emollient Compounding base
Aerogels and Xerogels	Inorganic, composed of silica, and produced by supercritical drying. Inorganic, composed of silica, produced by drying under normal pressure	Aerosil (only patented prototypes)	No pharmaceutical commercial product for topical
Bigels	Mixture of an oleogel and hydrogel without the addition of a surfactant	Bi-Gel Testosterone	Anti-inflammatory (Clinical stage)

Table no. 2: Various Antipsoriatic drugs loaded in Nanoparticles.

Antipsoriatic Drug	Method of preparation	Ingredients used in Nanoemulsion
Acitretin	solvent diffusion technique	Oleic Acid and Tween 80
Cyclosporine	High-shear homogenizer	Nutmeg oil, virgin coconut oil, tween 80, xanthan gum
Tacrolimus	Hot melt high pressure homogenization method	Compritol ATO 888 , Capmul® MCM C8, Pluronic® F-68
Turmeric oil	Emulsification method	Tween 20, tween 80, lecithin, labrasol, isopropyl alcohol
MTX	Hot homogenization ultrasonication techniques	Witepsol1 S51, Oleic acid, Polysorbate 60, Polysorbate 80
Curcumin	Nanoemulsification and ultrasonication	Precirol ATO 5 , Tween 80, Capmul MCM
Psoralens(8-MOP)	Emulsification method	Precirol ATO 5, Myverol 18-04 K, Tween 80, soybean phosphatidylcholine, squalene, Pluronic F68 (PF68)

REFERENCES

1. M.A. Lowes, M. Suarez-Farinas, J.G. Krueger, Immunology of psoriasis, Annu. Rev. Immunol, 2014; 32: 227e255.
2. G.K. Perera, P. Di Meglio, F.O. Nestle, Psoriasis, Annu. Rev. pathology, 2012; 7: 385e422.
3. B.B. Davidovici, N. Sattar, J. Prinz, L. Puig, P. Emery, J.N. Barker, et al., Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions, J. Investigative Dermatology, 2010; 130: 1785e1796.
4. A. Di Cesare, P. Di Meglio, F.O. Nestle, The IL-23/Th17 axis in the immunopathogenesis of psoriasis, J. Investigative Dermatology, 2009; 129: 1339e1350.
5. Sarac G, Koca TT, Baglan T. A brief summary of clinical types of psoriasis. Northern Clinics of Istanbul, 2016; 3(1): 79-82.
6. Henseler T, Christophers E. Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. J Am Acad Dermatol, 1985; 13: 450–6.
7. Goodfield M, Hull SM, Holland D et al. Investigations of the ‘active’ edge of plaque psoriasis: vascular proliferation precedes changes in epidermal keratin. Br J Dermatol, 1994; 131: 808–13.
8. Martin BA, Chalmers RJ, Telfer NR. How great is the risk of further psoriasis following a single episode of acute guttate psoriasis? Arch Dermatol, Jun, 1996; 132(6): 717-8.
9. Hawilo A, Zaraa I, Benmously R, et al. Erythrodermic psoriasis: epidemiological clinical and therapeutic features about 60 cases. Tunis Med., 2011; 89: 841–7.

10. Rosenbach M, Hsu S, Korman NJ, et al. Treatment of erythrodermic psoriasis: from the medical board of the National Psoriasis Foundation. J Am Acad Dermatol, 2010; 62: 655–62.
11. Farley E, Masrour S, McKey J, Menter A. Palmoplantar psoriasis: a phenotypical and clinical review with introduction of a new quality-of-life assessment tool. J Am Acad Dermatol, Jun, 2009; 60(6): 1024-31. [PubMed]
12. Omland SH, Gniadecki R. Psoriasis inversa: a separate identity or a variant of psoriasis vulgaris? *Clin Dermatol*, 2015; **33**(4): 456–461. doi:10.1016/j.clindermatol.2015.04.007 [PubMed] [CrossRef] [Google Scholar]
13. Syed ZU, Khachemoune A. Inverse psoriasis: case presentation and review. *Am J Clin Dermatol*, 2011; **12**(2): 143–146. doi:10.2165/11532060-000000000-00000 [PubMed] [CrossRef] [Google Scholar]
14. Körber A, Mössner R, Renner R, Sticht H, Wilsmann-Theis D, Schulz P, Sticherling M, Traupe H, Hüffmeier U. Mutations in IL36RN in patients with generalized pustular psoriasis. J Invest Dermatol, Nov, 2013; 133(11): 2634-2637. doi: 10.1038/jid.2013.214. Epub 2013 May 6. [PubMed]
15. Sugiura K. The genetic background of generalized pustular psoriasis: IL36RN mutations and CARD14 gain-of-function variants. J Dermatol Sci., Jun, 2014; 74(3): 187-92. doi: 10.1016/j.jdermsci.2014.02.006. Epub 2014 Mar 5.
16. Weinstein GD, van Scott EJ. Autoradiographic analysis of turnover times of normal and psoriatic epidermis** from the Dermatology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, Public Health Service, U.S. Department of Health, Education and Welfa. J Invest Dermatol, 1965; 45: 257–262.
17. Weinstein GD, McCullough JL, Ross PA. Cell kinetic basis for pathophysiology of psoriasis. J Invest Dermatol, 1985; 85: 579–583.
18. Voorhees JJ. Pathophysiology of psoriasis. Annu Rev Med., 1977; 28: 467–473.
19. Gudjonsson, J.E. et al. Immunopathogenic mechanisms in psoriasis. Clin. Exp. Immunol, 2004; 135: 1–800.
20. Laws PM, Young HS. Current and emerging systemic treatment strategies for psoriasis. Drugs, Oct, 2012; 72(14): 1867-80.
21. Rehman K, Zulfakar MH. Recent advances in gel technologies for topical and transdermal drug delivery. Drug Dev Ind Pharm, Apr, 2014; 40(4): 433-40.
22. Abdallah DJ, Weiss RG. Organogels and low molecular mass organic gelators. Adv Mater, 2000; 12: 1237–47.

23. Vintiloiu A, Leroux JC. Organogels and their use in drug delivery – a review. J Control Release, 2008; 125: 179–92.
24. Peppas NA, Bures P, Leobandung W, Ichikawa H. Hydrogels in pharmaceutical formulation. Eur J Pharm Biopharm, 2000; 50: 27–46.
25. Poonia N, Kharb R, Lather V, Pandita D. Nanostructured lipid carriers: versatile oral delivery vehicle. *Future Sci OA.*, 2016; 2(3): FSO135. doi: 10.4155/fsoa-2016-0030.
26. Selvamuthukumar S, Velmurugan R. Nanostructured lipid carriers: a potential drug carrier for cancer chemotherapy. *Lipids Health Dis.*, 2012; 11: 159. doi: 10.1186/1476-511x-11-159. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
27. Saraceno R, Chiricozzi A, Gabellini M, Chimenti S. Emerging applications of nanomedicine in dermatology. Skin research and technology, Feb., 2013; 19(1): e13-9.
28. Vincent N, Ramya DD, Vedha HB. Progress in psoriasis therapy via novel drug delivery systems. Dermatology reports, Feb 17, 2014; 6(1).
29. López-García R, Ganem-Rondero A. Solid Lipid Nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC): Occlusive Effect and Penetration Enhancement Ability. *J Cosmet Dermatol Sci Appl*, 2015; 5(2): 62–72. doi: 10.4236/jcdsa.2015.52008.
30. Iglic A, Kulkarni C, Rappolt M. Advances in Biomembranes and Lipid Self-Assembly. 1st ed. UK: Academic Press, 2016.
31. Shah R, Eldridge D, Palombo E, Harding I. Lipid Nanoparticles: Production, Characterization and Stability. UK: Springer, 2015.
32. Shi L, Li Z, Yu L, Jia H, Zheng L. Effects of surfactants and lipids on the preparation of solid lipid nanoparticles using double emulsion method. *J Dispers Sci Technol*, 2011; 32(2): 254–9. doi: 10.1080/01932691003659130.
33. Gasco MR. Method for producing solid lipid microspheres having a narrow size distribution. U.S. Patent No. 5250236, 1993.
34. Jaiswal P, Gidwani B, Vyas A. Nanostructured lipid carriers and their current application in targeted drug delivery. *Artif Cells Nanomed Biotechnol*, 2016; 44(1): 27–40. doi: 10.3109/21691401.2014.909822. [PubMed] [CrossRef] [Google Scholar]
35. Naseri N, Valizadeh H, Zakeri-Milani P. Solid lipid nanoparticles and nanostructured lipid carriers: structure, preparation and application. *Adv Pharm Bull.*, 2015; 5(3): 305–13. doi: 10.15171/apb.2015.043.
36. Fang CL, Al-Suwayeh SA, Fang JY. Nanostructured lipid carrier (NLCs) for drug delivery and targeting. Recent Pat Nanotechnol, 2013; 7(1): 41-55.

37. Sun J, Zhao Y, Hu J. Curcumin inhibits imiquimod-induced psoriasis-like inflammation by inhibiting IL-1beta and IL-6 production in mice. PLoS One, 2013; 8: 67078.
38. Rahman M, Alam K, Ahmad MZ, et al. Classical to current approach for treatment of psoriasis: a review. Endocr Metab Immune Disord Drug Targets, 2012; 12: 287-302.
39. Rapali VK, Kaul V, Waghule T, Srividya G. Curcumin loaded nanostructured lipid carriers for enhanced skin retained topical delivery. European journal of pharmaceutical sciences, 152(10): 105438.
40. Zhao Z, Liu T, Zhu S, Yang Y, Wang Z. Development and evaluation studies of Corylin loaded nanostructured lipid carriers gel for topical treatment of uv-induced skin aging. Experimental Gerontology, 2021; 153: 111499.