IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 20, Issue 6 Ser. II (Nov. – Dec. 2025), PP 01-05
www.iosrjournals.org

Chrysin And Probiotics Loaded Nanostructured Lipid Carriers: A Possible Topical Treatment for Psoriasis

Abstract:
Psoriasis is an autoimmune, recurrent, common, long lasting, multifactorial skin disease. It is affected by genetic, environmental factors and dysbiosis of skin. As per world psoriasis day consortium, it affects 125 million peoples worldwide. The etiology of psoriasis is unknown, but the existing data represents that, the over stimulation of immune system produces the cytokines, which leads to hyper proliferation of keratinocytes. The currently available topical, oral treatments in the market are able to produce symptomatic relieve, severe side effects poor efficacy, frequent recurrence and no patient's compliance. However, the most accepted treatment strategy in clinical view is biologicals but, it is not economical. Thorough literature search related to psoriasis condition helped in the identification of further improvements in treatment and requirement of formulation development. Recent studies of Chrysin (CS) on imiquimod induced psoriasis model, has shown antipsoriatic effect. It reduced the anti microbial peptides, TNF-α, IL-17A and IL-22 induced CCL20. CS is an economical and natural compound indicating its easy availability, cost effectiveness and better safety. It has been reported that the clinical evidence of novel Bifidobacterium infantis 35624 probiotic has decreased the levels of the TNF-α, CRP and IL-6, when administered orally. By considering the potential effects of CS and Bifidobacterium infantis 35624 in psoriasis management, a combinational approach in the form of nanostructured lipid carriers (NLCs) has been proposed wherein both CS and probiotics are loaded in NLCs and converted in to gel. The gel upon topical application at skin would offer a very good efficacy against psoriasis.
Keywords*: Psoriasis, Chrysin, Bifidobacterium infantis 35624, Nanostructured lipid carriers and hypothesis*

Date of Submission: 14-11-2025 Date of Acceptance: 29-11-2025

I. Introduction:

Psoriasis is an autoimmune, chronic skin disease, which appears as demarcated red plaques with silver scales, mainly on skin, elbows, knees, umbilicus and nails (Dobrica et al., 2022). It is a multifactorial disease, triggered by genetics, environmental changes, stress, trauma, drugs (Lithium, and β-blockers), excessive alcohol intake, dietary conditions and skin dysbiosis (Chen et al., 2020; Dobrica et al., 2022; Martins et al., 2020). It is associated with various comorbidities that include diabetes, cardiovascular diseases, metabolic syndrome, lymphoma, Parkinson's disease, sleep apnea, psoriatic arthritis, inflammatory bowel disorder, anxiety and depression etc (Oliveira Mde et al., 2015). According to the world psoriasis day consortium (WPSD) in 2016, psoriasis affects 125 million peoples globally (WHO). Based on the 2020 census data, psoriasis affects 8 million US adults aged 20 years (NSF). However, the prevalence rate was varied from one region to other region. Paris et al., on behalf of the Global Psoriasis Atlas, in 2020, performed the systematic psoriasis analysis and modelling study up to October 2019 data, reported the prevalence rate of psoriasis. It was reported that prevalence rate of psoriasis was 0.14 % in East Asia, 1.99 % in Australasia, 1.07 % - 3.46 % in a Western Europe, 0.62 % -5.32 % in central Europe, 0.63 % -3.60 % in North America, 0.36 % -2.96 % in Southern Latin America and in India 0.54 % - 0.58 % (Parisi et al., 2020;Choon et al., 2022) In addition to that, psoriasis prevalence differs by race/ethnicity. High prevalence 3.6 % has been reported in non Hispanic white than non Hispanic black (1.5 %) (Parisi et al., 2020; Armstrong et al., 2021)

Although, the mortality rate of psoriasis is low, it has negative impact on quality of life of psoriasis patients and even they lose professional activities. It makes socioeconomic burden for treatment expenses(Chen et al., 2022). Despite having the high prevalence rate, and socioeconomic burden, the currently available oral, and topical treatment options are less effective. They show severe side effects such as itching, stinging, burning, dryness, redness, swelling, tenderness, skin thinning, tuberculosis and peeling of skin (Rendon and Schakel, 2019). The systemic therapy has shown success in management of psoriasis, but it is not economical, less efficacious and recurrence after discontinuation of treatment(Rendon and Schakel, 2019; Zhou et al., 2022)

II. Pathogenesis of psoriasis:

The exact cause of psoriasis is unclear, some of the reported factors that trigger psoriasis are injury in the skin, drugs, trauma, stress, leaky gut, skin dysbiosis, and skin infection caused by *Staphylococcus aureus, Corynebacterium, Propionibacterium, and Streptococcus aureus* which results in stimulation of innate immune system. These stimuli cause damages in the keratinocytes that lead to the synthesis of antimicrobial peptides (LL37, β-defensins, and S100). Among these peptides, LL37 forms a complex with deoxyribonucleic acid (DNA) as well as ribonucleic acid (RNA) of the damaged cells. The LL37-DNA complex bind to the Toll like receptors (TLR-9) on the plasmacytoid dendritic cells (DC).The activated plasmacytoid DC produces type-1 interferon (IFN)-α, Type-1 IFN activates myeloid dendritic cells (mDCs) to release IFN-γ. The activation of T-helper cell-1(Th-1), and Th-17 leads to production of interleukin (IL)-17, tumor necrosis factor-α (TNF-α), IL-1, and IL-6. When LL37complexes with RNA, it activates myeloid DCs and secretes more amount of TNF-α, IL-23, and IL-12. The over expression of above mentioned cytokines cause inflammation and hyper proliferation of the keratinocytes. These initial psoriatic inflammatory process further stimulate the adaptive immune response through distinct T cells.Th-17 cells releases IL-17, IL-21 and IL-22 which stimulate keratinocyte proliferation in the epidermis. The most clinically significant signalling is stimulated by IL-17A and IL-17F, each of which acts via the same receptor but have diverse binding affinities. The recruitment of the ACT1 adaptor protein occurs when IL-17A binds to its trimeric receptor complex, which consists of two IL-17RA subunits and one IL-17RC subunit. All extracellular signal-regulated kinase (ERK), p38 MAPK, TGF-beta-activated kinase 1 (TAK1), I-kappa B kinase (IKK), and glycogen synthase kinase 3 beta (GSK-3 beta) are activated when ACT1 interacts with the IL-17A receptor complex. All kinase facilitate the generation of chemokines, AMP and cytokines via nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), AP-1 and C/EBP transcription process. On the other hand, γδT cells together with Th1 and Th17 releases IL-17 without involvement of stimulation of IL-23. Th1and Th2 helps in the stimulation of cytokines through the Janus kinase (JAK)-STAT signaling pathways. The released cytokines overactivates the epidermis which leads to hyper proliferation of the keratinocytes. (Rendon and Schakel, 2019; Zhou et al., 2022; Wilsmann-Theis et al., 2018). The sequences involved in the immune pathogenesis of psoriasis is illustrated in the Figure .1

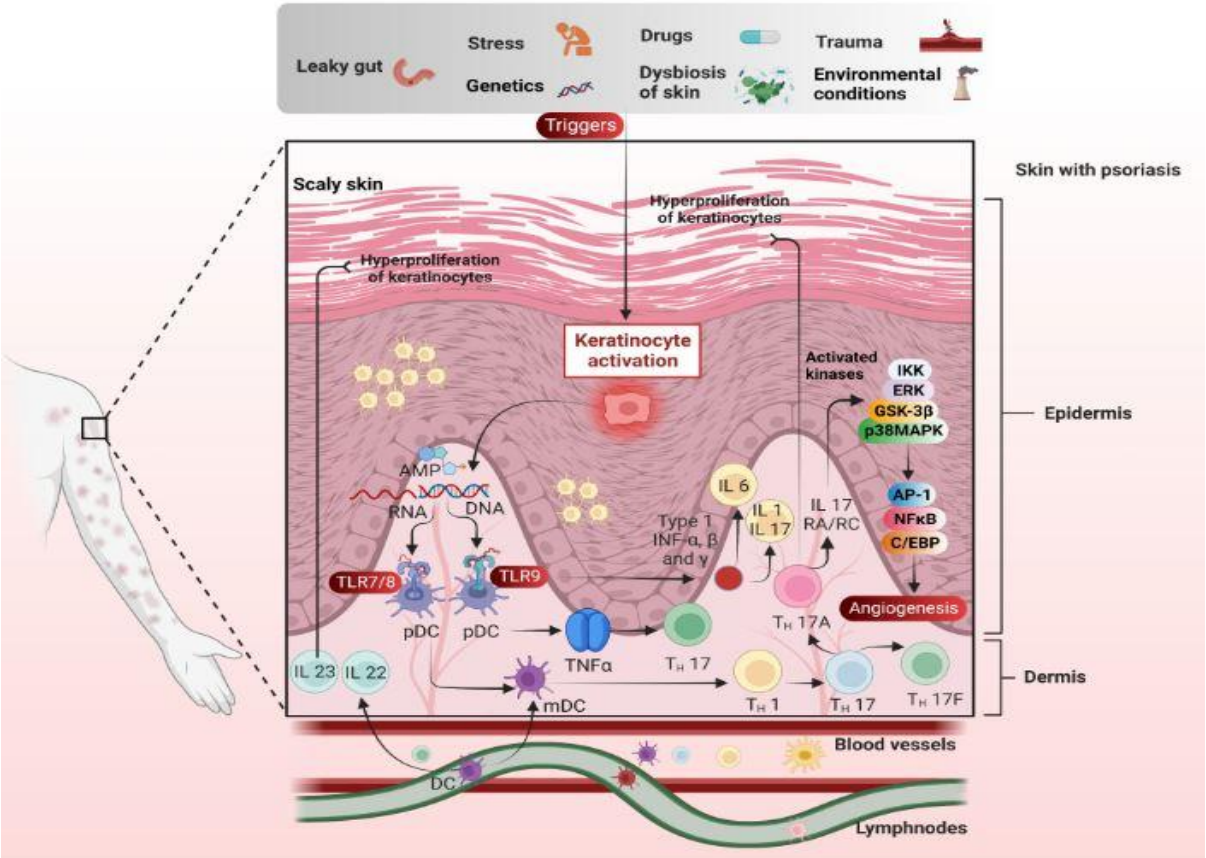

Figure 1. The sequences involved in the immune pathogenesis of psoriasis

III. Role of Chrysin:

Plant derived, bioactive polyphenols such as *Amentoflavone, Apigenin, Astilbin, Baicalin, Rottelerin, Genestin, Quercetin, Luteolin etc* have been found to be safe and effective to treat psoriasis. They act through inhibition of multiple pathways associated with psoriasis. Among them, (CS) has been reported to be very effective in treating psoriasis through topical administration (Bonesi et al., 2018).

CS is a dietary phytochemical, abudently found in nature. CS is obtained from passion fruit, bitter melon (*Momordica charantia),* wild Himalayan pear *(Pyrus pashia), Radix scutellariae*, mushroom (*Pleurotusostreatus),* honey and propolis. Recent research studies have confirmed that the CS is present in Diaphragm *juglandis fructus,* walnut pellicle, flowers of *Juglans regia*, leaves and fruits of doum palms (*Hyphaene thebaica*), Banxiaxiexin, *Chaetomium globosum* fungus, green marine algae and *Cytisusvillosus* Pourr. Chemically it comes under class of flavonoid. CS has anticancer, antidiabetic, antioxidant, antiinflammtory, antiallergic, neuroprotectve, antidepressing, hepatoprotective, antiallergic, nephroprotective, colon protective, cardioprotective pharmacological propertise (Mani and Natesan, 2018; Naz et al., 2019). Dispite of having these many pharmacological actions, CS poorly soluble in water and undergoes first pass effect, when administered orally. To avoid that effect of CS, it can be adminstered topically in the management of psoriasis (Gao et al., 2021)

Lie et al., in 2020 reported that CS underlying mechanism involves the amelioration of inflammation in psoriasis by reduction of TNF –α, IL-17A, IL-22 induced CCL20 and antimicrobial peptides released from epidermal keratinocytes. The reduction of inflammatory mediators, via regulation of MAPK, JAK-STAT and IKK/NFkB signalling pathways. Furthermore, CS is also reported for reduction in the production of ROS (Li et al., 2020).

IV. Role of probiotics:

In recent literaure it has also been found that there exists close relation between probiotics and psoriasis. Certain therapeutic microbial agent, such as *Lactobacillus pentosus GMNL-77, Lactobcillus sakei Probio65, Escherichia coli Nissle 1917* have shown effect in management of psoriasis, upon oral and topical administration preclinically. Among them a novel *Bifidobacterium infantis 35624*, has been reported to exert immunoregulatory effect and reduced the TNF-α, IL-6 and plasma CRP levels upon oral administration in clinical studies. The results indicated that the modulation of cytokines beyond the gut is the promising way in the regulation of psoriasis (Groeger et al., 2014; Zeng et al., 2021). In addition to that it also reporetd as it induced the IL-10, which helps in the reduction of psoriasis.

V. Challenges of topical drug delivery in psoriatic skin:

There are many factors influencing the delivery of drug to the psoriatic skin, which include dry skin, sensitivity, imbalanced lipids, thickened inflammed skin with excessive differentation of corneocytes. In addition to above mentioned factors, poor penetration of drugs via stratum corneum, increased levels of cholesterol, decreased levels of ceramides and reduction of natural moisturizing agent also influences the topical delivery of drugs. Moreover topical absorption of drugs depends upon the anotomical site of skin. This could be due to the areas with face and intertriginous region more suspetable to absorption. In case of scalp psoriasis, presence of hair makes treatment challenging and in nail psoriasis it is difficulty to achieve significant amount of drug in nails bed. Due to the influenc of aforementioned factors it becomes challenging to target the drug at paticular site of skin. This causes poor therapeutic efficacy of drug substances or developed formulations. In order to avoid such effects, a novel drug delivery system is the most suitable and effective approach for topical administration of drugs for the treatment of psoriasis (Hoffman et al., 2016; Katare et al., 2010).

VI. Role of nanostructured lipid carriers (NLCs) in psoriasis:

A thorough analysis of factors influencing the psoriatic skin, it is required to select the suitable drug delivery system to manage the psoriatic condition. NLCs offer a unique solution to overcome the problems associated with psoriasis by increasing the permeability and penetration of drugs through the skin. In addition they hydrate the skin by forming occlusive layer, and reducing the transepithelial water loss. NLCs are considered as the smarter, latest generation lipid nanoparticles, due to the presence of high drug loading capacity and entrapment efficiency. NLCs overcome the drawbacks of conventional therapy related to psoriasis treatment, such as, poor drug's penetration through skin, hyper pigmentation, burning sensation on normal and diseased skin in case of topical treatment. NLCs minimize the doses, systemic toxicity, and necrotizing effects of drugs available for psoriasis. NLCs offer effective drug targeting, skin retention property and sustained drug release feature that might be suitable in successful management of psoriasis. NLCs could be potential, safe and biocompatible drug delivery system for the treatment of psoriasis as for as topical administration is concerned. Furthermore, these NLCs can be converted into solid products upon lyophilisation or spray drying and further

converted into tablets, pellets, capsules, and powder for reconstitution (Mohd Nordin et al., 2021; Petit et al., 2021; Singh et al., 2021).

VII. The proposed hypothesis:

Looking at the multiple etiology of psoriasis a novel combination therapy has been proposed by utilizing the inhibitory mechanism of CS and probiotic in the form of NLCs. As mentioned above CS inhibits TNF-α, IL-17A and IL-22, similarly probiotics reduced the TNF-α, IL-6 and induce the IL-10. Loading them in to the NLCs and applying them topically in the form of gel would allow better penetration of CS in to the psoriatic skin and elicit its action. Furthermore, conversion of CS NLCs in to gel would offer longer retention of CS and probiotic in localized surface of psoriatic skin. The addition of probiotic would offer additive effect. The overall process involved in formulation of NLCs, topical application, absorption of NLCs in psoriatic skin and mechanism of action of CS and probiotic are demonstrated in Figure 2, Hence overall the treatment strategy could open a new avenue in the field of topical therapy for psoriasis.

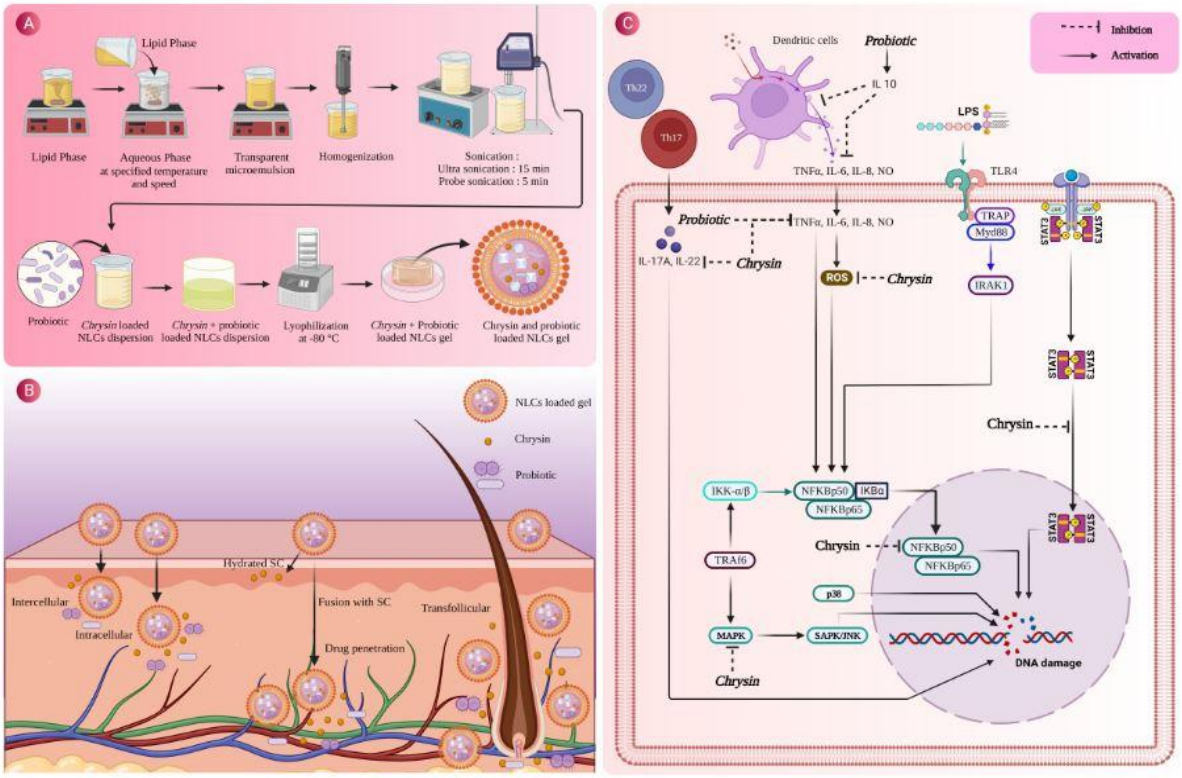

Figure 2 The overall process involved in formulation of NLCs, topical application, absorption of NLCs in psoriatic skin and mechanism of action of CS and probiotic

VIII. Conclusion

In the present manuscript a combinational therapy of nanostructured lipid carreirs loaded with CS and probiotic gel has been proposed. By considering the challenges associated with psoriatic skin, dysbiosis of skin, multifactorial pathological pathways of psoriasis. Using multifaced role of CS and probiotic attenuates the psoriasis by reduction of skin lesions and imunemodulatory effect. This combination might be helpful in overcome the drawbacks of excisting topical treatments in management of psoriasis. It is pertinent to add here that NLCs loaded with CS and probiotic combination has never been reported earlier for psoriasis treatment in topical route. The above mentioned hypothesis is a totally new concept in the treatment of psoriais.

Funding statement
This work was not funded

Declartion of competng interest:
Authors declares that they have no competing finacial interests or personal reltionships that could have apperaed to influence the work reported in this paper.

Abbreviations: **CS**: Chrysin, **NLCs:** Nanostructured lipid carriers, **AMP**: antimicrobial peptides, **ROS**: Reactive oxygen species, **DC:** Dendritic cells, **TLR7/8/9**: Toll like receptors 7, 8 and 9. **pDC:** plasmacytoid

dendritic cells, **mDC**: myeloid dendritic cells, **INF α, β and γ**: Interferon α, β and γ, **TNF-α:** Tumor necrosis factor alfa, **IL:** Interleukins-12/23/22/17A/17F/21/1, **Th1 and Th17**: T helper 1 and 17 cells, **NFkB**: Nuclear factor kappa light chain enhancer of activated B cells, **ERK:** Extracellular signal regulated kinase, **TAK1:**TGF beta activated kinase 1, **IKK:** I kappa B kinase **GSK-3β;** Glycogen synthase kinase 3 beta, **JAK/STAT**-Janus kinase signal transducer and activator of transcription proteins signalling pathaways **p38MAPK**: Mitogen activated protein kinase **C/EBP**: Protein family forms the transcription factor and **T:** T cell

References:

[1]. Armstrong, A.W., Mehta, M.D., Schupp, C.W., Gondo, G.C., Bell, S.J., Griffiths, C.E.M., 2021. Psoriasis Prevalence in Adults in the United States. JAMA Dermatol 157, 940-946.

[2]. Bonesi, M., Loizzo, M.R., Menichini, F., Tundis, R., 2018. Flavonoids in Treating Psoriasis. 281-294.

[3]. Chen, L., Li, J., Zhu, W., Kuang, Y., Liu, T., Zhang, W., Chen, X., Peng, C., 2020. Skin and Gut Microbiome in Psoriasis: Gaining Insight Into the Pathophysiology of It and Finding Novel Therapeutic Strategies. Front Microbiol 11, 589726.

[4]. Chen, Y., Lian, P., Peng, Z., Wazir, J., Ma, C., Wei, L., Li, L., Liu, J., Zhao, C., Pu, W., Wang, H., Su, Z., 2022. Alpha-7 nicotinic acetylcholine receptor agonist alleviates psoriasis-like inflammation through inhibition of the STAT3 and NF-kappaB signaling pathway. Cell Death Discov 8, 141.

[5]. Choon, S.E., Wright, A.K., Griffiths, C.E.M., Tey, K.E., Wong, K.W., Lee, Y.W., Suvelayutnan, U., Mariapun, J., Ashcroft, D.M., Global Psoriasis, A., 2022. Incidence and prevalence of psoriasis in multi-ethnic Johor Bahru, Malaysia: a population-based cohort study using electronic health data routinely captured in Teleprimary Care (TPC(R)) clinical information system from 2010 to 2020. Br J Dermatol.

[6]. Dobrica, E.C., Cozma, M.A., Gaman, M.A., Voiculescu, V.M., Gaman, A.M., 2022. The Involvement of Oxidative Stress in Psoriasis: A Systematic Review. Antioxidants (Basel) 11.

[7]. Gao, S., Siddiqui, N., Etim, I., Du, T., Zhang, Y., Liang, D., 2021. Developing nutritional component chrysin as a therapeutic agent: Bioavailability and pharmacokinetics consideration, and ADME mechanisms. Biomed Pharmacother 142, 112080.

[8]. Groeger, D., O'Mahony, L., Murphy, E.F., Bourke, J.F., Dinan, T.G., Kiely, B., Shanahan, F., Quigley, E.M.M., 2014. Bifidobacterium infantis35624 modulates host inflammatory processes beyond the gut. Gut Microbes 4, 325-339.

[9]. Global reports on psoriasis, **2016** World Health Organization (www.who. int)

[10]. Hoffman, M.B., Hill, D., Feldman, S.R., 2016. Current challenges and emerging drug delivery strategies for the treatment of psoriasis. Expert Opin Drug Deliv 13, 1461-1473.

[11]. Katare, O.P., Raza, K., Singh, B., Dogra, S., 2010. Novel drug delivery systems in topical treatment of psoriasis: rigors and vigors. Indian J Dermatol Venereol Leprol 76, 612-621.

[12]. Li, H.-J., Wu, N.-L., Pu, C.-M., Hsiao, C.-Y., Chang, D.-C., Hung, C.-F., 2020. Chrysin alleviates imiquimod-induced psoriasis-like skin inflammation and reduces the release of CCL20 and antimicrobial peptides. Scientific Reports 10.

[13]. Mani, R., Natesan, V., 2018. Chrysin: Sources, beneficial pharmacological activities, and molecular mechanism of action. Phytochemistry 145, 187-196.

[14]. Martins, A.M., Ascenso, A., Ribeiro, H.M., Marto, J., 2020. The Brain-Skin Connection and the Pathogenesis of Psoriasis: A Review with a Focus on the Serotonergic System. Cells 9.

[15]. Mohd Nordin, U.U., Ahmad, N., Salim, N., Mohd Yusof, N.S., 2021. Lipid-based nanoparticles for psoriasis treatment: a review on conventional treatments, recent works, and future prospects. RSC Advances 11, 29080-29101.

[16]. Naz, S., Imran, M., Rauf, A., Orhan, I.E., Shariati, M.A., Iahtisham Ul, H., IqraYasmin, Shahbaz, M., Qaisrani, T.B., Shah, Z.A., Plygun, S., Heydari, M., 2019. Chrysin: Pharmacological and therapeutic properties. Life Sciences 235, 116797.

[17]. National Psoriasis foundation (Http://www.psoriasis.org/psoriasis-statistics)

[18]. Oliveira Mde, F., Rocha Bde, O., Duarte, G.V., 2015. Psoriasis: classical and emerging comorbidities. An Bras Dermatol 90, 9-20.

[19]. Parisi, R., Iskandar, I.Y.K., Kontopantelis, E., Augustin, M., Griffiths, C.E.M., Ashcroft, D.M., Global Psoriasis, A., 2020. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ 369, m1590.

[20]. Petit, R.G., Cano, A., Ortiz, A., Espina, M., Prat, J., Munoz, M., Severino, P., Souto, E.B., Garcia, M.L., Pujol, M., Sanchez-Lopez, E., 2021. Psoriasis: From Pathogenesis to Pharmacological and Nano-Technological-Based Therapeutics. Int J Mol Sci 22.

[21]. Rendon, A., Schakel, K., 2019. Psoriasis Pathogenesis and Treatment. Int J Mol Sci 20.

[22]. Singh, S., Sharma, N., Behl, T., Sarkar, B.C., Saha, H.R., Garg, K., Singh, S.K., Arora, S., Amran, M.S., Abdellatif, A.A.H., Bilgrami, A.L., Ashraf, G.M., Rahman, M.S., 2021. Promising Strategies of Colloidal Drug Delivery-Based Approaches in Psoriasis Management. Pharmaceutics 13.

[23]. Wilsmann-Theis, D., Schnell, L.M., Ralser-Isselstein, V., Bieber, T., Schön, M.P., Hüffmeier, U., Mössner, R., 2018. Successful treatment with interleukin-17A antagonists of generalized pustular psoriasis in patients without IL36RN mutations. The Journal of dermatology 45, 850-854.

[24]. Zeng, L., Yu, G., Wu, Y., Hao, W., Chen, H., 2021. The Effectiveness and Safety of Probiotic Supplements for Psoriasis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials and Preclinical Trials. J Immunol Res 2021, 7552546.

[25]. Zhou, X., Chen, Y., Cui, L., Shi, Y., Guo, C., 2022. Advances in the pathogenesis of psoriasis: from keratinocyte perspective. Cell Death & Disease 13.