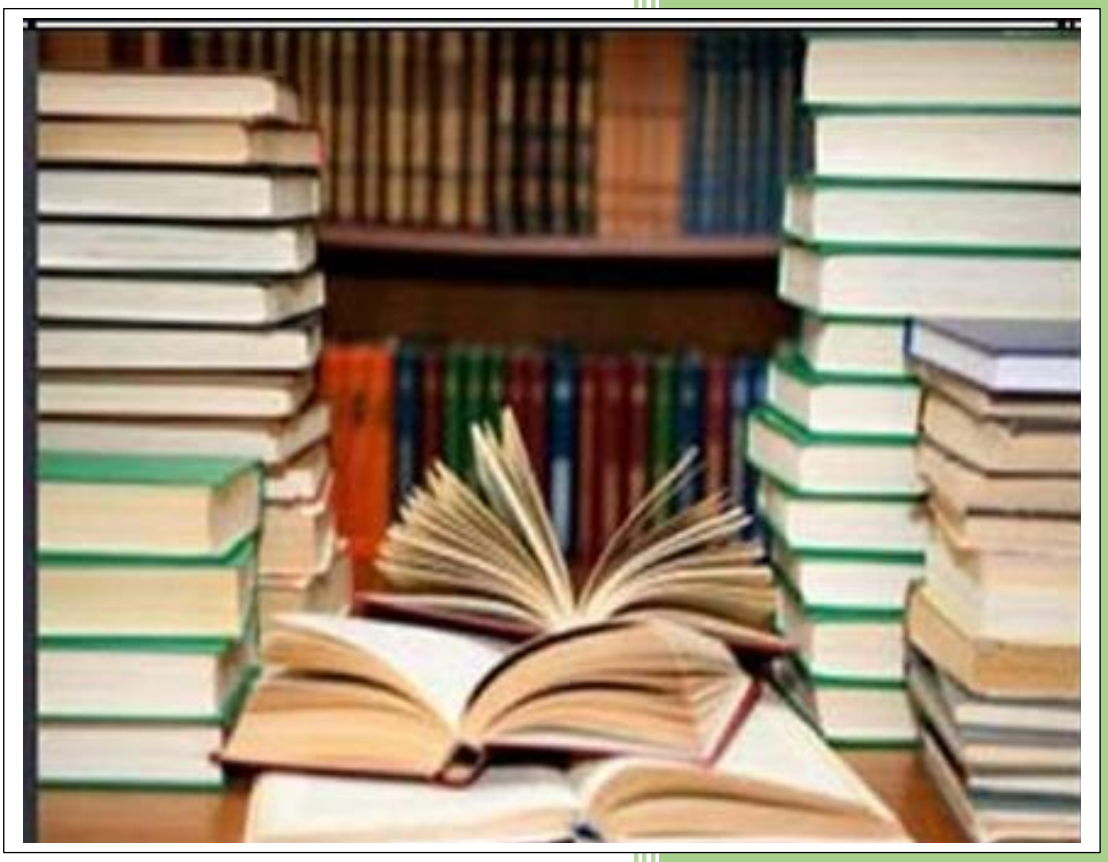
CHAPTER 2: LITERATURE REVIEW



Study of Vineet were aimed to develop tamoxifen citrate loaded Squalene integrated NLC based carbopol 940 and HEC gel to increase skin deposition in skin by maintaining lipid and moisture content of skin, it will improve the efficacy of drug against psoriasis. Methods that they have used for the preparation of NLC was emulsification cum-solidification by using high speed homogenizer, after characterization it is converted into gel having pH similar to skin. The result of the study reviled restricted permeation through the skin, slow drug release, and higher retention of the drug in epidermal and dermal layer. It also enhanced more than 45% moisture content and more than 35% lipid content of the skin. So, this study proved that the due to semisolid consistency it ensures longer stay on skin. It also helps in improving skin moisture and lipid content **(Sharma *et al.*, 2020).**

Results of Aljuffali.A report revealed that the development of "squarticles," nanoparticles formed from sebum-derived lipids such as squalene and fatty esters, for use in achieving targeted drug delivery to the follicles. Two different Nano systems, nanostructured lipid carriers (NLC) and Nano emulsions (NE) were prepared. As per the results of Aljuffali.A, the DPCP deposition within skin from squarticles was higher ($p < 0.05$) than that from the reference control. A varying lipid matrix changed the results of the skin deposition, with the NE type showing a greater enhancement ratio ($ER = 3.5$) as compared to the NLC type ($ER = 2.5$). Determination of the penetrated drug in the receptor can indicate its presence in systemic circulation if used in vivo. DPCP flux across the skin was in the order of NE > NLC > free control, the same as observed for recovery from the skin reservoir **(Aljuffali *et al.*, 2014).**

As per study of Suresh P.K revealed that in recent years, several novel carriers like liposomes, nanostructured lipid carriers (NLC), etc. have been used in psoriasis, with promising results. Small and relatively narrow size distribution with novel carriers permits site specific delivery to the skin, with improved drug solubilization of hydrophobic drugs and bioavailability **(Suresh *et al.*, 2013).**

As Zhanga Z. revealed that the penetration of ultra-small nanoparticles (size smaller than 40nm) into skin strata, the targeted delivery of the encapsulated drugs to hair Follicle stem cells, and the combination of nanoparticles and microneedle array technologies for special applications such as vaccine delivery are discussed **(Zhang *et al.*, 2013).**

Results of Nakaguma H. report revealed that Rat UV-B dermatitis was characterized by a sharply demarcated brownish-red lesion with scale formation lasting for 10 days. Histologically, microvascular dilatation, intraepidermal accumulation of polymorphonuclear leucocytes with microabscess, mononuclear cell infiltration at the papillary dermis and hyperproliferation of epidermal cells were observed. These features were similar to those of clinical psoriasis vulgaris in man **(Nakaguma *et al.*, 1995).**

Psoriasis vulgaris is the best-understood and most accessible human disease that is mediated by T cells and dendritic cells. Inflammatory myeloid dendritic cells release IL-23 and IL-12 to activate IL-17-producing T cells, Th1 cells, and Th22 cells to produce abundant psoriatic cytokines IL-17, IFN-γ, TNF, and IL-22. As per Lowes M.A. review these cytokines mediate effects on keratinocytes to amplify psoriatic inflammation. Therapeutic studies with anticytokine antibodies have shown the importance of the key cytokines IL-23, TNF, and IL-17 in this process. We discuss the genetic background of psoriasis and its relationship to immune function, specifically genetic mutations, key PSORS loci, single nucleotide polymorphisms, and the skin transcriptome. The association between comorbidities and psoriasis is reviewed by correlating the skin transcriptome and serum proteins. Psoriasis-related cytokine-response pathways are considered in the context of the transcriptome of different mouse models **(Lowes *et al.*, 2007)**.

Studies reviled that Rapalli has formulated curcumin loaded topical N L C s

(nanostructured lipid nanocarriers) and analytical validation parameters were also developed and described as per International Conference of Harmonization (ICH) guidelines by using the UV-Visible spectroscopy **(Rapalli *et al.*, 2020).**

Walunj have prepared Cyclosporine loaded cationic liposomal nanocarriers for the treatment of psoriasis this study showed reduction in the level of tumor necrosis factor-α,IL-17, and IL-22 in in-vivo imiquimod-induced psoriatic plaque models and it found to be effective in the treatment of psoriasis **(Walunj *et al.*, 2020).**

Sathe *results* indicate in terms of PASI score reduction has seen in the psoriatic symptoms and reduction in immunohistochemistry like tumor necrosis factor-α, IL-17, and IL-22 as a comparison to the negative control has also seen for this Sathe has formulated dithranol loaded topical NLC gel and applied on the IMQ-induced psoriatic plaque model **(Sathe *et al.*, 2019).**

Essaghraoui have prepared and optimized Cyclosporine loaded topical nanostructured lipid carriers and solid lipid nanoparticles and the comparative studies showed that SLNs are safe and retain Cyclosporine A in pork skin as compared to NLCs **(Essaghraoui *et al.*, 2019).**

Sousa have developed a novel nanoformulation i.e. polymeric micelles loaded with Salinomycin, and investigated its impact in the growth and proliferation of bacterial cells as well as the tumor A549 cells, and alveolar type II adenocarcinoma cell line. The developed formulation promotes a high drug intracellular accumulation, thus increasing drug sensitivity it seems to be able to deliver SAL into human cancer cells promoting a **(Sousa *et al.*, 2019).**

The goal of Bhoir study was to look into the in vitro and in vivo efficacy of a petroleum ether extract of Annona squamosa seeds that inhibited keratinocyte cell proliferation and found that its growth inhibitory property was significantly higher

than that seen in the presence of clobetasol propionate, a corticosteroid. The use of Annona squamosa seeds reduced erythema, edoema, and increased levels of cytokines IL6, IL17, TNF-, INF-, GMCSF, and infiltration of CD4 T cells observed in psoriasis lesions, which was comparable to treatment with 0.05 percent clobetasol propionate cream in Oxazolone-induced psoriasis to the ears of Balb/C mice **(Bhoir *et al.*, 2019).**

On experimental autoimmune uveoretinitis, Kasper produced topically applied everolimus (EV)-loaded methoxy-poly (ethylene-glycol)-hexyl substituted poly (lactic acid) (mPEGhexPLA) nanocarriers. Immunochemistry findings in both eyes, topical use of an everolimus formulation improved EAU. Because multiple systemic cellular immune responses were altered, the impact could be linked to systemic immunosuppressive effects **(Kasper *et al.*, 2018).**

Despotopoulou has suggested that the benefits of transdermal administration, such as patient compliance, drug escape from first-pass elimination, a good pharmacokinetic profile, and extended-release features, have attracted a lot of interest. However, the stratum corneum, the skin's most critical barrier that protects the body from the insertion of chemicals from the environment, is only partially penetrated by these systems. Transdermal drug delivery methods attempt to disturb the stratum corneum, allowing active medicinal substances to reach the bloodstream effectively. As a result, nanoparticles hold considerable promise since, due to their small size and other physicochemical qualities that will be thoroughly examined in this research, they can operate as excellent penetration enhancers. A comparison of the different types of nanoparticles will be undertaken in addition to the examination of physicochemical properties. To arrive at some meaningful conclusions about how the mentioned parameters affect skin permeability, the complexity of skin architecture and the uncertain mechanisms of penetration must be taken into account. This is one of the few publications in the literature, to the best of the authors' knowledge, that describes

the technology of transdermal delivery systems and how this technology influences biological activity **(Despotopoulou *et al.*, 2021).**

Lampis have created lamellar liquid crystals containing lysozyme and caffeine Due to the release of lysozyme from lipid formulations, it retains its biological activity **(Lampis *et al.*, 2018).**

Hashim has created topical delivery methods for Acitretin by combining it with cyclodextrin and encapsulating it in nanostructured lipid to investigate its critical role as a topical delivery system for successful psoriasis treatment. The benefits of the created Act nano niosomal gel as a promising topical administration technology with improved penetration, drug deposition into deeper skin layers, and reduced systemic absorption were highlighted in this study **(Hashim *et al.*, 2018).**

Khurana's review concentrated on nanotechnology-based drug delivery systems, which have enormous potential to improve the bioavailability and effectiveness of pharmaceuticals in their dosage forms, particularly lipophilic medications. The lipid imbalance and normal moisturising factors can be overcome with a lipid-based carrier system. He also said that nanoemulsions, as a novel carrier, have the potential to solve a variety of issues associated with topical antipsoriatic therapy. This delivery technique could be a viable option for treating psoriasis on the skin. The effectiveness of topical treatment for psoriasis depends not only on how nanoemulsions are made, but also on the active chemicals utilised and the oil chosen. A proper combination of both active and appropriate oils would result in a more effective treatment and effect **(Khurana *et al.*, 2018).**

Na Takuathung showed the therapeutic potential of Wannachawee Recipe on antiproliferant activity was investigated by using imiquimod-induced psoriasis of BALB/c mice by topical application of imiquimod for 15 consecutive days, followed by oral gavage of Wannachawee Recipe for 10 days because of which dermatitis is

seen on the shaved dorsal skin and right ear pinna. Reduced levels of Th17 cytokines (IL-17A, IL-22, and IL-23) were seen in both serum and dorsal skin after blood samples were taken for phenotypic observations, histological exams, and skin ELISA **(Na Takuathung *et al.*, 2018).**

Nimisha formulated a Berberis aristata extract nanovesicular gel and tested it for anti-inflammatory and antipsoriatic activities. In comparison to traditional gel formulation, topical use of extract loaded transferosomal gel resulted in a significant reduction in epidermal thickness and rete ridge length. B. aristata extract loaded transferosomal gel could be used as an anti-inflammatory and anti-psoriatic formulation, according to the findings **(Nimisha *et al.*, 2017).**

Prabhu have developed a nanoemulsion containing cyclobenzaprine. The optimised nanoemulsion formulation for maximal drug release was created as a unique cyclobenzaprine nanoemulgel with appropriate viscosity for topical application. The in-vitro results demonstrated that the developed nanoemulsion-based gel containing cyclobenzaprine hydrochloride has a high potential to deliver a better therapeutic impact locally when applied topically **(Lakshmana Prabu *et al.*, 2017).**

Nanoemulgels, according to Aithal's research, are suitable candidates for drug administration due to their dual character, i.e. the combination of a nanoscale emulsion and a gel base, both mixed in a single formulation. The active moiety is protected by the nanoemulsion component of the nanoemulgel, which prevents enzymatic degradation and certain processes like hydrolysis. The gel base gives the emulsion thermodynamic stability by raising the aqueous phase's viscosity and decreasing interfacial and surface tension. Nanoemulgels have rheological properties that make them ideal for topical and other forms of delivery, such as dental delivery, because they improve patient acceptability. Because the globule size is present in the nano form, using particular penetration enhancers can improve the formulation's

efficiency by increasing permeability and diffusibility. With an overview of a few illustrations supporting the case, this detailed review illustrates the merits of nanoemulgel as a viable carrier for medication delivery **(Aithal *et al.*, 2020).**

Several illnesses have invaded the outer layer of skin and the underlying soft tissue layer. Various topical formulations, such as nanoemulgel, niosomal gel, liposomal gel, and others, can be used to treat infection on local tissue. Nanoemulgel has a high level of activity locally in order to provide a considerable effect of drug delivery. Nanoemulsion is an emulsion with homogenous and extremely small droplet sizes in the region of 20-200 nm. Oil-in-water or water-in-oil emulsions are both possible. The penetration of pharmacological compounds through the skin can be improved with this approach. Nanoemulgel is made by combining nanoemulsion with a gel base to increase the penetration of pharmacological compounds through the skin. Nanoemulgel is a possible carrier for a large amount of allowed medications to provide a topical impact. Effective adhesion properties and extensive solubilization of the drug in oil or water phase result in a greater concentration gradient towards the skin, which promotes drug material penetration through the skin even more. This research sheds light on how nanoemulgel can be used to produce a more effective and efficient medication delivery mechanism for the topical system **(Padhy *et al.*, 2021).**

Bhardwaj in his review mentioned that psoriasis is an auto-immune, chronic inflammatory disease that affects about 2% of the world's population. The current psoriasis treatment has drawbacks, such as systemic adverse effects and limited percutaneous permeability, necessitating the development of a new lipoidal nanocarrier technology. Nano-emulgels are made by mixing a nanoemulsion system with a hydrogel matrix utilising high and low energy processes. Lipoidal nanocarriers in topical treatment have been described in several literatures, with decreased doses, improved percutaneous absorption, and greater bioavailability of

lipophilic medications with nano-emulgel delivery via topical route. There are several approved marketed preparations available that strongly support the efficacy and safety of these nanocarriers. This supports the use of a topical nano-emulgel system to administer lipophilic medicines in order to avoid the drawbacks of oral administration and enhance patient compliance. As a result, it is indicated as a promising approach for successful psoriasis care via topical route in the near future **(Bhardwaj and Tiwari, 2021).**

Hussain formulated a topical nanoemulsion gel for the administration of amphotericin, and the results demonstrate that the drug solution has a greater skin percutaneous penetration flux rate than the drug solution, which is supported by hemolytic and histological tests in local skin fungal infection **(Hussain *et al.*, 2016).**

Polymeric micelles and nanoemulsions have been investigated by Gupta as tumor-targeted medication carriers. Intravital imaging showed intricate information of carrier and drug activity in circulation and tissue in a study of nanoparticle extravasation and tumor accumulation. This knowledge is critical for the future therapeutic use of drug nanocarriers. The findings pave the way for new possibilities in drug nanocarrier optimization, with the optimization of relative rates of carrier internalisation, drug release, and drug and carrier diffusion in tumour tissue being of particular interest **(Rapoport *et al.*, 2015).**

Kjaer et al., 2015 used the IMQ induced Psoriasis mouse model to figure out how resveratrol works to lower necrosis factor levels and modulate the genes, pathways, and interleukins that mediate psoriasis contributing factors. The activity of resveratrol on cytokine translation through the appropriate mRNA was validated by polymerase chain reaction tests **(Kjær *et al.*, 2015).**

Psoriasis, according to Bracke, is a complicated inflammatory skin disease with a wide range of clinical symptoms. Human b defensin-2 (HBD-2) is a biomarker for

disease activity that is substantially upregulated in psoriatic lesions. In a bioengineered skin humanised mouse model for psoriasis, they investigated the potential benefits of targeting HBD-2 by topical application of DEFB4-siRNA-containing SECosomes. Histological testing revealed a significant improvement in the psoriatic phenotype, with normalisation of the skin architecture and a reduction in the number and size of blood vessels in the dermal compartment **(Bracke *et al.*, 2014).**

Isotretinoin-loaded SLNs and NLCs have been developed by Raza for the treatment of acne. Apart from establishing isotretinoin as an antibacterial agent against acne-causing bacteria, nano colloidal carriers such as SLNs and NLCs have enormous potential for treating acne more effectively **(Raza *et al.*, 2013).**

Gupta developed an O/W cream comprising a methanolic extract of Cassia tora L. leaves to produce in vivo antioxidant activity and discovered that the formulation could decrease oxidative stress caused by UV-B light in rats, which could be used to treat psoriasis **(Gupta *et al.*, 2013).**

Rawat has designed, improved, and evaluated the potential of solid lipid nanoparticles (SLNs) as a topical delivery system for Fluocinolone acetonide for targeted and extended release (FA). FA-loaded SLNs were successfully created utilising an emulsification–ultrasonication process and optimised using Design Expert software's 17-run, 3-factor, 3-level Box–Behnken design. The drug release investigation found that SLNs released drugs more slowly when using Higuchi release kinetics (R2 = 0.995), whereas pure drug suspension released drugs faster when using zero order release kinetics (R2 = 0.992). A three-month stability investigation at 4 ^{0}C confirmed that SLNs were stable. Furthermore, in vitro skin distribution tests revealed that when skin was treated with FA loaded SLNs suspension, a large amount of FA was present on the epidermal layer, whereas

simple FA suspension revealed a little amount of FA in the epidermis and dermis. Rawat further claims that accumulating FA selectively in the epidermis could prevent the negative side effects of systemic exposure. The findings showed that FA-loaded SLNs could be a promising therapy option for psoriasis, but more research in clinically relevant models is needed to prove the system's clinical value **(Pradhan, Singh, and Singh, 2015).**

RAWAT aimed to develop and optimize Fluocinolone acetonide (FA) loaded nanostructured lipid carriers (NLC) and to evaluate its potential as topical delivery system for management of psoriasis. FA loaded NLCs were successfully developed by modified microemulsion method and optimized using 3-level Box–Behnken design. After evaluation transmission electron microscopy confirmed spherical shape of prepared NLCs. Complete encapsulation of drug in the nanoparticles was confirmed by XRD and DSC. Release study showed prolonged drug release from the NLCs following Higuchi release kinetics and Zero order release kinetics, whereas pure FA suspension exhibited faster drug release following Zero order release kinetics with R2 value of 0.995. Stability study confirmed that NLCs were stable for 3 months at 4 C. Furthermore, in vitro skin distribution studies showed presence of significant amount of FA in the epidermal and dermal layer of skin when treated with FA loaded NLCs suspension while plain FA suspension showed significantly lesser amount of FA in the epidermis and dermis. Moreover, selective retention of FA in the epidermis might eliminate adverse side effects associated with systemic exposure. Thus FA loaded NLCs could be a potential system for psoriasis treatment but to create clinical value of the present system further studies are needed in clinically relevant models **(Pradhan, Singh, Murthy, *et al.*, 2015).**

According to Basse's study, lipids in the skin's outermost layer, the stratum corneum (SC), play a significant role in skin barrier qualities. Ceramides, cholesterol, and free fatty acids are the three primary lipid groups. Basse's goal in this study was to create

a psoriasis SCS (PS-SCS) that mimicked certain characteristics of the lipid composition of psoriasis patients' SC. The lipid organisation of PS-SCS differed from that of SCS. The existence of an orthorhombic packing was reduced, and the level of crystalline cholesterol was higher. Because of these alterations, hydrocortisone flux was lower in PS-SCS than in SCS and SC, which was most likely due to the increased level of phase separated crystalline cholesterol in PS-SCS. Because propylene glycol (PG) is commonly employed in dermatological formulations, the interaction of PG with SC and SCS membranes was examined in following investigations. These investigations discovered that PG improved hydrocortisone permeability by preferentially removing cholesterol from SCS and SC membranes. This could play a key role in PG's penetration-enhancing effect **(Basse *et al.*, 2013).**

Szoka created a library of polymer diacyl chain lipids with low polydispersity (1.04–1.09) and similar polymer molecular weights (2.1–2.5 kDa), which he then incorporated into 100 nm liposomes with a narrow polydispersity (0.25–1.3) made up of polymer–lipid/hydrogenated soy phosphatidylcholine/cholesterol/diD: 5.0/54.5/40 They found that HPMA, PVP, PMOX, PDMA, and PAcM modified liposomes increased rodent circulation times and that PVP, PDMA, and PAcM do not cause the ABC effect. They show for the first time that HPMA does not cause an ABC effect in rats, whereas PMOX causes a strong ABC effect. They discovered that a single dose of liposomes coated with PEG and PMOX causes rats to develop an IgM response to each polymer. They found a positive connection (R = 0.84 in rats, R = 0.92 in mice) between the circulation time of polymer-modified liposomes and polymer viscosity in this homologous polymer series; the most viscous polymers were PEG and PMOX, which can begin an ABC response. Their findings imply that non-ABC polymers, such as HPMA or PVP, should be investigated further as polymer coverings to increase the circulation of liposomes and other nanoparticles

(Kierstead *et al.*, 2015).

Fadda created new penetration enhancer-containing vesicles (PEVs) by mixing several hydrophilic penetration enhancers with standard phosphatidylcholine vesicles (control liposomes): Oramix® NS10 (OrNS10), Labrasol (Lab), Transcutol (Trc), and propylene glycol (PG). Vesicles were identified as being tiny, negatively charged, non-deformable, and multilamellar. PEVs have a higher fluidity than typical liposomes, according to rheological experiments. Ex vivo diffusion experiments through new born pig skin were used to investigate the effect of the obtained PEVs on (trans)dermal delivery of tretinoin using formulations with the drug both inside and outside the vesicles, as well as formulations with TRA only inside, in comparison to non-incorporated drug dispersions of the same composition used to produce the studied vesicles. The main outcome of these tests was an increase in cutaneous drug buildup and a decrease in transdermal TRA delivery (except for PG-PEVs). PEV-provided TRA deposition was greater in dialyzed vesicles than in non-dialyzed vesicles. The accumulation increased in the following order: control liposomes, PG-PEVs, Trc-PEVs, Or-PEVs, and Lab-PEVs. PEVs' potential to strongly interact with intercellular lipids, generating an expansion of this region, was demonstrated by SEM analysis of the skin **(Manconi *et al.*, 2011)**.

The goal of this investigation was to see how well Transcutol (Trc) could form elastic vesicles using soy lecithin (SL) and how the vesicles affected in vitro (trans)dermal delivery of minoxidil. Trc aqueous solutions (5–10–20–30 percent v/v) were used as the hydrophilic phase to make so-called penetration enhancer-containing vesicles (PEVs). As a control, SL liposomes lacking Trc were employed. The results showed that all of the synthesised PEVs had good entrapment efficiency (E percent 67), which was comparable to that of ordinary liposomes. Only when minoxidil was put in 5 and 10% Trc-containing vesicles did Trc-containing PEVs appear to be more malleable than liposomes. PEVs have a higher fluidity than

typical liposomes, according to rheological tests. The examination of zeta potential and size distribution over three months revealed that all PEVs were more stable than liposomes. Trc-containing PEVs were able to distribute minoxidil to deep skin layers without any transdermal penetration, according to the results of in vitro diffusion trials **(Mura *et al.*, 2011).**

In the present study Ferreira used deformable liposomes to improve drugs transdermal delivery. These vesicular systems were used to distribute piroxicam through the skin to treat inflammatory illnesses while avoiding negative side effects. Ferreira found that using -cyclodextrin inclusion complexes to entrap piroxicam in the aqueous compartment allowed for better entrapment efficiency (63.27 percent more than when entrapped in the lipid bilayer). The population of optimised deformable liposomes was homogeneous (PDI 0.1) in size (108.93 3.74 nm) and had a spherical shape. The vesicles remained steady in size after two months of storage, according to size stability analyses. In vitro permeation study revealed that the vesicles have adequate deformability to pass through pores 45 percent smaller than their own size. The penetration of deformable liposomes including piroxicam_ cyclodextrin complexes decreases significantly in studies conducted on pig skin. Due to the existence of the stratum corneum, the skin's major barrier, only 1.1-3.2 percent of the initial population reached the liquid receptor after 24 hours of diffusion. Nonetheless, histological examinations showed that deformable liposomes were equally distributed on the skin structure, allowing for percutaneous penetration of their contents. These findings indicate the feasibility of using this mixture to treat inflammatory diseases on a topical basis **(Ferreira *et al.*, 2015).**

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corneum, the skin's major barrier, only 1.1-3.2% of the initial population reached the liquid receptor after 24 hours of diffusion. Nonetheless, histological examinations showed that deformable liposomes were equally distributed on the skin structure, allowing for percutaneous penetration of their contents. These findings indicate the feasibility of using this mixture to treat inflammatory diseases on a topical basis. They included psoriasis studies that reported the percentage of subjects who met desired efficacy endpoints, as well as studies that reported the subjects' mean change in symptoms from baseline. Based on these findings, the researchers concluded that Clobetasol propionate is a highly effective psoriasis treatment. In clinical trials, ointment preparations exhibit similar efficacy to other preparations. In clinical practise, when patient preferences are more likely to influence compliance, it may be advisable to use the vehicle that patients prefer **(Warino *et al.*, 2006)**.

According to Reygagne, proper pharmacological formulations are required for the treatment of hairy skin, hence Galderma R&D, Inc. produced a new particular shampoo formulation including clobetasol propionate 0.05 percent. 151 patients with moderate to severe scalp psoriasis were randomised to 4 weeks of treatment with clobetasol propionate shampoo or calcipotriol solution in a multicenter, randomised, investigator-masked, parallel group research. Clobetasol propionate outperformed calcipotriol solution (total severity score: mean difference 0.51, 95 percent confidence interval 0.05–0.97, p = 0.028; global severity score: mean difference 0.43, 95 percent confidence interval 0.08–0.78, p = 0.016). The calcipotriol group had more adverse events than the clobetasol propionate shampoo group. Telangiectasia and skin atrophy did not differ substantially across treatments; however, the calcipotriol solution group had a considerably higher rate of burning sensations. Short contact therapy for scalp psoriasis with this new clobetasol propionate shampoo formulation was much more effective and well tolerated than calcipotriol solution for the treatment of scalp psoriasis, according to the findings **(Reygagne *et al.*, 2005).**

Feldman and Yentzer compared conventional ointment and cream formulations with newer clobetasol propionate 0.05 percent formulations. While there are few direct comparison studies between clobetasol propionate in different vehicles, efficacy rates (defined as clear or nearly clear psoriasis) for more recent formulations are high, with most patients achieving success after 2–4 weeks of treatment in well-controlled clinical trials, with response rates comparable to those with traditional clobetasol propionate ointment. Small changes in vasoconstrictor efficacy or cutaneous absorption have been observed among the formulations, but their clinical importance is difficult to determine. The relevance of drug adherence in the therapy of psoriasis has been highlighted in recent study. Small changes in drug administration are unlikely to be a far more important driver of effectiveness than adherence to therapy, especially in actual clinical use rather than the well-controlled setting of clinical trials. Adherence and outcomes are likely to be better with the more modern formulations than with the conventionally prescribed ointment for patients who want a less messy carrier **(Feldman and Yentzer, 2009).**

Hair follicles, hair shafts, and sebaceous glands make up the pilosebaceous unit. This three-dimensional complex structure seen on the surface of mammalian skin has long been thought to be a key channel for topically applied medications and delivery systems to absorb. This mechanism could be used for localised medication delivery for disorders connected with the pilosebaceous gland rather than systemic drug absorption for diseases linked with the pilosebaceous gland. To rationally design medication delivery systems targeted to hair follicles, a thorough understanding of pilosebaceous anatomy and its surrounding environment is required. The current paper provides an overview of hair follicle anatomy, as well as the rationale, opportunities, methods, and strategies for drug targeting to the pilosebaceous compartment at deformable liposomes that were uniformly distributed **(Singh *et al.*, 2000)**.

Van der Fits reported that topical application of imiquimod (IMQ), a TLR7/8 ligand and potent immune activator, can induce and exacerbate psoriasis, a chronic inflammatory skin disorder. Recently, a crucial role was proposed for the IL-23/IL-17 axis in psoriasis. They hypothesized that IMQ-induced dermatitis in mice can serve as a model for the analysis of pathogenic mechanisms in psoriasis-like dermatitis and assessed its IL-23/IL-17 axis dependency. Daily application of IMQ on mouse back skin induced inflamed scaly skin lesions resembling plaque type psoriasis. These lesions showed increased epidermal proliferation, abnormal differentiation, epidermal accumulation of neutrophils in microabcesses, neoangiogenesis, and infiltrates consisting of CD4 T cells, CD11c dendritic cells, and plasmacytoid dendritic cells. IMQ induced epidermal expression of IL-23, IL-17A, and IL-17F, as well as an increase in splenic Th17 cells. IMQ-induced dermatitis was partially dependent on the presence of T cells, whereas disease development was almost completely blocked in mice deficient for IL-23 or the IL-17 receptor, demonstrating a pivotal role of the IL-23/IL-17 axis. In conclusion, the sole application of the innate TLR7/8 ligand IMQ rapidly induces a dermatitis closely resembling human psoriasis, critically dependent on the IL-23/IL-17 axis. This rapid and convenient model allows further elucidation of pathogenic mechanisms and evaluation of new therapies in psoriasis **(Van der Fits *et al.*, 2009).**

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Psoriasis is a chronic inflammatory skin condition that causes erythematous, papulosquamous lesions on the skin. Excessive proliferation and abnormal differentiation of keratatinocytes define this condition. Traditional topical treatments,

such as coal tar and dithranol, have minimal efficacy and poor visual and cosmetic appeal, resulting in low patient compliance, whereas systemic medicines, such as methotrexate, cyclosporine, and acitretin, have substantial adverse effects. Several new carriers, such as liposomes, nanostructured lipid carriers (NLC), and others, have been employed in psoriasis in recent years, with promising outcomes. Small and narrow size distribution with innovative carriers allows for site-specific administration to the skin, with better drug solubilization and bioavailability of hydrophobic medicines. This study focuses on recent advances in the realm of new carriers for antipsoriatic active moieties and bioactives topical applications **(Suresh *et al.*, 2013).**

The goal of this study was to create a topical gel with clobetasol propionate niosomes to extend the duration of action and reduce negative effects. The clobetasol propionate niosomes were made by varying the ratios of non-ionic surfactants (Span 40, 60, 80) and cholesterol using three different methods: thin film hydration, ether injection, and hand shaking. Drug content, entrapment efficiency, size analysis, and in vitro drug release investigations were all performed on the generated niosomes. The Span 60 niosomes (ratio of surfactant, cholesterol- 1: 0.5) generated by thin film hydration process had a greater entrapment effectiveness (91.37 percent) and were assessed for their stability and manufactured as gel formulation. Drug content analyses, in vitro drug release tests, and in vivo pharmacodynamic investigations were performed on the manufactured niosomal gel (G2) and the commercialised gel (G3). Our findings imply that clobetasol propionate delivered via niosomal delivery in carbopol gel base is an effective topical medication delivery strategy for extending the duration of action **(Abraham Lingan, 2008).**

Feldman develops and characterises Acitretin-loaded Nanostructured Lipid Carriers (ActNLCs) in order to better understand in vitro drug release and clinically analyse the gel's efficacy in the treatment of psoriasis. The ActNLCs were made utilising a

solvent diffusion process and a 32-factorial design. In vitro skin deposition experiments in Human Cadaver Skin and double-blind clinical investigations in psoriatic patients were undertaken using NLCs integrated in a 1% w/w Carbopol 934 P gel base. The optimised ActNLCs had a spherical form, with an average particle size of 223(8.92) nm, a zeta potential of 26.4 (0.86) mV, and an EE of 63.0(1.54%). The development of NLCs was confirmed by DSC and XRD data. ActNLC gel produced much more Acitretin deposition in human cadaver skin (81.38.23%) than Act simple gel (47.28.02%). Clinical tests with ActNLCs loaded gel showed a significant improvement in therapeutic response and a reduction in local adverse effects, indicating its efficacy in the topical treatment of Psoriasis **(Feldman and Yentzer, 2009).**

Agrawal plans to use in vitro and in vivo research to investigate the potential of solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) in enhancing capsaicin (CAP) topical distribution. The average particle size, zeta potential, and entrapment efficiency of the lipidic nanoparticles were measured using the solvent diffusion method. The particles were nanometric in size, according to TEM photomicrographs. In comparison to SLNs (79.7% 2.93 percent), NLCs can encapsulate a higher quantity of CAP (87.4 3.28%). In comparison to plain drug solution and SLNs, the cumulative levels of CAP penetrated through the skin and maintained in the SC were larger in the case of NLCs. The irritation in SLNs and NLCs was little to non-existent. Overall, NLCs and SLNs demonstrated a decent ability to promote drug accumulation in various skin layers, but NLCs may be a more promising carrier for topical delivery of CAP for effective psoriasis treatment **(Agrawal *et al.*, 2015).**

Pradhan investigated the efficacy of Fluocinolone Acetonide (FA) loaded NLCs and plain Salicylic Acid (SA) containing new gels (FSG) for psoriasis treatment. Plain FA and SA-containing traditional gel (PFSG) formulations were also made for

comparison. The FSG formulation released FA for more than 24 hours, but the PFSG formulation released more than 90% of FA in less than 7 hours. Ex-vivo permeation studies demonstrated that both the FSG and PFSG formulations had little drug absorption into the systemic circulation; however, cutaneous pharmacokinetic studies revealed considerably higher (P 0.05) FA retention from the FSG formulation compared to the PFSG formulation. FA loaded NLCs were strictly contained to the epidermal and deep dermal layers of the skin, whereas PFSG was mostly restricted to the outside layer of skin, according to a confocal laser scanning microscopic research. In vivo, topical use of the FSG formulation caused no skin irritation, whereas topical application of the PFSG formulation caused minor irritation. Histopathological investigations suggested that FSG might successfully reduce psoriatic signs in the IMQ-induced model. The PASI scoring system was also used for this test. Furthermore, the FSG considerably reduced the levels of prime pathogenic cytokines (TNF-, IL-17, and IL-22) when compared to the PFSG and IMQ groups, according to the results of the ELISA investigation. Overall, the findings imply that nanocarrier loaded gel formulations are more effective than simple gel formulations **(Pradhan *et al.*, 2021).**