CHAPTER 2: LITERATURE REVIEW

- **Sharma *et al.*, 2020** have developed squalene integrated NLC based carbopol 940 and HEC gel of tamoxifen citrate to increase lipid and moisture content of skin and to create a local drug depot in the skin for improved efficacy against psoriasis. The results prove the clinical pertinence of this stable gel as it ensured longer stay (due to semisolid consistency) over the skin, increased skin moisture (hydrophilic gelling polymer) and lipid content (due to the presence of the natural skin lipid component), and improved drug retention in the skin along with higher efficacy against psoriasis.

- **Rapalli *et al.*, 2020** have formulated curcumin loaded topical nanostructured lipid nanocarriers and developed analytical validation parameters described as per International Conference of Harmonization guidelines using the UV-Visible spectroscopy.

- **Intagliata *et al.*, 2019** reviewed that resveratrol, a natural polyphenol has many therapeutic benefits but this bioactive suffers from different challenges which restrict its clinical efficacy such as low aqueous solubility and high rate of degradation and elimination, but these challenges can be overcome by using various approaches based on polymeric and lipidic nanocarriers.

- **Walunj *et al.*, 2019** have prepared cationic liposomal nanocarriers loaded with Cyclosporine in the imiquimod-induced psoriatic plaque model. Results showed that with*in vivo* model there is a reduction in the levels of tumor necrosis factor-α, IL-17, and IL-22 and found to be effective in the treatment of psoriasis.

- **Sathe *et al.*, 2019** has formulated topical NLC gel loaded with dithranol and applied on the IMQ-induced psoriatic plaque model. Results indicated that there is a reduction in the symptoms of psoriasis in terms of PASI score and there is a

reduction in immunohistochemistry like tumor necrosis factor-α, IL-17, and IL-22 as a comparison to the negative control.

- **Essaghraoui *et al.*, 2019** have prepared and optimized topical solid lipid nanoparticles and nanostructured lipid carriers loaded with Cyclosporine A. Results show that SLNs are safe and retain Cyclosporine A in pork skin as compared to NLCs.

- **Sousa *et al.*, 2019** have developed a novel nanomedicine i.e. Salinomycin loaded polymeric micelles, 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 seems to be able to deliver SAL into human cancer cells promoting a high drug intracellular accumulation, thus increasing drug sensitivity.

- **Bhoir *et al.*, 2019** aimed to investigate the *in vitro* and *in vivo* efficacy of petroleum ether extract of *Annona squamosa* seeds which showed inhibition of cell proliferation of keratinocytes and found growth inhibitory property of it was significantly higher than that was observed in presence of corticosteroid i.e clobetasol propionate. Oxazolone induced psoriasis to the ears of Balb/C mice showed a marked reduction in erythema, edema and increased levels of cytokines IL6, IL17, TNF-α, INF-γ, GMCSF, and infiltration of CD4 T cells observed in psoriasis lesions were decreased by using *Annona squamosa* seeds, which was comparable to treatment with 0.05% clobetasol propionate cream.

- **Kasper *et al.*, 2018** have developed topically everolimus (EV)-loaded methoxy-poly (ethylene-glycol)-hexyl substituted poly (lactic acid) (mPEGhexPLA) nanocarriers on experimental autoimmune uveoretinitis. Results from immunochemistry Topical administration of an everolimus formulation improved EAU in both eyes. The effect might also be related to systemic immunosuppressive effects, as several systemic cellular immune responses were influenced.

- **Khan *et al.,* 2018** reviewed the literature and revealed many researchers have used propylene glycol, poloxamer P407, monoolein, transcutol P, and choline loaded with finasteride in topical formulations. Moreover, among all drug delivery systems, the finasteride liposomal gel system consisting of methylcellulose and gel system containing poloxamer P407 exhibited the highest flux.

- **Lampis *et al.,* 2018** have prepared lamellar liquid crystals, which were prepared loaded with lysozyme and caffeine Although lysozyme retains its biological activity due to release from the lipid formulations.

- **Csanyi *et al.,* 2018** have reviewed current therapies, active agents, drug carrier systems, and evaluation methods in connection with the treatment of skin cancer and outlines Critical Quality Attributes of formulation development in the view of QbD approach which needs to be considered during the preparation of a nanosized dermal anticancer formulation.

- **Hashim *et al.,* 2018** have developed topical delivery systems for Acitretin through complexation with cyclodextrin, and encapsulation in nanostructured lipid to explore its pivotal role as a topical delivery system for effective treatment of psoriasis. This study highlighted the merits of the developed Act nano niosomal gel as a promising topical delivery system with prominently enhanced permeation, drug deposition into deeper skin layers, and diminished systemic absorption.

- **Na Takuathung *et al.,* 2018** This study investigated the therapeutic potential of Wannachawee Recipe on antiproliferant activity using imiquimod-induced psoriasis-like dermatitis on the shaved dorsal skin and right ear pinna of BALB/c mice by topical application of imiquimod for 15 consecutive days after which Wannachawee Recipe was administered to the mice by oral gavage for 10 days.

Blood samples were collected for phenotypical observations, histopathological examinations, and ELISA of skin and found reduced levels of Th17 cytokines (IL-17A, IL-22, and IL-23) in both serum and dorsal skin.

- **Nimisha *et al.*, 2017** have developed a novel nanovesicular gel of Berberis aristata extract and evaluated for its anti-inflammatory and antipsoriatic activity. Topical application of extract loaded transferosomal gel showed a marked reduction in thickness of the epidermis, length of rete ridges as compared to conventional gel formulation. It can be inferred that B. aristata extract loaded transferosomal gel can function as a potential anti-inflammatory and antipsoriatic formulation.

- **Pentek *et al.*, 2017** have prepared a dendrimer composite of resveratrol for enhancing its stability and solubility by avoiding the use of harsh organic solvent and stable formulation is available as an anti-aging cream and is ready to be commercially marketed.

- **Prabhu *et al.*, 2017** have developed cyclobenzaprine-loaded nanoemulsion. The optimized nanoemulsion formulation, which exhibited maximum drug release, was formulated as a novel nanoemulgel of cyclobenzaprine with suitable viscosity for topical administration. The *in-vitro* results revealed that the developed nanoemulsion based gel containing cyclobenzaprine hydrochloride has great potential to provide a better therapeutic effect locally through topical application.

- **Singh *et al.*, 2017** investigated the effect of resveratrol on mice at different doses against intracerebroventricular-collagenase-induced intracerebral hemorrhage and found there is a decrease in levels of nitro-oxidative stress and TNF-α level.

- **Barbosa *et al.*, 2016** formulated nanostructured lipid carriers loaded with resveratrol to modulate human dendritic cells. They concluded that resveratrol-

NLCs were able to inhibit nuclear factor κ beta phosphorylation and significantly decrease the level of interleukin-12/23, both upregulated in response to TNF-α.

- **Hussain *et al.,* 2016** have prepared a topical nanoemulsion gel for delivery of amphotericin and results show the higher skin percutaneous permeation flux rate as compared to drug solution which is confirmed by Hemolytic and histopathological studies in local skin fungal infection.

- **Conte 2016** reviewed that polyphenols like resveratrol, quercetin, epigallocatechin-3-gallate, and curcumin have potential biological activities like anti-aging, anti-inflammatory, and cancer. But these bioactive suffer from long-term stability, degradation in light, having low water solubility, and poor bioavailability, So nanocarriers are advantageous in combating the problems of bioactive and deliver them safely to the targeted location.

- **Qadri *et al.,* 2016** have prepared and characterized invasomes loaded with isradipine, The results revealed that formulation has high transdermal flux through rat skin in the management of blood pressure.

- **Gupta *et al.,* 2015,** have studied polymeric micelles and nanoemulsions as tumor-targeted drug carriers. A study of nanoparticle extravasation and tumor accumulation revealed, via intravital imaging, intimate details of carrier and drug behavior in circulation and tissue. This information is vital for future clinical application of drug nanocarriers. The results pave the way for new directions in the optimization of drug nanocarriers of paramount importance is the optimization of relative rates of carrier internalization, drug release, and drug and carrier diffusion in the tumor tissue.

- **Gambini *et al.,* 2015** have reviewed the therapeutic properties of resveratrol due to donating properties and binding with the biomolecules, but all these activities i.e. anticancer agent, anti-aggregation agent, antioxidant, antiaging, antifragility,

anti-inflammatory, antiallergenic need to be confirmed through *in vitro* and *in vivo* models.

- **Kjaer *et al.*, 2015** have exploited the IMQ induced Psoriasis mice model and sought to identify the resveratrol mechanism for downregulating the levels of necrosis factor and modulating the genes, pathways, and interleukins mediating contributory factors of psoriasis. Results from polymerase chain reaction studies confirmed a decline in cytokine translated through the corresponding mRNA due to the action of resveratrol.

- **Kjaer *et al.*, 2015** have suggested that the Sirtuin1 enzyme thought to mediate the effects of resveratrol is present in the skin, and resveratrol is known to down-regulate NF-κB; an important contributor in the development of psoriasis. Consequently, they investigated whether Resveratrol affects an Imiquimod-induced psoriasis-like skin inflammation in mice and sought to identify candidate genes, pathways, and interleukins mediating the effects. After studying they concluded that Resveratrol ameliorates psoriasis, and changes the expression of retinoic acid stimulated genes, IL-17 signaling pathways, IL-17A and IL-19 mRNA levels in a beneficial manner, which suggests resveratrol, might have a role in the treatment of psoriasis and should be explored further in a human setting.

- **Sharma *et al.*, 2015** have developed topical microemulsion loaded with Benzyl Benzoate and found there is an increase in skin bioavailability of the drug through skin histopathology and dermatokinetic studies on mice abdominal skin.

- **Bracke *et al.*, 2014** have suggested that psoriasis is a complex inflammatory skin disease that presents a wide variety of clinical manifestations. Human b defensin-2 (HBD-2) is highly up-regulated in psoriatic lesions and has been defined as a biomarker for disease activity. They explored the potential benefits of targeting HBD-2 by topical application of DEFB4-siRNA-containing SECosomes in a

bioengineered skin humanized mouse model for psoriasis. A significant improvement in the psoriatic phenotype was observed by histological examination, with a normalization of the skin architecture and a reduction in the number and size of blood vessels in the dermal compartment.

- **Raza *et al.*, 2013** have developed Isotretinoin-loaded SLN's and NLC's for the treatment of acne. Besides establishing isotretinoin as an antimicrobial agent against acne-causing bacteria, there is the immense potential of nano colloidal carriers like SLNs and NLCs to treat acne more efficiently.

- **Gupta *et al.*, 2013** have prepared O/W cream containing methanolic extract of *Cassia tora* L. leaves to produce *in vivo* antioxidant activity and found formulation having the capability to prevent the oxidative stress-induced in rats by exposure to UV-B light to treat psoriasis.

- **Hangun-Balkir and Mckenney 2012** have developed the ultraviolet-visible method of resveratrol and found antioxidant activity using the DPPH assay, they also determined IC50 value which is having the capability to the reduction in 50% free radical concentration.

- **Ndiayea *et al.*, 2011** have reviewed that resveratrol which is present in red grapes, and found it is having antioxidant effects against UV-induced oxidative stress, hence helpful in the management of skin aging and associated skin related problems.

- **Hung *et al.*, 2008** firstly reported the permeation profiles for topically applied resveratrol and concluded that the resveratrol is very effective when administered by topical route. *In vivo* skin irritation studies denied any type of erythema which ratified that no toxic effect or deleterious effect on skin surface was observed.

- **Zhang *et al.*, 2007** have concluded the benefits of resveratrol as antioxidant moiety and free radical neutralizer but its poor physicochemical properties hinder its benefits. Resveratrol triphosphate is a novel derivative of resveratrol with inherent properties like the parent molecule. Several *in vivo* studies confirmed that the molecule was found to have higher bioavailability in the epidermis when applied topically as compared to the parent molecule.

- **Docherty *et al.*, 2004** attempted a comparative study between resveratrol cream, 10% docosanol cream (Abreva), and 5% acyclovir ointment (Zovirax). 12.5 and 25% resveratrol cream effectively suppressed lesion formation. Results showed no apparent dermal toxicity such as erythema, scaling, crusting, lichenification, or excoriation in resveratrol-treated animals. It was confirmed that it inhibits HSV lesion formation in the skin of mice with topically applied resveratrol.

- **Sen *et al.*, 2002** reviewed that the wound healing process gets promoted by a combination of grape seed proanthocyanidin extract and resveratrol facilitates inducible VEGF expression, a key element supporting wound angiogenesis. Strategies to manipulate the redox environment in the wound are likely to be of outstanding significance in wound healing.

- **Guenther *et. al.*, 2002** have reviewed the use of tazarotene and found that in psoriasis concerning other topical retinoids, it normalizes keratinocyte differentiation, reverses keratinocyte hyperproliferation, and has better anti-inflammatory effects. In the case of acne, it should be used with a topical corticosteroid or phototherapy, or an antibiotic.