SUMMARY

CHAPTER - 1

A number of factors have been known to be involved in psoriasis - a hyperproliferative and inflammatory skin disorder with an unknown etiology. TEWL is also known to be high. In normal human skin, the lipids derived from the lamellar body secretion form broad bilayered sheets in the corneycyte intercellular spaces, which accounts for the barrier properties of the epidermis. The current observations, showed an abnormal configuration of lipid lamellae in the lamellar bodies of psoriatic epidermis. The intercellular lipids of the corneocytes contain huge lacunae, while the bilayers are not compact and are disarranged in whorls breaking up at many loci. The study indicates that abnormal processing of lamellar lipids and possibly lamellar enzymes and retention of desmosomes could together lead to an anomaly in corneocyte cohesion and dyshesion in psoriatic lesions. Retention of nuclear material and lipid droplets in the outermost layer of stratum corneum suggest an abnormality in the processing of the cell organelles during epidermal differentiation in psoriasis.

CHAPTER - 2

Various animal models have been developed to study the pathology underlying psoriasis - a hyperproliferative, scaling skin disorder. The granular layer is absent both in the parakeratotic involved epidermis of psoriasis, and the interscale parakeratotic epidermis of rat tail skin, because of which this model has been proposed, to study the pathology underlying this scaling disorder. In the present study, histochemical observations on lipid, calcium and nucleic acid distribution in the epidermis was carried out to compare if there is any similarity in tail and psoriatic parakeratosis,

as these parameters play an important role during epidermal differentiation. Present observations showed that rat tail skin and psoriatic skin showed more disparity in the distribution pattern of all the parameters mentioned above. The possible explanation could be that parakeratosis in rat tail skin is a normal process, while as in psoriatic patients it is a pathological condition.

CHAPTER - 3

Glycerol is known to be a good and a commonly used skin conditioner. The avian corneocytes have a paucity of keratin filaments and transepidermal water loss in higher than mammals, which gives the epidermis a dry and scaly appearance. Ultrastructural studies, with topical application of glycerol on pigeon apterial skin as a 'dry and scaly' skin model was thus carried out.

Normally, the avian corneocytes are termed 'sebokeratocytes' as the lamellar body (LB) contents fuse with each other to form neutral lipid droplets which are then secreted into the intercellular space. In mammals, these intercellular lipids form broad bilayered sheets which in turn form the barrier to transepidermal water loss. Glycerol treatment shows a comparative increase in the number of lamellar bodies in the transitional layer. The outer border of the lamellar bodies is seen to have a lamellar pattern and the core having translucent lipid droplets. These lipid droplets are retained intracellularly till the upper corneocyte layer. The findings suggest a possible role for glycerol to induce lipid synthesis in the avian epidermis and further reduce transepidermal water loss.

CHAPTER - 4

Topical drug delivery is preferred over the systemic therapy as it reduces the chances of toxic side effects. Liquid crystalline cream, a mixture made from Brij 96 and water, is being developed as a means for transdermal drug delivery. Topical application of this cream on rat pup skin has further confirmed the earlier findings that the route of permeation of any substance through the skin is via the intercellular spaces of the corneocytes, that consist of a mortar of intercellular lipids. Studies revealed that Brij 99 causes domain separation within SC bilayers by forming lacunae that serve as channels for permeation. This can also create 'reservoirs' for the drugs miscible in these creams; which can further facilitate the formation of prodrugs. Enough time can also be provided for the drug to act before it is removed systemically. This vehicle also has an effect on the regular, normal process of intercellular lipid bilayer formation, as a result of lamellar body secretion. Instead large focal areas of nonlamellar lipid domains are seen in the epidermis of treated animals, which can also facilitate faster percutaneous permeation by providing a passage for the cream through the intercellular spaces.

CHAPTER - 5

Structural lipids also play an important role in the water holding property of the skin. β emitters are known to pass through the skin barrier. A permeability cell was constructed and tritiated water was used to determine the rate of *in vitro* water permeation through the skin.

The epidermal sheets from different classes of vertebrates were compared for water permeation. Some of the samples were treated with solvents,

surfactant and conditioners, to fathom permeability changes of the epidermis after these treatments at various time intervals.

Solvent treated epidermal sheets show very high degree of permeation, both in rat pup skin and pigeon skin. Glycerol, Brij 99 and beewax treated skin shows negligible permeation; or rather, helps in retention of water compared to normal and solvent treated skin. Comparison of water permeation in rat, pigeon and lizard skin showed that reptilian integument is more efficient as it allows very less permeation of water compared to rat pup and pigeon epidermis. These observations suggest that tritiated water could be ideal, for determining in vitro water permeation through the epidermis.

CHAPTER - 6

Buffalos have a typical, adaptive, behavioural thermoregulation. Earlier studies on rat, catecean and avian skin have shown that epidermal lipids play a vital role for the animal to adapt to varied climatic conditions. The epidermal lipids are mainly derived from sebaceous secretion and from the lamellar bodies. The granular cells of buffalo epidermis show abundant lamellar bodies and the discharged intercellular lipids seem to occupy a small surface area compared to rat epidermis. Keratohyalin granules are not as distinct in size, as seen in rat epidermis. These findings indicate that some change in the processing of the lamellar body derived intercellular corneocyte lipids could lead to a fault in the barrier function. Permeability experiments with $LaNO_3$ (Lanthanum nitrate) as a tracer also shows lanthanum precipitates even in the stratum corneum interstices which indicates an increased transepidermal water loss in these animals. The animal, thus has to adapt to behavioural thermoregulation to reduce transepidermal water loss in the tropical condition.