3. SKIN PENETRATION

Two potential drug penetration paths across the intact skin of the body are known, namely the Trans-epidermal and Trans-appendage paths. The trans-epidermal route includes molecules moving through the stratum corneum, an architecturally complex, multi-layered, cellular membrane. It can be termed intra- or intercellular trans-epidermal penetration. The intracellular path through corneocytes, terminally differentiated keratinocytes, enables hydrophilic or polar solutes to be transported. Transport through intercellular spaces allows the continuous lipid matrix to disperse lipophilic or non-polar solutes. The trans appendage path includes molecules going through sweat glands and through the hair follicles (Fig. 2) [7].

To establish efficient TDD systems, knowing the kinetics of skin permeation is very important. For the evaluation of TDDS, a critical step is to check the percutaneous absorption of molecules. Absorption across percutaneous layer; the primary route for drug entry into the bloodstream [8].

Percutaneous absorption of drug molecules is a process involving the following steps

1. Penetration of a drug from the outer skin layer to the deep layers of the skin
2. Partitioning of drugs in the aqueous and lipophilic layers
3. Diffusion into the upper dermis through the viable epidermis
4. Permeation of molecules from one surface to another, which is functionally and structurally distinct from the first layer
5. Absorption of the drugs into the blood circulation

Enhancers of penetration are also known as accelerators, promoters of absorption or enhancer of permeation. The protective role the stratum corneum is due to its barrier function, but at the same time, this may be an obstacle for the transdermal drug delivery through it. Since the drug's main route is through the intracellular channels, in the first stage of absorption, the lipid portion is a viable determinant [9].

Chemical permeation enhancers work by one or additional of the subsequent three principal mechanisms:
Relaxation of the stratum corneum
Interaction with lipid bilayer's aqueous domain
Enhanced drug partition by applying enhancer or suitable solvent to the skin

Chemical permeation enhancers achieve their influence by changing the structure of the skin above; they interact with the polar head groups via hydrogen bonding and ionic interactions. Due to subsequent disturbance in lipid hydration and changes in the properties of the head unit induce relaxation in the portion of the brain [10]. Thus the relaxation will reduce resistance to polar molecules in this lipid concentrated area. An additional factor could be increased in water surface volume, causing more influx of water via the tissue, the process considered to be solvent swelling, thus providing increased surface area for diffusion of polar molecules [11].

Techniques to alter the barrier property of the stratum corneum:

The following categories of techniques are used for controlling the barrier properties of the top layer of the skin to improve drug penetrations and absorption. Chemical enhancement.

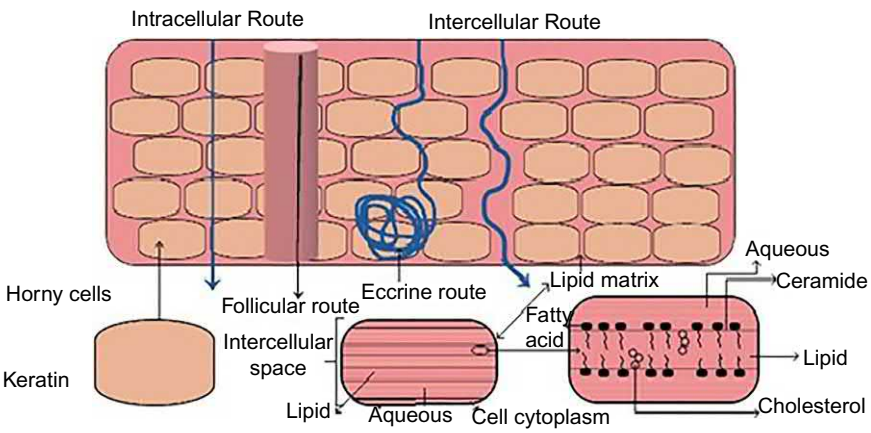

FIG. 2 Routes of drug penetration through skin.