

Industrial pharmacy/ 5th stage
Transdermal DDS lec 12
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- Most efforts in drug delivery has focused on an oral route of administration for several considerations, namely: **patient compliance and a high degree of flexibility on dosing.**
- The oral route is not without profound drawbacks posed by the **hostile environment in the GIT** in addition to the **first-pass effect** encountered directly after absorption, which constrains the administration of essential biologics orally

- In 1979, with the introduction of a scopolamine transdermal patch for the prevention of motion sickness by Alza corporation, the era of transdermal drug delivery was started virtually and divert the conventional perspective towered the skin from topical use to alleviate dermal ailments into a promising site for percutaneous absorption

- Transdermal drug delivery is a way to achieve a systemic effect by applying drugs topically; upon contact with skin, the drug proceeds to penetrate the epidermis passing through its different layers **without localization** reaching the dermal circulation to be accessible for systemic absorption

Release from the base material of the patch

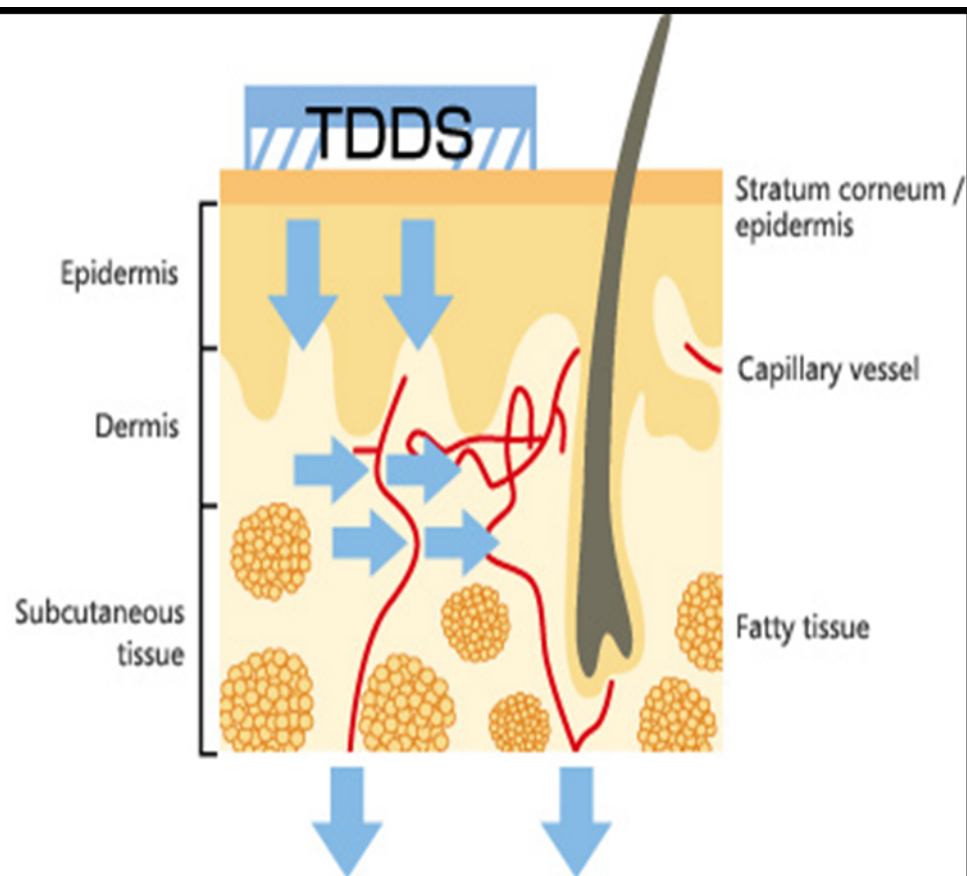
Diffusion to the stratum corneum

Diffusion to the epidermis

Diffusion to the dermis

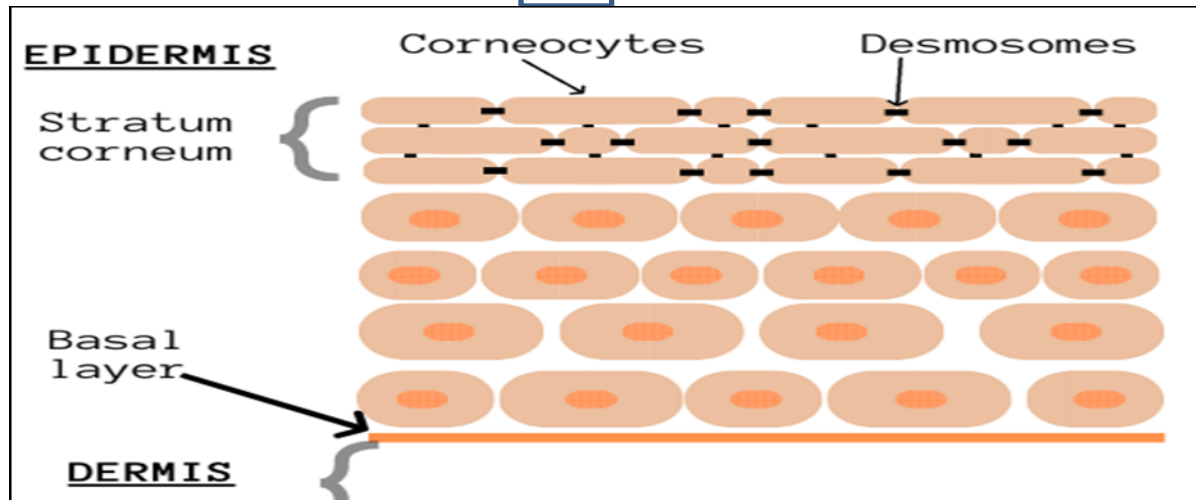
Migration to the capillary vessels

Migration to the affected area



- Besides being **patient-friendly**, transdermal drug delivery impart further merits such as:
- 1) **escaping the first-pass metabolism**
 - 2) **minimizing variation in drug blood concentration** by controlled delivery over time
 - 3) suitability as an **alternative route** whenever oral dosing is impermissible
 - 4) the existence of antigen-presenting cells copiously in skin layers may render the skin as an **upcoming site for vaccination**

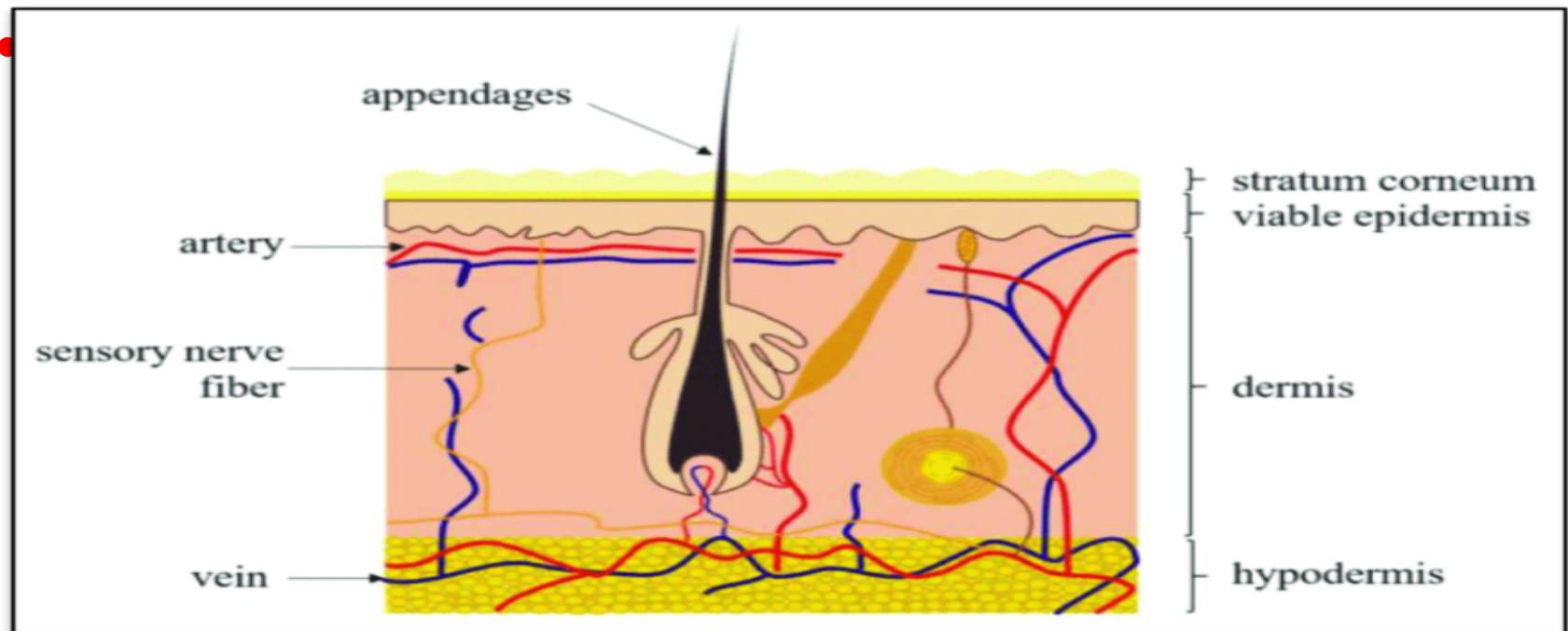
- Despite these remarkable features, the number of drugs has been launched to the market is yet limited, which is an anticipated finding as a consequence of impermeable nature of skin which serves as a physiological barrier for the entrance of drug molecule



➤ Nevertheless, the market of transdermal drug delivery has attained substantial growth, which surpasses the oral route; therefore, considerable attention has been paid to overcome obstacles imposed by skin complex structure aiming to better utilization of skin as a route of administration

- The skin is an exceptional organ in terms of histology and function; the skin plays a multi-functional pivotal role as being a protective barrier against chemicals, UV radiation, and microorganisms;
- the skin is implicated in thermal coordination, fluid balance, besides, being sensory and endocrine organ

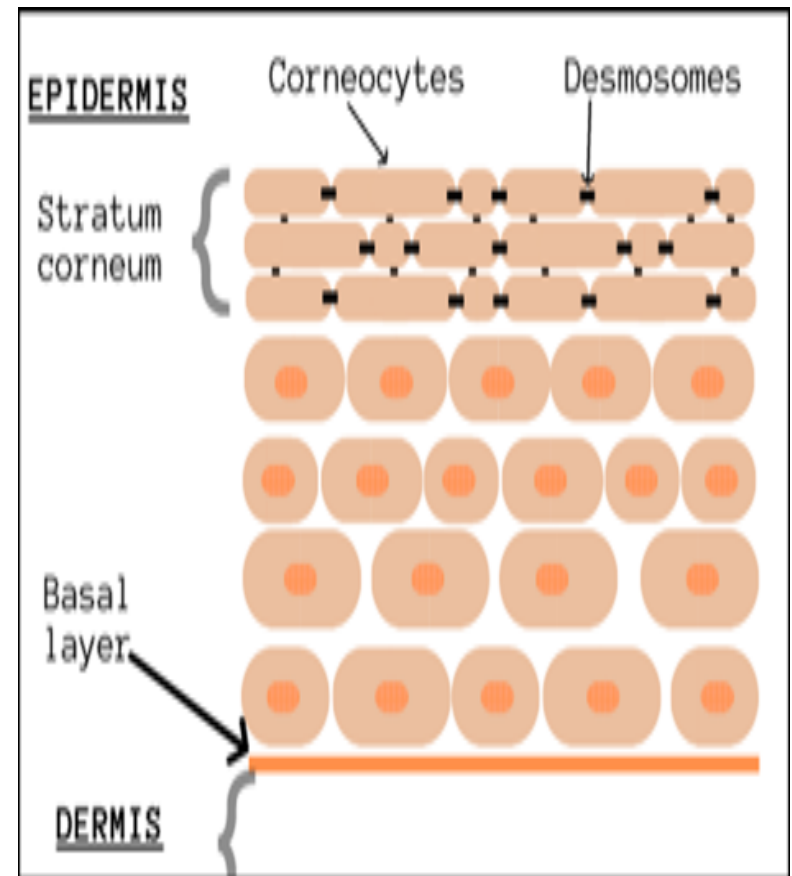
- The skin is a multilayered organ with three distinguished layers which is from top to bottom: **epidermis**, **dermis**, and **hypodermis**



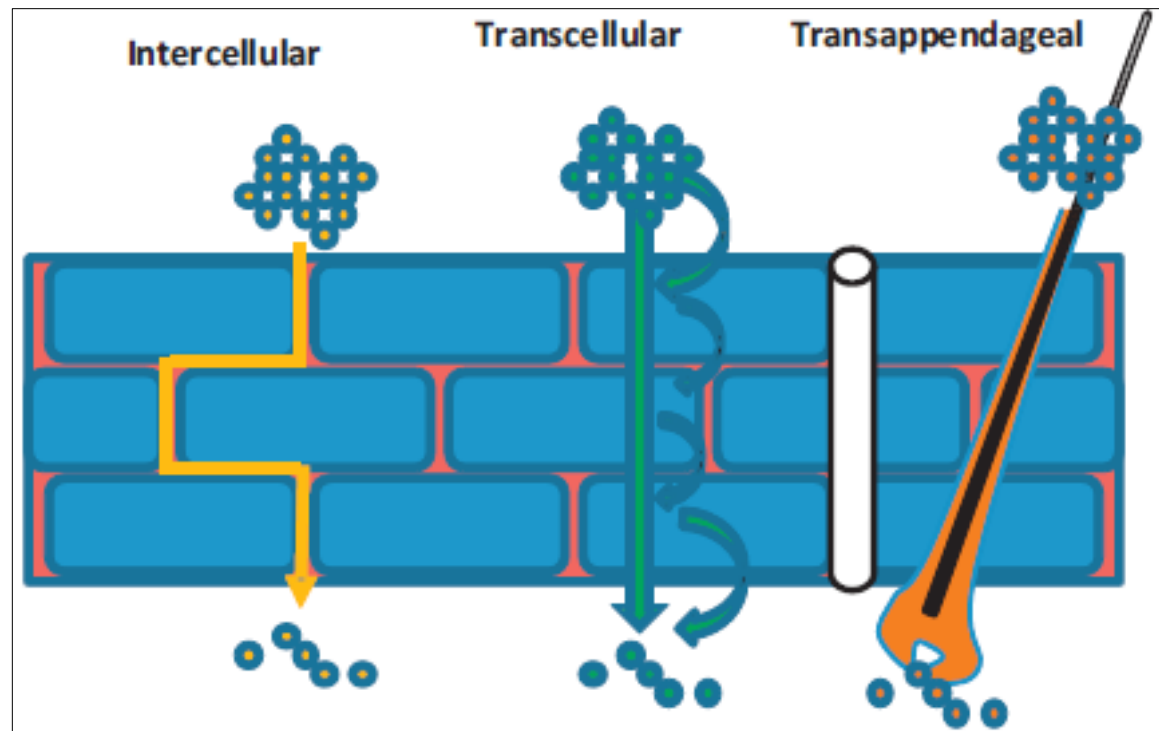
- The uppermost layer epidermis is subdivided into the viable **epidermis and superficial stratum corneum**;
- the major components of the viable epidermis are **keratinocytes**; furthermore, melanocytes and Langerhans cells also exist

Stratum corneum cells are keratin-rich cells called **corneocytes** which are terminally differentiated keratinocytes, polyhedral, acutely flatted, arranged in **15-25 layers** with 10-15 μ m thickness in a dry state, **pervaded with intercellular lamellar lipid bilayers** consists of a mixture of ceramides, cholesterol, cholesterol esters.

The stratum corneum is organized in a unique style comparable to a wall of "**bricks and mortar**" afford the skin its defensive, impermeable properties



- According to the heterogeneous skin anatomy, a drug molecule should penetrate the barrier of the stratum corneum to approach viable skin tissue through the well-acknowledged pathways, which are: **intercellular route, transcellular route, and trans appendageal route**



- The intercellular pathway is considered the essential route for drug penetration, in which the drug molecules pass through tortuous, lipid-rich gaps around the corneocytes
- The transcellular is direct path towered the dermis in which the penetrant molecules transported through corneocytes cytoplasm and extracellular lipid, the sequential series of partition and diffusion; inevitably, complicate the penetration process

- The trans appendageal route has minor contribution in transdermal transport as it occupies only 0.1% of skin surface area
- The penetrant molecules that overcome the stratum corneum barrier diffuse through viable epidermis to the dermis where the blood and lymphatic vessels eventually remove the drug from the skin to be absorbed