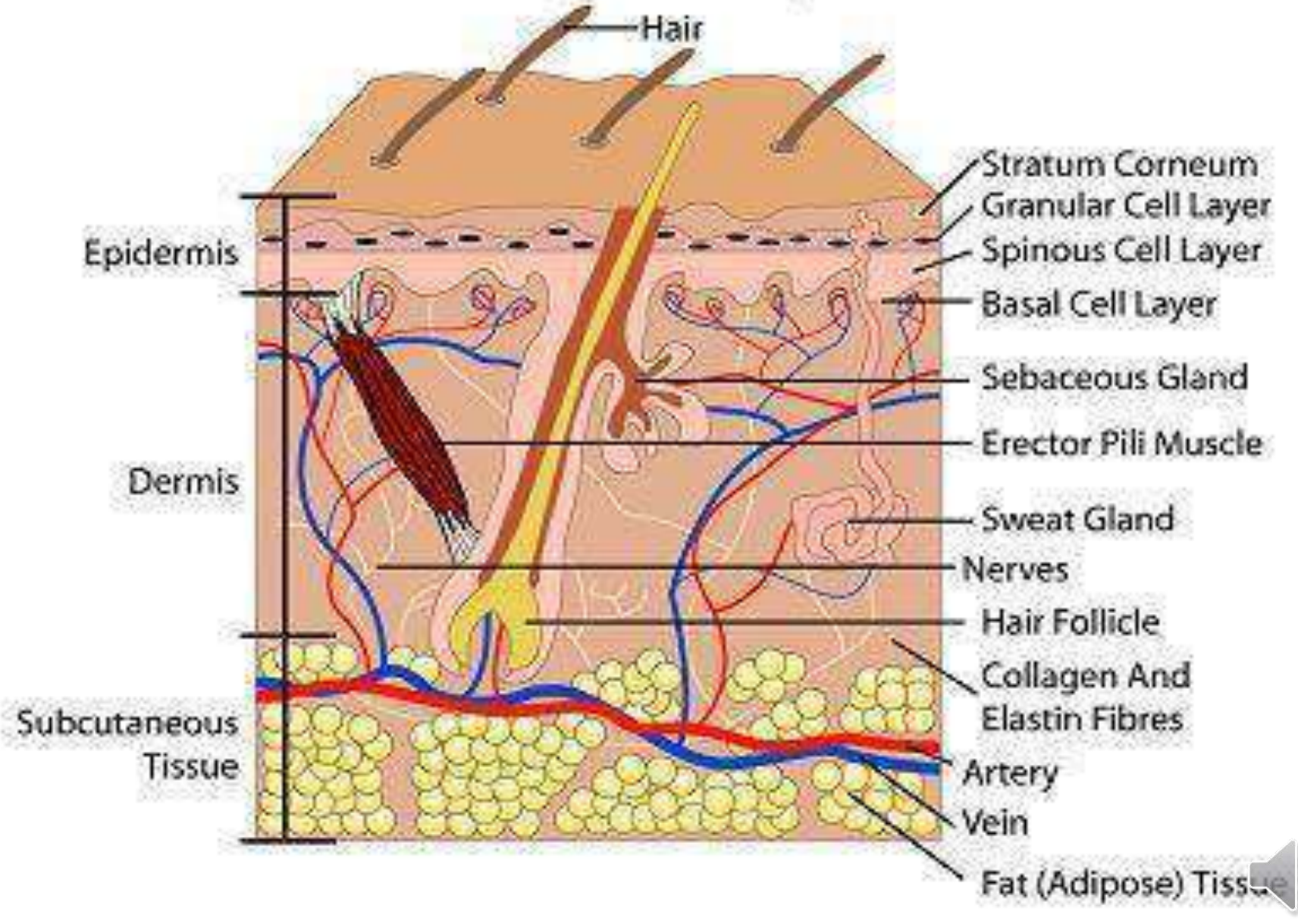
Pharmaceutics 1

Chapter 2

The skin & semisolid dosage form

Lecture 3

Human Skin Diagram



- The skin often has been referred to as the largest of the body organs: an average adult's skin has a surface area of about 2 m_2.
- It is probably the heaviest organ of the body. Anatomically, human skin may be described as a stratified organ with three distinct tissue layers:
- The epidermis,
- The dermis,
- The subcutaneous fat layer .

(1) Epidermis, the **outermost skin layer, consists of stratified squamous epithelial cells**. Keratinized, flattened remnants of these actively dividing epidermal cells accumulate at the skin surface as a relatively thin region (about 10–20 μm thick) termed **the stratum corneum, or horny layer.**

- The stratum corneum functions as a
- Protective physical and chemical barrier
- Is only slightly permeable to water ,
- It retards water loss from underlying tissues,
- Minimizes ultraviolet light penetration,
- Limits the entrance of microorganisms, medications, and toxic substances.

- Thus, it tends **to be thicker in regions more subject to abrasion. Its regeneration is provided by rapid cell division in basal cell layer of epidermis.**
- **An acidic film, (pH ranging between 4 and 6.5, depending on the area tested)** made up of **emulsified lipids, covers the surface of the stratum corneum.**

(2) The dermis can be described as a gel structure involving a fibrous protein matrix (including collagen and elastin fibers), the dermis supports and interacts with the epidermis, facilitating its conformation to underlying muscles and bones.

- Blood vessels, lymphatics, and nerves are found within the dermis, although only nerve fibers reach beyond the dermal ridges or papillae into the germinative region of the epidermis.

- Collagenous fibers from the dermis thread between the accumulations of fat cells, providing a connection between the superficial skin layers and the subcutaneous layer.
- Human skin has numerous surface openings (i.e., hair follicles and sweat glands) extending well into the dermis .
- Hair follicles, together with the sebaceous glands that empty into the follicles, make up the pilosebaceous unit.

Histology of skin

- The skin is divided histologically into the stratum corneum (the outer layer), the living epidermis, and the dermis, collectively a laminate of barriers protecting against permeation by external agents and loss of water from the body.
- Blood capillaries and nerve fibers rise from the subcutaneous fat into the dermis and up to the epidermis.
- Sebaceous glands, sweat glands, and hair follicles originating in the dermis and subcutaneous layers rise to the skin's surface

- The stratum corneum is the desquamating horny layer, a 10- to 15-μm thick layer of flat, partially desiccated, dead epidermal cells .

- The stratum corneum is composed of approximately 40% protein (mainly keratin) and 40% water, with the balance being lipid, principally as triglycerides, free fatty acids, cholesterol, and phospholipids.

- On the surface is afilm of emulsified material composed of a complex mixture of sebum, sweat, and desquamating epidermal cells.

- The film covering the stratum corneum varies in composition, thickness, and continuity as a result of
- differences in the proportion of sebum and sweat produced
- the extent of removal through washing & sweat evaporation.
- It offers little resistance to drug penetration.

- Hair follicles and gland ducts can provide entry for drug molecules, but because their relative surface area is so minute compared to the total epidermis, they are minor factors in drug absorption.

- The stratum corneum, being keratinized tissue, behaves as a **semipermeable artificial membrane**, and drug molecules can penetrate by **passive diffusion.**
- The rate of drug movement across this skin layer depends on
- the drug concentration in the vehicle,
- its aqueous solubility,
- and the oil–water partition coefficient between the stratum corneum and the product's vehicle .

- Substances with both aqueous and lipid solubility characteristics are good candidates for diffusion through the stratum corneum.
- Once through the stratum corneum, drug molecules may pass through the deeper epidermal tissues and into the dermis.
- If the drug reaches the vascularized dermal layer, it becomes available for absorption into the general circulation.

Drugs are applied to the skin to elicit one or more of four general effects:

1-an effect on the skin surface,

2-an effect within the stratum corneum

3- a more deep-seated effect requiring penetration into the epidermis and dermis,

4-a systemic effect resulting from delivery of sufficient drug through the epidermis and the dermis to the vasculature to produc therapeutic systemic concentrations.

1-An effect on the skin surface

- Drug activity on the skin surface may be in the form of a protective film (e.g., a zinc oxide cream), an action against surface microorganisms, or a cleansing effect.
- The vehicle must facilitate contact between the surface organisms and the active ingredient.

2-An effect within the stratum corneum

a-Sunscreens drug effects within the stratum corneum

;**p-aminobenzoic acid** is an example of a sunscreening agent that both penetrates and is substantive to stratum corneum cells.

b-Skin moisturization takes place within the stratum corneum.

Whether it involves the hydration of dry outer cells by surface films or the intercalation of water in the lipid-rich, intercellular laminae, the increased moisture results in the softening of the skin.

c- Keratolytic agents, such as salicylic acid, act within the stratum corneum to cause a breakup or sloughing of stratum corneum cell aggregates.

- **This is particularly important in conditions of abnormal stratum corneum such as psoriasis, a disease characterized by thickened, scaly plaques.**

3- a more deep-seated effect requiring penetration into epidermis &dermis,

- The examples on these drugs required to absorb deeply to the internal part of dermis as antiwrinkles drug

4-Systemic action of topical dosage form

- Successful candidates for transdermal drug delivery should be nonirritating and nonsensitizing to the skin.
- Since relatively little drug may reach systemic circulation over relatively long time, drug candidates should be relatively potent drugs.

- In addition, the limitation to relatively potent drugs can ease problems formulation, since the amount of drug that can be incorporated in the formulation may be limited by physicochemical considerations, such as solubility.

- Percutaneous absorption involves the transfer of drug from the skin surface into the stratum corneum, under the aegis of a concentration gradient, and its subsequent diffusion through the stratum corneum and underlying epidermis, through the dermis, and into the microcirculation.

- Occlusion of the skin surface also increases skin temperature (~2°–3°), resulting in increased molecular motion and skin permeation.
- Hydrocarbon bases that occlude the skin to a degree will bring about an increase in drug penetration.

The end of lecture