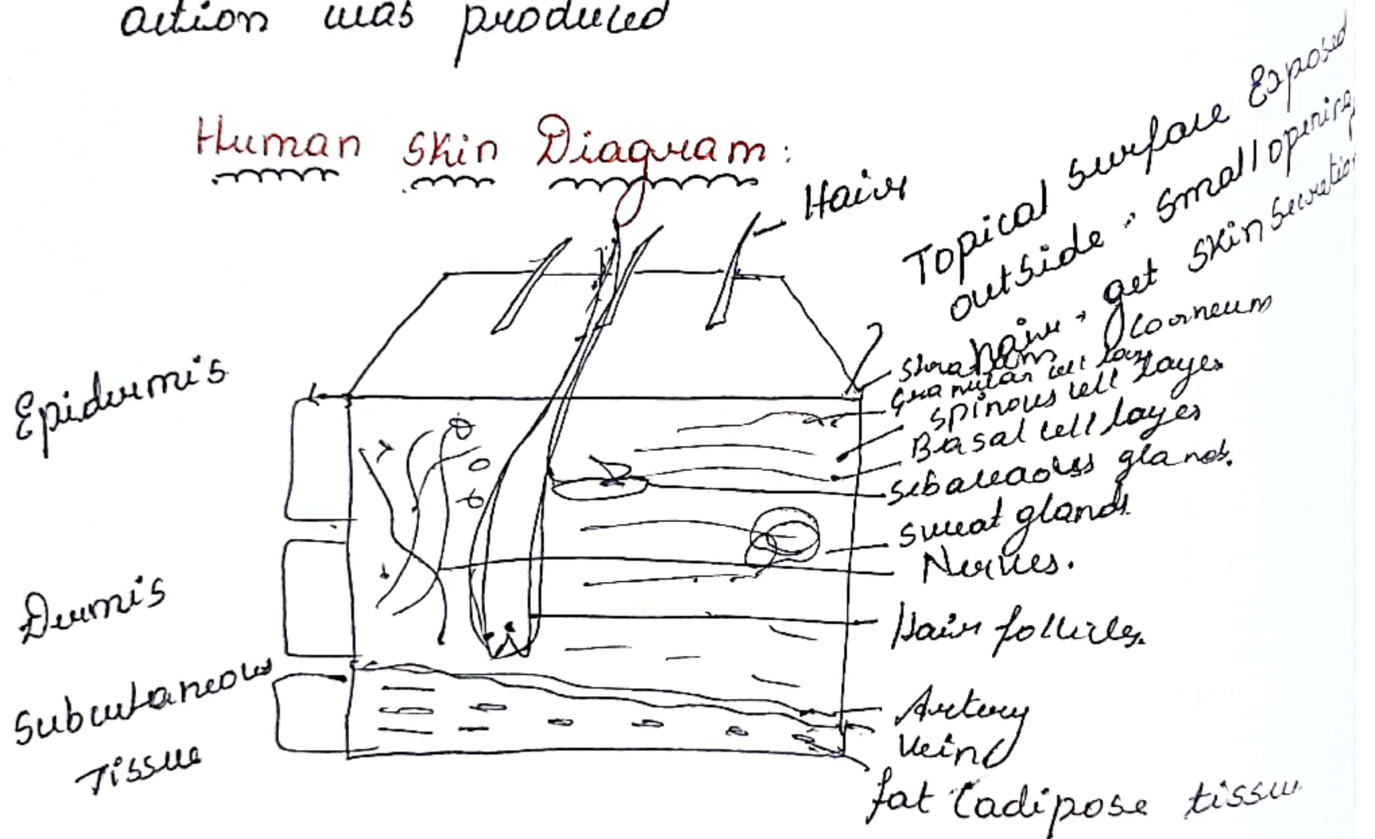


# Mechanism of dermal penetration of drugs

- Semi solid dosage forms are actually applied topically on the skin surface or mucous membrane
- Drug penetrates in to the surface as a result action was produced

## Human Skin Diagram:



- Consists of 3 layers:
- ① Epidermis
  - ② Dermis
  - ③ Subcutaneous tissue

## Epidermis:-

- outermost layer consists of

- ① Stratum Corneum
- ② Granular cell layer
- ③ spinous cell layer
- ④ Basal cell layer
- ⑤ sebaceous gland - release sebum  
↓  
which keeps the body hydrated

Dermis consists of

- ① Erector pill muscle
- ② Nerve Ending
- ③ Sweat Gland.
- ④ Hair follicle

Subcutaneous tissue:-

- ① Collagen kind, Elastic fibre
- ② Artery
- ③ Veins
- ④ fat (adipose) tissue

Excessive production of Glucose & Glycogen converted into fats accumulated beneath the surface of subcutaneous tissue layer.

- Drug applied on skin surface  
↓  
Dermal penetration occurs  
↓  
and eventually reaches → S.C layer  
↓  
Exchange of medicament & <sup>blood</sup> ~~drug~~ takes place b/w  
↓  
Sweat gland & Nerve fiber  
↓  
or in to the artery & vein

### Mechanism:

- Dermal penetration of drug occurs through skin  
→ Skin is very effective in selective absorption of drugs  
→ Epidermis layer is the major important controlling layer for drug penetration.

mechanism occurs through 3 routes

- ① Trans follicular Route
- ② Trans cellular Route
- ③ Intercellular Route

## Transfollicular route : (Appendage Route)

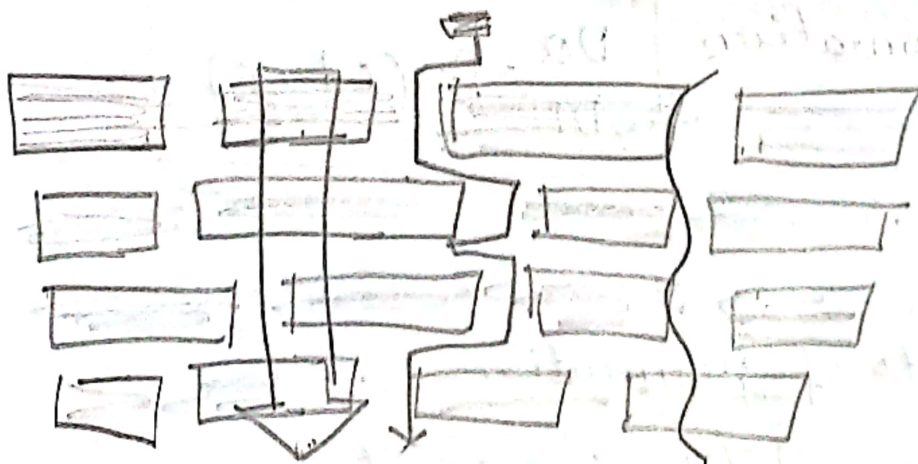
- Follicles are minor openings of the follicles of hair or the follicles of sebum through which dermal penetration of drug occurs
- It is the shortest pathway for drug passage and provides larger area for drug diffusion.
- Transfollicular pathway gives quick and rapid action

## Transcellular route :

- Drug passes through between 2 corneocytes which are hydrated hydrophilic pathway.

## Intercellular Route :-

- Drug diffuses through continuous lipid matrix present between the cells



Transcellular    Intercellular    Appendageal

- low molecular weight molecules penetrate easily through stratum corneum
- skin appendages are main route for electrolytes, polar steroids, antibiotics and colloidal particles
- Hair follicle route is important for penetration through stratum corneum
- Topical agents may form a depot or reservoir by attaching them with stratum corneum for longer duration.
- Average residence time of drug in dermis may be for a period of 1 min, before it gets washed away
- NSAIDs reach far down to muscles to form depots.

Rate of permeation

$$\frac{DQ}{DT} = P_s (C_d - C_r)$$

where

$\frac{DQ}{DT}$  = Rate of permeation

$P_s$  = permeability coefficient

$C_d$  = Concentration in donor compartment

$C_r$  = Concentration in Receptor compartment

# Factors influencing dermal penetration of Drugs

## Biological factors

- ① Skin conditions
- ② Skin age
- ③ Blood flow
- ④ Regional skin site
- ⑤ Skin metabolism
- ⑥ Species difference

## Physicochemical factors

- ① Skin hydration
- ② Diffusion coefficient
- ③ Drug solubility characters
- ④ Drug concentration
- ⑤ Penetration enhancers
- ⑥ Temperature & pH
- ⑦ Molecular size and shape

## Biological factors:

### Skin Condition:

- The penetration of drugs through skin is affected by age, disease, climate and injury.
- Drug absorption occurs rapidly in children
- Diseases and injured skin increases drug penetration.
- Drug penetration is <sup>less in</sup> healthy skin

### Skin age:

- young skin is more permeable than older
- Skin of the children are more sensitive to the drugs.

### Blood flow :

- Blood flow through the skin also affects the dermal penetration of drugs
- when blood flow is reduced, amount of drug penetration rises

### Regional skin site :

- Dermal penetration of drugs changes with varying of skin thickness
- Facial skin is generally more permeable compare to other body sites.

### Skin metabolism

- The skin metabolizes steroid hormones chemical carcinogens and some other drugs
- So skin metabolism determines efficacy of drug permeated through skin

### Species difference :

- The condition and thickness of skin varies in different species
- Mice, rat, rabbits have more follicles but they lack sweat glands, so drug penetration is different in their skin compare to human skin

## Physico-chemical factors

### Temperature & pH

- The increase in temperature increases the dermal penetration of drugs through skin
- Drugs with pH value near 5 easily penetrate through skin

### Skin hydration

- when the amount of water is sufficient on in excess the tissue swells & softens.
- Drugs through this softens tissues easily penetrates the skin
- Hence, hydration rises drug penetration

### Diffusion Co-efficient

- Diffusion coefficient of drug depends on the properties of drug & diffusion medium

### Drug solubility

- Highly lipid soluble drugs easily penetrate the skin compare to hydrophilic drugs.

### Drug concentration

- Drug penetration depends upon the concentration gradient
- Concentration gradient will be higher if concentration of drug will be more across

The barrier

### penetration Enhancers

Dimethyl Sulphoxide (DMSO)

Dimethyl formamide (DMF)

Azone

} widely used as  
penetration  
Enhancers

→ These solvates the subcutaneous and bring  
configuration changes in skin protein structure

↓  
Results in swelling

↓  
as a result drug gets easily penetrated  
through the skin

### Molecular Size & Shape

1) Penetration of drugs inversely depends  
on size

2) Small particles penetrates faster than  
larger ones