Transdermal drug delivery system

Transdermal drug delivery system

- **Definition:**

- Transdermal drug delivery systems are defined as a self contained discrete dosage forms, which when applied to the intact skin, will deliver the drug at a controlled rate to the systemic circulation.

- Transdermal delivery may be defined as the delivery of a drug through ‘intact’ skin so that it reaches the systemic circulation in sufficient quantity, to be beneficial after administration of a therapeutic dose.

Transdermal drug delivery system

- Transdermal systems are ideally suited for diseases that demand chronic treatment.

- Topical formulations containing drugs showing systemic action are called **transdermal delivery systems** (TDS) or **transdermal therapeutic systems** (TTS).

Transdermal drug delivery system

Advantages

- Can avoid gastrointestinal drug absorption difficulties covered by gastrointestinal pH, enzymatic activity and drug interaction with food, drink and other orally administered drugs.

- Can **substitute oral administration** of medication when the route is unsuitable as with vomiting and diarrhea.

- To avoid the **first pass effect** e.g. Transdermal Nitroglycerin. It is rapidly metabolized by the liner when taken orally.

- **Noninvasive**, avoiding the inconvenience of parenteral therapy.

- They provided **extended therapy** with a single application, improving compliance over other dosage forms requiring more frequent dose administration e.g. (Transdermal clonidine 7 day).

- The activity of drugs having a start half life is extended through the **reservoir of drug** in the therapeutic delivery system and its controlled release.

- Drug therapy may be **terminated rapidly** by removal of the application from the surface of the skin.

Disadvantages

- Some patients develop contact **dermatitis** at the site of application from one or more of the system components, necessitating discontinuation.
- Only **potent drugs** are suitable candidates for transdermal patch because of the natural limits of drug entry imposed by the skin's impermeability.
- Long time **adhere** is difficult.

ANATOMY AND PHYSIOLOGY OF SKIN

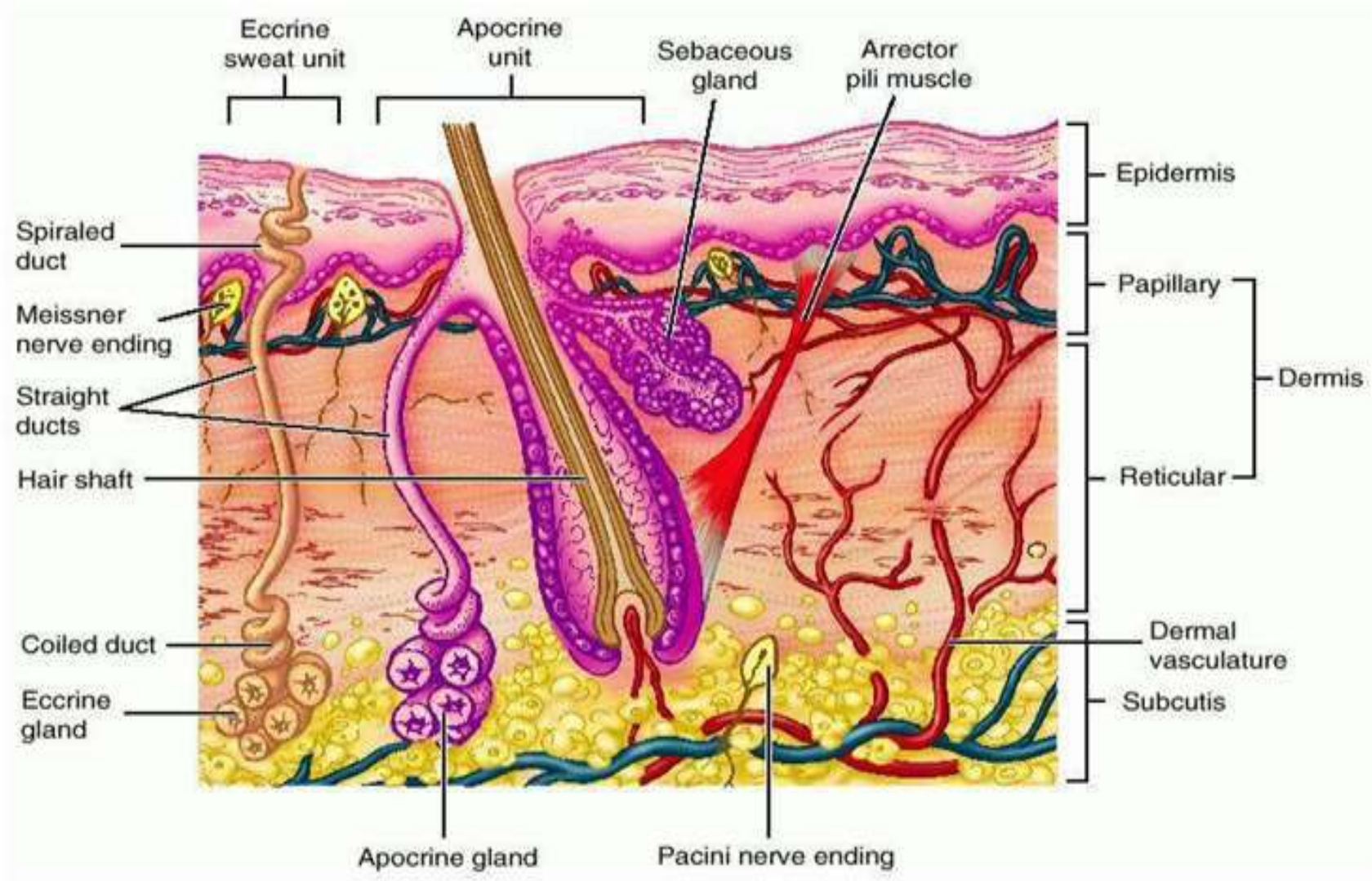


Figure 1: Anatomy of Skin

Routes of drug absorption through skin

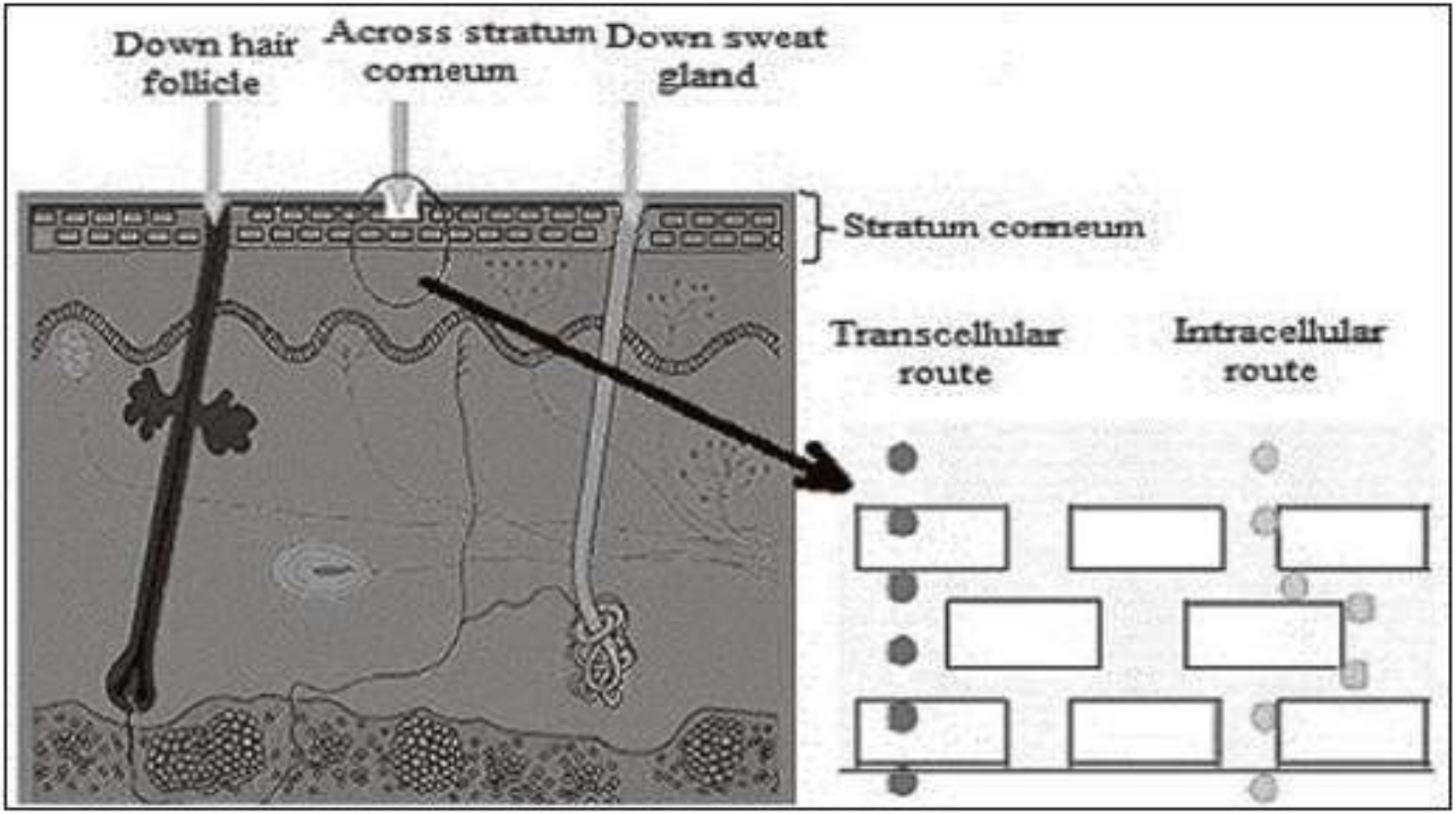
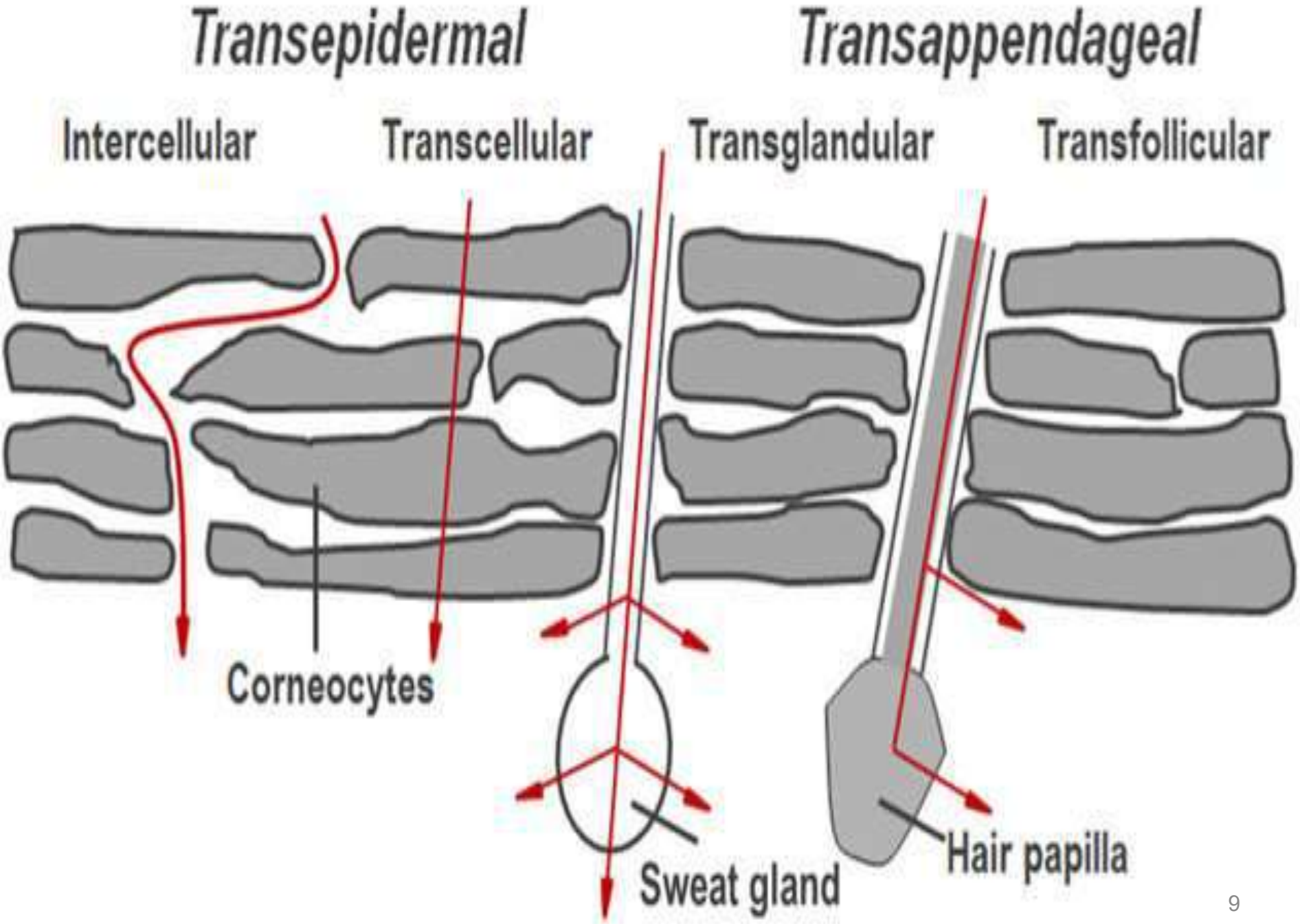


Figure 2: Drug penetration pathways across skin


Transepidermal
Transappendageal
Intercellular
Transcellular
Transglandular
Transfollicular
Corneocytes
Sweat gland
Hair papilla

BASIC COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEM

COMPONENT OF TRANSDERMAL DEVICE INCLUDE:

1) POLYMER MATRIX.

2) THE DRUG.

3) PERMEATION ENHANCER.

4) OTHER EXCEPIENTS.

Basic components of Transdermal drug delivery

Backing

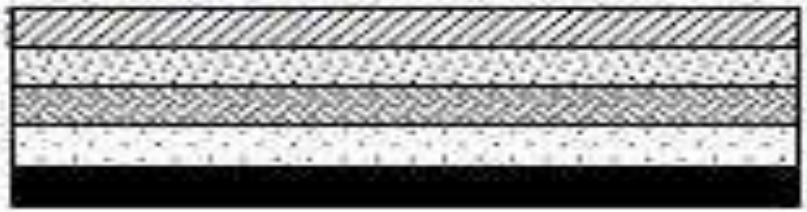
Drug

Membrane

Adhesive

Liner

Reservoir system



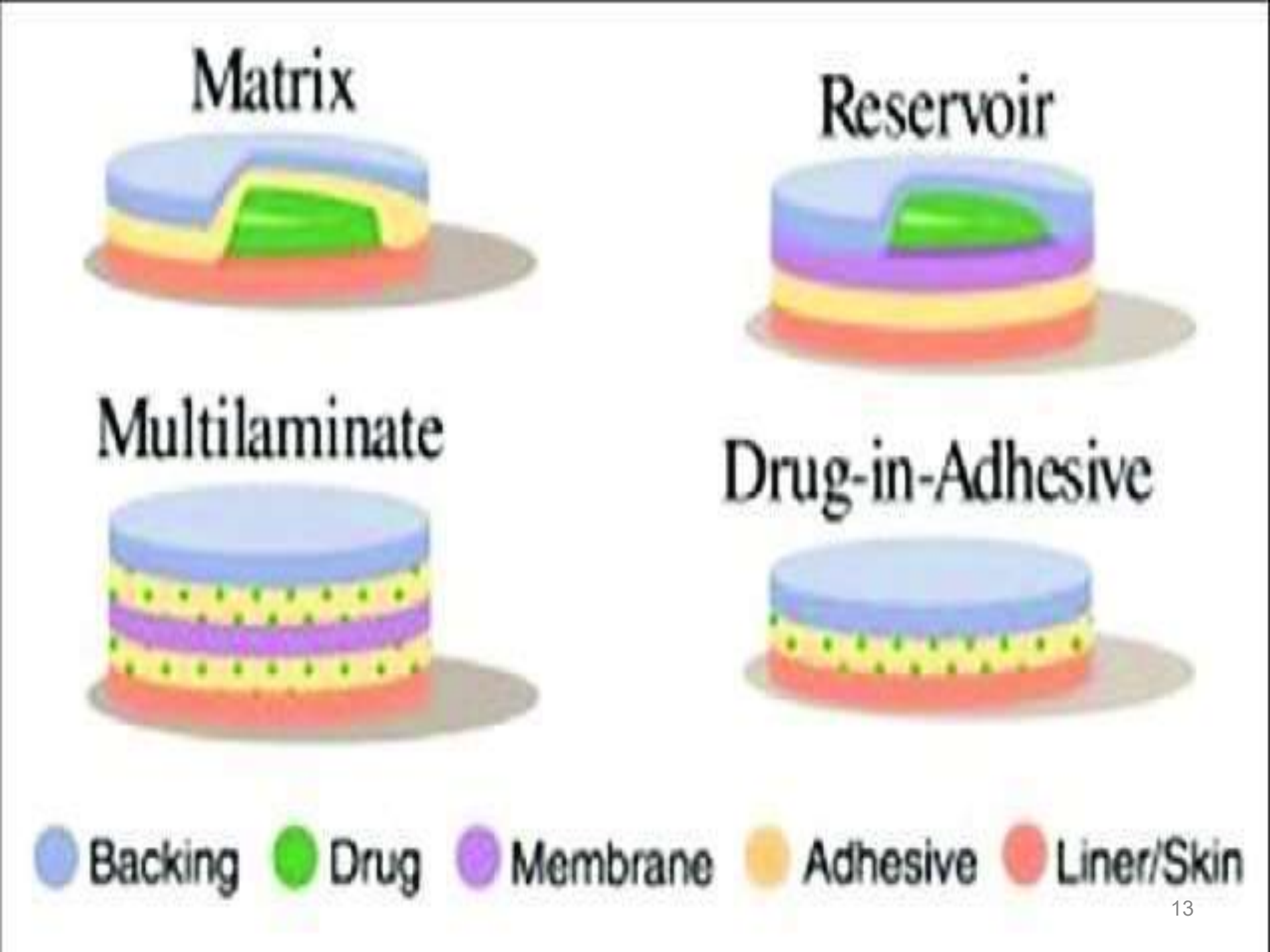
- Backing
- Drug reservoir
- Membrane
- Drug-in-adhesive
- Liner

Matrix system without a rate-controlling membrane

- Backing
- Drug-in-adhesive
- Liner

Matrix system with a rate-controlling membrane

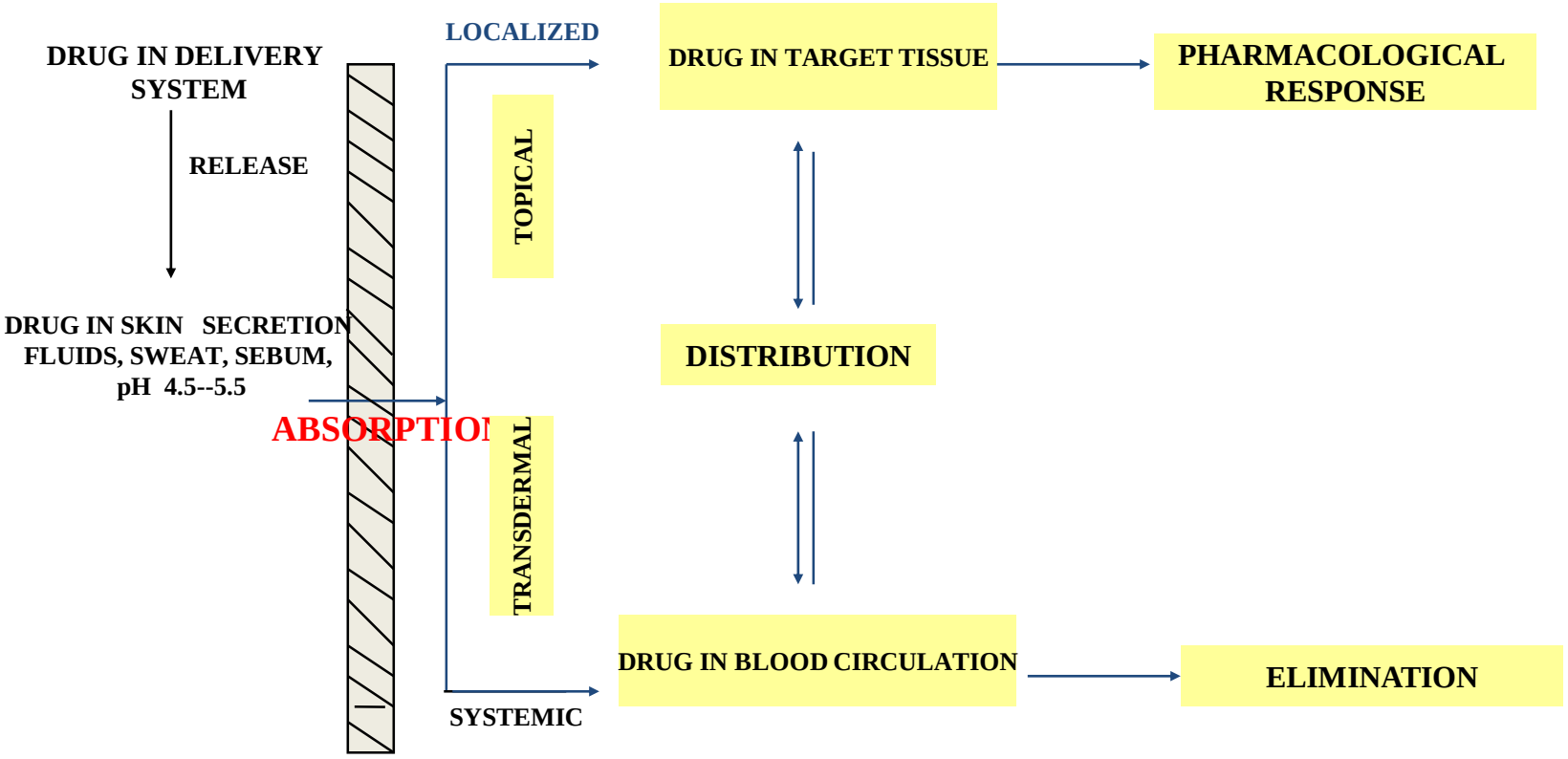
- Backing
- Drug-in-adhesive
- Membrane
- Drug-in-adhesive
- Liner


Matrix
Reservoir
Multilaminate
Drug-in-Adhesive
Backing
Drug
Membrane
Adhesive
Liner/Skin

The various steps involved in transport of drug from patch to systemic circulation are as follows:

- ✓ Diffusion of drug from drug reservoir in the rate controlling membrane.
- ✓ Diffusion of drug from rate limiting membrane to stratum corneum.
- ✓ Sorption by stratum corneum and penetration through viable epidermis.
- ✓ Uptake of drug by capillary network in the dermal papillary layer.
- ✓ Effect on target organ.

Topical application-absorption & action of drugs



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KINETICS OF TRANSDERMAL PERMEATION

Transdermal permeation of a drug involves the following steps:

- Sorption by stratum corneum.
- Penetration of drug through epidermis.
- Uptake of the drug by the capillary network in the dermal papillary layer.

KINETICS OF TRANSDERMAL PERMEATION

This permeation can be possible only if the drug possesses certain physiochemical properties. The rate of permeation across the skin is given by:

$$dQ/dt = Ps\ (Cd - Cr)$$

Where **Cd and Cr** are the concentration of the skin penetrant in the donor compartment i.e. on the surface of stratum corneum and in the receptor compartment i.e. **body respectively**. **Ps** is the overall permeability coefficient the skin tissue to the penetrant.

KINETICS OF TRANSDERMAL PERMEATION

❖This permeability coefficient is given by the relationship:

$$Ps = Dss\ Ks/\ hs$$

Where;

Ks: is the partition coefficient for the interfacial partitioning of the penetrant molecule from a solution medium or a transdermal therapeutic system on to the stratum corneum

Dss: is the apparent diffusivity for the steady state diffusion of the penetrant molecule through a thickness of skin tissues and **hs:** is the overall thickness of skin tissues.

Formulation of transdermal drug delivery system

Drug substance:

For successfully developing a transdermal drug delivery system, the drug should be chosen with great care. The following are some of the desirable properties of a drug for transdermal delivery.

Formulation of transdermal drug delivery system

A. Drug substance

Physicochemical properties:

- The drug should have a molecular weight less than 1000 Daltons.
- The drug should have affinity for both lipophilic and hydrophilic phase.
- The drug should have low melting point.
- **Drug should be very potent ,i.e. it should be effective in few mg/day**

Formulation of transdermal drug delivery system

B. Biological Properties:

- The drug should not be irritant and non allergic to human skin.
- The drug should be stable when contact with the skin.
- They should not stimulate an immune reaction to the skin.
- Dose is less than 50 mg per day and ideally less than 10 mg per day.
- The drug should not get irreversibly bound in the subcutaneous tissue.
- The drug should not get extensively metabolized in the skin.

Formulation of transdermal drug delivery system

C. Polymer matrix:

Polymers are the **backbone** of transdermal drug delivery systems. System for transdermal delivery are fabricated as multi layered polymeric laminates in each a drug reservoir or a drug polymer matrix is sandwiched between two polymeric layers, an outer impervious backing layer that prevents the loss of drug through the backing surface and an inner polymeric layer that functions as an adhesive, or rate controlled membrane.

Formulation of transdermal drug delivery system

Ideal properties of a polymer to be used in a transdermal system:

- The polymer should be stable.
- The polymer should be nontoxic .
- The polymer should be easily of manufactured.
- The polymer should be inexpensive.
- The polymer and its deaggration product must be non toxic.
- Large amounts of the active agent are incorporated into it.

Formulation of transdermal drug delivery system

TABLE 2: USEFUL POLYMERS FOR TRANSDERMAL DEVICES

Natural Polymers	Synthetic Elastomers	Synthetic Polymers
Cellulose derivatives	Polybutadiene	Polyvinylalcohol
Arabino Galactan	Hydrinrubber	Polyethylene
Zein	Polysiloxane	Polyviny Chloride
Gelatin	Acrylonitrile	Polyacrylates
Proteins	Neoprene	Polyamide
Shellac	Chloroprene	Acetal copolymer
Strarch	Silicon rubber	Polysyrene

Formulation of transdermal drug delivery system

Penetration Enhancers:

These are compounds which promote the skin permeability by altering the skin as barrier to the flux of a desired penetrate.

Surfactants	Na-lauryl sulfate Polyoxyethylene-9-laurylether, Bile salts: Na-deoxycholate Na-glycocholate Na-taurocholate
Fatty acids	Oleic acid,
Cyclodextrins	α-, β- and γ cyclodextrins, Methylated β cyclodextrins
Chelating agents	EDTA, Polyacrylates
Positively charged polymer	Chitosan salts, Trimethyl chitosan

Factors affecting transdermal permeation

A. Biological factors:

1. Skin conditions (complex dense structure of stratum cornium).

2. Skin age: Adults and young ones are more permeable than the older ones. Children shows toxic effects because of the greater surface area per unit body weight, thus potent steroids, boric acid, hexachlorophene have produced severe side effects.

3. Blood Supply: Changes in peripheral circulation can affect transdermal absorption.

Factors affecting transdermal permeation
Biological factors

4. Regional skin site: Thickness of skin, nature of stratum corneum and density of appendages vary site to site. These factors affect significantly the transdermal penetration.

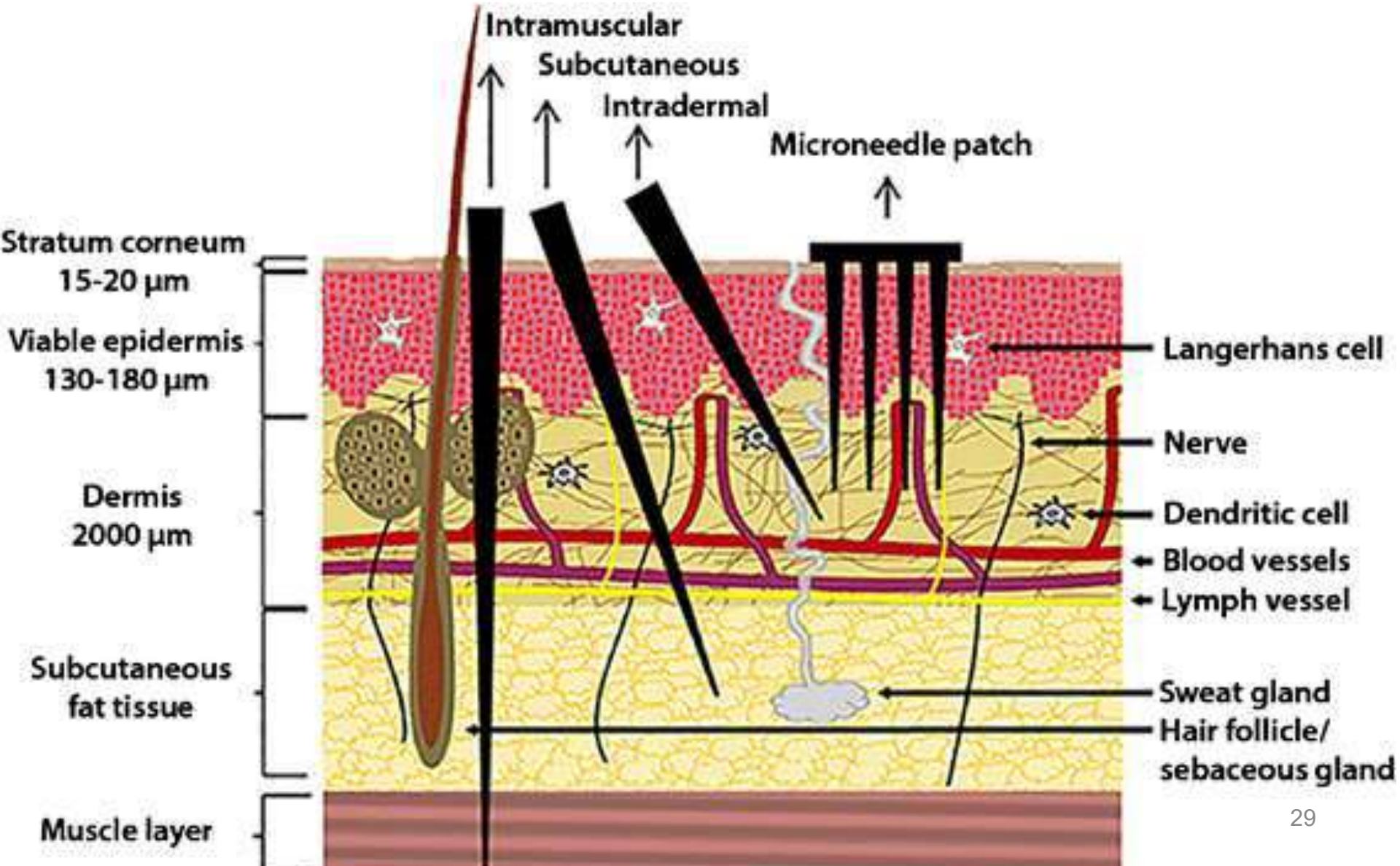
5. Skin metabolism: Skin metabolizes steroids, hormones, chemical carcinogens and some drugs, so skin metabolism determines efficacy of drug permeated through the skin.

6. Species differences: The skin thickness, density of appendages of skin vary species to species, so affects the penetration. (**Inter and intraindividual variability)**

Factors affecting transdermal permeation
Physicochemical factors

- **Skin hydration:** In contact with water the permeability of skin increases significantly. Hydration is most important factor increasing the permeation of skin.
- **Temperature and pH:** The permeation of drug increases ten folds with temperature variation. The diffusion coefficient decreases as temperature falls.
- **Diffusion coefficient and Partition coefficient:** Penetration of drug depends on diffusion coefficient of drug. At a constant temperature the diffusion coefficient of drug depends on properties of drug, diffusion medium and interaction between them.
- **Drug concentration:** The flux is proportional to the concentration gradient across the barrier and concentration gradient will be higher if the concentration of drug will be more across the barrier.
- **Molecular size and shape:** Drug absorption is inversely related to molecular weight, small molecules penetrate faster than large ones.

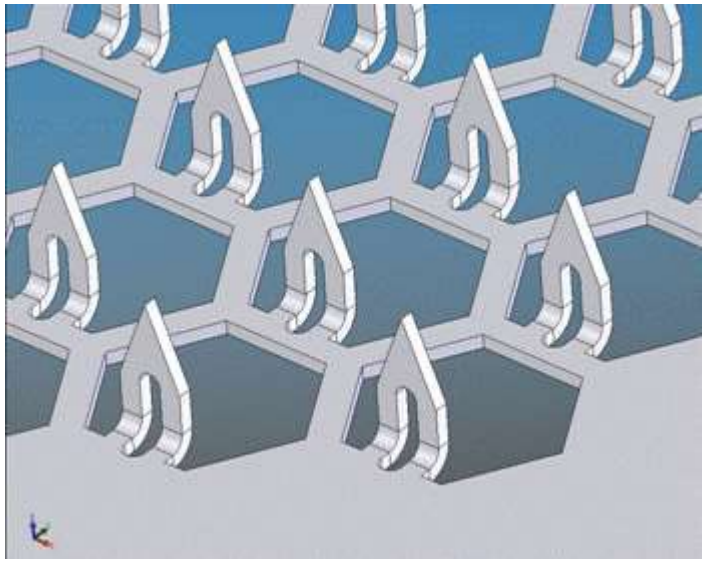
ADVANCED RESEARCHES



ADVANCED RESEARCHES

MICROARRAY NEEDLE

- Advanced micro-needle Patch transdermal system allowing continuous delivery through the skin of proteins and water-soluble drugs.



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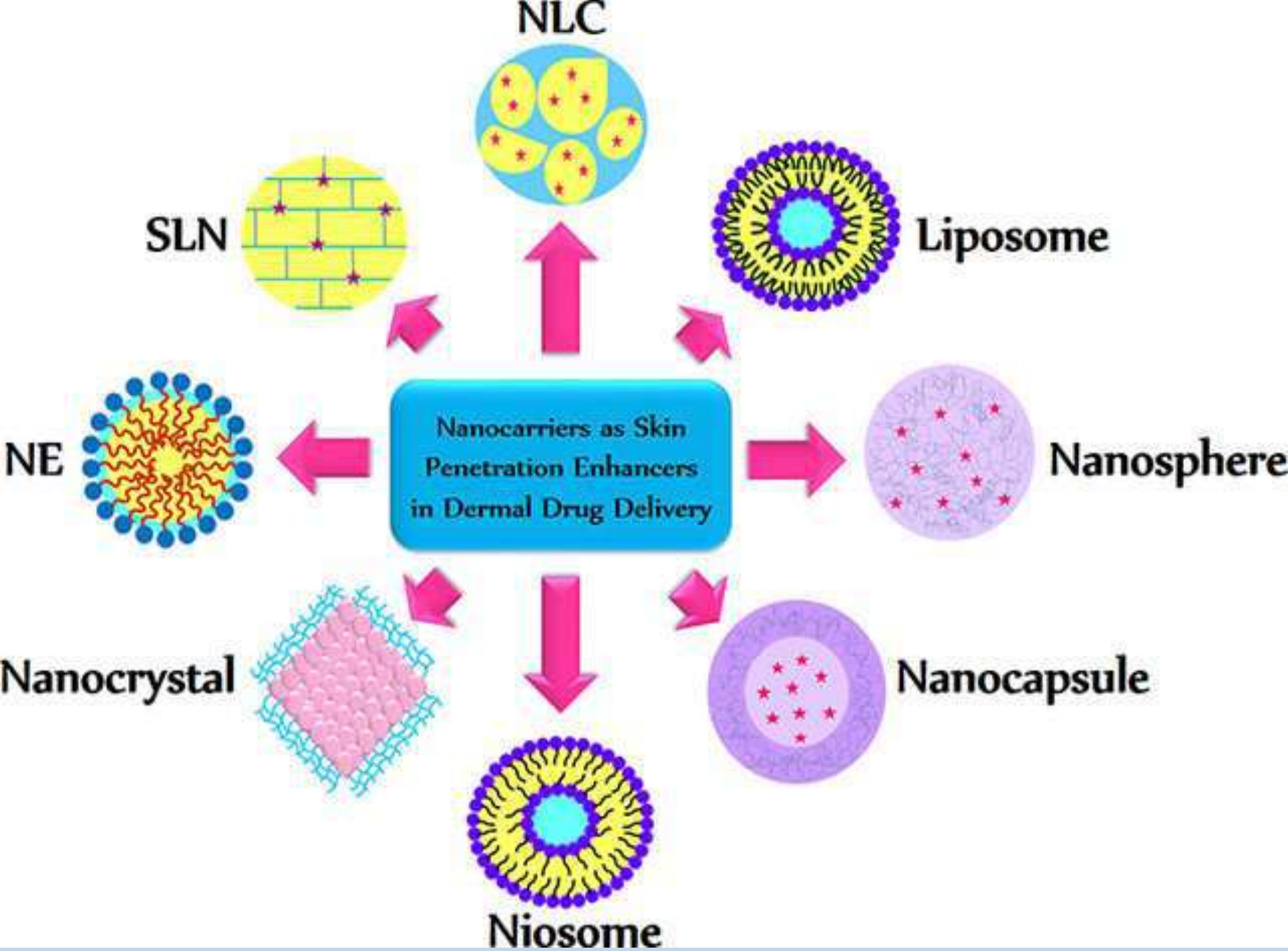
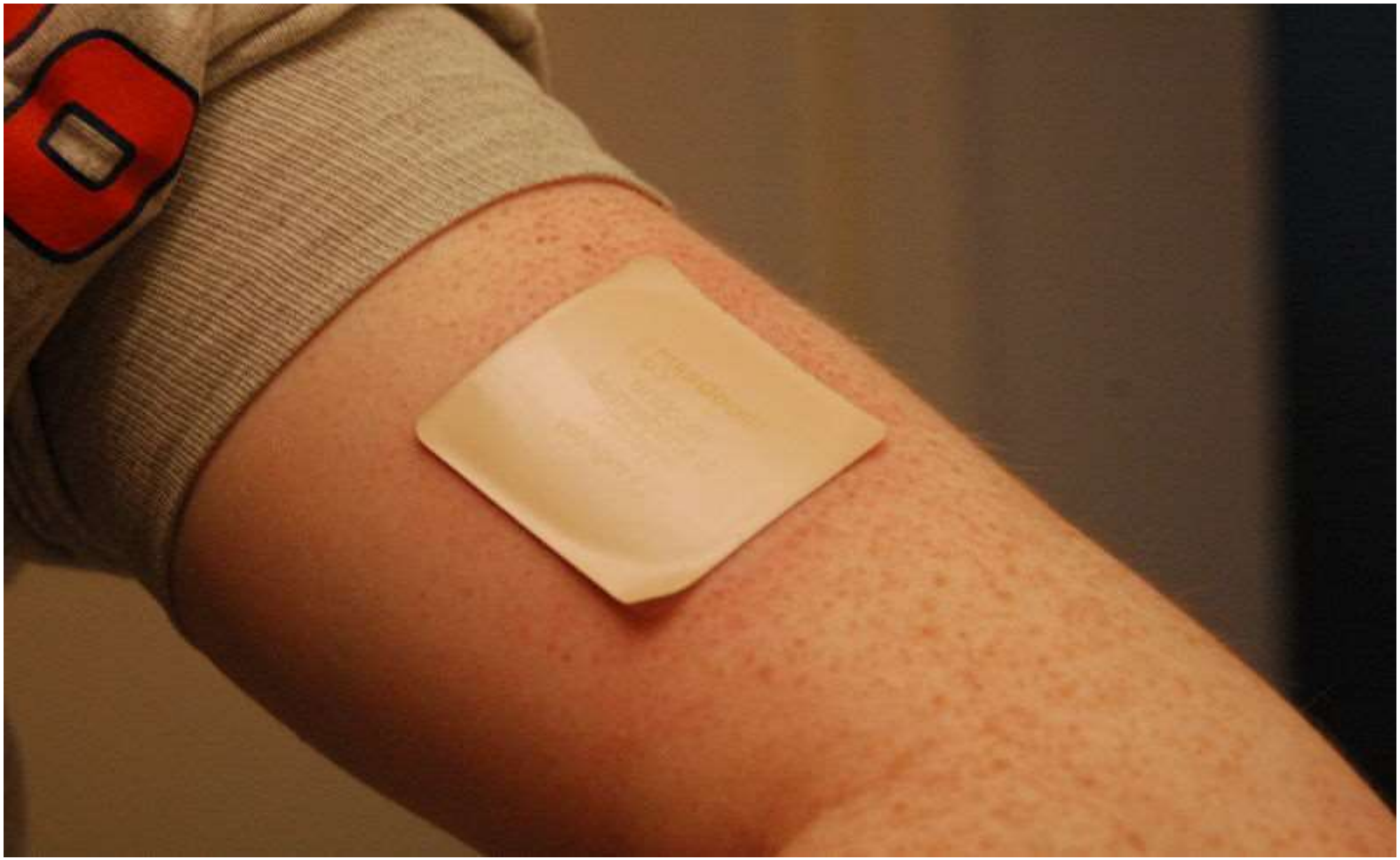

NLC
SLN
Liposome
NE
Nanocarriers as Skin Penetration Enhancers in Dermal Drug Delivery
Nanosphere
Nanocrystal
Nanocapsule
Niosome

Find an appropriate place to put the patch



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GOOD LUCK