Transdermal drug delivery system

Dr. Meenakshi Gupta
Senior Assistant Professor
University Institute of Pharmacy
C. S. J. M. University Kanpur U.P

Transdermal drug delivery system

- **Definition:**

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

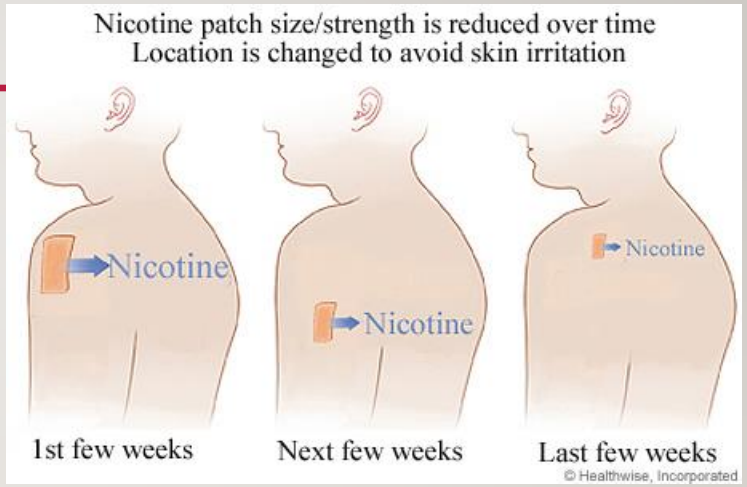
POTENTIAL BENEFITS OF TRANSDERMAL DRUG DELIVERY (ADVANTAGES)

- Easy to use.
- Avoid GIT absorption problems for drugs.
- Avoids FP hepatic metabolism of drugs.
- More improved and convenient patient compliance.
- Rapid termination in case of toxicity is possible.
- Self medication is possible.
- Reduces frequency of dosing.
- Maintains therapeutic level for 1 to 7 days.
- Controlled delivery resulting in more reliable and predictable blood levels.

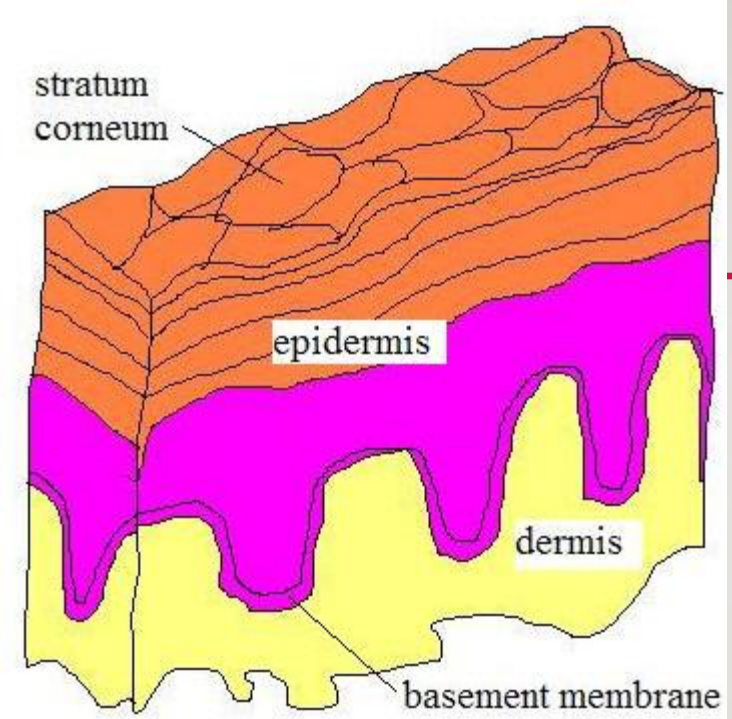
DISADVANTAGES

- Daily dose of more than 10mg is not possible.
- Local irritation is a major problem.
- Drug requiring high blood levels are unsuitable.
- Drug with long half life can not be formulated in TDDS.
- Uncomfortable to wear.
- May not be economical.
- Barrier function changes from person to person and within the same person.
- Heat, cold, sweating (perspiring) and showering prevent the patch from sticking to the surface of the skin for more than one day. A new patch has to be applied daily.

LIMITATIONS OF TRANSDERMAL DELIVERY SYSTEMS



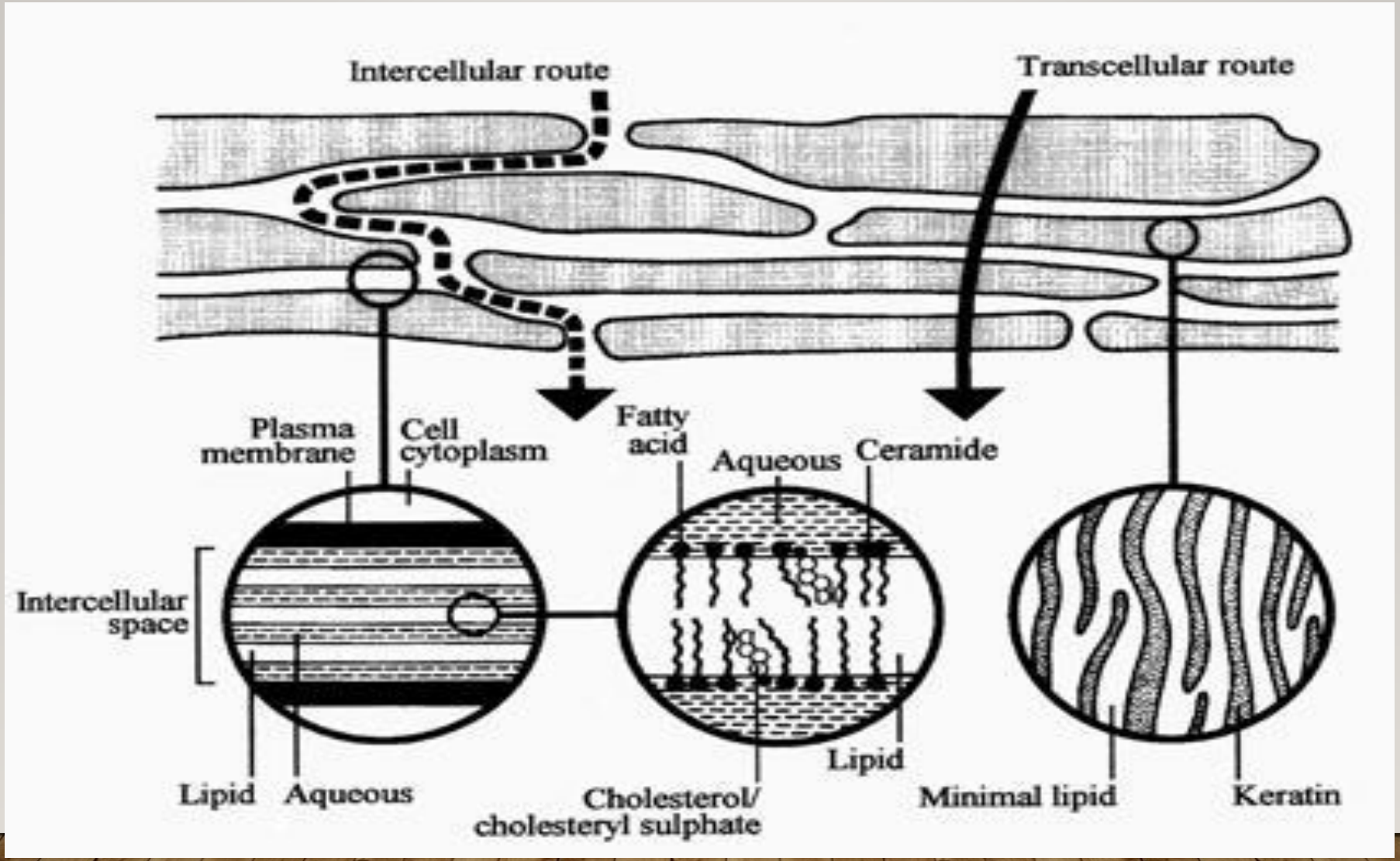
- Skin structure poses a barrier on the mw of the drug (< 500 Da)
- Usually reserved for drugs which are extremely potent (thus requiring a dosage of only a few mg).
  - The largest daily dose of a drug from a patch is the nicotine patch, with delivers a daily dose of only 21 mg.



The drug must traverse three layers, the stratum cornium, the epidermis, and the dermis.

Of these, the toughest barrier is the stratum corneum, which consists of 10-25 layers of keratinized cells.

ROUTES OF DRUG ABSORPTION THROUGH SKIN



FACTORS AFFECTING TRANSDERMAL PERMEABILITY

- **Physico chemical properties of parent molecule**
- **Physico chemical properties of drug delivery system**
  - **Physiological and pathological condition of skin**
  - **Biological factors**

WHAT KIND OF DRUGS CAN BE INCORPORATED INTO A PATCH?

- Compounds with low logP will not diffuse into skin lipids
- However, compounds with high logP also have difficulties, this time associated with their diffusion out of the stratum corneum.
- The accepted range of logP values is between 1 and 3.

BASIC COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEM

COMPONENT OF TRANSDERMAL DEVICE INCLUDE:

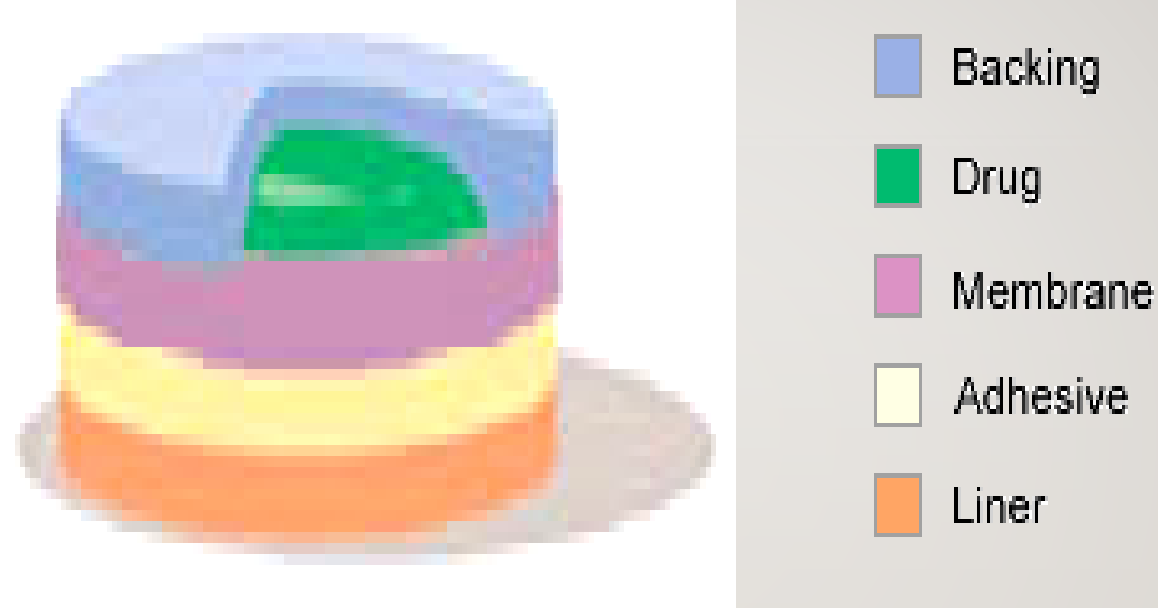
1) POLYMER MATRIX

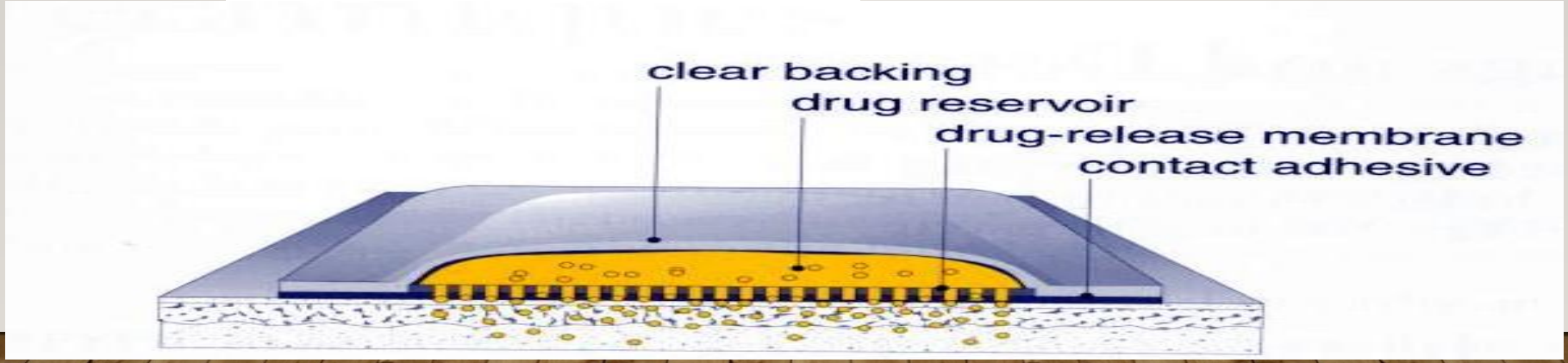
2) THE DRUG

3) PERMEATION ENHANCER

4) OTHER EXCEPIENTS

BASIC COMPONENTS OF TRANSDERMAL DRUG DELIVERY

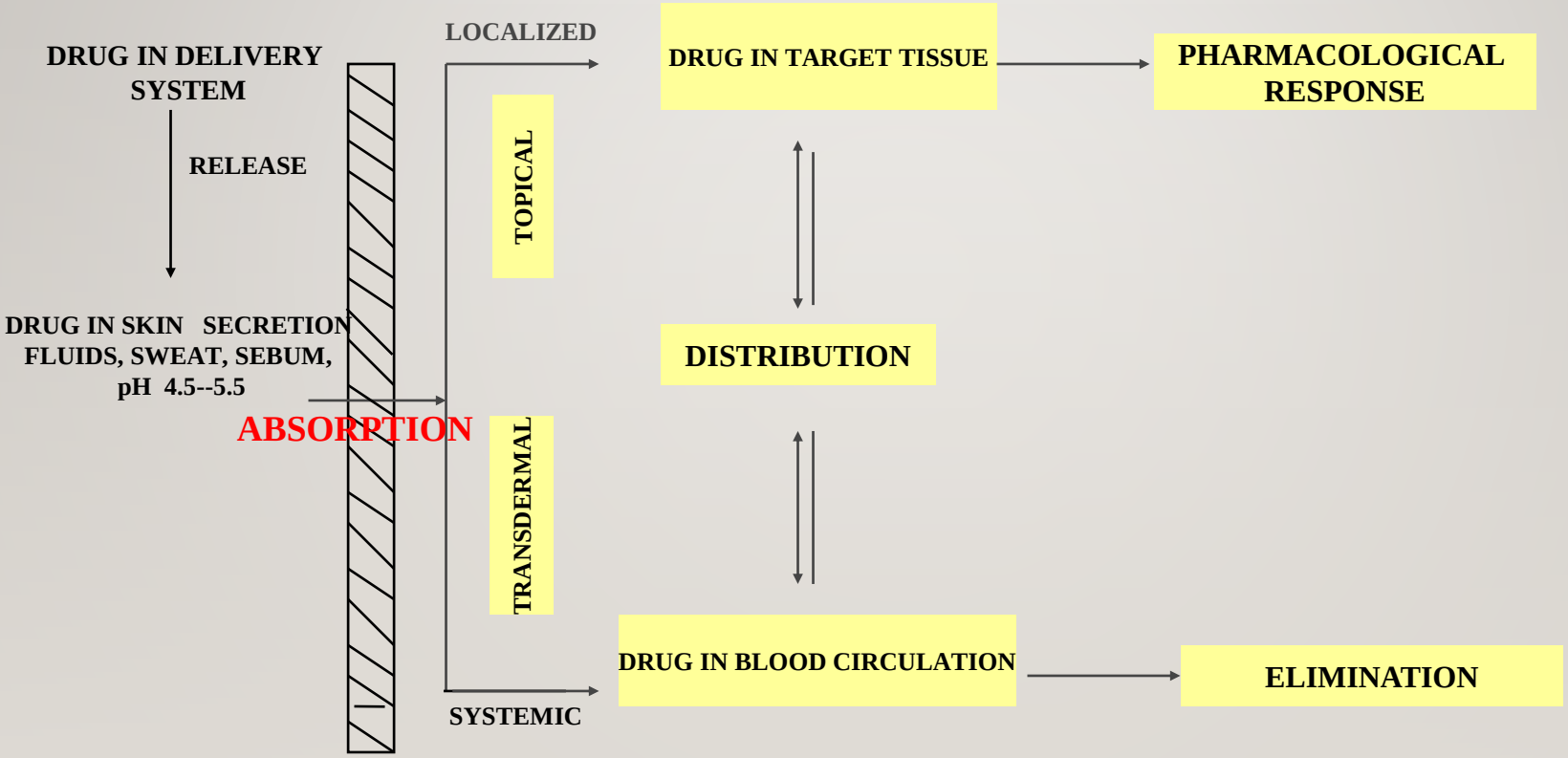




TYPES OF PATCHES: DEFINITIONS

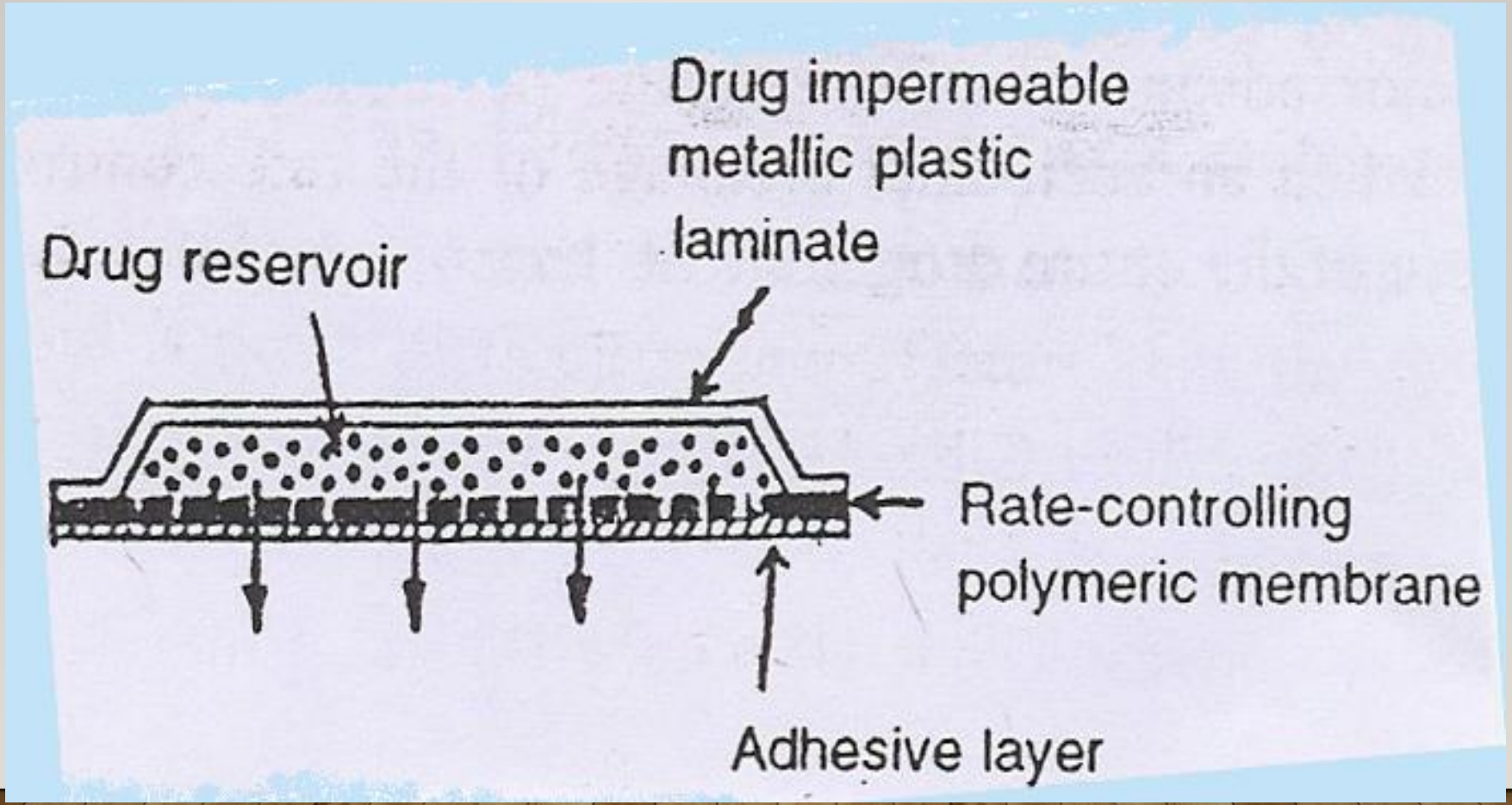
- Liner: Protects the drug during storage and is removed prior to use
- Drug
- Adhesive: Serves to bind the components of the patch to the skin
- Membrane: Controls the release of the drug from the reservoir in certain types of patches
- Backing: Protects the patch from the outer environment.

Topical application-absorption & action of drugs

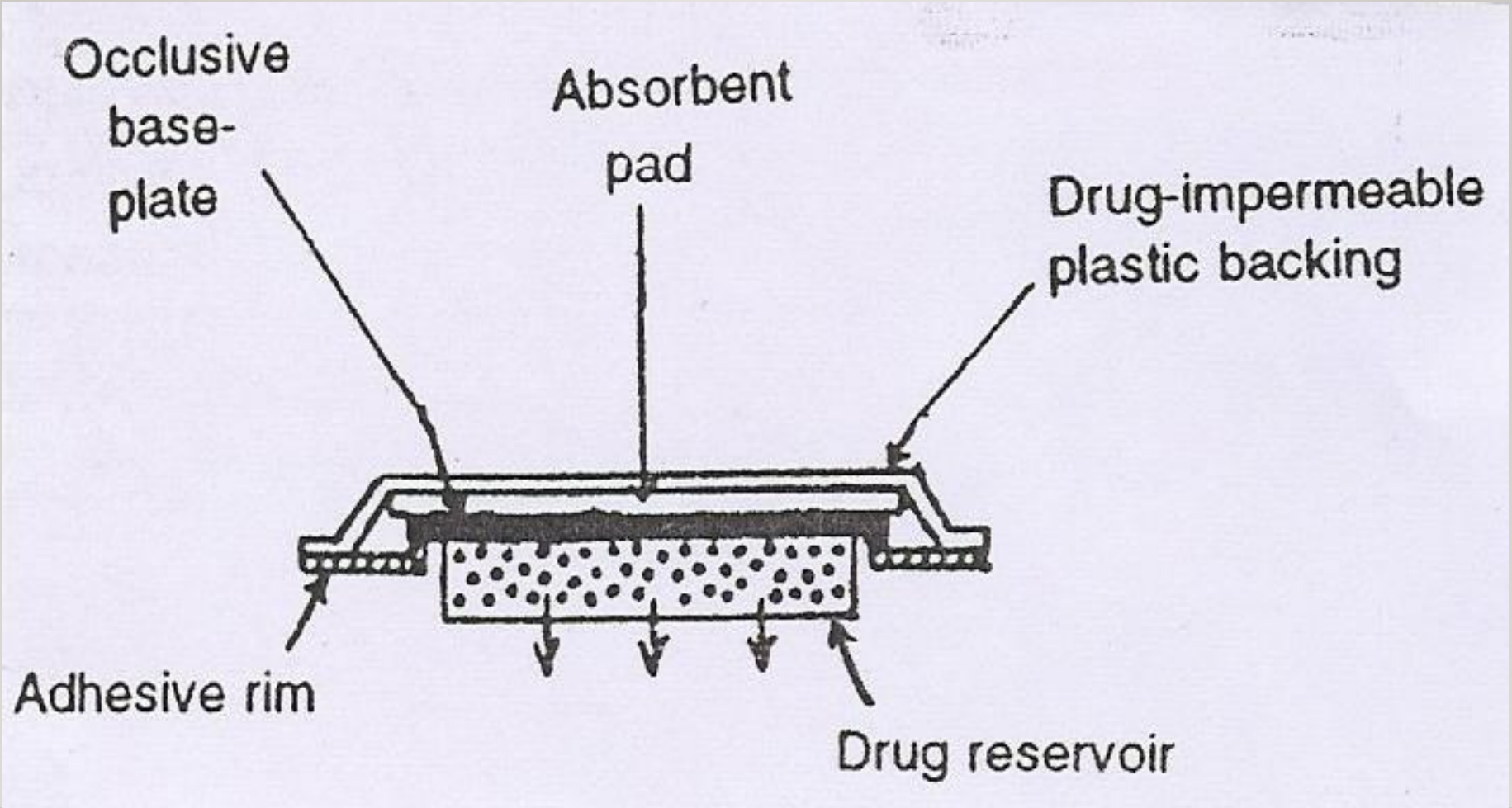


FORMULATION APPROACHES FOR DEVELOPMENT OF TRANSDERMAL DRUG DELIVERY SYSTEM

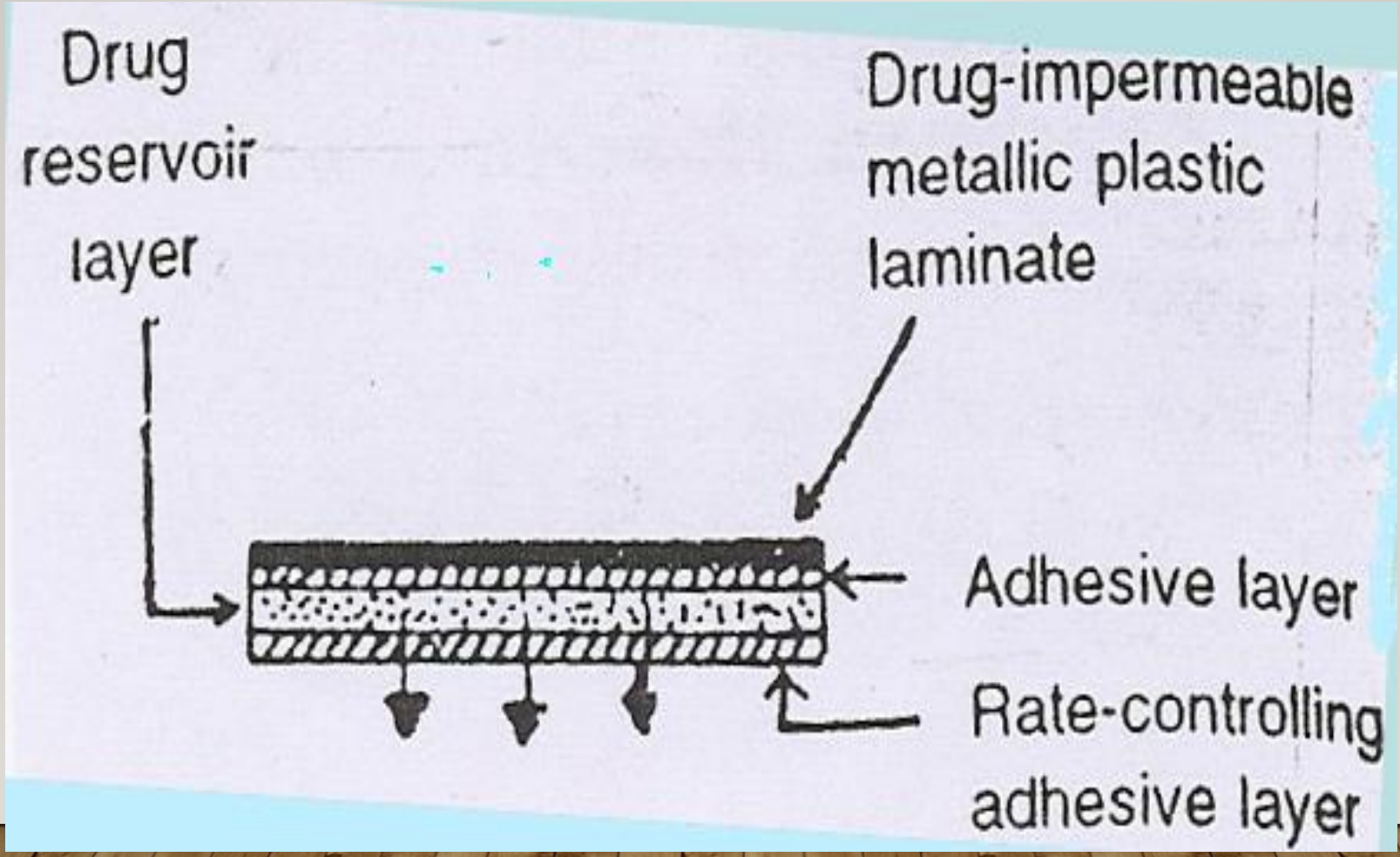
1. POLYMER MEMBRANE PERMEATION CONTROLLED SYSTEM



2. POLYMER MATRIX DIFFUSION CONTROLLED TDDS SYSTEM

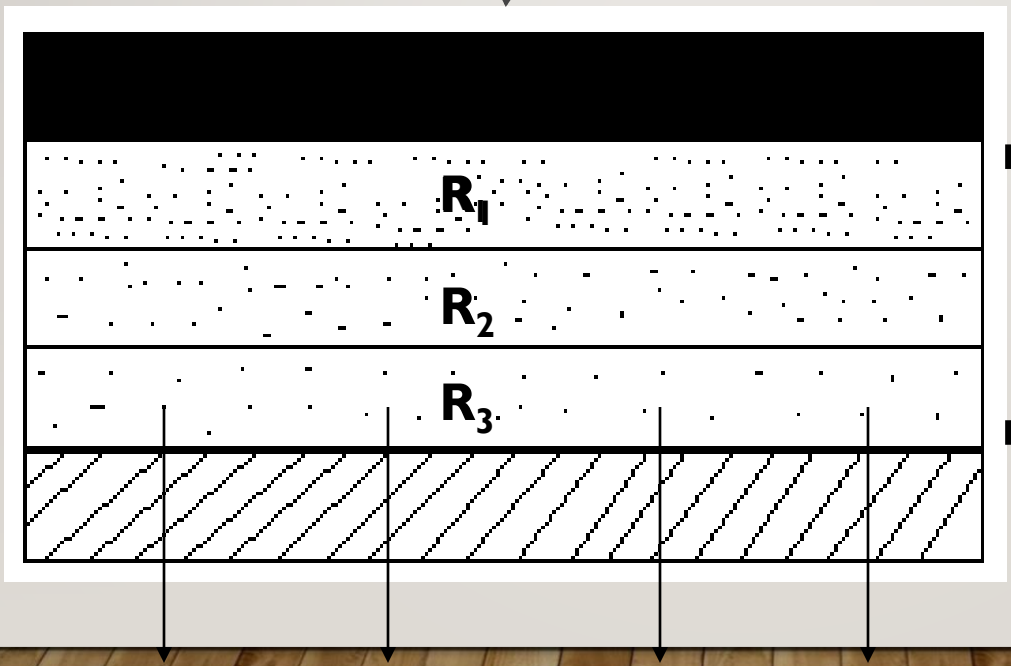


3. ADHESIVE DISPERSION-TYPE SYSTEM



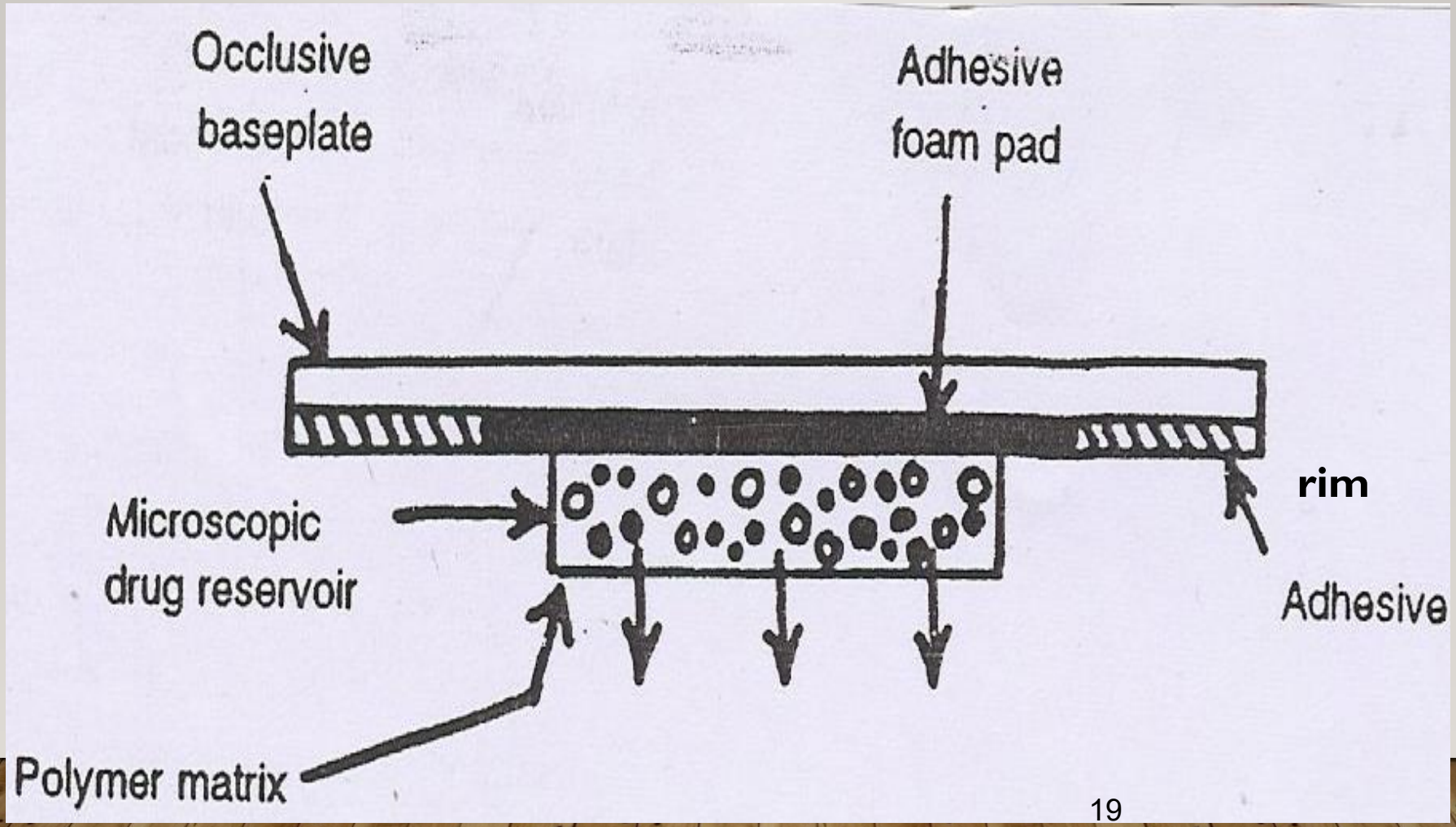
4. GRADIENT CONTROLLED TDDS

Drug – impermeable metallic plastic laminate



Drug reservoir gradient layers $R_1 > R_2 > R_3$

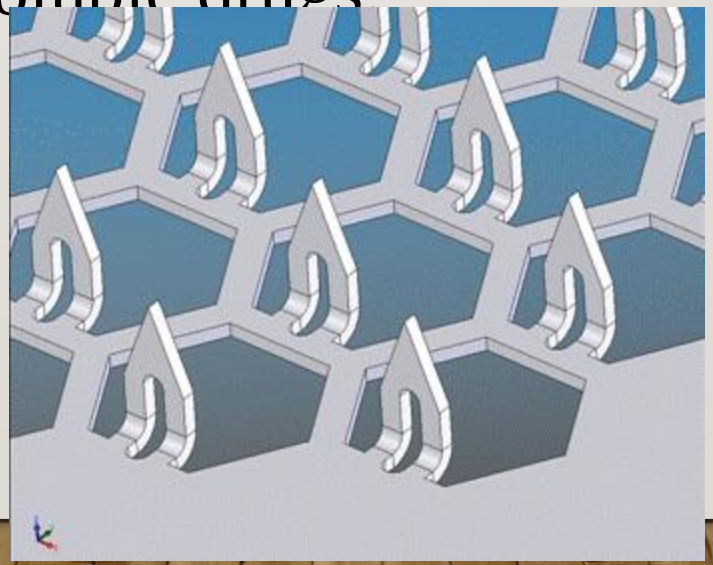
5. MICRORESERVIOR TYPE OR MICROSEALED DISSOLUTION CONTROLLED SYSTEM



ADVANCED RESEARCHES

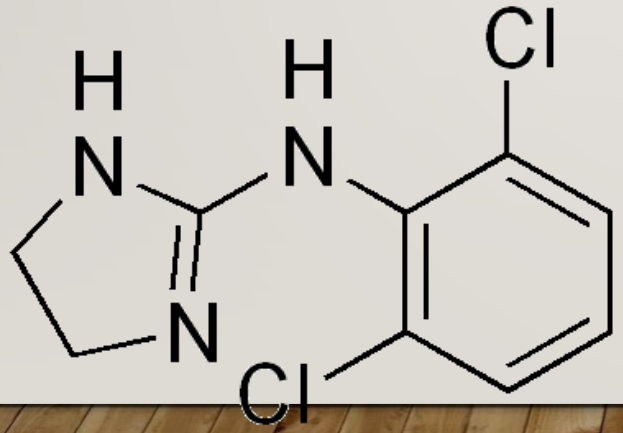
MICROARRAY NEEDLE

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

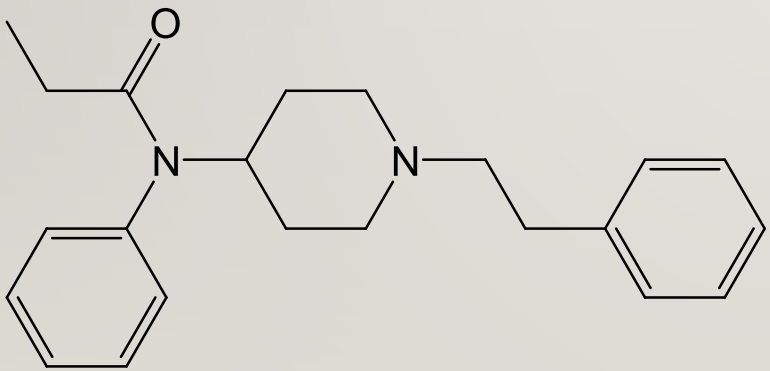


PRODUCTS ON THE MARKET, OR IN DEVELOPMENT INCLUDE:

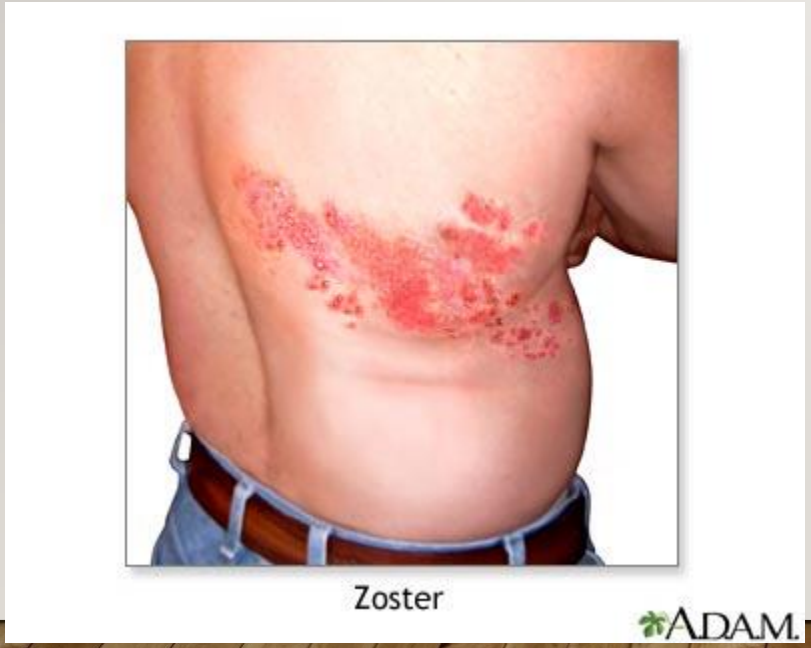
- Clonidine
- Works as an agonist of adrenaline at the presynaptic α_2 adrenergic
- Product name = Catapres-TTS®
- used to treat hypertension

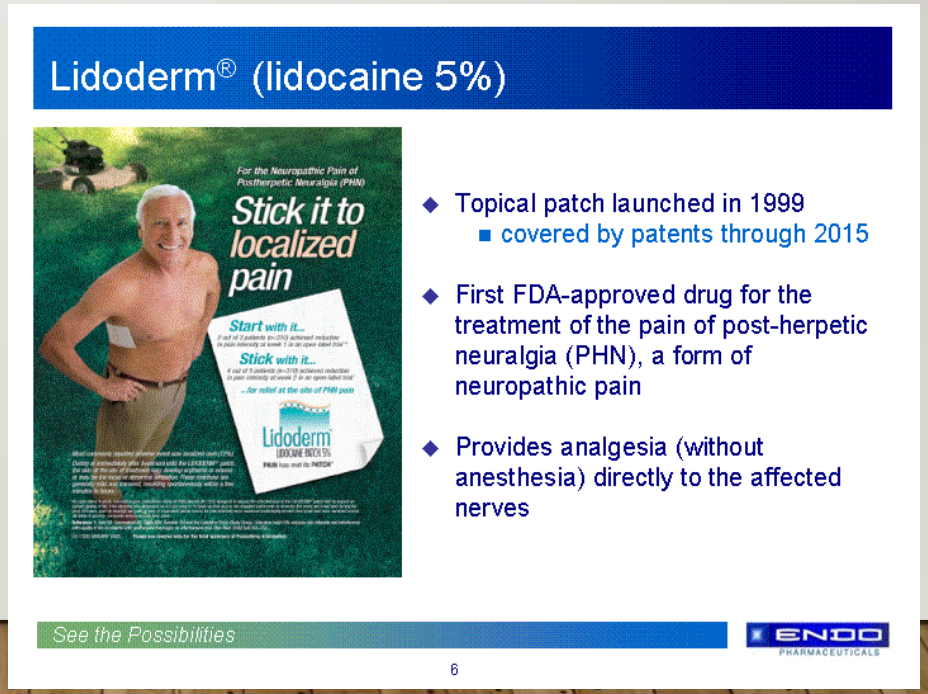


- Fentanyl
- Product Name = Duragesic®
- Used for: Analgesia
- Type of Patch = Drug-in-Adhesive
- Frequency of Application = Weekly

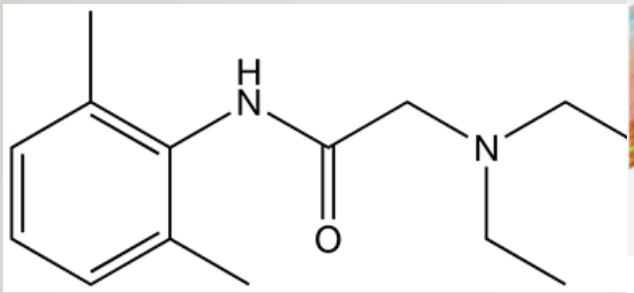


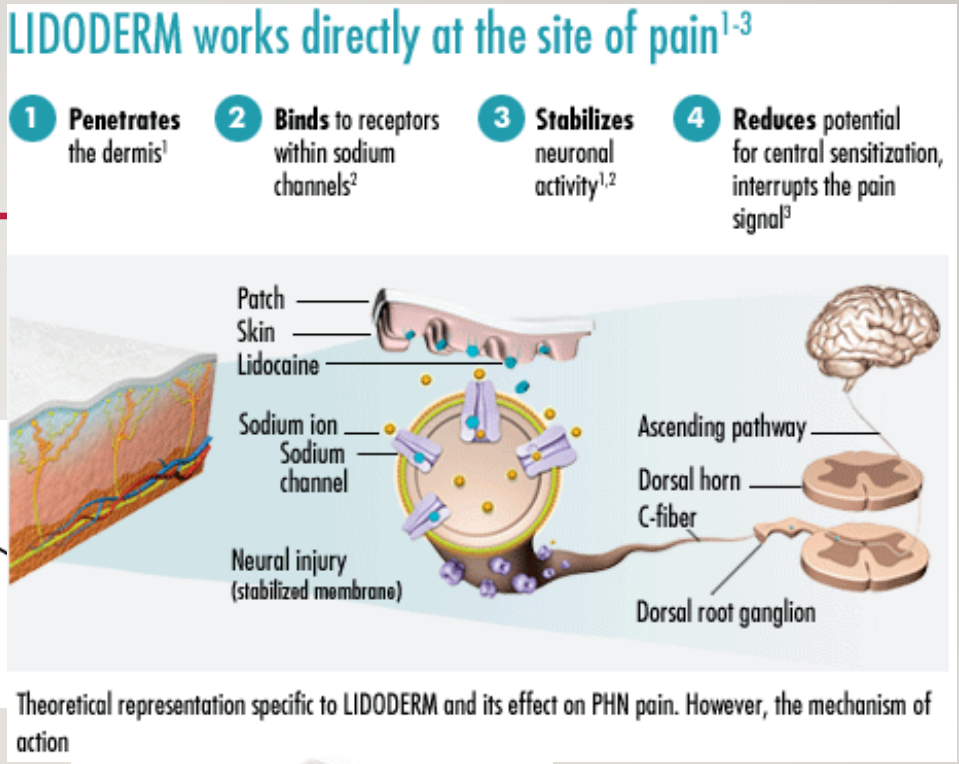
- Lidocaine
- Product Name = Lidoderm®
- Used ~~for: analgesia of postherpetic neuralgia (PHN)~~, a painful condition caused by the varicella zoster virus (herpes zoster = shingles)





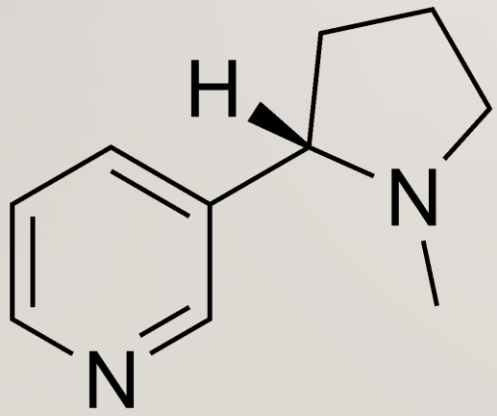
LIDODERM PATCH





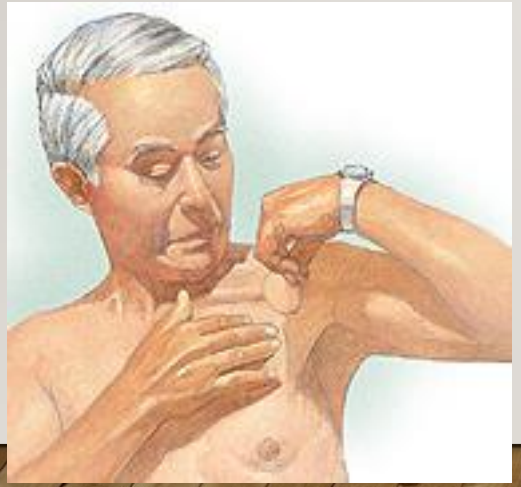
- Type of Patch = Reservoir
- Frequency of Application = Daily

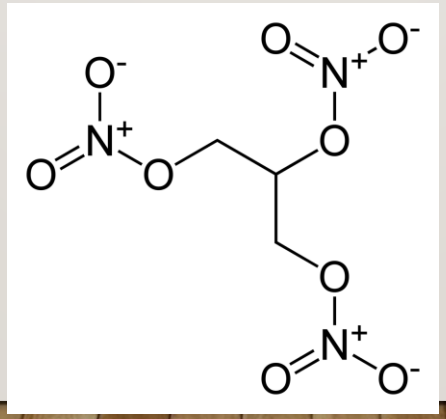
- Nicotine
- Product name = Habitrol®, Nicoderm – CQ®, Nicotrol®, Prostep®
- Used for: Smoking cessation
- Frequency of administration = Daily



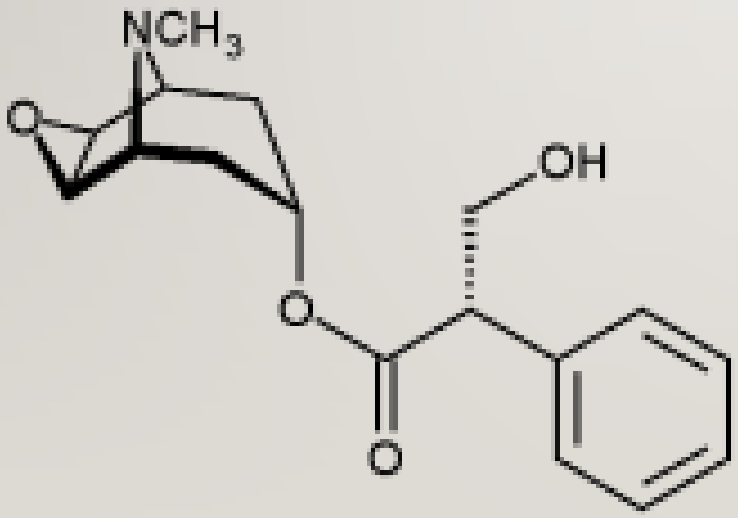
- Nitroglycerin
- Works by producing nitric oxide (NO), which then acts as a vasodilator
- Product Names = Nitro-Dur®, Transderm-Nitro®
- Used for: Angina
- Type of Patch = Nitro-Dur is Drug-in-adhesive

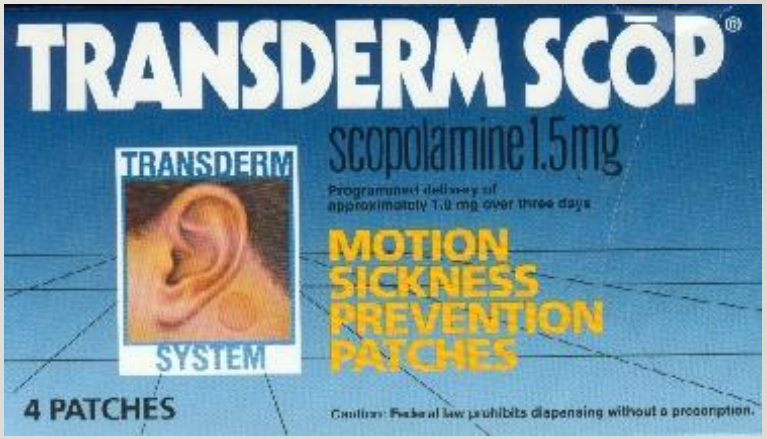
  Nitrodisc is reservoir
- Frequency of administration = Daily



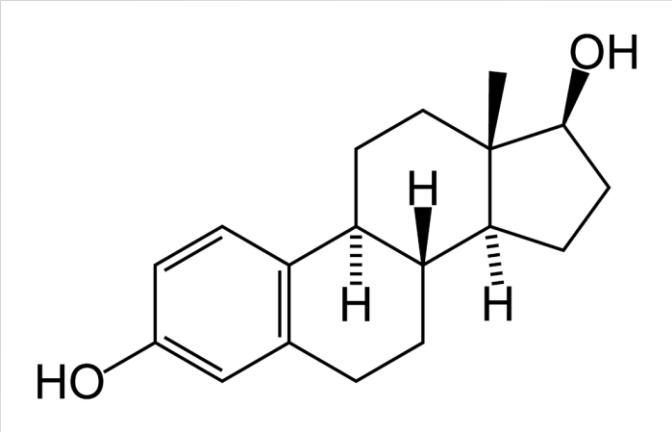


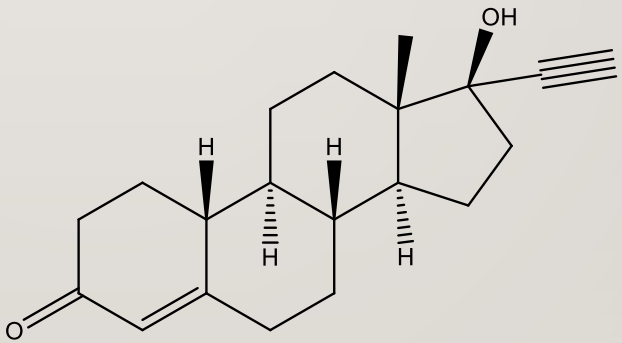
- Scopolamine
- Works as competitive antagonist of acetylcholine at the muscarinic receptor
- Product Name = Transderm Scop®
- Used for: Motion Sickness





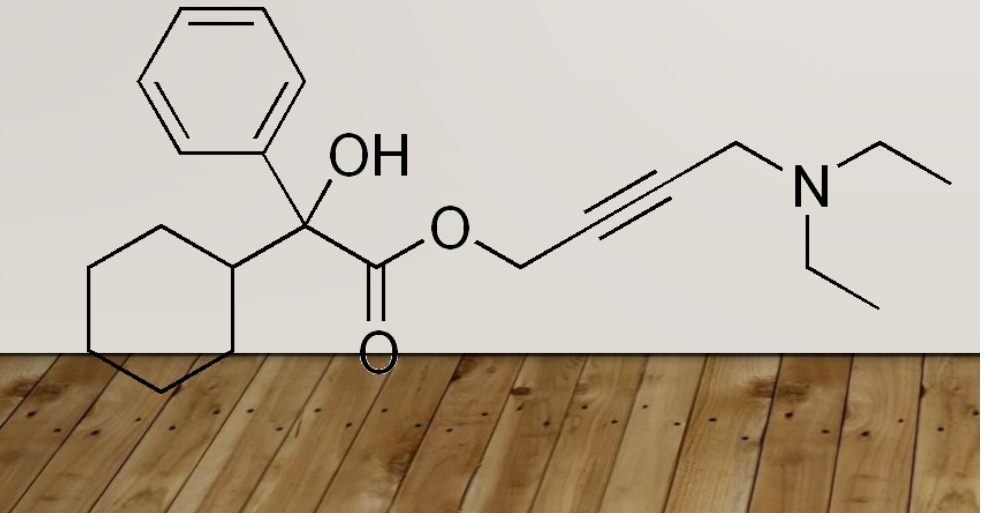
- Estradiol + Norethindrone
- Product name = CombiPatch®
- Used for: Hormone Replacement





Norethindrone

- Oxybutynin
- Works as competitive antagonist of the muscarinic acetycholine receptor
- Product name = Oxytrol®
- Used for: Overactive bladder (antispasmodic)
- Type of Patch: Drug-in-adhesive
- Frequency of application = twice a week



OXYTROL™
Oxybutynin Transdermal System

Oxytrol Patch Approved by FDA for Overactive Bladder

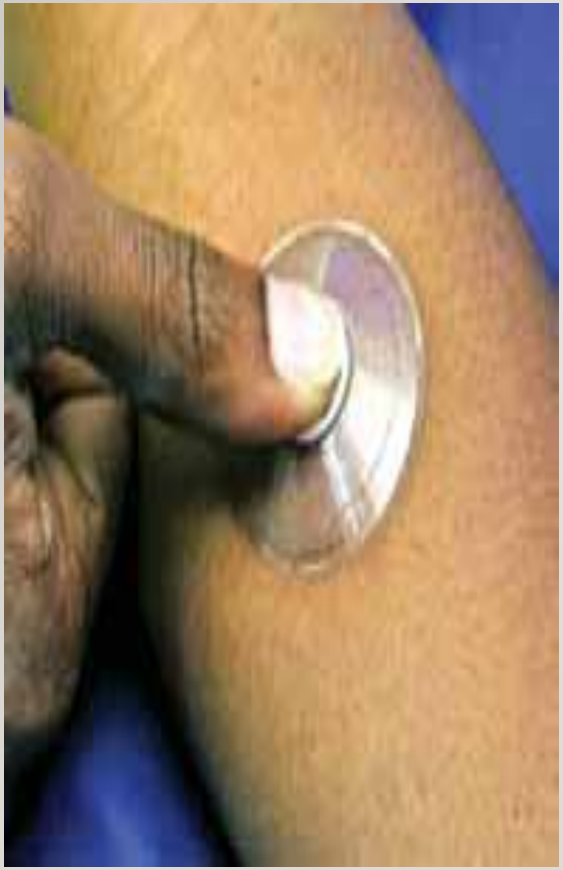
CORONA, Calif., Feb 26, 2003---Watson Pharmaceuticals, Inc. announced today that the U.S. Food and Drug Administration has approved Oxytrol (oxybutynin transdermal) for treatment of overactive bladder (OAB). The patch is the first transdermal system for treatment of this condition, which is estimated to affect more than 33 million Americans.

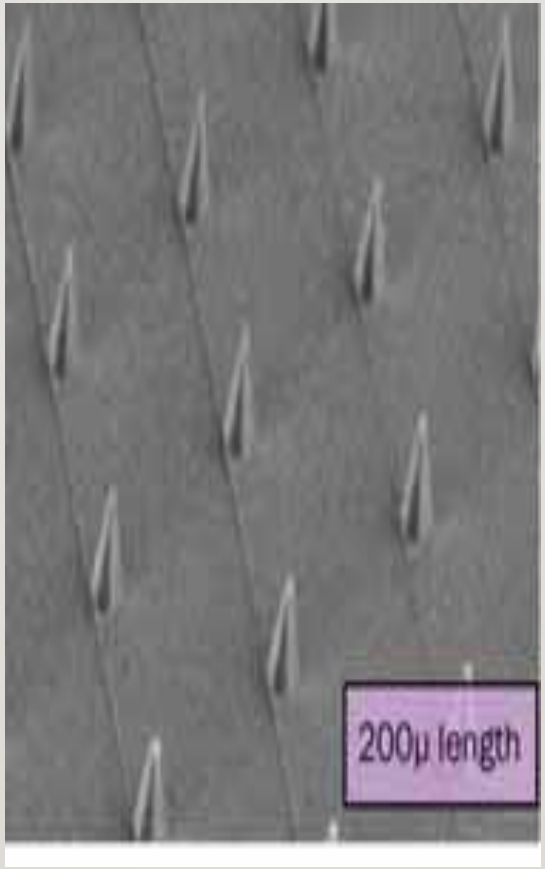
Although the active ingredient (oxybutynin) has been available in pill form for years, side effects---especially dry mouth and constipation---have been a limiting problem for many patients. With the patch, these side effects are less frequent and less severe than with oral forms of the drug. In the clinical trials leading to FDA approval, side effects in the Oxytrol group were about the same as in the placebo group. Thus, transdermal delivery of the drug appears to offer an advantage over the oral route of administration in some patients. Head-to-head comparisons of the two forms of delivery are not currently available.

ADVANCED RESEARCHES

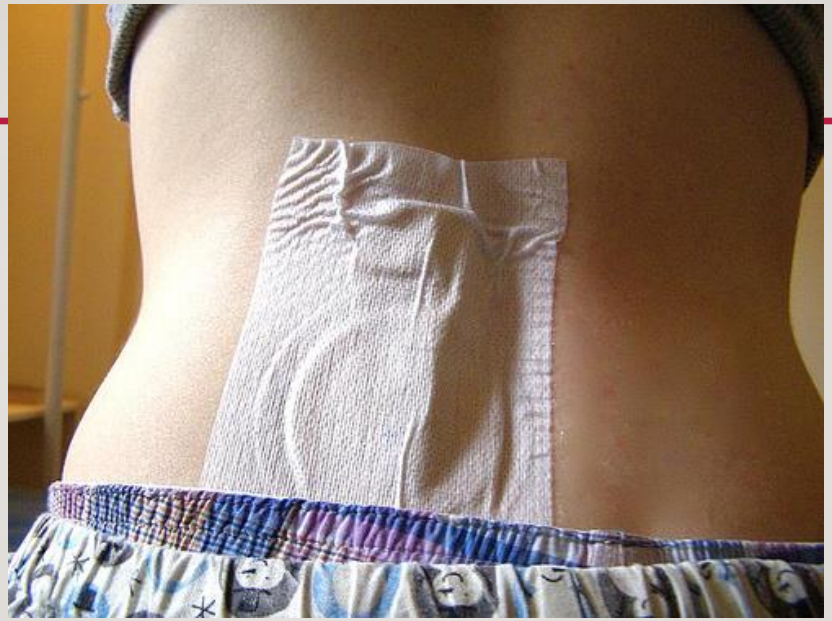
- The device create painlessly micropores in the S.C. known as microstructered arrays or microneedles.
- These devices have about 400 microneedles.
- The solid silicone needles (coated with drug) or hollow metal needles (filled with drug solution) penetrate the horny layer without breaking it or stimulating nerves in deeper tissues.
- Flux increase up to 1,00,000 fold are reported.

MICRONEEDLE ARRAY



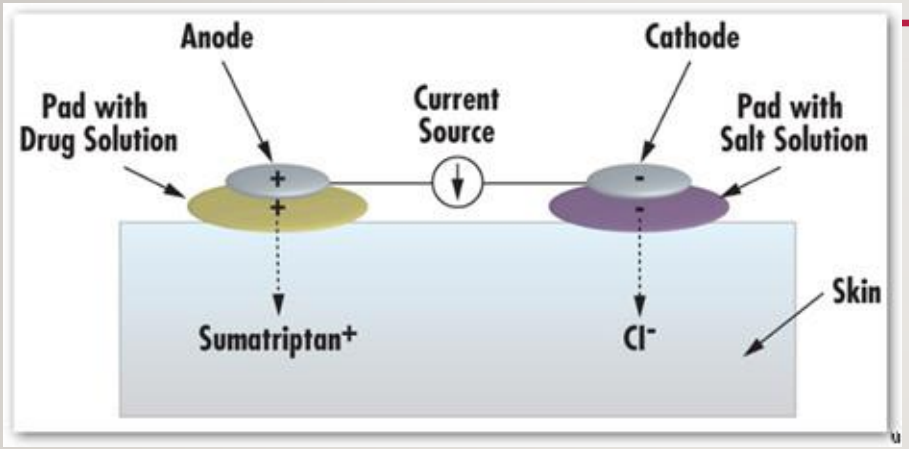


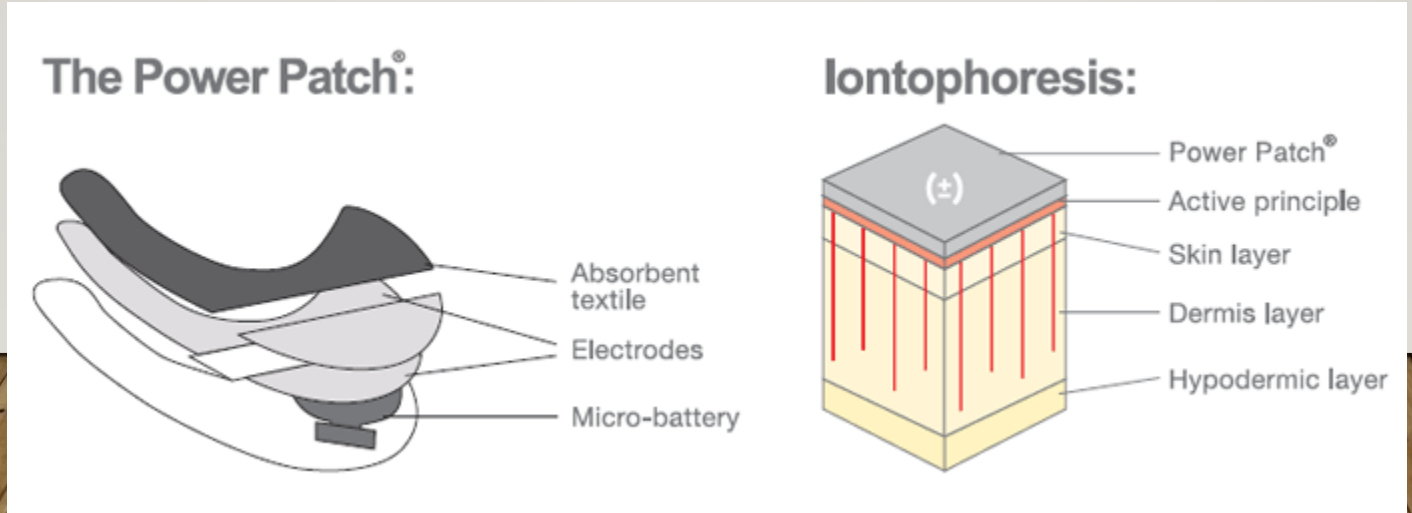
IONTOPHORETIC PATCHES



- Iontophoretic patches use a tiny electrical current to promote flow of the drug (usually charged) through the skin.

Iontophoretic Patches





IONTOPHORETIC PATCHES