

Topical vs. transdermal

- Topical dosage forms: gels, ointments, emulsion
 - Target organ: skin
 - Promotes drug residence in skin
- Transdermal dosage forms: patches
 - Systemic delivery
 - Promote drug migration through the skin to underlying blood supply w/o buildup in skin

Skin and percutaneous absorption:

- Stratum corneum is rate-limiting barrier to transdermal drug transport
 - Partially non-living: 40% protein (keratin); 40% water, 20% lipids
- Rate of drug movement across stratum corneum depends on:
 - Drug concentration
 - Aqueous solubility
 - Partition coefficient
- Other preferred factors
 - MW 100-800 (preferable <400) w/ good adequate lipid & aqueous solubility
 - Good hydration of skin; patches act as occlusive moisture barrier
 - Application area with thin layer of skin and longer application time

Matrix (monolithic) TDDS:

1. Outer backing: impermeable metal/plastic laminate
2. Drug-loaded adhesive matrix
 - a. Rim around drug matrix
 - b. Matrix itself may be adhesive
3. Release liner

Indications for transdermal opioid patch:

- CHRONIC PAIN
- Can't take oral meds: NV, mucositis, dysphagia
- Poor compliance: cognitive impairment, elderly

Fick's First Law of Diffusion

$$\frac{dq}{dt} = D_m K_r^m A \frac{C_r - C}{h}$$

dq/dt = rate of diffusion

D_m = diffusion coefficient for drug through membrane

K_r^m = partition coefficient for drug b/w reservoir & membrane

A = surface area of patch

C_r = dissolved drug concentration in the reservoir

C = drug concentration at skin

h = thickness of membrane

Rate of drug transport in TDDS: controlled by the rate of drug release from the patch OR the rate of permeation through the skin membrane

→ whichever is lower

Membrane-controlled TDDS:

1. Protective liner (peel strip): prevent adhesive from sticking to packaging or unwanted sites prior to use
 - Impermeable to drug
 - Removed & discarded prior to application
2. Adhesive layer: allows patch to remain in place
 - Must be permeable & biocompatible
3. Rate controlling drug membrane
4. Drug reservoir: holds drug dispersion
5. Outer backing: protection of patient & drug; provides identification of drug
 - Occlusive to prevent transmission of water vapor
 - Impermeable to penetration of drug

Advantages of transdermal route for opiates

- Avoidance of hepatic first pass metabolism
- Continuous pain relief
- Improves pt compliance
- Constant drug delivery → more stable plasma concentration without peaks
- Ease of administration despite NV & difficulties swallowing
- Absorption independent of food or fluid intake

Fentanyl citrate: absorbed easily through skin; low risk for skin irritation; 1000 x more potent than morphine; less constipation; less nausea and vomiting → IN OPIOID NAÏVE PATIENTS, COMMENCE AT LOWEST DOSE

Use of TDDS

- Percutaneous absorption varies with the site of application; rotate locations within that site to regain normal permeability (w/in a week) and to prevent skin irritation
 - Fentanyl patch: torso or upper arm
- Applied to clean, intact, dry skin that is free of hair and not oily
 - Wet skin can accelerate drug permeation beyond intended rate
 - Oily skin can impair adhesion of patch
 - Removal of stratum corneum by wet-shaving can affect drug absorption rate
- Avoid using skin lotion at the application site → affects hydration of skin & drug partition between patch and skin
- Should NOT be cut for dose adjustment
- Avoid touching adhesive layer with fingers when removing the protective lining
- Should be pressed firmly against the skin with the heel of the hand for 10-30 seconds to ensure uniform contact and adhesion
- Patches can be left on when showering, bathing or swimming
 - If patch prematurely dislodges, reapply it or replace with a fresh one (worn for a full period)
- Clean hands thoroughly before and after applying a patch; don't rub eyes or touch mouth during handling of patch
- Seek for re-evaluation when skin shows sensitivity or intolerance to the TDDS
- Upon removal, a used TDDS should be folded in half with adhesive layer together so that it cannot be re-used
 - Used patch (contains residual drug) should be discarded in a manner safe to children & pets

FENTANYL: wait 24 h before evaluating pain relief and replace patch every 72 h