1996a(13): Describe briefly the factors determining transdermal uptake of drugs and give examples. Outline the advantages and disadvantages of transdermal administration of drugs

General: Transdermal application of drugs can be achieved through use of
- Patch eg fentanyl, GTN, oestrogen, nicotine

All applications require the drug to diffuse through epidermis to access target site, dermal vessels for systemic absorption
- Behave in accordance with Fick’s Law of Diffusion
  \[ F = \frac{A \times \text{sol} \times P_{1-2}}{T \sqrt{\text{MW}}} \]
  where F=rate of diffusion, A=surface area for diffusion, \( T \) = thickness of barrier, \( P_{1-2} \) = conc gradient of drug across barrier

Factors affecting uptake
A: surface area of diffusion
  - ↑surface area (by ↑size of patch) will ↑rate of diffusion
T: Barrier thickness
  - Thicker barrier (eg back) will ↓rate of diffusion
  - Inner thigh/mucosal, relatively thin barrier have ↑rate of diffusion
Sol: Drug solubility
  - ↑lipid solubility will ↑uptake (↑unionised portion of drug)
  - ↑hydration of skin will ↑penetration of horny layer
  - Electrical current will ↑solubility
MW: <1,000 Da → ↑uptake

\( P_{1-2} \): ↑conc applied will ↑conc gradient across skin barrier → ↑diffusion
  - Vascularity of site → ↑systemic absorption → maintain gradient for uptake
  - ↑CO → ↑systemic absorption

Advantages/Disadvantages of Transdermal application

Advantages:
- Avoid 1st pass metabolism
  - Only other route injectable
- Avoid use of needles/invasive administration
  - ↓risk blood-borne disease
  - ↓discomfort
- Slow release application
  - Controlled dose over long period → prevents peak-trough phenomenon with po/Intermittent injection
  - Patches worn for 12-18hours
  - GTN patch suitable for stable angina
- Abuse potential low
  - Sustained release formulations of fentanyl/buprenorphine

Disadvantages:
- Allergy
  - To adhesive component
  - Preservatives/buffers in formulation → skin irritant
  - Anaphylaxis rare
- Continued absorption after removal of patch
- Latent effect
  - Acts as a depot

  - Tachyphylaxis
    - Especially a problem with GTN → requires o/night break (on 12hrs, off 12hrs) or loses effectiveness

- Slow SoO
  - GTN patch unsuitable for Rx during AMI
  - Delayed onset → 4hrs for effect with patch v almost immediate

- Risk of inadvertent overdose
  - Forgotten patch → >1 patch on at a time
  - Application heat → deaths 2° heat pack over fentanyl/buprenorphine patch → ↑rate of diffusion → opioid OD
  - Electricity → GTN patch and external defibrillator → ↑diffusion (explosion potential)