



Routes of Drug Administration

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1

Drug Absorption, Bioavailability

- Absorption describes the rate at which a drug leaves its site of administration and the extent to which this occurs
- Bioavailability is a term used to indicate fractional extent to which dose of a drug reaches its site of action or a biological fluid from which drug has access to site of action

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2

Factors Deciding Choice of Route

- Type of described effect, systemic or local
- Physiochemical properties, solid or insoluble
- Rapidity of effect, oral, intramuscular (IM), intravascular (IV)
- Quality of effect, Magnesium sulphate orally is purgative but rectally ↓ I/c tension
- Condition of patient, conscious or unconscious, vomiting

Topical Application- Mucous Membrane

- Conjunctiva, nasopharynx, oropharynx, vagina, urethra, urinary bladder, ear, nose, anal canal for local effects
- Synthetic ADH to nasal mucosa for systemic effects
- Absorption rapid
- Local anesthetic for local effects rapidly absorbed, produce systemic toxicity
- Ointment, cream, drops, jelly, powder, tablet, suppository, pessary

Topical Application- Skin

- Absorption- surface area, lipid solubility
- Few drugs readily penetrate skin
- Burned, denuded, abraded, inflammation increase systemic absorption
- Toxicity by highly lipid soluble **insecticides**
- Controlled- release topical patches- **post-aural scopolamine patches** for prophylaxis of motion sickness

Topical- Application Disadvantage & toxicity

- Adrenal steroids and neomycin to skin
- Atropine to eyes
- Timolol eye drops contraindicated in bronchial asthma and COPD
- High local conc. without systemic toxicity

Topical Application

- For systemic effect, Transdermal Delivery System (TDS) release drug through rate controlling membrane into skin and to systemic circulation.
- This avoid fluctuation in plasma conc.
- Glyceryl trinitrate or Nitroglycerine or Nitro disc is applied on chest wall
- Estrogen patches is given in postmenopausal hormone replacement therapy (HRT)

Topical Injection

- Intraarticular adm. of hydrocortisone
- Intrathecal into subarachnoid space of L2-3 or L3-4, Lidocaine, Amphotericin-B
- Intramedullary into bone marrow
- Intraarterial, anticancer drugs in limbs cancer
- Retro bulbar, behind eyeball, hydrocortisone hemisuccinate
- Intrapleural, anticancer agents
- Intraperitoneal, anticancer agents

Systemic Routes

- **Enteral through GIT**
 - Orally
 - Buccal or sublingual
 - Rectal
- **Parental:** Par- way, enterm- intestine
 - Intravenous (IV)
 - Intramuscular (IM)
 - Subcutaneous (SC)
 - Transdermal Therapeutic system (TTS)
- **Inhalation**

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9

Oral Ingestion / Swallowing

- Absorption variable
- Most conventional, economical, more safe and acceptable to patient
- Absorption delayed, reduced after food
- **Antimuscurainic and opoids** inhibit gut motility, absorption slow or irregular
- Presystemic elimination causes interindividual variation

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10

- **Gentamicin not absorbed**
- **Insulin, oxytocin destroyed in gut**
- Esophageal ulceration
- Tablets, capsules, powder, syrup, mixture suspension or emulsion

ORAL

- Absorption from stomach and upper intestine is affected by:-
 - Surface area
 - Blood flow to site of absorption
 - Physical state: solid, solution, suspension
 - Water solubility
 - Conc. at the site of absorption
 - Rate of dissolution
 - Rate of disintegration
 - Particle size

Sublingual

Clinically useful drugs:

- Nitroglycerine
- Isosorbide dinitrate
- Buprenorphine
- Clonidine
- Isoprenaline
- Methyl testosterone

Rectal Administration

- Used when recurrent **vomiting or unconscious**
- **50% absorbed drug bypass liver**
- Absorption incomplete, irregular in lower rectum by external haemorrhoidal veins
- Bisacodyl, glycerine, indomethcine, phenylbutazone
- Paraldehyde, tribromo-ethanol, prednisolone, soap water & barium sulphate as enema
- Inconvenient & embarrassing
- Rectal inflammation occurs

Paraenteral Injections

- IV, IM, SC
- SC, IM absorption simple diffusion from drug depot to plasma
- First- pass elimination in lungs
- Lungs storage site for drugs

Intravenous (IV)

- **Advantages :-**
- IV inj. Immediate effects
- Valuable for **emergency use**
- Suitable for **large volume, irritating drugs**
- Permits titration of dose for protein & peptide drugs
- **Bolus or very slow** (as drip)
- Must inject slowly as a rule
- **Complete bioavailability**
- Thiopentol, furosemide, diazoxide, sodium nitroprusside, **diazepam IV** for quick effect

IV- Route Disadvantages

- Not suitable for oily solutions & insoluble substances
- Drug administered cannot be withdrawn
- **Thrombophlebitis** occurs at inj. site
- Lack of sterility may cause **viral hepatitis or AIDS**
- **Increased risk of ADR**

Subcutaneous (SC) Route

- Rate of absorption slow, sustained
- **Vasoconstrictor retards absorption**
- Inj. of drug into *subcutaneous site*
- Rapid effect from aqueous solution
- Suitable for *insoluble suspension & solid pellet implantations*
- Only nonirritant drugs
- Not suitable for large volume

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- Pain, necrosis, tissue sloughing
- Absorption of solid pellets implanted under the skin occurs *slowly over weeks or months*, e.g *Testosterone*
- ***Insulin, adrenaline, heparin, vaccines inj. SC***

Intramuscular (IM) Inj.

- *Deltoid, gluteus maximus*
- Rapid effect from aqueous solution, vastus lateralis
- ***Slow, sustained effect from depot preparation***
- Moderate volume, oily vehicles, irritant, penicillin's, amino glycosides, iron
- Pain, Abscess
- Avoid during *anticoagulant therapy*
- **Abs. depends upon rate of blood flow to the injection site**

Intraarterial

- Direct inj. into artery
- Localization of effect in particular tissue or organ
- *Liver tumors, head & neck cancers*
- *Diagnostics agents*
- **Reserved route for experts**

Intradermal (ID)

- Drug inj. into layers of skin
- Multiple puncture of epidermis
- *BCG, Small pox vaccination*
- **Testing drug sensitivity- Penicillin's and
ATS**

Intrathecal

- Blood Brain Barrier & Blood CSF Barrier slow **drug entry into CNS**
- Used when local and rapid effects of drugs on the meninges or cerebrospinal axis desired
- *Spinal anesthesia*
- *Acute CNS infections*
- Into **spinal subarachnoid space**
- Direct *intraventricular drug in brain tumors*

Inhalation Drug Administration

- **Volatile liquids, gaseous anesthetics and therapeutics gases**
- *Amylnitriate pearl* is broken in handkerchief and inhaled
- Dry powder inhaler- *chromolyn sodium*
- **Metered dose aerosol inhaler**- salbutamol, beclomethasone, ipratropium, salmeterol
- **Compressed air driven nebulised solution inhaler**
- Cumbersome methodology

Pulmonary Absorption

- Important route for drugs abuse
- Access to circulation rapid large surface area of lungs
- *Fine drug droplets in air (aerosol) inhaled*
- *Instantaneous absorption*
- **Avoids hepatic first-pass loss**
- Local application at the desired site of action in **pulmonary disease**
- **Treatment of bronchial asthma**

Aerosol Delivery

- Only 2-10 % dose deposited in lungs
- 90 % dose is swallowed
- Use of spacer, a tube fits between inhaler and mouth
- **Metered dose inhaler discharges into spacer and patient inhales**
- Metered dose inhaler, nebulizer
- **Inhaler cheaper and portable**
- **Nebulizer do not require coordination**
- **Dry powder inhaler**

Controlled Release drug Delivery System

- Transdermal (transcutaneous) drug delivery system
- Transmucosal drug delivery system

Transdermal Therapeutics system(TTS)

- Used for percutaneous drug absorption
- Adhesive patch on surface of skin
- Patch delivers drug at constant rate
- Absorption occurs via skin by diffusion
- Single patch for continuous absorption for 7 days
- **Site:** chest, abdomen, upper arm, lower back, mastoid area, pinna

TTS drugs

- Glyceryl trinitrate / Nitroglycerin
- Isosorbide dinitrate
- Scopolamine
- Clonidine
- Verapamil
- oestradiol
- Nicotine
- Fentanyl
- Testosterone

TTS Advantages

- Longer duration of action
- Decreased frequency of administration
- Stable plasma conc.
- Decreased adverse effects
- Improved patient compliance
- Patch can be removed if ADRs occur

Newer TTS

- Dermojet injection- Needle not used, High velocity jet of drug solution from microfine orifice, painless
- Implantable miniature syringes pump for insulin
- Iontophoresis- galvanic current based deeper tissue penetration e.g Salicylates in arthritis
- Inunction provides abs. into blood by rubbing nitroglycerine ointment on skin

Transmucosal Drug Delivery System absorption

- Used for slow mucosal absorption of *pilocarpine, progesterone*
- Ocular insert (**OCUSERT**) of *PILOCARPINE* placed directly under eyelid, delivers low amount of drug at steady rate for 7 days, PILO- 20, PILO- 40
- Need for repeated eye drops avoided

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- **Progesterone I/U contraceptive device,**
- Provides controlled release of Progesterone in uterus for one year
- **Ocular, soft contact lenses, collagen shields**
- Ointment: *miotics, cycloplegics, antibiotics*

Thank you