Drug administration and absorption

*مقتبس من تيم ٤٣٥

Objectives:

- Know the meaning of pharmacology and its branches.
- Discuss the different routes of drug administration.
- Identify the advantages and disadvantages of various routes of drug administration.
- Know the various mechanisms of drug absorption.
- List different factors affecting drug absorption.
- Define bioavailability and factors affecting it.

Titles
Very important
Extra information
Terms

The roots of education are bitter, but the fruit is sweet

Pharmacology

Pharma: drug , logy: science

A science that deals with the drugs regarding classification, pharmacokinetics, pharmacodynamics, side effects and uses.

Pharmacokinetics:
(what the body does to a drug?)

Pharmacodynamics
(what the drug does to the body? And what is the other action for the drug)

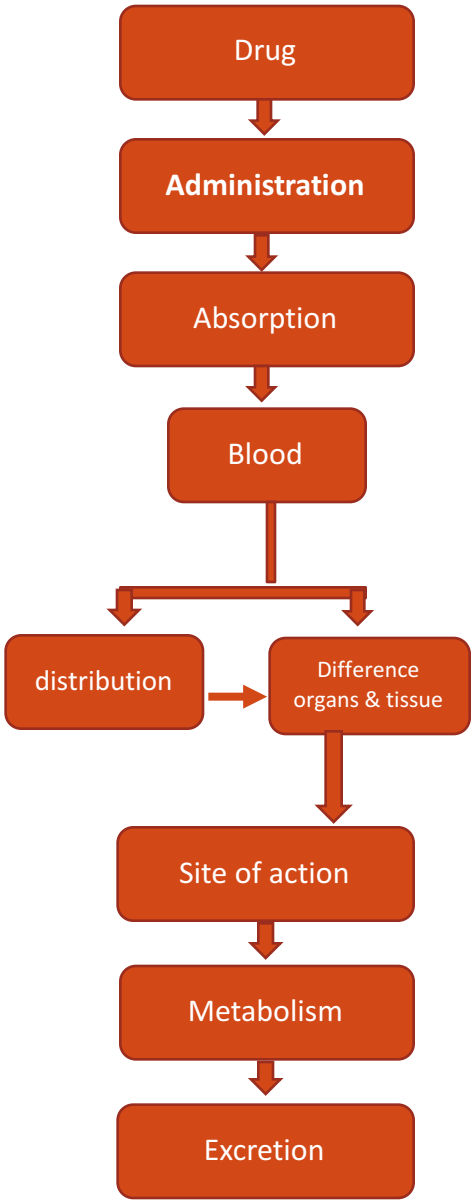
Pharmacodynamics:

1. Mechanismsof drug action
2. Pharmacological effects of drugs

Pharmacokinetics(ADME) :

- **A**bsorption
- **D**istribution*
- **M**etabolism
- **E**xcretion**

* the drug distribute all over the body, which will give the wanted effect and unwanted effect (side effect)
** usually in urine from kidney or faces from the liver



Routes of drug administration:

1. Enteral via gastrointestinal tract GIT (Oral – Sublingual –Rectal)
2. Inhalation
3. Parenteral(Injections)
4. Topical application

Routes of drugadministration:

1- Enteral via gastrointestinal tract (GIT):

	Advantage	Disadvantage
Oral	• Common • Easy • Self use • convenient • Cheap • No need for sterilization.	• Slow effect, GIT irritation. • Destruction by pH and enzymes. • Food - drug interactions. (if there is food inside the stomach) • Drug-drug interactions. (if the patient use more than 1 drug) • First pass effect. • No complete absorption. (because of the pH, enzymes, food-drug interaction) • Low bioavailability. (the conc. of drug in blood). • Not suitable for vomiting and unconscious patient and emergency (because it has slow effect) and bad taste drugs.
Sublingual	• Rapid effect • can be used in emergency (direct absorption) • High bioavailability • No first pass effect. (direct absorption) • No GIT irritation • No food drug – interaction • Dosage form: friable tablet (easily breaks and dissolves)	• not suitable for : ○ Irritant drugs ○ Frequent use
Rectal	• Suitable for children, vomiting, unconscious patients • Irritant & bad taste drugs • less first pass metabolism (50%) • Dosage form suppository or enema	• Irritation of rectal mucosa • Irregular absorption & bioavailability

First pass effect:

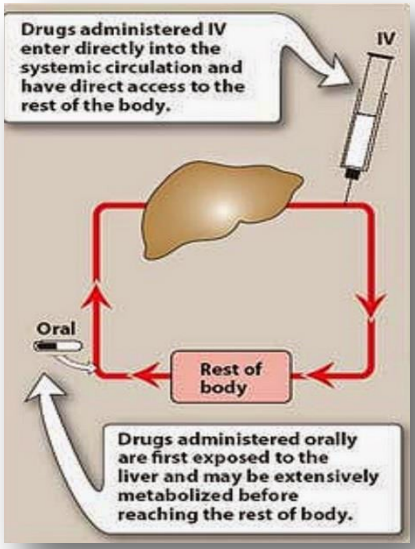
Drugs given orally → via portal circulation → taken to the liver and metabolized (first metabolism) → reaching to the blood to be distributed to body compartments

أي بمعنى لمن ناخذ الدواء orally على طول يروح للكبد ويصير له تكسر (first metabolism) فبالتالي نخسر جزء من الدواء فراح يقل الbioavailability، بعد ما يخلص من الكبد يروح للدم (Absorption)

First pass metabolism results:

- **Low bioavailability** (low conc. of drug in blood).
- **Short duration of action** (t½).
- drugs with high first pass effect should **not** be given orally **but** parenterally.*

  * لأن راح يتكسر جزء كبير من الدواء و ماراح يضل جزء كافي إنه يعطيني التأثير



Where it occur:

- Liver (mainly).
- GIT Wall.
- GIT Lumen.

Oral Dosage Forms “oral formulations”:

Tablets: Coated tablets: sugar-coated to mask bad taste
Enteric coated tablets: dissolve only in intestine

Capsules: Hard gelatin capsules: (contain powder ’solid’)
Soft gelatin capsules: (contains liquid)

Syrup: (e.g. Cough syrups) "كمية قليلة من الدواء مذابة في محلول السكر عشان تحسن الطعم خصوصًا للأطفال"

Suspension: “mixture of solid in liquids” e.g. antibiotics

Routes of drug administration:

2- Inhalation:

	Advantage	Disadvantage
Inhalation	• Rapid absorption (due to large surface area) • Immediate Effects • limited systemic effect (because it is in one place or Local Effect) • Ideal For Gases • Effective • Local action • Dose Can Be Titrated • Suitable For Emergency • Fewer Side Effects • No first pass effect • Dosage form: • volatile gases e.g. anesthetics • liquids given by aerosol, nebulizer for asthma treatment	• addictive route • patients may have difficulty using inhalers • patients may have difficulty regulating dose • Not suitable for irritant drugs • Only few drugs can be used

3- Parenteral (injection):

	Advantage	Disadvantage
Parenteral	• No first-pass metabolism • Have Highest Bioavailability • No food-drug / drug-drug interaction • No gastric irritation • Suitable for Vomiting, unconscious ,Irritant & bad taste drugs.	• Need skill • Pain, tissue necrosis or abscess (I.M) • Anaphylactic reaction (I.V)

Type of Parenteral:

Intradermal (I.D) **(into skin)**	**Subcutaneous** (S.C) **(Under skin)**	**Intramuscular** (I.M) **(into muscle)**	**Intravenous** (I.V) **(into veins)**
Intra-arterial (I.A) **(into arteries)**	**Intrathecal** (I.T) **(cerebrospinal fluids)**	**Intraperitoneal** (I.P) **(peritoneal cavity)**	**Intra-articular (Synovial fluids)**

Parentral

	Advantage	Disadvantage	Volume
Intradermal (I.D)	• suitable for vaccinations • sensitivity test (sensitivity of some medications or food)	• Not suitable for large volumes.	**0.1 ml**
Subcutaneous (S.C)	• Used for sustained release effect (راح يأخذ وقت عشان يمتص فيجلس بالجسم فترة طويلة فما يحتاج آخذه أكثر من مرة باليوم) • Suitable to poorly soluble suspensions & for Instillation of slow-release implants e.g. insulin zinc preparation	• Not suitable for large volumes	**0.1ml –1ml**
Intramuscular (I.M)	• prolonged duration of action • oily preparations* or poorly soluble substances can be used	• Not suitable for irritant drugs • pain, abscess, tissue necrosis may happen	**3-5ml**
Intravenous (I.V)	• Large volume • Rapid action (emergency) • High bioavailability 100% (becase it will go directly to the blood stream) • No food-drug interaction • No first pass metabolism • No gastric irritation • Suitable for Vomiting, unconscious ,emergency, Irritant & bad taste drugs.	• used only for water soluble drugs (because the blood is water soluble, so we can't use oily preparations) • Infection • Anaphylaxis • Sterilization • Expensive • Not suitable for oily solutions or poorly soluble substance • Must inject solutions slowly as a rule	**500ml**

* oily preparation: drug dissolved in oil solvent which won't be mixed with bloodstream so we inject it in muscle

4 Topical application

Drugs are mainly applied topically to produce local effects. They are applied to

- Skin (percutaneous) e.g. allergy test, topical antibacterial and steroids and local anesthetics.
- Mucous membrane of respiratory tract (Inhalation) e.g. asthma
- Eye drops e.g. conjunctivitis
- Ear drops e.g. otitis externa
- Intranasal e.g. decongestant nasal spray

Transdermal patch:

Is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. Girl's definition: are medicated adhesive patch applied to skin to provide systemic effect 'all around the body' (prolonged drug action)

- e.g. the nicotine patches (quit smoking).
- e.g. Scopolamine (vestibular depressant, antiemetic for motion sickness).

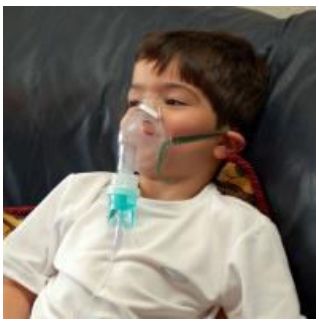
Ampoule (single use)

Vial (repeated use)

(Parenteral Dosage Forms)

Atomizer

Nebulizer



(Inhalation Dosage Forms)

Drug Absorption

DEFINITION: the passage of a drug from it's site of administration to site of action across cell membranes.

EXCEPTION: Except for intravenous administration, all routes of drug administration require that the drug be absorbed from the site of administration into the systemic circulation (blood).

(I.V. administration requires no absorption)

Mechanisms of drug absorption

- Simple Diffusion (Passive Diffusion)
  - **Aqueous Diffusion**: low molecular weight & water soluble drugs diffuse through aqueous channel or pores in cell membrane (filtration).
  - **Lipid Diffusion**: low molecular weight & lipid soluble drugs diffuse through lipid cell membrane.
- Facilitated Diffusion
- Active Diffusion
- Pinocytosis
  - Endocytosis: uptake of membrane-bound particles
    - for high molecular weight drugs such as peptides
    - high polar substances such as vitamin B12(combines with intrinsic factor) &iron (combines with transferrin)
  - Exocytosis: expulsion of membrane-bound particles

Passive Diffusion	Active Diffusion	Carrier-Mediated Facilitated Diffusion
ALONG Concentration Gradient	AGAINST Concentration Gradient	ALONG Concentration Gradient
No Energy & Carrier	Requires Energy & Carrier	No Energy But Requires Carrier
Common	Uncommon	_____
Not Saturable	Saturable	Saturable
Non Selective	Selective (Specific)	Selective
DEPEND ON Lipid Solubility	E.G. Absorption of Sugar & Amino Acid	Similar to Entry of Glucose into Muscle (GLUT 4)
DEPEND ON Pka of Drug & pH of the Environment (It can be fluid of the cell body, blood, urine)	Uptake of Levodopa by Brain (treatment of Parkinsons)	_____

pka effect & pH

pKa (dissociation/ionization constant): pH at which half of the substance is ionized & half is unionized.

- The lower the pKa value (pKa < 6) of the acidic drug, the stronger the acid ,e.g Asprin (Pka= 3.0)
- The higher the pKa value (pKa >8) of a basic drug, the stronger the base, e.g propranolol(pKa= 9.4)

- Drugs can exist in 2 forms in equilibrium :

ionized (polar) > water soluble

unionized (nonpolar) > lipid soluble

- Most drugs are weak basic or weak acid
- Only UNIONIZED form is absorbable (because it is lipid soluble and can soluble easily in cell membrane which has lipid bilayer)
- Ionization of drugs reduces passage of drugs across cell membranes. (because it is water soluble and can't soluble easily in cell membrane which has lipid bilayer)
- The degree of ionization of drugs is determined by their pKa and pH of the surrounding.

Affects degree of ionization of drugs:

- Weak Basic drugs are best absorbed in the intestine. (because the intestine is a basic medium, so the drug won't ionized and will be unionized or lipid soluble, so it will easily absorbed)
- Weak Acidic drugs are best absorbed in the stomach. (because the stomach is an acid medium, so the drug won't ionized and will be unionized or lipid soluble, so it will easily absorbed)

Factors affecting absorption:

Route of administration	**Dosage forms** (depending on particle size and disintegration, ease of dissolution) (solution > suspension > capsule > tablet)	**Molecular weight of drug** Small molecular absorbed better than large molecular
Lipid and drug solubility (aqueous preparation better than oily, suspension preparation)	**Degree of ionization** Less ionized better absorbed	**Chemical instability in gastric pH** Penicillin and insulin
Surface area available for absorption (small intestine has large surface area than stomach due to intestinal microvilli)	**Blood flow to absorptive site** (greater blood flow increases bioavailability) (intestine has greater blood flow than stomach)	**Intestinal motility (transit time)** (Diarrhea reduces absorption)
Gastric emptying (drugs that increase gastric emptying enhances absorption 'metoclopramide').	**Drug interactions**	**Food** (Slow gastric emptying, generally slow absorption) e.g. Tetracycline, aspirin, penicillin V (A fatty meal increases the absorption of fat soluble antifungal drug (e.g. griseofulvin,)

Quick quiz

Videos :

The First Pass Effect of the Liver

Bioavailability

Pharmacology Team :

Boys	Girls
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عبدالعزيز رضوان	روان سعد القحطاني
عبدالرحمن المالكي	أميرة نيازي
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فارس النفيسة	رانيا العيسى
خالد العيسى	غادة المزروع
معاذ الفرحان	لمى الفوزان
محمد الاسمري	نورة الشبيب
محمد خوجة	أسيل ناصر بادخن
عمر التركستاني	أنوار نجيب العجمي