Lecture (1)

Drug administration and absorption

pharmacology
Team 438

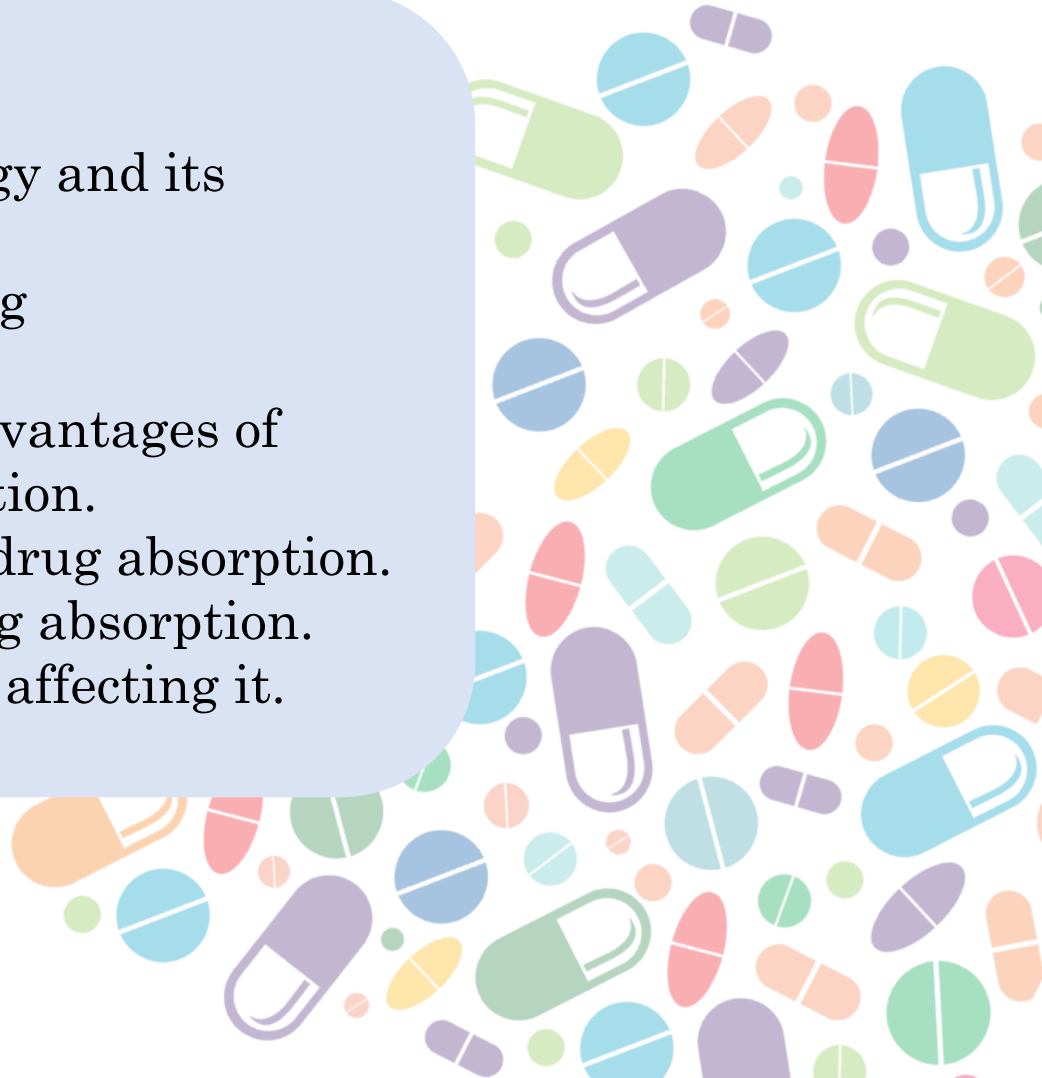
MED438
KING SAUD UNIVERSITY

- Red : important
- Black : in male / female slides
- Pink : in girls slides only
- Blue : in male slides only
- Green : notes, Extra

Reviewed by Razan AlRabah & Khalid Alkhani

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.



Pharmacology:

Is the science that deals with the drugs regarding names, pharmacokinetics, pharmacodynamics, side effects and uses.

Also defined as the study of how chemical agents affect living processes. E.g. hormones, neurotransmitters & drugs.

Examples of drugs:

1. Acetylsaliclic (ASA) or Aspirin can reduce inflamation, pain & fever.

It inhibit the action of a human cell membrane enzyme known as cycloxygenase.

2. penicillin cures certain bacterial infections, distrupts the synthesis of cell walls in susceptible bacterial stains by inhibiting a key enzyme.

Pharmacokinetics:

"what the body does to the drug"

Pharmacokinetics (ADME) :

- Absorption
- Distribution
- Metabolism
- Excretion

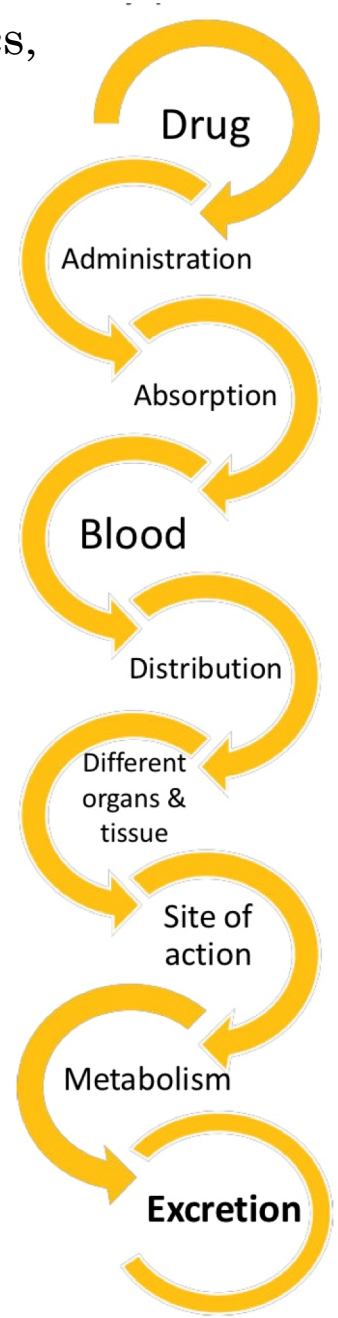
Pharmacodynamics:

" what the drug does to the body"

- Mechanisms of drug Action
- Pharmacological effects of drugs

Routes of drug administration:

1. Enteral via GIT (Oral –Sublingual –Rectal)
   *GIT=gastrointestinal tract
2. Inhalation
3. Parenteral (Injections)
4. Topical application قد يكون لغرض تجميلي او علاجي



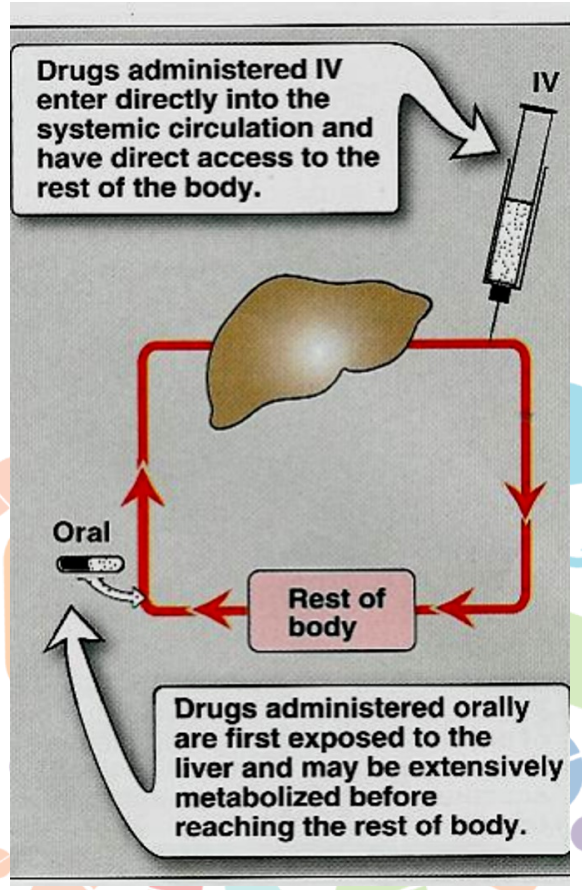
Routes of drug administration:

1- eternal via Gastrointestinal tract

	oral	sublingual	rectal
advantages	• Common. • Easy. • Self-use. • Convenient. • No need for sterilization. • Cheap.	• rapid effect because it goes to blood circulation directly • can be used in emergency • High bioavailability • No first pass effect • No GIT irritation • No food-drug interaction • Dosage form: friable tablet (easily breaks and dissolves)	Suitable for • children, vomiting, unconscious patients • Irritant & bad taste drugs • less first pass metabolism (50%) • Dosage form: suppository or enema
disadvantages	• Slow effect, GIT irritation. • Food - drug interactions. • Drug-drug interactions. • Destruction by PH & enzymes e.g. Penicillin and insulin. • First pass effect. • No complete absorption. • Low bioavailability. NOT SUITABLE FOR • Vomiting & unconscious patient. • Emergency & bad taste drug.	NOT SUITABLE FOR • Irritant drug. • Frequent use.	NOT SUITABLE FOR • Irritation of rectal mucosa • Irregular absorption & bioavailability

Bioavailability:

the amount of **unchanged** drug that enters systemic circulation after administration and becomes available to produce pharmacological actions. Bioavailability is the concentraion of the drug in the blood.



First pass effect:

Drugs given orally → Taken to the liver(via portal circulation)&meta bolized → Reaching the blood circulation to be distributed to all body compartments

First pass metabolism results in:

- **Low bioavailability** (low conc. of drug in blood).
- **Short duration of action** ($t\,^{1}/_{2}$).
- Drugs with high first pass effect should not be given orally but parenterally.

Where does it occur? Liver, GIT wall, GIT lumen.

Oral dosage forms (oral formulations):

1. **Tablets:**
    I. Coated tablets: sugar-coated to mask bad taste.
    II. Enteric coated tablets: dissolve only in intestine.
2. **Capsules:**
    I. Hard gelatin capsules: (contain powder).
    II. Soft gelatin capsules: (contain liquid).
3. **Syrup:** e.g. Cough syrups.

4. **Suspension:** "mixture of solid in liquids" e.g. antibiotics.

tablet

Syrup

Soft / hard capsule

Routes of drug administration:

2-Inhalation

Inhalation	
advantages	• rapid absorption (due to large surface area) • suitable for emergency • provide local action • limited systemic effect • less side effects • no first pass effect • Dosage form: i. volatile gases e.g. anesthetics ii. liquids given by aerosol, nebulizer/inhaler for asthma treatment
disadvantages	• Not suitable for irritant drugs • Only few drugs can be used

(Inhalation Dosage Forms)

Atomizer

Nebulizer

Routes of drug administration:

3- parentral administration. (INJECTION)

(Suitable route to provide rapid effect)

	Parental (injections)
advantage	• No gastric irritation • No food-drug interaction • No drug-drug interaction • No first pass metabolism • higher availability than oral
disadvantage	• Need skill • Pain, tissue necrosis or abscess (I.M.) • Anaphylactic or hypersensitivity reaction (I.V.)

(Parenteral Dosage Forms)

Ampoule (single use)

Vial (repeated use)

Types of parenteral:

Intradermal (I.D) (into skin)	Subcutaneous (S.C) (Under skin)	Intramuscular(I.M.) (into muscles)	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)

من الابطأ بالاستجابة الى الأسرع

I.V

I.M

S.C

I.D

	Intradermal (I.D) Volume: 0.1 ml	Subcutaneous (S.C) Volume: 0.1ml - 1 ml	Intramuscular (I.M) Volume: 3ml - 5ml	Intravenous (I.V) Volume: 500 ml
advantages	• suitable for vaccinations • sensitivity test	• Used for sustained release effect • Suitable for poorly soluble suspensions e.g. insulin zinc preparation	• prolonged duration of action • oily preparations or poorly soluble substances can be used	• Large volume (can be given by infusion) • Rapid action (emergency) • High bioavailability • No food-drug interaction • No first pass metabolism • No gastric irritation • Suitable for Vomiting, unconscious ,Irritant & bad taste drugs.
disadvantages	• Not suitable for large volumes.	Not suitable for large volumes	• Not suitable for irritant drugs • pain, abscess, tissue necrosis may happen	• Used only for water soluble drugs • Must inject slowly as a rule • Infection • Anaphylaxis • Sterilization • Expensive • Not suitable for oily solutions or poorly soluble substance

Routes of drug administration:

4-Topical Application

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

- **Skin** (percutaneous) e.g. allergy test, topical antibacterial, 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:

medicated adhesive patch applied to skin to provide systemic effect (prolonged drug action)

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

Drug Absorption

DEFINITION: the passage of drug from its 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: The transport of drugs across cell membrane occurs through one or more of the following processes:

- Simple diffusion (passive diffusion):

  -Aqueous diffusion: low molecular weight & water soluble drugs diffuse through aqueous channels or pores in cell membrane (filtration).

  -Lipid diffusion: low molecular weight & lipid soluble drugs diffuse through lipid cell membrane.

- Facilitated diffusion
- Active transport
- Pinocytosis /Phagocytosis :

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)

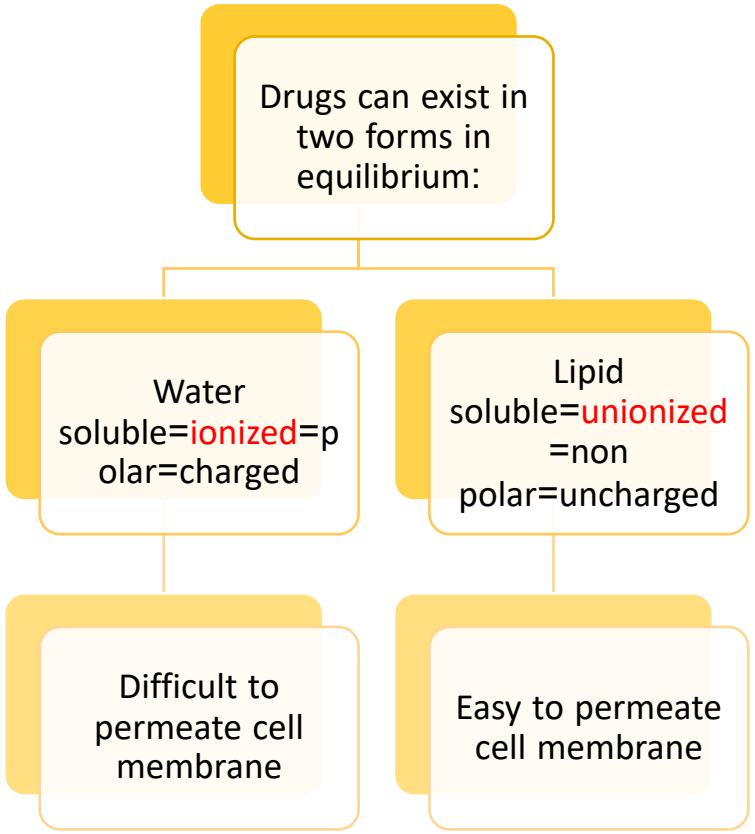
Passive Diffusion	Active Diffusion	Facilitated Diffusion (Carrier mediated)
ALONG Concentration Gradient	AGAINST Concentration Gradient	ALONG Concentration Gradient
No Energy & Carrier	Requires Energy & Carrier	No Energy But Requires Carrier
Common	Uncommon	_____
Not Saturable	Saturable	Saturable
Non Selective	Selective (Specific)	Selective
DEPENDS ON Lipid Solubility	E.G. Absorption Of Sugar & Amino Acid	E.G. Similar To Entry Of Glucose Into Muscle (GLUT 4)
DEPENDS ON Pka Of Drug & PH Of The Environment (it can be fluid of the cell body, blood, urine)	Uptake Of Levodopa by Brain (levodopa is used in treatment of parkinsonism)	_____

Pka & pH effect

pKa of the drug (dissociation or 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)



- Most drugs are weak basic or weak acid

- Only **unionized form** is absorbable.
- Ionization of drugs reduce passage of drugs across cell membranes.
- The degree of ionization of drugs is determined by their Pka and pH of the surrounding.

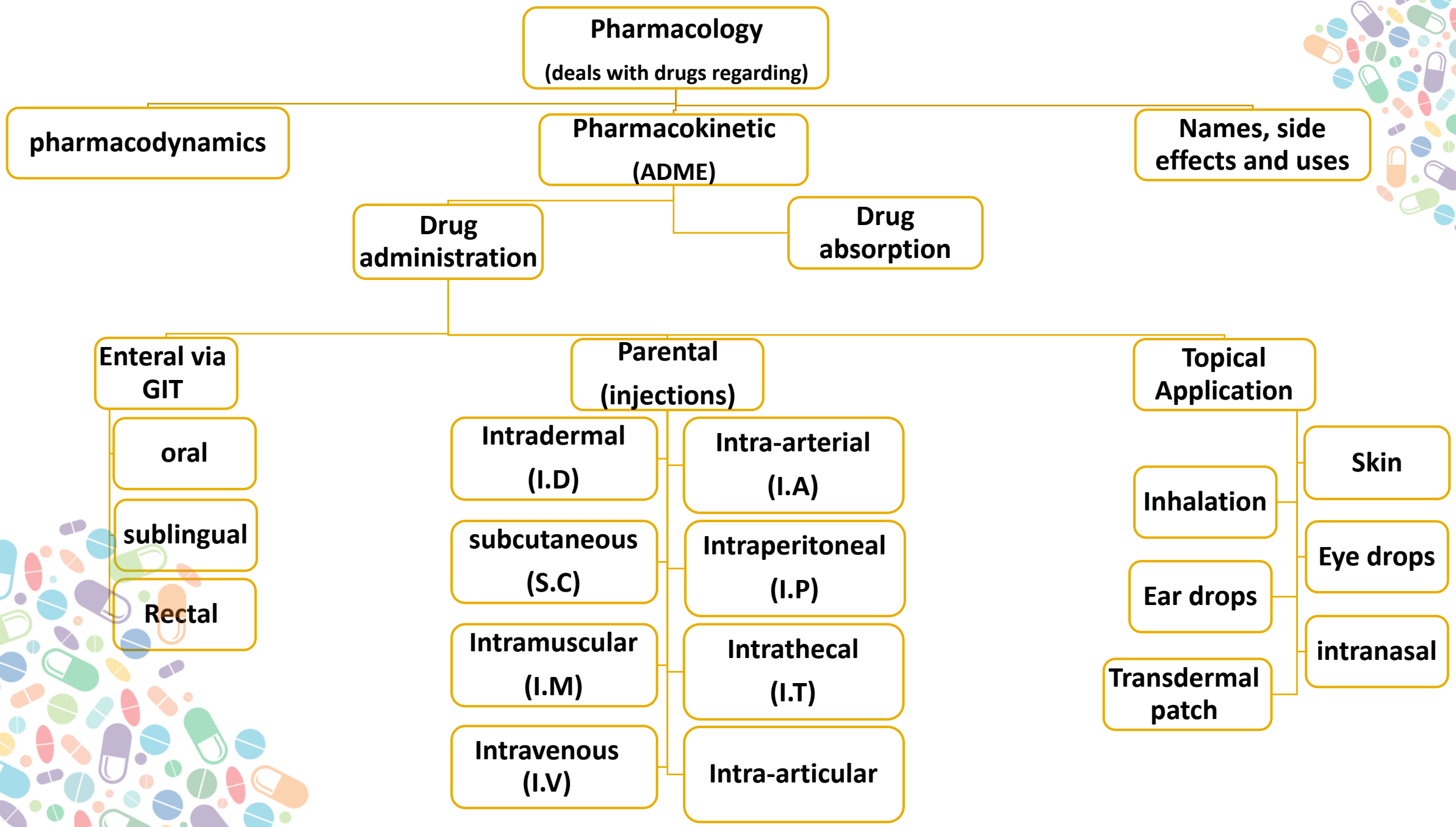
- Affects degree of ionization of drugs:

- Weak acidic drugs are best absorbed in the **stomach** (because the stomach is an acidic medium, drug exists in unionized form that is lipid soluble and easily absorbed).
- Weak basic drugs are best absorbed in **intestine** (because the intestine is a basic medium, drug exists in unionized form that is lipid soluble, and easily absorbed).

Note: If an acidic drug entered a basic medium the drug will become ionized and the drug won't show its effect Same thing will happen if a basic drug entered an acidic medium

Factors affecting absorption

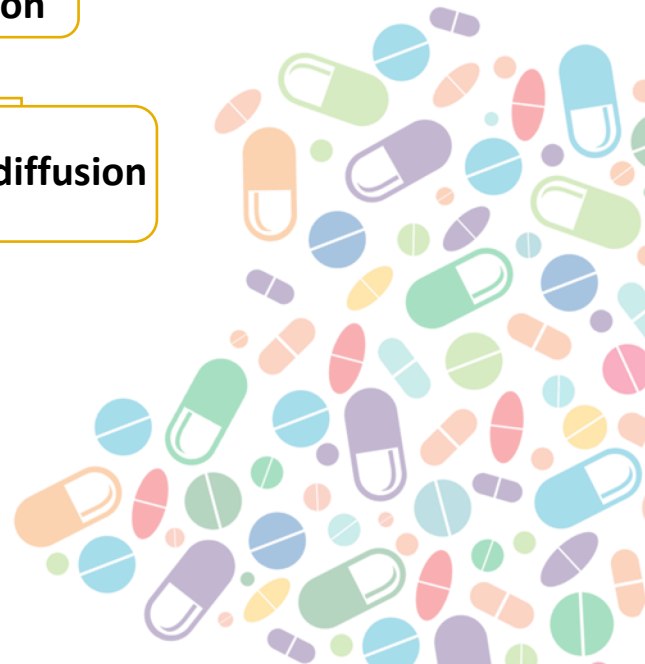
Route of administration	**Dosage forms** Depends on (particle size, disintegration ,ease of dissolution) (solution > suspension > capsule > tablet)	**Molecular weight of drug**
Lipid and drug solubility (aqueous preparation better than oily, suspension preparation)	**Degree of ionization**	**Chemical instability in gastric pH** (Penicillin & 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 enhance absorption-metoclopramide-)	**Food** • Slow gastric emptying. • generally slow absorption. • Tetracycline ,aspirin ,penicillin V. • A fatty meal increases the absorption of fat soluble antifungal drug (e.g. Griseofulvin)	**Drug interactions**


Pharmacology
(deals with drugs regarding)
pharmacodynamics
Pharmacokinetic
(ADME)
Names, side effects and uses
Drug administration
Drug absorption
Enteral via GIT
oral
sublingual
Rectal
Parental
(injections)
Intradermal
(I.D)
Intra-arterial
(I.A)
subcutaneous
(S.C)
Intraperitoneal
(I.P)
Intramuscular
(I.M)
Intrathecal
(I.T)
Intravenous
(I.V)
Intra-articular
Topical Application
Skin
Inhalation
Eye drops
Ear drops
intranasal
Transdermal patch

Pharmacology

(deals with drugs regarding)

- pharmacodynamics
- Pharmacokinetic (ADME)
  - Drug administration
  - Drug absorption
    - Factors affecting absorption
      - Route of administration
      - Molecular weight of drug
      - Degree of ionization
      - Intestinal motility
      - Food
      - Surface area available for absorption
      - Dosage forms
      - Lipid and drug solubility
      - Drug interactions
      - Blood flow to absorptive site
      - Gastric emptying
      - Chemical instability in gastric pH
    - Mechanism of drug absorption
      - Pinocytosis/ phagocytosis
        - endocytosis
        - exocytosis
      - Active transport
      - Facilitated diffusion
      - Simple diffusion
        - Aqueous diffusion
        - Lipid diffusion
    - I.V administration requires NO absorption
- Names, side effect and uses



Quiz

Q1/ The right order of the pharmacokinetic procedure is :			
A- Distribution 》 absorption》 metabolism 》 excretion	B- Absorption 》 distribution 》 metabolism 》 excretion	C- Absorption 》 metabolism 》 distribution 》 excretion	D- Distribution 》 metabolism 》 absorption 》 excretion
Q2/ Which route produces 100% bioavailability:			
A- Intradermal	B-Subcutaneous	C-Intramuscular	D-Intravenous
Q3/ The site of First Pass Metabolism is :			
A-Spleen	B- Muscles	C- Liver	D- Lungs
Q4/ Acidic drugs are best absorbed in :			
A- Intestine	B- Stomach	C- Liver	D- Urinary Bladder
Q5/ Which factor decreases absorption:			
A- Increased surface area available of absorption	B- Increased gastric emptying	C- Increased Blood Flow to site of absorption	D- Increased intestinal motility

Answers: b, d, c, b, d

Good luck

Thanks to the pharma team 435

PHARMACOLOGY 435

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