Pharmacology
Team 437

MED437
KING SAUD UNIVERSITY

Drug administration and absorption

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 Terms Extra informations

Success Doesn't Come To You, You Go To It!

Meaning Of Pharmacology And Its Branches

Pharma : drug.
ology: science.

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

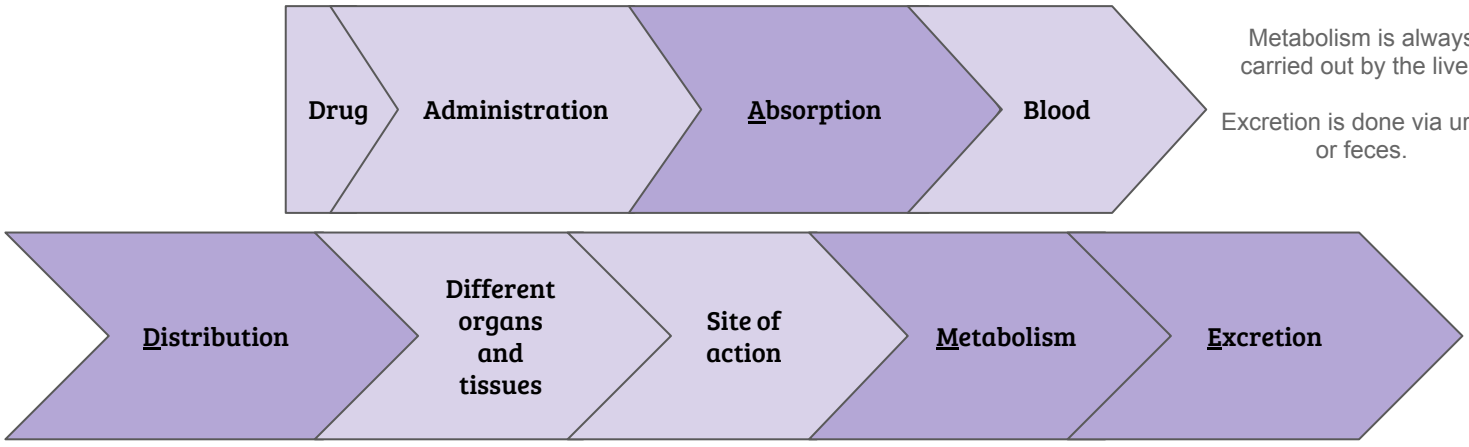
Pharmacological effects of drugs are the **uses** (wanted effects) of that drug. Any other effects caused by that drug are known as **side effects (unwanted effects).**

حركة الدواء

Pharmacokinetics
Are studies of the absorption, distribution, metabolism & excretion of drugs.
"What the body does to drugs?"

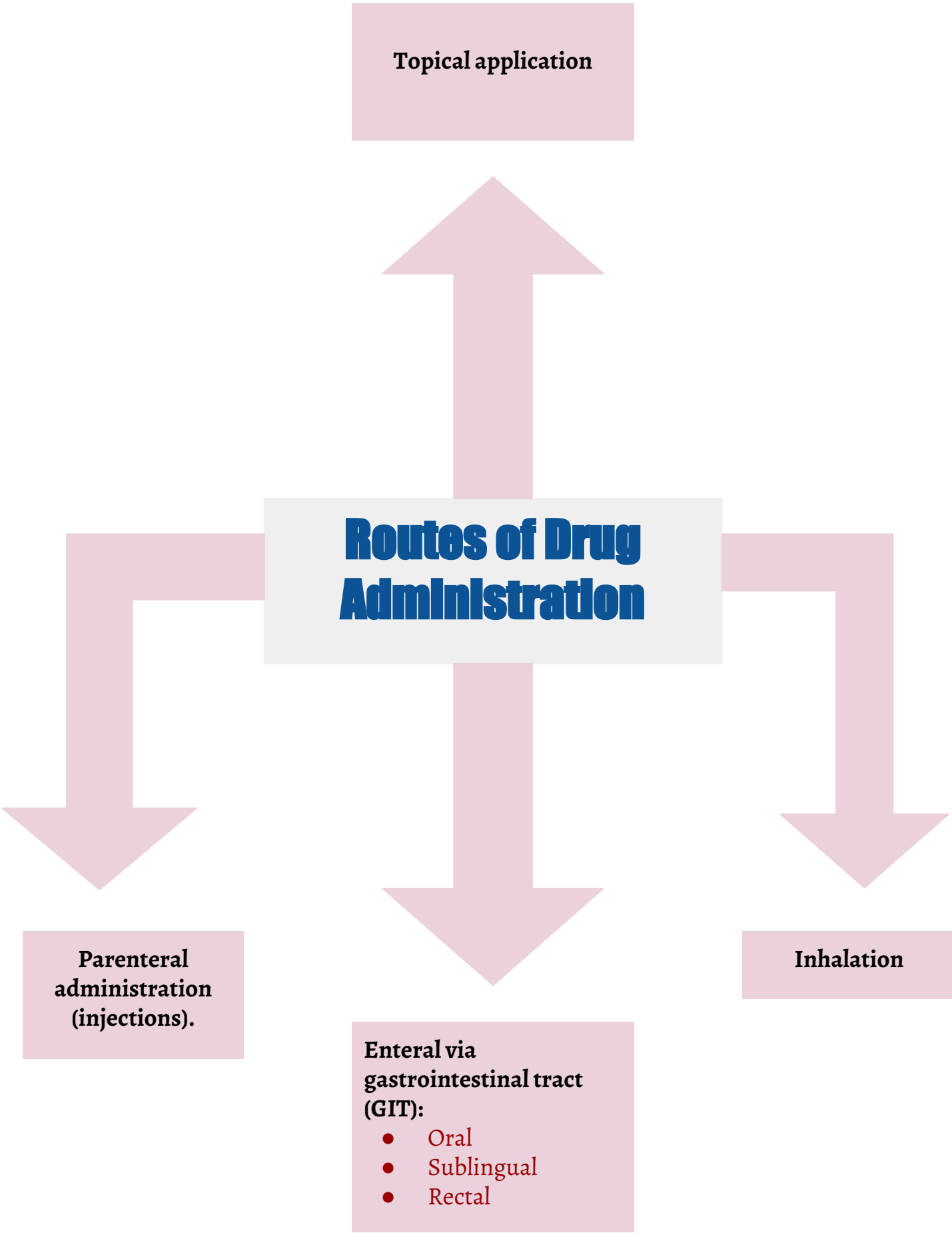
Pharmacodynamics
Are studies of :
1-mechanism of drug action.
2- pharmacological effects of drugs.
"What the drug does to the body?"

ADME
1-Absorption
2-Distribution
3-Metabolism
4-Excretion



Metabolism is always carried out by the liver.

Excretion is done via urine or feces.


Topical application
Routes of Drug Administration
Parenteral administration (injections).
Enteral via gastrointestinal tract (GIT):
Oral
Sublingual
Rectal
Inhalation

Bioavallability

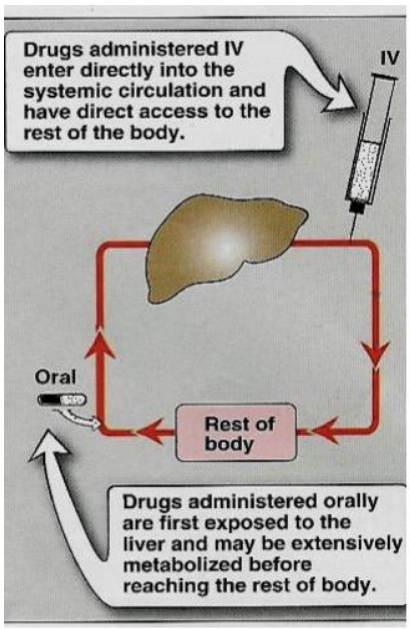
Is the amount of unchanged drug that enters systemic circulation after administration and becomes available to produce pharmacological actions.

* هو كمية الدواء الذي يصل للدم بحالة سليمة دون تغيير، أو تكسر يقلل من فاعليته، "بمعنى آخر هو الجزء الذي يعطي مفعوله من الدواء"* .

- **First pass** effect

Drugs given orally → ***Taken to the liver (via portal circulation) and metabolized*** → ***Reaching to the blood to be distributed to body compartments***

*الدواء قبل أن يدخل blood circulation يدخل على الكبد حيث يوجد عدد من الإنزيمات التي من الممكن أن تكسر جزء منه، مما يقلل من فعاليته.
فقط يحدث لبعض الأدوية



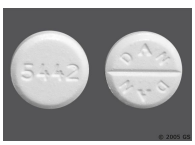
- **First pass** metabolism

Where does it occur?
- ➢ Liver
- ➢ GIT wall
- ➢ GIT lumen

Results in:
- ➢**Low bioavailability** (low conc. of drug in blood).
- ➢**Short duration of action (t ½).**
- ➢Drugs with high first pass effect should **not** Given orally **but** parenterally.

لأنه مارح يعطي المفعول orally

Oral dosage forms (oral formulation)



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

Capsules:
- Hard gelatin capsules: contain powder
- Soft gelatin capsules: contain liquid

Spansule oral capsule:
*a capsule which when swallowed releases one or more medicinal drugs over a set period.

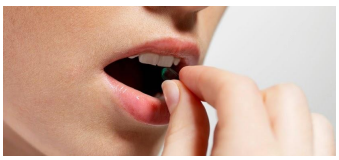
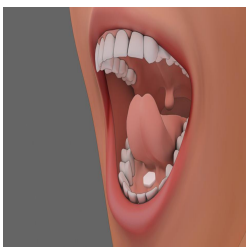
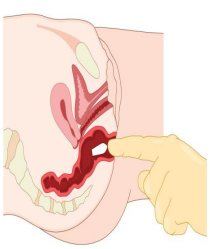
Has a long duration of action.

Syrup: e.g. cough syrup

Suspension: (mixture of solid in liquids e.g. antibiotics).

Routes of drug administration:

1- Enteral via gastrointestinal tract GIT:

	Advantages	Disadvantages
Oral 	• Common • Easy • Self use • convenient • cheap • No need for sterilization * Sterilization = عملية تعقيم هو رخيص لأنه لا يحتاج لعملية تعقيم.	• Slow effect (takes 1-2 hours to reach circulation), GIT irritation • Destruction by pH & enzymes • Food-drug interactions. • Drug-drug interactions (when multiple drugs are taken at the same time) • First pass effect . • No complete absorption *كمية الدواء التي وصلت للدم ليست كافية بسبب العمليات الحيوية في الجهاز الهضمي. • Low bioavailability. Not suitable for : vomiting, unconscious patient, emergency & bad taste drugs لاينفع في الحالات الطارئة بسبب بطء الامتصاص و نحتاج أن ننقذ المريض فورا
Sublingual 	• Rapid effect • can be used in emergency • High bioavailability * لأن تحت اللسان فيه blood vessels فيدخل على طول قبل blood circulation لا يتكسر من الإنزيمات الموجودة بالفم • No first pass effect. • 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%) *فيه قابلية أن الدواء ما يتكسر بنسبة 50% Dosage form: suppository or enema	• Irritation of rectal mucosa • Irregular absorption & bioavailability *Absorption done in the small intestine NOT in large intestine. وهو يدخل على الأمعاء الغليظة بالتالي عملية الامتصاص وفاعلية الدواء تكون قليلة.

Intradermal
(I.D.)
(into skin)

Subcutaneous
(S.C.)
(under skin)

Intramuscular
(I.M.)
(into muscles)

Intravenous
(I.V.)
(into veins)

2- Parenteral Administration

Intra-arterial
(I.A.)
(into arteries)

Intrathecal (I.T.)
(cerebrospinal fluids)

Intraperitoneal
(I.P.)
(peritoneal cavity)
= In abdominal area

Intra-articular
(synovial fluids)

*داخل المفصل=

Parenteral Administration (Injections)

Advantages	Disadvantages
• No gastric irritation • No food-drug interaction • No drug-drug interaction • No first pass metabolism • higher availability than oral	• Need skill • Pain,tissue necrosis or abscess(خراج) (I.M.) * في حالة الحقن بطريقة خاطئة • Anaphylactic or hypersensitivity reaction (I.V.) *رد فعل تحسسي لما يحقن بمادة يتحسس منها

Ampoule

Single Use

Vial

Repeated Use

Injection	Advantages	Disadvantages
Intradermal (I.D.)	• Minute volume of drug (0.1 ml). • suitable for vaccinations. • sensitivity test.	**Not suitable for** large volumes
Subcutaneous (S.C.)	• volume of drug (0.1 ml – 1 ml). • used for sustained release effect (prolonged duration of action). • suitable for poorly soluble suspensions and for instillation of slow-release implants e.g. insulin zinc preparation.	**Not suitable for** large volumes
Intramuscular (I.M.)	• moderate volumes (3-5 ml) . • prolonged duration of action. • oily preparations or poorly soluble substances can be used. Oily preparation :الدواء ذائب في سائل له خصائص الزيت.	**Not suitable for** • irritant drugs. • pain, abscess, tissue necrosis may happen.
Intravenous (I.V.)	• Large volume (500ml can be given by infusion). I.V infusion : drop by drop .يعني أحقن كميات كبيرة بس ليست بدفعة واحدة إنما بالتقطير. • Rapid action (emergency). • High bioavailability. • No food-drug interaction. • No first pass metabolism. • No gastric irritation. • No absorption required. **Suitable for:** • Vomiting & unconscious. • Irritant & bad taste drugs.	• used only for water soluble drugs. • Infection. • Anaphylaxis (hypersensitivity). • Sterilization. • Expensive. **Not suitable** for oily solutions or poorly soluble substance. *the poorly soluble substitute could cause Heart attack using the IV

3- Topical Application

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

Skin (percutaneous)
e.g. Allergy test, topical antimicrobial, steroids and local anesthetic.

Inhalation
(Mucous membrane of respiratory tract) e.g. asthma.

Intranasal
e.g. decongestant nasal spray

Ear drops
e.g. otitis externa

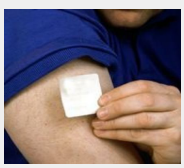
Eye drops
e.g. conjunctivitis

Inhalation

Advantages	Disadvantages
• 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:** • volatile gases e.g. anesthetics • liquids given by aerosol, nebulizer for asthma treatment	• **Not suitable for** irritant drugs • Only few drugs can be used

Transdermal Patch

They are 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**(مضاد للقيء) **for motion sickness)**



*devices for converting a drug in liquid form into a mist or fine spray .

Nebulizer

Atomizer

Drug Absorption

Definition:the passage of a 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 require 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 & lipids soluble drugs diffuse through lipid cell membrane itself.
- **Facilitated Diffusion**
- **Active Diffusion**
- **Pinocytosis**
  - **Endocytosis:** uptake of membrane bound particles.
    *for high molecular weight drug such as peptides.
    *high polar substances such as vitamin B12 (combines with intrinsic factor) & iron(combines with transferrin)
  - **Exocytosis:** Expulsion of Membrane bound particles.

أي شيء فيه carrier protein يكون selective و saturable .
Selective | carriers for acidic drugs and carriers for basic drugs.
Saturable| لما تكون كل carries مشغولة بالنقل .

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
Commen	Uncommon	_____
Not saturable	Saturable	Saturable
Non selective	Selective (specific)	Selective
Depends on lipids solubility	E.G. Absorption of sugar & amino acid	Similar to entry of glucose into muscle (GLUT4)
DEPENDS ON Pka of drugs & pH of the environment (it can be fluid of the cell body, blood, urine)	Uptake of Levodopa by brian (treatment of Parkinsons)	_____

pka effects & pH

Pka(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 aspirin (Pka =3)**
- **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
- Drugs can exist in two forms in equilibrium:

1-water soluble drugs=ionized = polar=charged are difficult to permeate cell membranes.
2-lipids soluble drugs=unionized =non polar =uncharged are easy to permeate cell membranes.

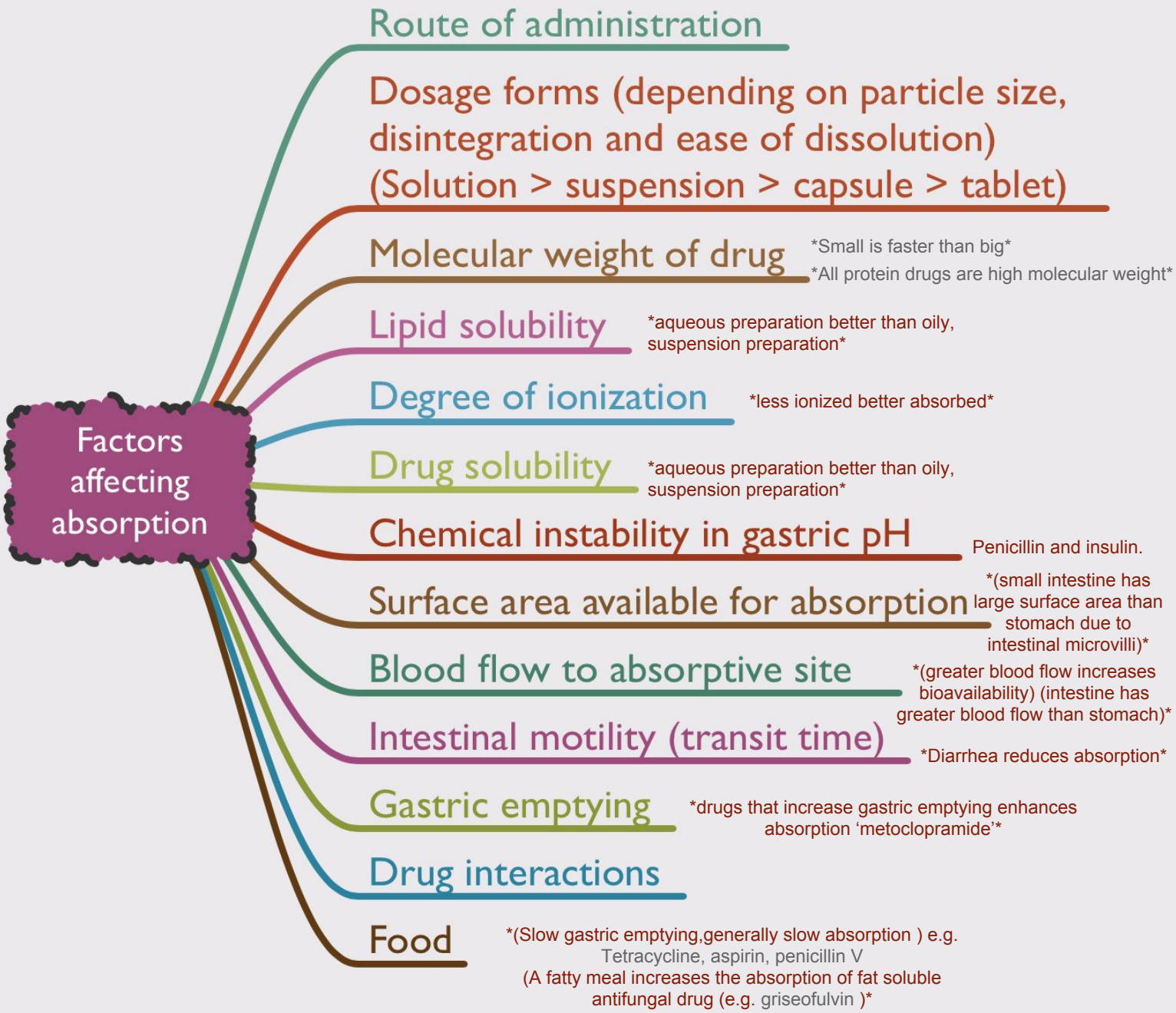
- Only **unionized form** is absorbable. *(because it is lipid soluble and can soluble easily in cell membrane which has lipid bilayer)*
- Ionization of drugs reduce passage of drugs across cell membranes. *opposite of ^*
- The degree of ionization of drugs is determined by their Pka and pH of the surrounding.

Affects degree of ionization of drugs:

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

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

Extra Explanation: When a basic drug is in a basic medium (with high OH^- concentration) it doesn't need to ionize and donate it OH^- group and therefore remains in unionized form, so its lipid soluble and can easily be absorbed/ pass through plasma membrane.
The same goes for an acidic drug, when it is in an acidic medium (with high H^+ concentration) is doesn't need to donate its H^+ group therefore remains in unionized form and can easily be absorbed.


Factors affecting absorption
Route of administration
Dosage forms (depending on particle size, disintegration and ease of dissolution) (Solution > suspension > capsule > tablet)
Molecular weight of drug
Small is faster than big
All protein drugs are high molecular weight
Lipid solubility
aqueous preparation better than oily, suspension preparation
Degree of ionization
less ionized better absorbed
Drug solubility
aqueous preparation better than oily, suspension preparation
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)*

Summary


Pharmacology
Deals with drugs regarding names
Pharmacokinetic
Absorption
Distribution
Metabolism
Excretion
Pharmacodynamics
Factors affecting absorption
Surface area available
Blood flow to absorptive site
Intestinal motility
Gastric emptying
Drug interactions
Food
Drug administrations
Enteral via GIT
Oral administration
First pass effect
Form [oral formulation]
Tablets
Coated tablets
Enteric coated tablets
Capsules
Hard gelatin capsules
Soft gelatin capsules
Syrup
Suspension
Ex: antibiotics
Sublingual
Rectal
Parental
Injections
Intradermal I.D
Subcutaneous S.C
Intramuscular I.M
Intravenous I.V
Intra-arterial I.A
Intraperitoneal I.P
Intrathecal I.T
Intra-articular
Topical application
Local effects
Inhalation
Drug absorption
I.V administration requires NO absorption
Mechanism of drug absorption
Simple diffusion [passive diffusion]
Aqueous diffusion
Water soluble
Through aqueous channels or pores in cell membrane [FILTRATION]
Lipid diffusion
Lipid soluble
Through lipid cell membrane
pH effect
Ionization of drug
Weak acidic
Intestine
Weak basic
Stomach
Active transport
Against concentration gradient
Requires carrier and energy
Facilitated diffusion
Along concentration gradient
No energy required
Requires carriers
Pinocytosis
Endocytosis
Occurs for :
High molecular weight drug
High polar substances
Exocytosis
Expulsion of membrane bound particles

MCQs

1-What's the most common way of drug administration?

A-Oral B-Sublingual
C-IV (intravenous) D-IT(intrathecal)

2-Which type of the drug administration has the highest bioavailability ?

A-Rectal B-IV(intravenous)
C-IA(intra-arterial) D-Inhalation

3-Pharmacokinetics of drugs are studies of drugs regarding...

A-AMDE B-MADE
C-ADME D-EMDA

4-The process where the drug is being metabolized in the liver before it distributed to all the body is called...

A-Excretion B-First pass effect
C-Absorption D-Distribution

5-Which type of the drugs administration is usually used with children ?

A-Inhalation B-Sublingual
C-Rectal D-Injections

6-Which type of the drug administration doesn't require absorption?

A-IM(intramuscular) B-Sc(subcutaneous)
C-ID(intradermal) D-IV(intravenous)

7-Which of the following answers is correct about the simple diffusion?

A- It Doesn't require energy, saturable
B-It requires energy,non selective
C-It Doesn't require energy,No carrier
D-It requires energy,with the concentration gradient

8-Most drugs are ..

A- Weak acids B-Weak bases
C-Strong acids D- A&B

9-Drugs are only absorbable in the

A-Ionized form B-Unionized form
C-acidic medium D- bases medium

10-Which one of the following sentences is correct?

A-Diarrhea increase absorption
B-Stomach has greater blood flow than intestine
C-Greater blood flow increases bioavailability
D-Food doesn't slow the absorption

Answers

1-A 2-B 3-C 4-B 5-C 6-D 7-C 8-D 9-B 10-C

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Team 437

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Useful videos:

Pharmacokinetics first 5 min

Routes of drug administration 3:30

Routes of drug administration (2)

Team members:

girls:

Alanoud Alessa
Alanoud Salman
AlFahdah alSaleem
Ghadah Alhenaki
Ghada Alqarni
Laila Alsabbagh
Norah Aldubaib
Nouf AlOtaibi
Rahaf AlShammari
Rahaf Althnayan
Reem Alqarni
Rinad Alghoraiby
Shaden AlOtay
Shahad Alzahrani
Shikah Alrwais

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