HANDWRITTEN NOTES

DAMS

α

PHARMACOLOGY

CRISP, CONCISE, CONCEPTUAL

Integrated Edition

Studentfirst @DAMS

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HOW TO MAKE BEST USE OF NOTES?

A Message by Mentor Duo Specially for you,

- *Read the notes thoroughly, they are absolutely concise, crisp & conceptual and hence it is best advised not to add a lot of extra information to them as that will dilute the quality.*
- *Images have been provided alongside to aid in better understanding and also help you solve image-based questions, these images have been specially picked by the faculty so have a high probability of being asked in exams.*
- *Notes are handwritten in a way to help make them easier to retain, a lot of tables, graphs and algorithms have been used to simplify the learning.*
- *While reading notes try and use the CFAQ technique —*
  - *A. Use the C to denote concept part in the notes and ensure you are clear with this part in the first go if not then it's advisable to listen to this part of the video from your course.*
  - *B. Use the F To denotes facts in your notes, it is okay if you can't remember them in first go but will need repeat reading. But these facts are important for exams as they could be integrated to clinical questions.*
  - *C. Use A to denote applied parts, this is how concepts and facts are asked indirectly in exams. This will also help you develop MCQ solving skill.*
  - *D. Use Q to denote areas where faculty has said it's a direct question or a PYQ or a potential question.*
- *This technique will help you summarize your notes In way that your second reading will become easy and faster.*
- *Active space has been provided with these notes to make your own annotations alongside and this will help you maintain one single notebook for one subject.*
- *Try and solve MCQs with every topic from DQB. Your goal should be to start with at least 30 MCQs every day and then increase to at least 50 MCQs every day. Also, when you do a topic wrong write it alongside the notes that this topic needs to be read again but mark only the specific area that you have done wrong not the whole topic.*
- *After the topic is covered then in the active space try and summarize the topic in the form of mind map. This will help in active recall and make your revision easier.*

Best Wishes & Happy Learning!!!!!

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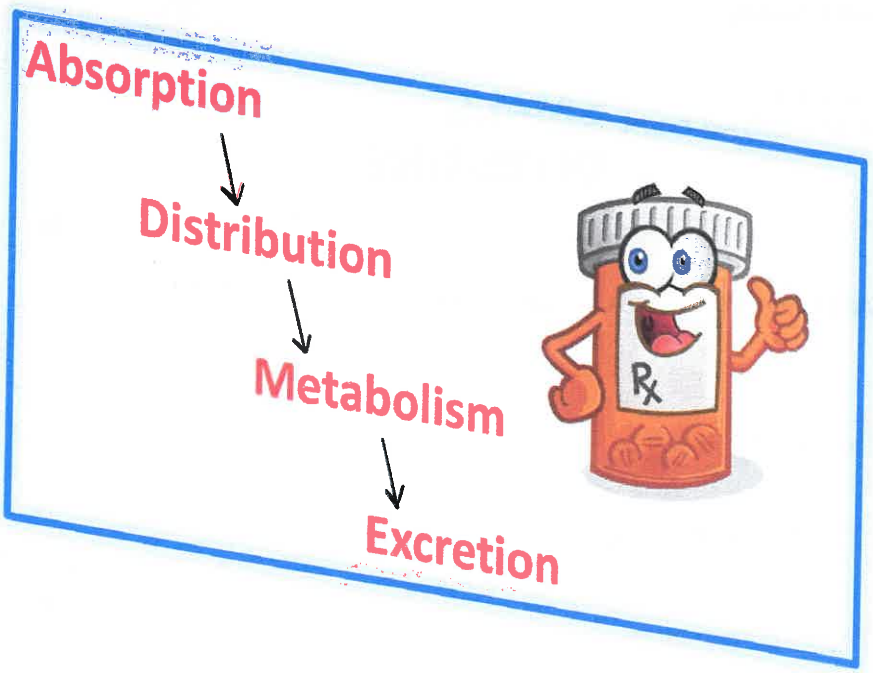
PHARMACOLOGY

General Pharmacology

PHARMACO KINETICS



DRUG ABSORPTION

For a drug to get better absorption, It should be

- LIPID SOLUBLE
- NON-IONISED

Aspirin (Acetylsalicylic acid)

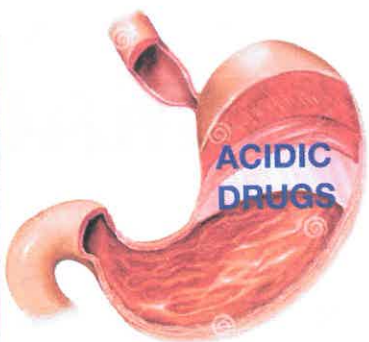
Ionisation of drug depends pH of the environment

FORMULA

Acidic drug NON IONISED– Acidic medium

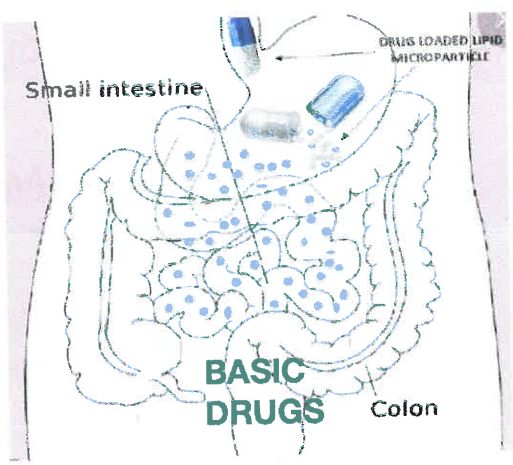
Basic drug NON IONISED- Basic medium

Acidic drugs- Better absorbed from STOMACH



Morphine (Alkali)

basic drugs- Better absorbed from SMALL INTESTINE



Comparison- stomach / intestine

Intestine has

- Large surface area
- Thin mucous membrane

Strongest acid/alkali drugs-

IONISED

Heparin ?

Strongest acid

Not absorbed via oral route
Hence, given i.v.

DVT- pregnancy

Not only for absorption

Even - For distribution & for crossing barrier-

NON- IONISED

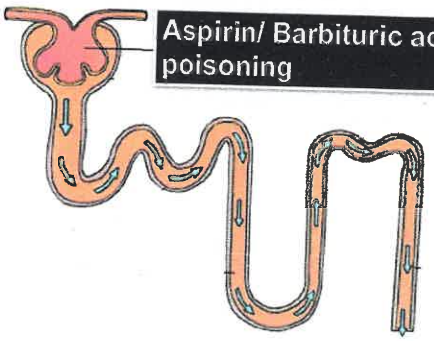
IN CASE OF DRUG POISONING-

HOW TO PROMOTE EXCRETION OF DRUG THROUGH URINE

Drug poisoning ?

- ANTIDOTE
- GASTRIC LAVAGE
- HEMODIALYSIS
- PROMOTING EXCRETION VIA URINE

Drug poisoning



Aspirin/ Barbituric acid poisoning

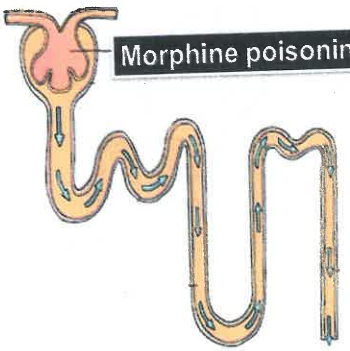
For excretion of Acidic drug

Forced alkalization

↓

Alkalization of urine done by

- Sodium bicarbonate
- Acetazolamide



Drug poisoning

ANTIDOTE-

NALOXONE

- i.v. Naloxone - DOC → ↓ $t_{1/2}$
- Oral Naloxone → Maintenance

For excretion of Alkali drug

Forced acidification

↓

Acidification of urine done by

- Ascorbic acid
- Ammonium chloride

Message

Drug Absorption — **NON-IONISED**

Drug Excretion — **IONISED**

HENDERSON HESSELBACH EQUATION

$$pH = pKa + \log \frac{\text{Ionized drug concentration } [A^-]}{\text{Unionized drug concentration } [HA]}$$

When pKA = pH means what is the inference?

↓

50% of drug is in ionized form
50% of drug is in non-ionized form

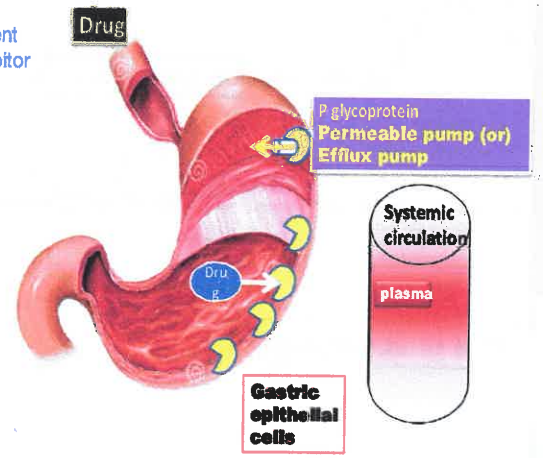
So, log (50/50) = log (1) = 0

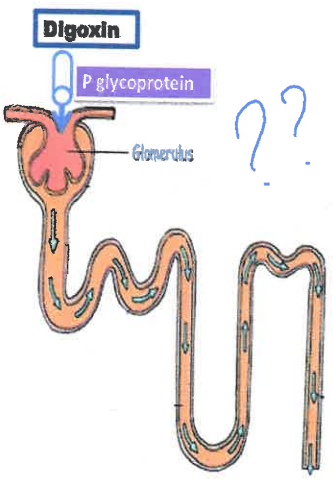
Bio availability

Fraction of drug % that effectively reaches systemic circulation.

P-glycoprotein inhibitors-

- V — Verapamil — Most potent P-gp inhibitor
- A — Amiodarone
- C — Cyclosporine
- I — Itraconazole
- N — Nifedipine
- E — Erythromycin
- Q — Quinidine





Quinidine + Digoxin – DRUG INTERACTION?

Quinidine interferes with renal excretion of Digoxin

P-glycoprotein inducers

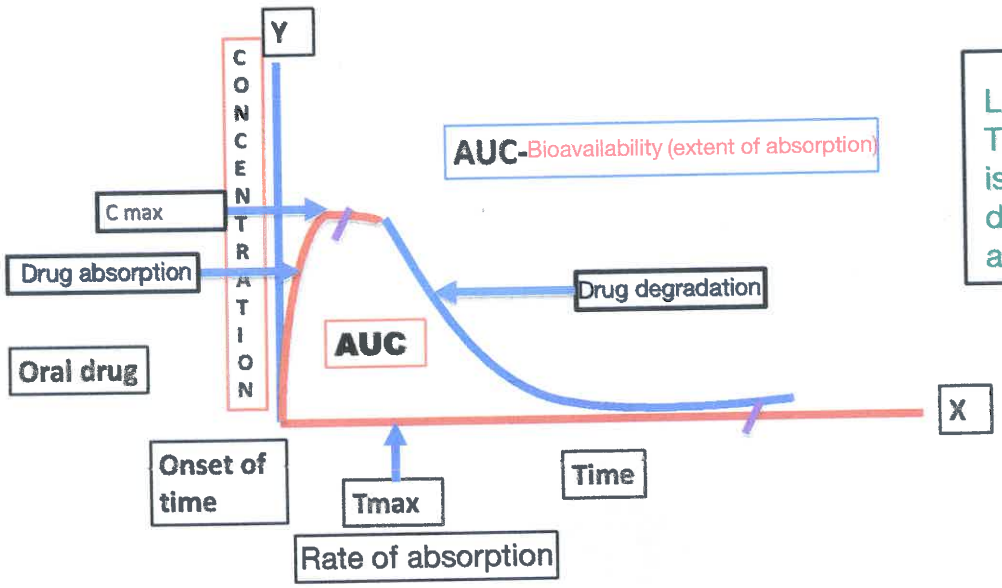
- Rifampicin
- St. John's wort (Herbal medicine (Antidepressant))
- Phenytoin
- Carbamazepine

P-gp also called as

- ABC - 1 (ATP binding cassette)
- MDR - 1

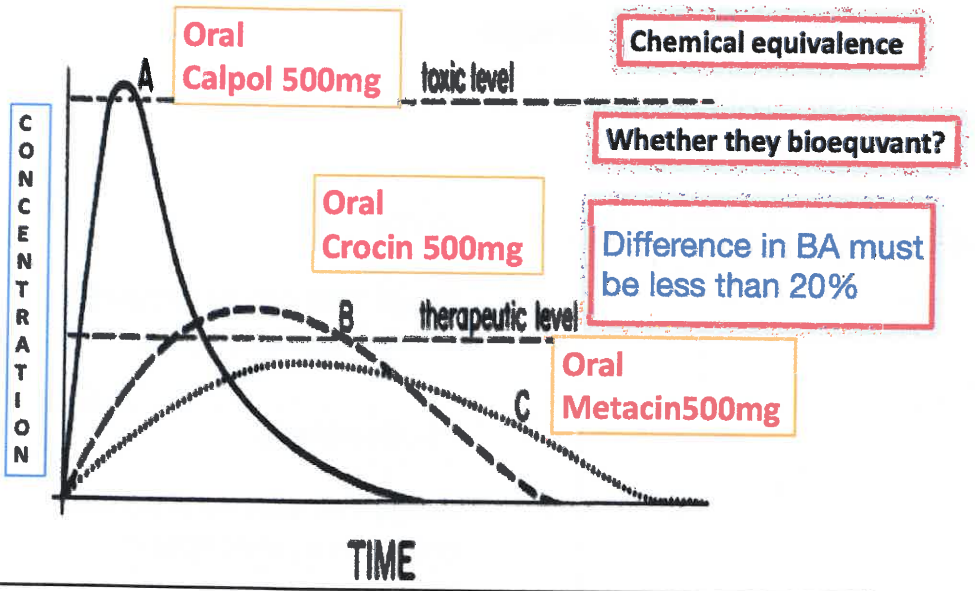
C max- Maximum concentration of drug in plasma

BIOAVAILABILITY



AUC- Bioavailability (extent of absorption)

Lower the Tmax, faster is the rate of drug absorption.



Same drug, same dose, same route - difference in BA < 20% - bio equivalent

Orphan drugs

For diagnosis/prevention & treatment of **RARE DISEASE**

Fomepizole — Antidote of methyl alcohol — MOA- Inhibits alcohol dehydrogenase

protamine sulfate — Antidote for Heparin — What type of antagonism? Chemical antagonism

- Heparin - acidic drug
- Protamine - basic drug

Digiband — Antidote for Digoxin

Liothyronine — ?. T3 - active form of thyroid hormone — USE- Myxoedema coma

Essential drugs

Those drugs that satisfy the priority healthcare needs of the majority of population

ESSENTIAL DRUGS SHOULD BE

- Affordable
- Available
- Single compound

?OTC-
OVER THE COUNTER DRUGS
Drugs that can be procured without a prescription.

? Schedule H-
PRESCRIPTION DRUGS
Drugs that can be procured only with a prescription.

PLACEBO- **Inert substance** available as Dummy medicine, use- satisfy the patient, clinical trail

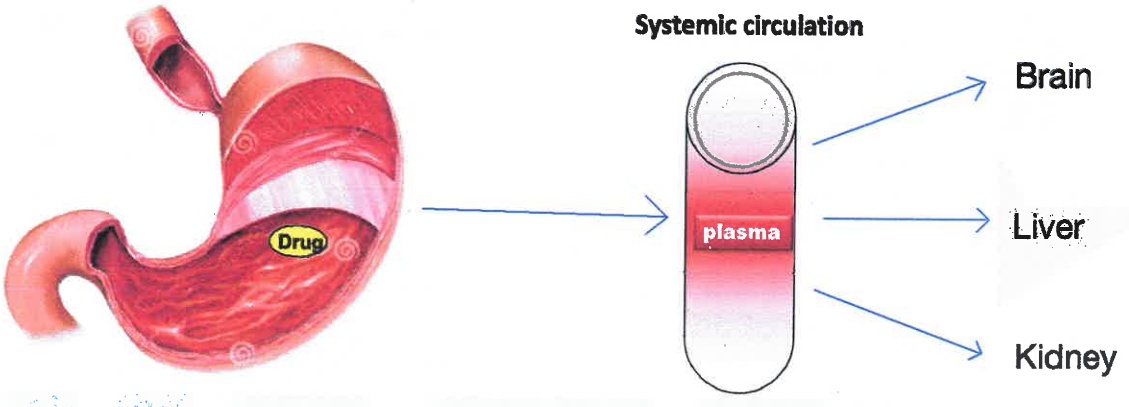
(placebo surgery)---? Sham surgery

Inert substance used along with an active ingredient- to make stability or to mask unpleasant taste- **EXCIPIENT**

If the labeling is deceptive, untrue or leaves out important safety information, the product may be **MISBRANDED.**

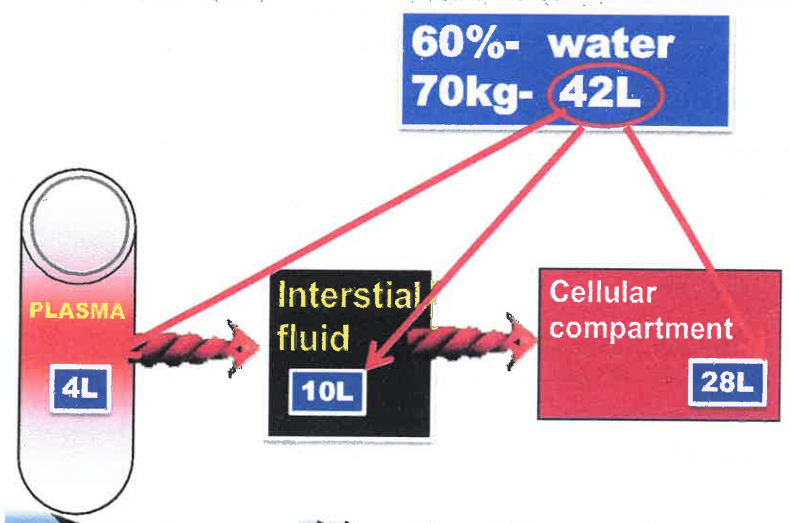
A counterfeit drug -will contain either deficient quantities of the necessary ingredients or they may be of substandard quality. In addition they may contain active ingredients that are not even in the label.

Drug distribution



PHYSIOLOGY

60% of the body weight is contributed by water.
Hence, a 72kg adult has 42L of water.



Drug distribution

Imagine- Given drug is

Lipid insoluble
Ionized
Highly protein bound
Large size

Distributed
Plasma compartment - 4L

Low Vd

In case of poisoning we can do
HEMODIALYSIS

Imagine- Given drug is

- Chloroquine
- Digoxin
- TCAs

Lipid soluble
Non Ionized
Free form

Distributed IN
Cellular compartment

Large Vd

Interstitial fluid 10 L

Cellular compartment 28L

In case of poisoning – there is no role for
NO ROLE FOR HEMODIALYSIS

No role for hemodialysis
(Large Vd)

A- Amphetamine
V- Verapamil
O- Opiods, OPC
I- Imipramine
D- Digoxin
Dialysis- Diazepam
Strong binding - plasma protein

Loading dose depends upon.... Vd

What type of drugs needs loading dose?
Large Vd

Vd = $\frac{\text{Total dose}}{\text{Plasma concentration}}$

PK formula

Loading dose=
Vd x Target plasma concentration

Half life= $\frac{0.693 \times Vp}{CL}$

clearance= (CL) $\frac{\text{Rate of elimination}}{\text{Plasma concentration}}$

Maintenance dose=
CL x Target plasma concentration

Free form → **Action**
Free form → **Metabolism**
Free form → **Excretion**
Free form → **ADR**

Bound form
(binding with plasma protein)

Temporary reservoir

What drug binds with what protein?

Acidic Drugs – Albumin

Basic Drugs - Alpha-1 Acid Glycoprotein

In case of Hemoglobinemia | Liver cirrhosis, Nephrotic syndrome → HYPOALBUMINEMIA

What happens to free level of Acidic Drugs ?

↑Free drug → Action + ↑ADR → Hence, less dose to avoid ADR

In case of Myocardial infarction or Burns or Trauma ↑ α-1acid glycoprotein

What happens to free level of basic Drugs ?

↓Free drug → More dose is required

Drug displacement – drug interaction

Salicylate displace.....Tolbutamide

Salicylate displace.....Warfarin

Salicylate displace .....Thyroxine

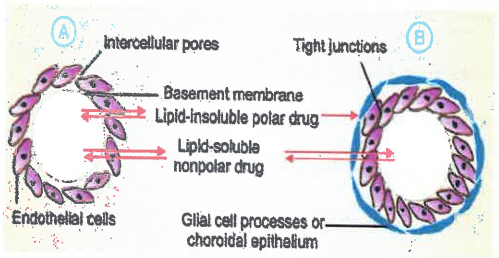
Sulphonamide displace.....Bilirubin.....

Kernicterus ?

Sulphonamide - unconjugated hyperbilirubinemia → BRAIN of newborn

BBB

Only lipid soluble & unionised drugs can cross BBB



Blood Brain Barrier absent --

Pituitary, Pineal, CTZ, Median eminence

Does not cross BBB-

Streptomycin, Neostigmine, Glycopyrrolate, Dopamine

PLACENTAL BARRIER

Only lipid soluble & unionised drugs can cross

Drugs with high molecular weight cannot cross **(Heparin, Insulin)**

ADR
TERATOGENICITY

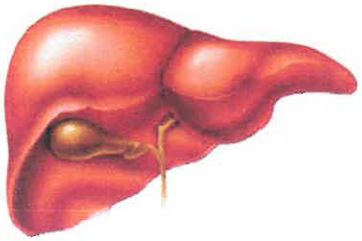
REDISTRIBUTION

EXAMPLE

Thiopentone sodium

- Ultra short acting barbiturate
- Induction in general anaesthesia

BIOTRANSFORMATION (METABOLISM)



? consequences

Drug metabolism

- **Inactivation**
  - WATER SOLUBLE
- **Active metabolite formation from an active drug**
  - Diazepam ⟶ OXAZEPAM
  - Spironolactone ⟶ CANRENONE
  - Primidone ⟶ PHENOBARBITONE
  - Phenacetin ⟶ PARACETAMOL
- **Activation of inactive drug** (INACTIVE DRUGS(PRO DRUG))
  - Levodopa ⟶ DOPAMINE
  - Minoxidil ⟶ MINOXIDIL SULPHATE
  - Enalapril ⟶ ENALAPRILAT
  - DIPIVEFRINE ⟶ EPINEPHRINE
  - All ACEI are prodrug EXCEPT- Captopril & Lisinopril

Drug metabolism

- **Phase - 1 reaction** (Non-synthetic)
  1. Oxidation
  2. Reduction
  3. Hydrolysis
  4. Cyclization
  5. Decyclization

  Microbial enzyme - *CYP450*
- **Phase - 2 reaction** (Synthetic/ Conjugation)
  - Glucuronidation
  - Sulfate conjugation
  - Glycine conjugation
  - Glutathione conjugation
  - Acetylation
  - Methylation

Acetaminophen
PARACETAMOL

- **PHASE I** (Minor pathway ~ 5-10%) — *CYPN2E1*
  - **NAPQI:** N-acetyl-p-benzoquinone imine
    - HEPATOTOXIC
    - Single dose of **10 - 15g**
- **PHASE II**
  - GLUTATHIONE CONJUGATION (Detoxification)
    - ANTIDOTE: N-acetyl cysteine (NAC)
  - Inactivation
  - Major pathway:
    - Glucuronidation (60-65%)
    - Sulphate conjugation (30-35%)

INH
Chronic alcoholic
CYP2E1 inducer