Toppersnotes
Unleash the topper in you

NEET-PG

PART-B

VOLUME-III

Pharmacology

SIERRA INNOVATIONS
Private Limited

PHARMACOLOGY

Toppersnotes
Unleash the topper in you

Pharmacology -

Science dealing ~ **DRUG**

1) what happens to drug
2) What happens to body due to drug

PK - effect of Body on drug

Pharmodynamics - effect of Drug on Body (HR, BP etc)

PHARMACOKINETICS

= A D M E → study
↓ ↓ ↓ ↓
absorp^n distribu^n Metabolism Excretion

ABSORPTION

ROUTE OF ADMINISTRATION

Absorp^n is movement of drug from site of administration to blood.

Drug should cross membrane for absorption.

Factors

1) Lipid solubility -

varies a/c to site.

$H_2O \rightleftharpoons H^+ OH^-$

Ionised form of drug is water soluble.

Non-ionised form of drug is lipid soluble

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⇒ It depend on

1) pH

2) medium

* When medium is same → drug will cross.
→ If drug is acidic – it will cross in acidic medium
→ Basic drug crosses in Basic medium

* Acidic Drug will not cross in Basic medium becoz it gets ionised (water soluble)

Drug	Med			
A	A	LS	Non-I	✓
B	B	LS	Non-I	✓
A	B	WS	Ion	×
B	A	WS	Ion	×

Drug = Acidic/Basic.

pH = ?

pKa (Acidic Dissociation constant)

That pH at ≤ 50% of drug can cross
• 50% is water soluble. (lipid-soluble)

eg An acidic drug having pKa = 6
Place the drug in mediums of different pH

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pH	LS	WS
3	99.9	0.1
4	99	1
5	90	10
6	50	50
7	10	90
8	1	99
9	0.1	99.9

Henderson Hasselbach Eqn

$$pH = pK_a + \log \frac{\text{Ionised}}{\text{Non-I}}$$

Eg a) Aspirin
acidic drug
absorbed from stomach due to acidic pH

b) Morphine
Basic drug.
can't be absorbed from stomach due to acidic
absorbed from intestine where pH is basic

So, Acidic Drug :- absorbed from stomach a/c to this eqn

Basic Drug :- absorbed from intestine a/c to this eqn.

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* But practically all ~~dtts~~ drugs are more absorbed from Intestine due to other factors -

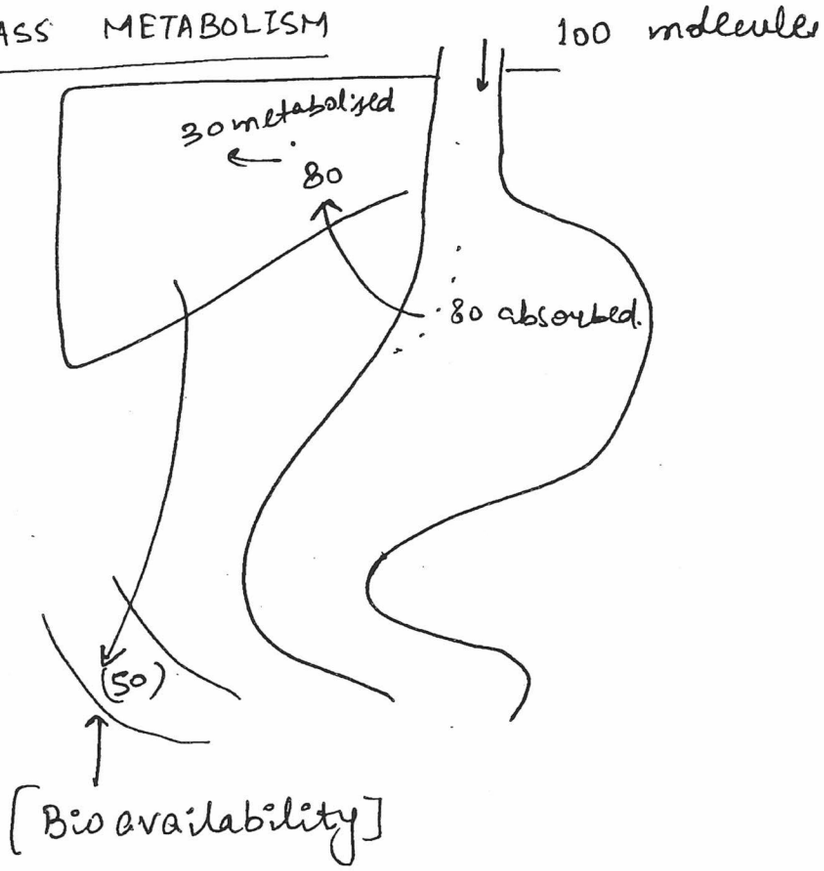
1) transit time

very less in stomach. (30min)
more in intestine

2) Surface area

more in intestine, hence more absorptn takes place..

FIRST - PASS METABOLISM



Bioavailability → biologically available, % of drug available for action.

can be in fraction (0.5) or %. (50%)

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* Clinical Importance -

1) Lesser bioavailability, more the dose.
   It determine the dosage
   If a drug given by I.V. route, bioavailability is 100%.

* FACTORS on ∝ bioavailability depends :-

1) Absorpⁿ.
   If more absorpⁿ, more bioavailability

2) First Pass Metabolism
   If more metabolism, less bioavailability
   max. 1st pass met. seen in oral route
   also seen in rectal route

eg. Nitroglycerin. → 100% absorpⁿ approx.
But bioavailability is very poor due to very high 1st pass metabolism
Hence given sublingual route

DRUGS ∝ High 1st Pass Met

L - Lignocaine
P - Propranolol
G - GTN.

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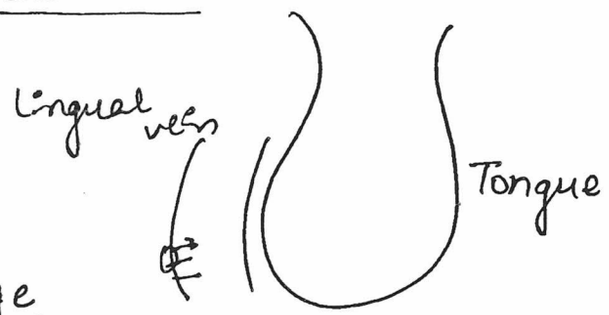
Sublingual Route :-



Advantage

1. 100% bioavailability
2. no 1st pass metabolism
3. Faster Action

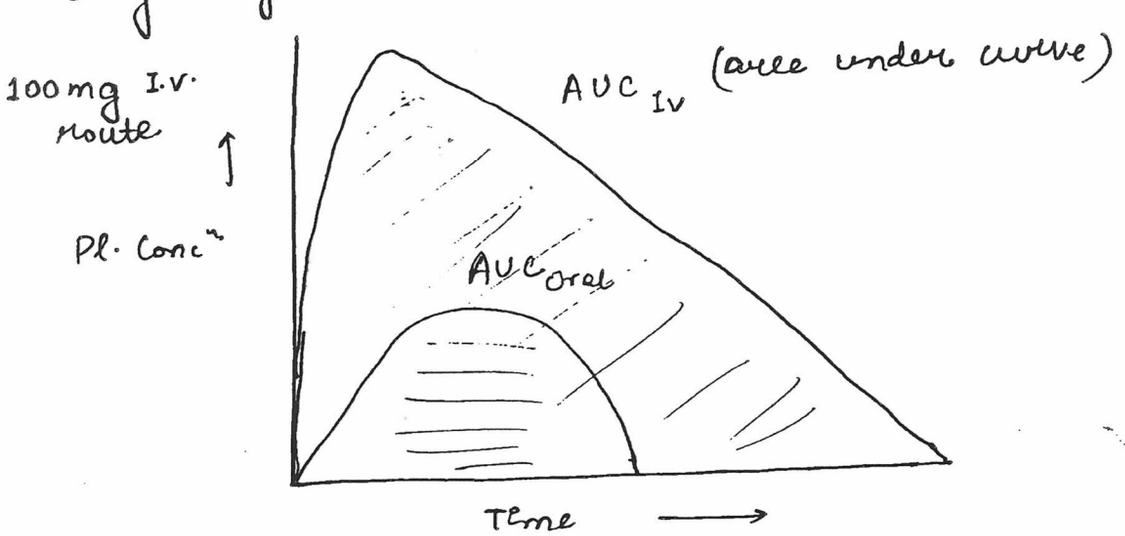
Hence useful in emergency

Eg. 10 mg of nitroglycerine is administered sublingually 5mg is absorbed, rest 5mg is in mouth

4. Rest drug can be spit thus effect can be terminated.
5. self administration is possible, no expertise reqd. hence I.V. route not used for NTG.

How to measure Bioavailability?

Drug A by oral route ?



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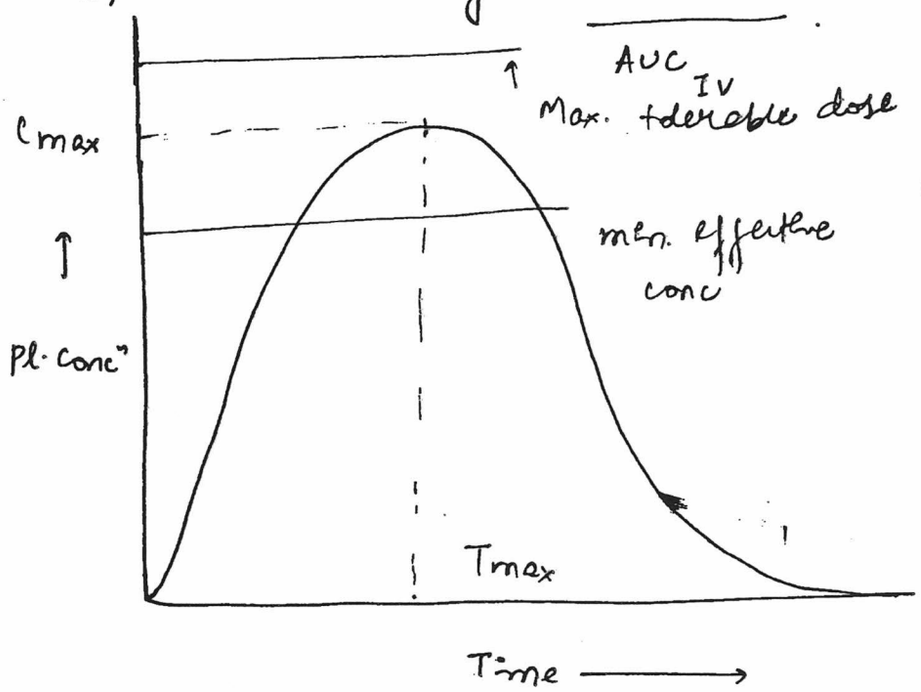
So, Bioavailability = $\frac{AUC_{oral}}{AUC_{IV}}$



AUC → extent of absorp"

AIIMS

Tmax - time at ⊆ Pl. conc" is max.
tells about rate of absorp".
Low Tmax → can be utilised in emergency

Cmax - max conc" obtained at that particular dose
It should lie bet" Max tolerable dose & Min. effective conc"

BIOEQUIVALENCE

If bioavailability of 2 brands of same drug is similar they are called bioequivalent

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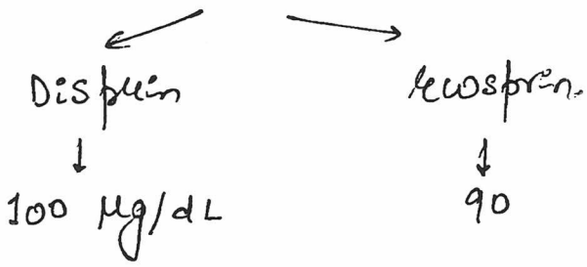
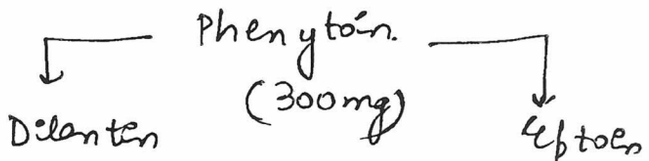
Eg Aspirin (500mg)



If bioavailability & varies ± 20%, Bioavailability is considered same. (Bioequivalent)

exception - Phenytoin → not bioequivalent

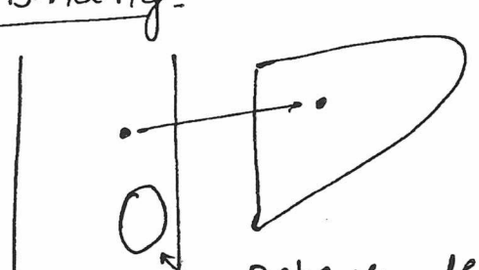


So, brand can't be changed for phenytoin

DISTRIBUTION

- The amount of drug c reaches blood gets distributed
- Depends upon ① Lipid solubility + other factors

② Plasma Protein Binding.



Behaves like big molecule due to plasma protein binding

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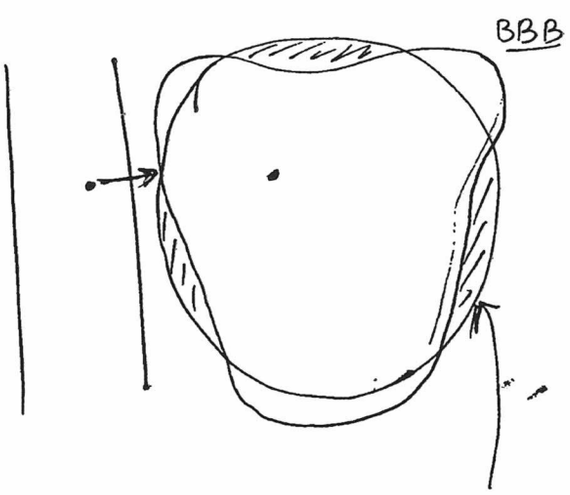
More PPB means less distribution

* Proteins on ⊂ drug Binds →

Albumin
↓
Acidic drugs binds to albumin

α_1 - Acid Gp
↓
Basic drugs bind to α_1-acid Gp.

③ BBB



* Areas where BBB is absent (Circum ventricular organs)

1> Area Postrema
2> Post. Pituitary
3> Lamina Terminalis
4) Organum Vasculosum
5) Chemo Receptor Trigger Zone (CTZ)

Har drug CTZ ko ungle kake nikal jata hai

↳ All drugs can cause ⊙ nausea vomiting except anti-emetic ante-psychotic

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* 2 Drugs Do not Cause Placenta :- Insulin
Heparin

Teratogenic Drugs

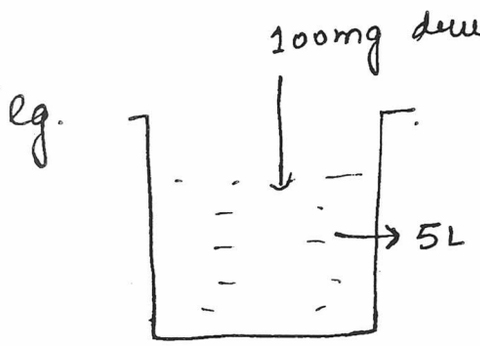
1) Thalidomide ⟶ causes Phocomelia
even single dose caused teratogenecity | or absent long Bones
sea-limbs

→ Nowadays used for Multiple myeloma + Anti-cancer

* How to measure Distribution ?

Volume of Distribution (V_D) or $a V_D$ = apparent V_D.

$$V_D = \frac{\text{Amount given}}{\text{Pl. conc}^n \text{ obtained}}$$

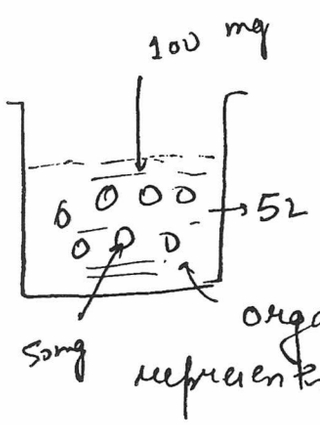


eg.

$$\text{Pl. conc}^n = \frac{100}{5} = 20 \text{ mg/L}$$

$$V_D = \frac{100}{20} = (5\text{ L})$$

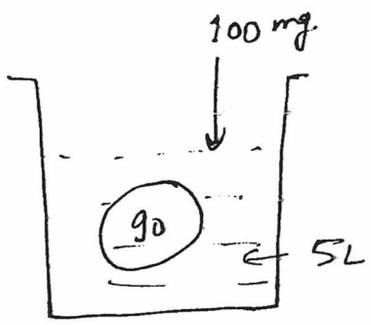
This happens when no distribution occurs.



$$PC = \frac{50}{5} = 10 \text{ mg/L}$$

$$V_D = \frac{100}{10} = (10\text{ L})$$

More the volume of Distribution, more drug is distributed in various organs.



Pl. Conc^n = $\frac{10}{5}$ = 2 mg/L

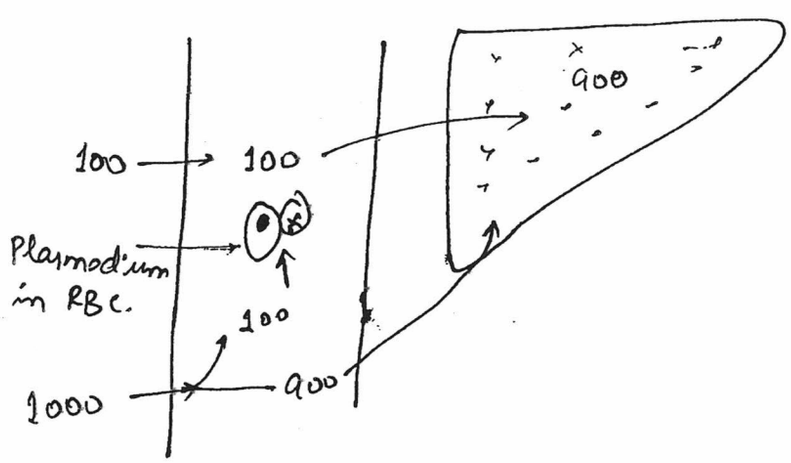
$V_D = \frac{100}{2}$ = 50L.

Clinical Importance-

Hypothetical vol req. to accomodate the drug

Eg Chloroquine → max. V_D. (V_D > 1300L)

Chloroquine is concentrated in Liver.



So, High Dose is required for action if V_D is more

Loading Dose -

Initial High Dose given to start the effect of a drug

So It depends upon distribution.

L.D. = V_D × target Pl. Conc^n

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Maintainance Dose

It doesn't depends on V_D

It depends upon clearance

M.D. = Clearance x Target Pl. Conc^n

If M.D. given as 20mg /hour in 24 hrs

& Total M.D. = 20 x 24.

ELIMINATION

Stoppage of action of drug is called elimination

2 methods

METABOLISM + EXCRETION

METABOLISM

TYPES

Active → Inactive

Active → Active

Inactive → Active [Prodrug]

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PRODRUGS

All - ACE ⊖ Except Captopril + Lisinopril

Prefer - PPI

Doing Dipivefrine → forms adrenaline

M - Methyldopa, Minoxidil, Mercaptopurine.

D - L-Dopa

In - Irinotecan

Clinical - Cyclophosphamide, Clopidogrel, Carbamazole

Subjects - Sulfasalazine

Purpose of Metabolism → to make drug water soluble.

CATABOLISM

Phase 1

(MC) oxidation

Reduction

Hydrolysis

Cyclization

Deamination..

ANABOLISM

Phase 2
(conjugation Rxns)

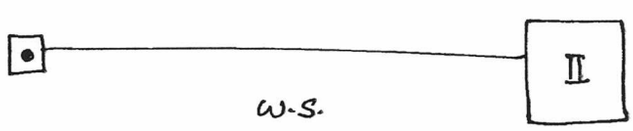
(MC) Glucuronide

Glutathione

Acetyl

Methyl

Sulfate



Func" of Phase-I ⇒ attach the functional group to the drug so that conjugation can be done

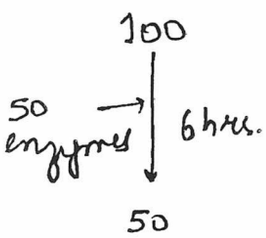
ENZYMES

Microsomal

Enzymes present inside microsome or endoplasmic reticulum

Can be induced / inhibited

eg. warfarin.



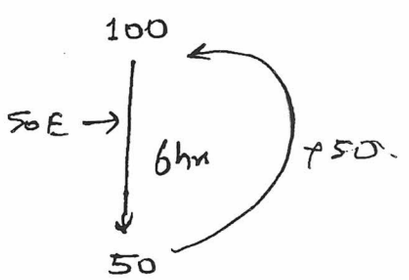
- on adding rifampicin (Enzyme inducer), metabolism of warfarin ↑ . So ↑ dose is required

- on adding cimetidine (Enzyme inhibitor), metabolism of warfarin ↓ . So ↓ dose is required

Non-Microsomal

Not present inside ER

Heparin.



* Enzyme Inducers

G - Griseofulvin

P - Phenytoin

R - Rifampicin

S - smoking → [Nicotene is not an enzyme inducer]

Cell - Carbamazepene

Phone - Phenobarbitone

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Smokers require high dose of theophylline + if they stop smoking dose readjusted

Enzyme Inhibitors

Vit - valproate

K - Ketoconazole

can Cimetidine

cause - ~~Cefp~~ ciprofloxacin.

Enzyme - Erythromycin

Inhibitor - INH

(vit K doesn't cause enzyme Inhibition)

CYP · Enzymes

Cytochrome P_{450} enzymes

↓

pigment & absorbs light of 450 nm λ.

CYP 3 A 4 → gene

↓ → subfamily

represents family

50% of drugs are metabolised

CYP 2 D 6

20% drugs are met·

Drugs Met· By CYP 3A4 — CT SCAN

C - CCB, cyclosporine

T - Tacrolimus

S - Statins → cause QT Prolongation

C - CAT drugs (Cisapride, Astemizole, Terfenadine)

CAT is QuTe (cute)

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A- Amiodarone

V- NAVIR

Drugs Metabolised by CYP 2 D 6 - sex ↓ anti-arrhythmics except Amiodarone

↓ Beta Blockers

↓ Depressen

- SSRI
- SNRI
- TCA
- MAO ⊖

CYP 2 C 1 9

↓ Clopidogrel

↓ CYP 2C19 ⟵ ⊖ prazole except Rabeprazole Pantoprazole

Active

CYP 2 C 9 → P - Phenytoin.

↓ Clotting → warfarin