Answer key

Pharmacodinamic & P.k

1st Class Evaluation Test ... Pharmacology, 3rd Year MBBS

MCQ Type

Time allowed: 15 min

2019

Total marks: 15

1. Drugs that are administered through IV route are:

(a) Rapidly excreted by kidneys
(b) 100% Bioavailable
(c) Rapidly metabolized by liver
(d) Subject to first pass metabolism

2. Drugs that are highly bound to Albumin:

(a) Effectively cross the BBB
(b) Are easily filtered at Glomerulus
(c) Have a large volume of distribution (Vd)
(d) can undergo competition with other drugs for albumin binding sites

3. The loading dose for a drug given IV with volume of distribution (Vd)= 42L, Target plasma conc. (Cp)=5mg/L and Clearance (CL)= 200L/min will be:

(a) 500mg
(b) 210mg
(c) 1G
(d) 40mg

4. Which of the following is a phase II drug metabolizing reaction? phase I

(a) Acetylation
(b) Deamination
(c) Hydrolysis
(d) Oxidation

5. The maintenance dose of a drug is usually based on the:

(a) Total body clearance (CL) of the drug
(b) Percentage of drug bound to plasma proteins
(c) Fraction of drug excreted unchanged in the urine
(d) Apparent volume of distribution (Vd)

6. A Prodrug is:

(a) The prototype member of a class of drugs
(b) The oldest member of a class of drugs
(c) An inactive drug that is transformed in the body to an active metabolite
(d) A drug that is stored in body tissues and is then gradually released in the circulation

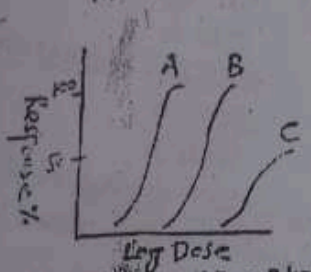
7. The Down Regulation of receptors can occur as a consequence of: Persistance use of drug

(a) Continuous use of agonists
(b) Continuous use of antagonists
(c) Chronic use of CNS depressants
(d) Denervation

8. If the effect of combination of two drugs is equal to the sum of their individual effects, the two drugs are exhibiting

(a) Potentiation (b) Synergism (c) Cross tolerance d) Antagonism

9. In this figure the correct response is:



(a) Drug B is more potent than Drug A (b) Drug A and Drug B have equal potency

(c) Drug A is more potent than Drug B (d) Drug C is the most potent

10. Factor which can affect the absorption of drug is:

(a) Dissolution rate (b) Particle Size
(c) Lipid Solubility (d) All the above

11. A patient was given 200mg dose of a drug IV and after 2 hours plasma conc. was 100mg. If the drug follows first order kinetics, what will be the plasma conc. 6 hours after its administration:

(a) 25mg (b) 50mg (c) 75mg (d) 100mg

12. An example of 2nd messenger for G Protein coupled receptor signaling is:

(a) Gs Protein (b) cAMP (c) Na+ (d) Cl-

13. Redistribution of drugs results in:

(a) Termination of drug action (b) Prolonged action of drug
(c) Shortened duration of action (d) Drug reaction

14. The ability of drug to cause fetal abnormalities is known as

(a) Teratogenicity (b) Carcinogenicity (c) Cross tolerance (d) Allergic reaction

15. The set of properties that characterize the effects of a drug on a body is called

(a) Distribution (b) Permeation
(c) Pharmacodynamics (d) Pharmacokinetics

Pharmakinetics

Q.no1:- (A) What do you understand by parenteral route of drug administration. Write at least four advantages and four disadvantages of this route. (1+2)

Ans:-

Parenteral route introduces drugs directly across body barriers/ defenses into systemic circulation. Parenteral (oral) administration is used for drugs that are unstable in GIT tract or poorly absorbed from GIT.

4 advantages:-

IV
- Have immediate effects, convenient,
- Suitable for irritating substances such as oily vehicle and complex mixtures.

* Ideal for inpatient who are vomiting or comatose.

IM
- Subcutaneous administration is suitable for slow release drugs
- Intramuscular administration is suitable if drug volume is moderate or large.

4 disadvantages:-

IV
- In IV strict aseptic techniques needed. Potentially more dangerous
- Bolus injections may result in adverse effects.

Transdermal has slow onset & Skin irritation.

- Sc Subcutaneous - Pain at the
  it may be irritating.
- It will be painful.

IM Limited amount is given & Risk of nerve damage

Qno 1(B):- A Patient Presented with acute aspirin toxicity due to overdose using your knowledge of aspirin pharmaKinetics how can you help this Patient get rid of high plasma aspirin through Urine? (2)

Ans:-

Urine is slightly acidic, It should be alkalanized by administering Sodium bicarbonate as a result aspirin becomes ionized in Kidney tubules and its lipid solubility decreases due to which its reabsorption from tubules back into blood stops and aspirin is excreted in urine.

NaCO3

Qno 2:-(A)

What is 1st Pass metabolism of drug?? Write its consequences with examples; (1+2)

When drug is absorbed across tract, it first enters the portal ial circulation before entering Systemic circulation and may be tensively metabolized in the liver.

Sequences & examples:-

→ Bioavailability of a drug decreases by first Pass metabolism.

→ If the drug is rapidly metabolized in liver → the amount of unchanged drug that gains access to systemic circulation is ↓. e.g Nitroglycerine is cleared during single Passage through liver. That's why it is administered Sub lingually.

Ans 2:-(b)

500mg dose of a drug was administered, a uniform Concentration of 10mg was achieved in the body. What will be the volume of distribution of this drug?

"Ans:-"

Amount of drug in body = 5...

Plasma drug Concentration = 10

V_D = ?

V_D = Amount of drug in b...
Plasma drug concentr...

$V_D = \frac{500}{10}$

V_D = 50mg

Qno 2:-(C)

What do you know loading dose of drug?? How can be calculated :(1)

Ans:-

Loading dose:-

A comparatively large dose c... at the begining of treat... to achieve maximum responce. ment therapeutic concentration

Loading dose = (V_d) × (desired steady - st... Plasma concentration)

bioavailability

For I.V Infussons L.D = V_D × plasma conc. / Bioavailability

OR

Loading dose of drug is...

of drug

Things to do

NOTES

1/12009

Lip.# 10-11

Binding ↓ protein

Significance of Plasma protein of Drugs

1) i- Reversible binding to plasma proteins in non-diffusible form that slows its transfer out of vascular compartment.

2) ii- Albumin is major drug binding protein act as reservoir. ⇒ they ↑ drug ↓ concentrations in tissues.

3) iii- Drug binding to plasma proteins ↑ the duration of drug.

4) iv- Plasma binding proteins prolong the actions of drug.

Example

Acrolein, the metabolite of cyclophosphamide, can cause hemorrhagic cystitis because it accumulates in bladder.

Appointments

Enteric-coated preparation

→ chemical envelope that resists the action of fluid and enzyme in the stomach but dissolve readily in the upper intestine

Example:

→ omeprazole → unstable in stomach

→ Aspirin → irritant effector for stomach
→ only dissolve in small intestine.

→ Enteral → oral / tubing
→ parenteral → IV

Extended released preparation

- Special coating or ingredients that control how fast the drug is release from pill into body
- Convenient → Ensure compliance
- maintain concentration of dosage for long time
- have short life
- Example
  morphine → 2-4 child
  Six time → 24 hour
  Adult

is administered to achieve the desired Plasma level rapidly.

Loading Dose = $\frac{Vd \times \text{Plasma drug Concentration}}{\text{Bioavailability}}$

Loading dose = $(Vd) \times \left(\text{desired steady state Plasma Conc}\right) / F$

For iv infusion, the bioavailability is 100% and the equation becomes

Loading dose = $(Vd) \times$ desired steady state Plasma Conc.

Ans 3:- (a) Write down the clinical significance of Plasma binding Protein of drugs with at least 1 example? (3)

Ans:-

1) Protein binding acts as a temporary store of a drug and tends to prevent large fluctuations in conc. of free drug in body fluids.

2) It delays metabolic breakdown and excretion of drug ↑ because only the unbound drug can be metabolized or excreted. On entering the

blood a portion of drug is bound to plasma protein (chief albumin) and a portion is free or unbound. Protein binding is reversible. The protein bound fraction is inactive pharmacologically. It can not leave the vascular space and not eliminated or metabolized so, it has longer half life. Only unbound drug is available for pharmacological action at receptors. Protein binding becomes clinically important when more than 90% drug present in blood.

Examples:-

Warfarin 99%
Phenytoin
Prazosin.

Ans 3:- (b)

A Patient was given 200mg dose of a drug IV and 100mg was eliminated during first two hours. If the drug follow first order elimination, how much

will remain 6 hours after its administration. (2)

Ans:-

half life = 2 hours

After 1st half life = 100mg remains

After 2nd half life = 50 mg

After 3rd half life = 25 mg

So after 6hrs 25mg remains.

Ans 4:- (a)

What is biotransformation.

Write names of two phase II reactions with examples. (2)

Biotransformation:- It is physico-chemical change of the drug molecule by the enzymatic process to make it more excretable.

An alteration of a substance typically of a drug by enzymes in the body is lipid soluble into water soluble to enhance elimination.

Phase II reactions:- Ab. "MSAG"

1) glucuronidation e.g. nitrophenol, morphine, Diazepam, Digoxin.
2) Acetylation e.g. Isoniazid : Sulfonamides
3) Sulfation e.g. Estrone : Phenol
4) Methylation e.g. Dobutamine : chlorpromazine

Qno 4 :- (B)

What are possible results of biotransformation write ē examples. (2)

(1) Biotransformation converts inactive drugs into their active products :.

e.g 6-mercaptopurine is converted into 6-mercaptopurine ribonucleotide.

(2) Sometimes an active drug is converted into another product which retains pharmacological activity and may be even more potent than parent drug.

e.g. Conversion of diazepam into oxazepam.

Diazepam oxazepam.

(3) Phenacetine is metabolized and converted to Paracetamol (acetaminophen) which acts as analgesic

(4) Drugs that are lipid soluble becomes water soluble to enhance excretion.

Qno 4:- (C)

What is maintenence dose of drug. How it is calculated ? (1)

Loading Dose:- Initially large amount of drug is given to achieve the max response

Maintance Dose:- The drug that is given to maintain loading dose

Maintenance dose:-

In maintenence dose steady state concentration of drug is maintained. At "steady state rate of adminestration equals to elimination rate given at intervals".

Maintenance dose = Clearance × Plasma drug conc. / bioavailability

Ans5:- (A) Explain enzyme induction of cyt. P450 with 2 examples which are clinically relavant?? (1+2) N.A

Ans:-

The cytochrome P450 dependent enzymes are an important target for Pharmacokinetic drug interactions: One such induction is cytochrome P isozymes

It is a process.

in which a molecule induces the expression of an enzyme.

Examples:-

- **Rifampin**, an antituberculosis drug, decreases the plasma concentration of HIV protease inhibitors, by diminishing their ability to suppress HIV virion maturation.
- **Phenobarbital** induces the metabolism of warfarin and phenytoin.

Q no 5 :-(B)
Define biotransformation. What are different phase 1 metabolic reaction, where do they occur? (2)

Ans:-

Biotransformation:- An alteration of a substance typically a drug within the body is called biotransformation.

Types of Phase 1 reactions:-

(ORH)

- Oxidation
- reduction ~~alkyl~~ aliphatic hydroxylation
- hydrolysis

where do they occur?

Principal organ for phase 1 reaction is liver, other organs include GIT, lungs, skin, Kidney.

Qno b:- (a)

What information do you get from plasma half life? (3)

Ans:- Plasma half life:-

Time period This is the period of time required for conc. or amount of drug in the body to reduced by one half. A drug plasma half life depends on how quickly the drug is eliminated from plasma. Half life of a drug is to volume of distribution and inversely proportional to clearance.

$$t_{1/2} = 0.693 \times \frac{V_D}{\text{Clearance}}$$

$t_{1/2} = 0.693$

Note:- We can maintain normal dose of drug. e.g. Penicillin → 0.5 hour
Amoxicillin → 1 hour
Ampicillin → 1.2 hour

Qno b:- (b)

What are different types of drug doses ? example. (3)

Ans:- Types of doses:-

i) Maintenence dose -

ii) Loading dose.

i) Maintenance dose:- The dose required for regular administration to maintain target Plasma level.

Maintenance dose = Clearance × Plasma
Bioavalability

Loading dose of drug is administered to achieve the desired plasma level rapidly.

L.D = V.D × Plasma drug Conc.
Bioavalbility

Q no 7:- (a)

Write importance of cyt P450 inhibition with 2 clinical examples. (2)

Ans:-

Inhibition of cytoP450 is an important source of drug interactions that leads to ~~serious adverse events~~.

If two drugs are administered together and one is metabolized by cyt. P450 dependent system but other drug is inhibitor of cyt. P450 as a result serious adverse effects may occur (it [illegible] ... [illegible] ... [illegible] duration of ... ...)

Examples:-

⇒ Omeprazole is Potent inhibitor of (warfarin) metabolism. If both taken together, Plasma Conc of warfarin ↑ which leads to hemorrhage and serious bleeding reactions. eg * Erythromycin * Ketoconazol * Ritonavir

⇒ Sematidin blocks the metabolism of theophylline, Clozapine and warfarin.

Ans 7:- (B)

Classify and Categorize drugs used in Pregnancy ??

According to FDA ratings of drugs safety in Pregnancy:-

i) Category A:-
- Folic acid (FLM)(FML)
- Magnesium Sulphate
- Levothyroxine

ii) Category B:-
- Amoxicillin (AEP) (CAP)
- Cyclobenzaprine
- Pantoprazole

iii) Category C:-
- Tramadole (TTGP)
- Trazodone
- Gabapentin (GT-PT)
- Prednisone

iv) Category D:-

- Alprazolam (ALCK)
- Lesarton / valsartan
- Clonazepam
- Lorazepam.

v) Category X:-

- warfarin. (MSW)
- Methotrexate.
- Simvastatin

vi) Category N:-

- Aspirin (AD).
- Diazepam.

Qno8:- (A) Write down a comparison between first and zero order Kinetics of elimination with graphs and examples:- (3)

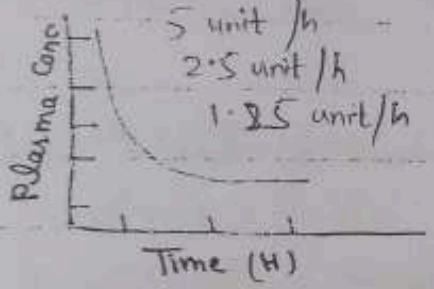
Ans:-

1st order Kinetics	Zero order Kinetics
1. Rate of metabolism is directly proportional to conc. of drug.	1. Rate of metabolism remains constant over time.
2. Plasma drug conc. is much less than K_m.	2. Plasma drug conc. greater than K_m

Rate of Drug Metabolism = $\frac{V_{max}[C]}{K_m}$ $V = V_{max}$

- Constant fraction of drug is metabolized per unit time.
- Clinically referred as linear Kinetics. elemination is directly proportional to the conc of free Drug

Graph

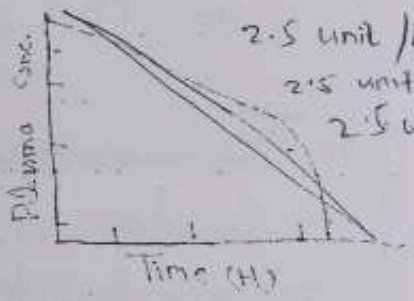


Examples

- Cisplatin
- Omeprazole

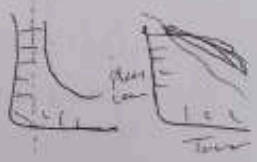
- Constant amount of drug is metabolized per unit time.
- Clinically referred as non-linear Kinetics. elemination is constant and does not Depends the drug conc.

Graph



Examples

- Aspirin
- ethanol
- Phenytoin



Qno 8:- (B)

What is plasma half life, how it can be calculated ?? (7)

Plasma half life:-

time in which conc. of drug becomes half of its intial conc.

$$t_{1/2} \text{ (Half life)} = \frac{0.693 \times Vd}{\text{Clearance}}$$

Factors of Dosage: • Particle size
• Disintegration time
• Dissolution rate
• formulation

Q no 9:- (a)

Write down different factors which effect the absorption of a drug?? (3)

shape and size
Lipid solubility
partition coefficient
Degree of ionization

Following factors influence absorption of drugs:-

1:- Blood flow to the absorption site:-

Blood flow to intestine is much greater than flow to stomach So absorption from intestine is favoured over stomach.

2:- Total surface area available for absorption:-

With a surface rich in brush borders containing microvilli the intestine has a surface area about 1000 fold that of the stomach making absorption of drug across intestine more efficient.

3:- Contact time at absorption surface:-

If a drug moves through GI tract very quickly it is not well absabed So for better absorption drug should stay at absorption site for greater time.

4. Low molecular weight:-
Low molecular weight drugs well absorbs e.g. heparin.

5. Lipid Solubility:-
Drugs that are lipid Soluble easily absorb e.g. aspirin.

6. Un-Ionized drugs:-
Un-Ionized drugs easily pass and absorb.

Qno 9:-(B)

What do you Know about bioavailability, bioequivalence and therapeutic equivalence? (2)

Ans:-

* Bioavailability:-
Fraction of drug in systemic circulation which by-passes the first pass effect: AUC

First pass hepatic metabol
Chemical instability
Nature of the drug formulat
Solubility of t drug

$$\text{Bioavailability} = \frac{AUC\ (\text{oral})}{AUC\ (\text{IV})} \times 100\%$$

* Bioequivalence:-
Two related drugs having same bioavailability known as bioequivalence.

* Therapeutic equivalence :-

Two similar drug products are therapeutically equal if they are pharmaceutically equivalent with similar clinical and safety profiles.

Ans no :- (A)

What do you Know drug elimination ??

Ans :-

Once a drug enters the body the the process of elimination begins. The three major routes involved are

1. Hepatic metabolism.
2. Elimination in bile.
3. Elimination in urine.

} Hepatic

Together, these elimination processes cause the plasma concentration of a drug to decrease exponentially ~~Most drugs are eliminated according to first order kinetics~~ while some like aspirin in high doses, eliminated through zero order or non-linear kinetics. Or first order kinetics.

Example

rate of drug metabolism elimination is directly proportional to concentration of free drug while in zero order the drug metabolism is constant and independent of drug close.

Qno 10:- (B)

What factors effect distribution of drug in body?? What is Vd??

Ans:-

Following factors effect distribution..

1. Ability of drug to cross biological membrane.
2. Lipid solubility of drug e.g. [illegible] Aspirin
3. Un-ionization of drug e.g. [illegible]
4. Low molecular weight e.g. [illegible]

Vd:-

It is the ratio of amount of drug in body to plasma drug concentration.

Vd = Amount of drug in body / Plasma drug conc.

Qno 11:- (A)

What is plasma half life?? what do you know about

Steady state Concentration of drug ??

Ans:-

Plasma half life:-

This is the period of time required for Concentration [amount of drug in the body to reduced by one half.

$t_{1/2} = 0.693 \times \frac{\text{Volume of clearance}}{V_D}$

Steady - state Concentration:-

A Condition in which rate of drug elimination is equal to rate of administration hence average total amount of drug in body does not change over multible dosing cycles.

Qno 11:-(B)

What are different methods of Prolonging drug action ??

There are following methods for Prolongation:-

A) Slow down absorption:- For orally administered drugs give along ē food use coated preparations change the

route e.g. transdermal.

For parentrally administered drug

↓ vascularity of area e.g Add adrenaline to Procane (local anesthetic),

↓ Solubility e.g Penicillin + Procaine.

Combine with Protein e.g. insulin + Protamine

(B) Distribution:-

Use drug ē higher Plasma Protein barrier e.g. Intermediate or long action sulfoxamide have ↑ PPB

(C) Inhibit metabolism:-

e.g. Pysostigmine inhibits metabolism at acetylcholine and Prolong its action.

(D) Reduced renal excretion:-

Identical PH ↑ back diffusion of drug (drug return to plasma) and Prolong action e.g. excretion of Penicillin is reduced by Probenecid.

Ans 12:- (A).-

What are different routes of drug administration?? What are advantages / Disadvantages of extral

Routes:

There are following routes of drug administration:-

1) Oral / Enteral
2) Intravenous
3) Subcutaneous
4) Intramuscular
5) Transdermal
6) Rectal
7) Inhalation
8) Sublingual

Enteral
Parenteral
Others

Enteral Route of Admi.

Advantages:-

1. Safest and most common.
2. Convienient and cheaper.
3. Self administered.
4. Have low risk of systemic infections.
5. Toxicities by oral route may be overcome by antidotes.

Disadvantages:-

1. Limited absorption of some drugs
2. Food may effect absorption.
3. Patient compliance is necessary.
4. Drugs may be metabolized before systemic absorption.

NAGMAN AFZAL, 4th/4yr.

Qno 12 :- (B)

What are different barriers to drug absorption limiting the drug access to certain area?? (1)

1) Blood brain barrier - Blod brain Barrier.
2) Placental barrier. - Placental Barrier.

Qno 12 :- (C) ×

What are Some special drug delivery system?? (1)

There are following routes:

1. Transdermal ---> Plasters
2. IU devices ← vaginal
3. Inhalation - [illegible]
4. Stants in CoA
5. Antigen directed drugs + antibody (illegible)

Biotransformation.

It is a Physico-chemical change of a drug molecule of a drug molecule by the enzymatic process to make it more excretable.

Sites
Liver, Mainly
Gut
Kidney
blood.

Mechanism of desensitization:

① change in receptor sensitivity

continuous administration of Narcotic analgesics leads to gradual "dec in sensitivity of opioid receptors". Mose drugs has to produce direct effect An opioid combining to specific receptors restrict the release of neurotransmitter Their withdrawl result is loss of synaptic inhibition - withdrawl syndrome is thus a manifested loss of synoptic inhibition.

② Enzymatic inhibition

Some drugs induce adaptive degrading enz- formulation. There is ↑ in metabolism of drug and ↓ duration and intensity of action.

e.g chronic alcoholic develop lower blood level when drug given I/V.

Dec Intestinal Absorption

chronic administration of some drugs orally for many years, leads to ↓ intestinal Absorption.

② Enumerate the components of drug dependence.

① withdrawl syndrome

② Euphoria

③ Tolerance