EXCRETION

Dr. Kamlesh P. Patel
Associate Professor
Department of Pharmacology
Smt. NHL Municipal Medical College
Ellisbridge, Ahmedabad

EXCRETION

- **Excreted in two forms :-**

- **1) Unchanged (Polar, Ionized)**
  (eg. Aminoglycosides, atenolol, neostigmine)

- **2) Changed** (highly lipid soluble & unionized)

- **Routes of Excretion :-**
- 1) Renal
- 2)Non – Renal
- 3) Others :- Saliva, Sweat, Milk, Tears, Hair

RENAL EXCRETION

- Major route of elimination
- 3 processes involved :-
- A) Glomerular Filtration (Passive)
- B) Renal Tubular Secretion / Excretion (Active)
- C) Renal Tubular Re – absorption (Passive)

RENAL EXCRETION

- **A) Glomerular Filtration (Passive) :-**

- Most drugs filtered through pores of the glomerular membrane
- **Renal blood flow And MW < 10000 determines the glomerular filtration**
- **Free drug can also be excreted**
- Drugs cannot be filtered are :-
- (i) Highly bound to plasma protein
- (ii) M.W. > 10,000 eg. Heparin, Dextran

RENAL EXCRETION

- **B) Renal Tubular Secretion / Excretion (Active) :-**

- Carrier mediated active transport process
- **Weakly acidic & weakly basic drugs are secreted by cells of proximal renal tubules from plasma**
- Conjugated metabolites are also excreted
- 2 System exists separately :-
- (i) Acidic drugs :- Penicillin & Probenecid, Aspirin (<2g)
- (ii) Basic Drugs :- **Morphine & Amiloride**

RENAL EXCRETION

C) Renal Tubular Re – absorption (Passive)

- Passive & bidirectional process
- **Depends on lipid solubility, degree of ionization (pKa) & pH of the medium**
- Acidic drugs (salicylates, barbiturates → at acidic pH of urine → **unionized** → **lipid soluble** → **Reabsorbed**
- **Basic drugs** → at basic pH of urine → **unionized** → **lipid soluble** → **Reabsorbed**
- Basic drugs (Pethidine, amphetamine) → **at acidic pH of urine** → **ionized** → **water soluble** → Excreted

C) Renal Tubular Re – absorption (Passive)…Contd…

- Clinical significance :–
- **Acidic drugs → in alkaline pH → ionized → water soluble (Polar) → Excreted readily in alkaline urine**
- **Basic drugs → in acidic pH → ionized → water soluble (Polar) → Excreted readily**
- ***In Poisoning with Acidic drugs → alkalinizing the urine → Removes (Excretes) the acidic drugs in alkaline urine & …Vice versa***
- ***In Renal Damage / failure :–***
- *(i) Completely metabolized & inactivated Drugs → Safely used eg. Secobarbitone (S.A. Barbiturates)*
- ***(ii) Drugs not metabolized & excreted unchanged → should be avoided or dose readjusted eg. Atenolol***

NON – RENAL EXCRETION

- (i) Hepato–biliary excretion & entero – hepatic circulation
- (ii) Faecal excretion
- (iii) Pulmonary Excretion

NON- RENAL EXCRETION

- **(I) Hepato-biliary excretion & entero – hepatic circulation :-**

- Liver, Hepatocytes → secretes drugs & their metabolites into bile → Bile salts circulates in intestine & portal blood → go to Liver 6-8 times in a day repeatedly → bile salts gets conserved

- Certain drugs → Secreted in bile → but not reabsorbed → eliminated in Faeces (Quinidine, colchicine, erythromycin, ampicillin, chlorpromazine)

- Certain drugs → Secreted in bile → reabsorbed → enter the liver again (undergo entero-hepatic circulation) → not eliminated (Rifampicin, oral contraceptives)

NON- RENAL EXCRETION

- Certain drugs → Excreted in bile after deconjugation in liver→ Not reabsorbed in intestine → hydrolysed in the gut by intestinal enzymes & bacteria → parent drug is released & reabsorbed → & reconjugated in liver
- (Morphine, Doxycycline, chloramphenicol, ethinyl estradiol) → not excreted.

- BUT, Rifampicin & its deacetylated metabolite → excreted in bile → Rifampicin alone is reabsorbed

(action prolonged due to entero – hepatic circulation) → its metabolite is eliminated in Faeces.

- Certain drugs → Secreted in bile without deconjugation → reabsorbed in intestine → undergoes entero-hepatic circulation → not eliminated (Digitoxin, indomethacin)

NON- RENAL EXCRETION

- **FAECAL :-**

- Streptomycin, Neomycin, Bacitracin → orally → **Not absorbed → Excreted in Faeces**

- **Erythromycin** → orally not absorbed → **excreted in Bile**

NON- RENAL EXCRETION

- **PULMONARY :-**

- **Volatile general anaesthetic agents**
  (Ether, halothane, Nitrous oxide)

- **Alcohol :- Conc in exhaled air is <2000 times the plasma concentration →** But still measurement of exhaled alcohol in air has medico-legal importance in suspected vehicle drivers

OTHER ROUTES OF EXCRETION

- 1) Saliva :- Heavy metals (Lead, arsenic etc); Phenytoin, Iodine, Lithium). Saliva conc of Lithium provides non-invasive method of TDM
- 2) Sweat :- Rifampicin (reddish orange)
- 3) Milk:- Highly lipid soluble drugs
- 4)Tears : Lithium, rifampicin
- 5) Hair :- Chlorpromazine, Flecainide, Haloperidol, Mercury, Iodides, Arsenic (accumulates in hair & excreted for many months) → give importance clue in homicidal poisoning & has medico-legal importance).

METHODS OF PROLONGING DRUG ACTION

Advantages :-

- Helps achieve sustained plasma concentration → Avoids fluctuation in Pl. Concentration.
- Minimizes side effects associated with large Pl. conc.
- Helps in controlling the effect of drug round the clock for 24 hrs.
- Decreases frequency of drug administration → Increase patient convenience
- Less chances of forgetting to take the drug
- Increases patient's compliance
- Helps in maintaining drug effect overnight → less chances of disturbing sleep in night
- Useful for drugs with T1/2 < 4 hrs

METHODS OF PROLONGING DRUG ACTION

- **Disadvantages** :-

- Not useful for drugs with Pl. T1/2 > 4 hrs

- Not useful for drugs used for short term management of symptoms or diseases eg. Headache, insomnia etc…

- Not applicable for those drugs having long duration of action eg. omeprazole, amlodipine, digoxin, azithromycin, doxycycline etc..

METHODS OF PROLONGING DRUG ACTION

(1) **By Prolonging Absorption of a Drug** :-

(A) ORAL :-

i) SR – sustained release tablets eg. Diclofenac (Voveran-SR 100mg).

ii) TR/CR – time/controlled release tablets eg. Nifedipine.

iii) Spansules – Iron supplements.

[SR – drug particles are coated with resins, plastic materials which slowly disperses and releases the active ingredients in GIT].

[TR / CR – utilizes semipermeable membrane to control the release of drug at different time interval from the dosage form].

METHODS OF PROLONGING DRUG ACTION

B) Parenteral :-

i) Drugs in insoluble forms :-

eg. (a) Lente Insulin for SC administration

(b) Procaine Penicillin G for i.m administration → 24 hrs duration

© Benzathine Penicillin G for i.m administration → 15 – 30 Days duration

ii) As Oily injection :- Testosterone Depot Inj. i.m

iii) Pellet implantation :- Contraceptives, Pilocarpine

iv) Sialistic & Biodegradable implants –Norplant

v) Adrenaline + Lignocaine injection

vi) Transdermal Patches :- GTN, Nicotine, Estrogen, Fentanyl, Scopolamine, Clonidine

METHODS OF PROLONGING DRUG ACTION

2) At Disribution site :-

i) Drugs highly Bound to Plasma protein → slowly released→ Longer duration of action

ii) Eg. Sulphadoxine → Effect lasts up to 9 days

3) At Metabolism site :-

i) By retarding rate of metabolism of drug

ii) Eg. Adding ethinyl group to estradiol → Longer acting OC pills.

iii) Inhibition of enzyme→ prolongs action eg. Allopurinol→ inhibits degration of 6-Mercaptopurine, ritonavir→ Boosts Indinavir levels.

iv) Cilastatin + Imipenem → cilastatin inhibits dehydropeptidase – I enzyme inbrush border cell of kidneys → prevents imipenem degradation → prolongs imipenem effect

METHODS OF PROLONGING DRUG ACTION

4) At Excretion site :-

i) By retarding renal excretion

ii) Eg . Penicillin / ampicillin + Probenecid

iii) Probenecid → inhibits tubular secretion of Penicillin & Ampicillin → Prolongs action of Penicillin & Ampicillin by retarding its excretion.

T H A N K Y O U