Unit V – Problem 9 – Pharmacology: Drug Elimination

- Most drugs are metabolized by the liver (e.g. CYP450 enzymes) to make them more polar (more water-soluble) and then excreted outside the body usually by the kidneys (but notice that certain drugs might be excreted in stool or with breath through the lungs).
- When reaching the kidneys, the drug or its metabolites are filtered in glomerulus, secreted to tubular fluid in Proximal Convoluted Tubules (PCT) and some amount is reabsorbed in Distal Convoluted Tubules (DCT).
- Clearance (Cl) expresses how much volume of plasma is cleared completely of a drug in a unit of time. Its clinical significance is that it plays an important role in regimen design that is dose and frequency of administration of a drug to keep in the therapeutic range rather than toxic or sub-theraputic (ineffective) one.
- Clearance follows first order in most drugs that is as dose increases, clearance increases. Very rarely, clearance follows zero order (as dose increases clearance may stop and drug accumulates due to saturation of metabolizing enzymes).
- **Methods of clearance calculation:**
  - **Clearance =** $\frac{Rate\ of\ elimination}{C\ (Concentration\ in\ plasma)}$
  - **Clearance =** $\frac{Dose}{AUC\ (Area\ Under\ Curve)}$
  - **Clearance =** $\frac{Dosing\ rate}{C_{ss}\ (Steady\ State\ Concentration)}$
  - **Clearance =** $\frac{Ke\ (Elimination\ constant)}{Vd\ (Volume\ of\ distribution)}$
  - **Clearance =** $\frac{0.7\ x\ Vd}{Half-life}$
- Modification of tubular pH enhances excretion of a drug by making it more polar (water-soluble). If the drug is acidic then alkalanization of urine makes the drug more polar and is excreted in urine. This approach is used clinically when a patient presents with an overdose.
- Certain diseases may cause reduced drug clearance. Renal failure in particular leads to this but other diseases that affect renal function like heart failure and hepatic failure may cause this too. These conditions lead to drug accumulation and toxicity.