- **Measuring drug efficacy and safety**:
- randomised controlled trials
- Steady state drug levels are continuously within a therapeutic range,

4 Absorption and distribution of drugs

- Absorption, Distribution, Metabolism, Excretion
- **Absorption** can be vascular (directly into bloodstream) or extravascular (cross biological membrane)
- Passive diffusion from exterior (relatively high drug concentration) to interior (relatively low drug concentration)
- Lipophilic/Lipophobic
- Octanol has similar properties to the hydrophobic portion of the cell membrane, water coefficient
- LogP (Log10 (Conc in octanol/conc in water) higher the value the more lipophilic, and LogD (Log10 (Conc in octanol/conc unionised and ionised in water)
- LogP/LogD ratio ideally between 0 and 3, exceptions
- pH of log D must be noted
- Passive diffusion, from high concentration to low concentration over a membrane
- Right combination of Hydrophilic/hydrophobic properties
- Most drugs are weak acids or weak bases, acid and base dissociate dissociated compounds form ions (ionised), ionised compounds will not partition into octanol
- Can be passed through by transporter proteins (proteins within cell membrane)
- All xenobiotics absorbed via oral route go to the liver
- Absorption is: generally maximal in small intestine, effect of food is unpredictable, first pass metabolism
- Affected by: patient disease state, age, site of absorption, co-administration, frequency of administration
- **Distribution** affected by LogP/LogD, blood flow to tissue or organ, molecular shape/size, binding of compound to blood and plasma proteins and membrane transporters
- Blood Brain Barrier, efflux transporter protects brain against harmful xenobiotics
- Partition coefficient
- Blood transports xenobiotics so areas with highest blood flow will be exposed to more of the drug in a given time
- Albumin is slightly basic so will bind acidic drugs i.e. warfarin
- Glycoproteins are slightly acidic so will bind basic drugs i.e phenytoin
- Transporter proteins have a pivitol role in mediating movement of drugs across membranes
- Membrane transporters are transmembrane proteins, divided into ATP-binding cassette (ABC) and solute carriers (SLC)
- P-glycoprotein (P-gp)