06 - B. Permeation

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© SPMM Course B. Permeation: Permeation of a drug is defined as the lipid membrane permeability of the drug molecule. After oral administration, a drug may be incompletely absorbed e.g. only 40% of a dose of chlorpromazine reaches the systemic circulation. This is mainly due to lack of absorption from the gut. Lipophilicity: Inherent properties of certain drugs can also affect their absorption e.g. highly hydrophilic drugs cannot cross the lipid cell membrane while highly lipophilic drugs will struggle to cross the water layer in the extracellular space. Drugs such as atenolol are too hydrophilic to be absorbed easily, and have a low bioavailability as a result. Apart from lipid solubility, concentration gradient affects permeation. Only free drug forms contribute to the concentration gradient. Hence, protein binding indirectly affects permeation. Permeation can take place either via simple diffusion i.e. along concentration gradient without any specific transport mechanism or facilitated diffusion i.e. along concentration gradient but ‘facilitated’ by the presence of carrier specific mechanisms. Active transport refers to transport against concentration gradient where ATP dependent energy expenditure takes place. Surface area and vascularity of the gut mucosa are important with regard to absorption of drugs into the systemic circulation. Only the nonionized form of a drug can cross lipid membranes of a cell. Many drugs are either weak acids or weak bases. These substances exist in either nonionized or ionized forms in equilibrium, in relation to the pH of the environment and their pKa (the pH at which the molecule is split into 50% ionized and 50% nonionized forms). The ionized form is more water-soluble than the nonionized form. As a consequence, ionized drug is more or less trapped in the glomerular filtrate and does not get reabsorbed. Hence, renal clearance is higher for ionized drugs. A weak base can be ionized by acidifying urine; a weak acid by alkalinising urine. Hence for salicylate (aspirin) overdose, and barbiturate overdose, alkalinization helps to reduce toxicity. Acidification may help in the elimination of amphetamines and phencyclidine (but often complications associated with this procedure overrides any benefits).

Revision #1
Created 2026-01-04 20:04:13 UTC by Omar Ayman
Updated 2026-01-04 20:04:13 UTC by Omar Ayman