

11 - F. Excretion

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© SPMM Course F. Excretion: The major routes of drug excretion are via urine, faeces and bile. Psychotropic drugs are also excreted in sweat, sebum, tears, saliva and breast milk. Both active forms and inactive metabolites can be excreted. Ionized and non-lipid soluble compounds are the most suited forms for renal excretion. The factors influencing excretion include □ Increased age (decreases excretion) □ Reduction in renal blood flow e.g. dehydration □ Renal impairment leading to decreased renal function □ Alterations in re-absorption: urine pH. (Changes in the p H of the tubular filtrate can alter the rate of elimination of the drugs. Normally urine is weakly acidic and good for excretion of drugs such as tricyclics and amphetamines. Alkaline diuresis is required to enhance elimination of drugs such as aspirin or phenobarbitone in overdose) and low sodium (Low sodium increases lithium reabsorption and decreases excretion leading to consequent toxicity) Clearance: Clearance is the term used to describe the rate of elimination of a drug. Clearance is defined as the volume of blood cleared of a particular drug in unit time. Total body clearance depends on renal and nonrenal clearance such as sweat, bile, etc. Clearance is directly proportional to the volume of distribution. $Cl = k \times V_d$, Where the constant of proportionality, k, is the first order elimination constant. Clearance is specific for each drug and does not depend on drug concentration in plasma (because if concentration increases, elimination will also increase under first order kinetics). It represents the relationship between the rate of drug elimination ($t_{1/2}$) and plasma level. For drugs with first order kinetics, clearance is constant irrespective of dose consumed because the rate of elimination is directly proportional to plasma level. Renal elimination without significant liver breakdown is seen for drugs such as lithium, amisulpride, sulpiride, gabapentin, acamprosate and amantadine. Both sulpride and amisulpride have up to 90% elimination via renal route – a minor portion is excreted via the biliary system. Amisulpride produces 2 weak metabolites following limited hepatic breakdown. Half-life: The half-life of a drug refers to the time taken for the plasma concentration of a drug to halve. It is represented by the expression ' $t_{1/2}$ '. Following intravenous injection, there is a rapid

Revision #1

Created 2026-01-04 20:04:15 UTC by Omar Ayman

Updated 2026-01-04 20:04:15 UTC by Omar Ayman