

extraction ratio and is simply one minus the ratio of concentration of drug in blood *leaving* the liver to that in blood *entering* the liver.

$$\text{extraction ratio } (E_H) = 1 - \frac{\text{concentration out}}{\text{concentration in}}$$

Equation 1.1

It will be apparent from the above that clearance is determined by the blood flow to an eliminating organ (Q_H in the case of the liver) and the efficiency of irreversible drug extraction from the blood by the organ (E_H). This is considered further in Chapter 4.

Obviously, the most drug that could be removed by the liver is all that enters the organ. In this case, the 'concentration out' would be 0.0, extraction ratio would be 1.0 and the hepatic clearance 90 L/hour. The further significance of the extraction ratio will be discussed in Chapter 4. For the present, it should be noted that the minimum clearance by an organ is zero and the maximum clearance by an organ is the blood flow to the organ.

CLEARANCE AND ELIMINATION RATE

Another definition of clearance is that it is the constant relating the concentration of drug in the plasma to the rate at which the drug is eliminated from the body.

$$\begin{array}{ccccc} \text{elimination rate} & = & \text{clearance (CL)} & \times & \text{plasma drug concentration (C)} \\ \text{(mg/hour)} & & \text{(L/hour)} & & \text{(mg/L)} \end{array}$$

Equation 1.2

It is apparent that for a given clearance, which is a constant characteristic of a particular drug and a particular patient, the elimination rate varies directly with the plasma drug concentration.

WHY IS CLEARANCE IMPORTANT?

Clearance is the one parameter that determines the maintenance dose rate required to achieve a target plasma concentration (and therefore effect) at steady state. Steady state is defined as the situation at which the rate of drug administration is equal to the rate of drug elimination so that the amount of drug in the body, and

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