Consider the compartment model in Figure 3.1 in order to understand the movement of a drug in the body. In the schematic representation given, it is very important to take note of the direction of the arrows – most of the processes involved can occur in both directions. Figure 3.2 is a more detailed representation of the factors affecting drug disposition.

3.1.1 Absorption

Absorption is essentially unidirectional and involves the movement of the drug from the site of administration into the bloodstream. The speed with which this occurs is largely dependent on the route of administration and determines the time taken for the response to occur. Solubility and physicochemical properties of a drug will also influence the rate of absorption. The oral route of administration generally results in slow rates of absorption and the greatest variability in the amount of drug entering the bloodstream. By comparison, intravenous administration bypasses the process of absorption, which dramatically reduces the induction time to immobilization.
3.1.2 Distribution

Distribution is a multifactorial process involving the movement of a drug from the bloodstream to various body tissues and organs. Immobilization occurs due to the effects of drugs on the brain and spinal cord (central nervous system); actions on tissues elsewhere in the body are termed ‘side effects’. Shortly after administration, the drug essentially moves in one direction from a higher concentration in the blood to a lower concentration in the tissues (i.e. a concentration gradient). Drug concentration and availability in the blood and, therefore, concentration and availability at the site of action are influenced by a number of factors. These include quantity of drug administered, amount bound to plasma proteins, pH, degree of hydration of the individual and presence of other drugs. The amount of drug entering the various tissues and organs depends on their perfusion by blood, ability to absorb the drug and the concentration gradient. Once the tissue concentration of the drug is relatively high, a dynamic process is established where the drug moves in both directions (from blood to tissues and from tissues to blood). In the absence of metabolism and excretion, a dynamic equilibrium would result where drug molecules would continue to move in both directions but the net concentration in both tissues and blood would remain the same. As the drug is metabolized, accumulates in muscle, fat and vessel-poor tissue and is excreted, its blood concentration starts to decline. This change in concentration gradient causes the drug to start moving out of the tissues, especially the central nervous system, and return to the bloodstream. Drug concentrations are forever changing: first increasing to a maximum and then decreasing as the drug is removed from the body. This can be illustrated by a graph of drug concentration in plasma as a function of time as shown in Figure 3.4. Note the influence of the route of administration on blood levels.

The most important physiological barriers that affect drug distribution are the blood-brain barrier and the blood-placenta barrier. Certain drugs are unable to cross these membranes, in which case no drug will be found in the brain or foetus respectively. It is therefore of paramount importance that if a drug is to exert its effect on the central nervous system, it must be able to effectively cross the blood-brain barrier. Drugs that are lipid soluble, un-ionized and not bound to plasma proteins are able to cross both the blood-brain barrier and the blood-placenta barrier. For this reason, drugs that induce immobilization will also affect the foetus should the animal be pregnant. All drugs used in the immobilization, tranquillization and sedation of wildlife due to their actions on the brain and spinal cord are inherently lipid soluble.