2. After this, the solute molecules must migrate through the boundary layers surrounding the crystal to the bulk of solution.

These stages, and the associated solution concentration changes, are illustrated in Figure 2.1.

These two stages of dissolution are now discussed in turn.

Interfacial reaction

Leaving the surface. Dissolution involves the replacement of crystal molecules by solvent molecules. This is illustrated in Figure 2.2.

The process of the removal of drug molecules from a solid, and their replacement by solvent molecules, is determined by the relative affinity of the various molecules involved. The solvent/solute forces of attraction must overcome the cohesive forces of attraction between the molecules of the solid.

Moving into the liquid. On leaving the solid surface, the drug molecule must become incorporated in the liquid phase, i.e. within the solvent. Liquids are thought to contain a small amount of so-called 'free volume'. This can be considered to be in the form of 'holes' that, at a given instant, are not occupied by the solvent molecules themselves (this point is discussed further in Chapter 3). Individual solute molecules are thought to occupy these 'holes', as shown in Figure 2.3.

The process of dissolution may be considered, therefore, to involve the relocation of solute molecules from an environment where they are surrounded by other identical molecules, with which they form intermolecular attractions, into a cavity in a liquid where they are surrounded by non-identical molecules, with which they may interact to different degrees.

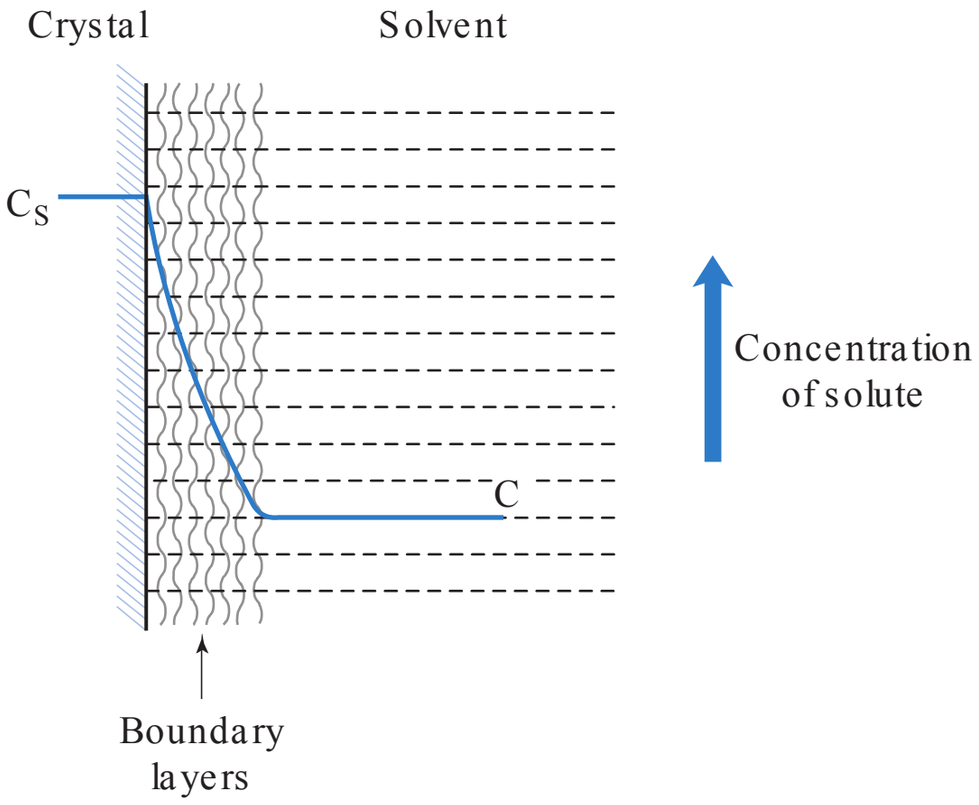

Fig. 2.1 • Diagram of boundary layers and concentration change surrounding a dissolving particle.

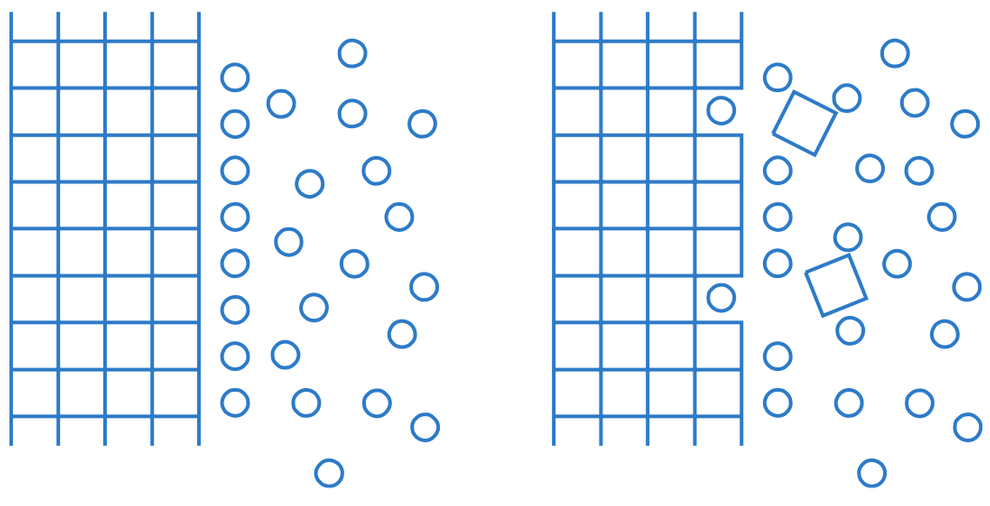

Fig. 2.2 • Schematic representation of the replacement of crystal molecules with solvent molecules during dissolution.

Diffusion through the boundary layer

This step involves transport of the drug molecules away from the solid/liquid interface into the bulk of the liquid phase under the influence of diffusion or convection. Boundary layers are static or slow-moving layers of liquid that surround all solid surfaces that are surrounded by liquid (discussed further later in this chapter and in Chapter 6). Mass transfer takes place more slowly (usually by diffusion; Chapter 3) through these static or slow-moving layers that inhibit the movement of solute molecules from the surface of the solid to the bulk of the solution. The solution in contact with the solid will be saturated (because it is in direct contact with undissolved solid). During diffusion, the concentration of the solution in the boundary layers changes from being saturated (C_S) at the crystal surface to being equal to that of the bulk of the solution (C) at its outermost limit, as shown in Figure 2.1.

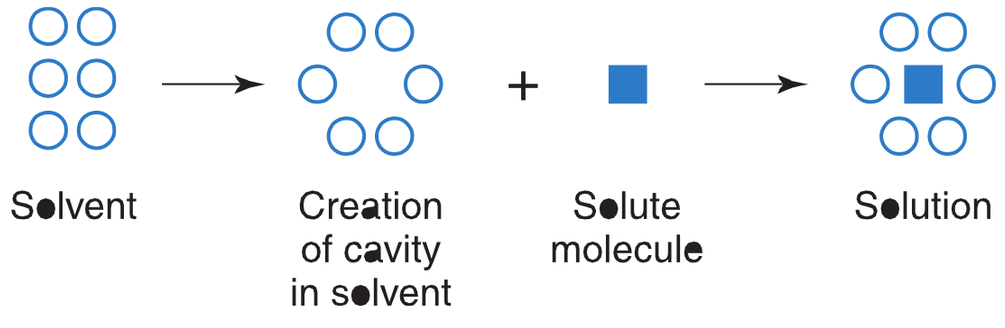

Fig. 2.3 • The theory of cavity creation in the mechanism of dissolution.