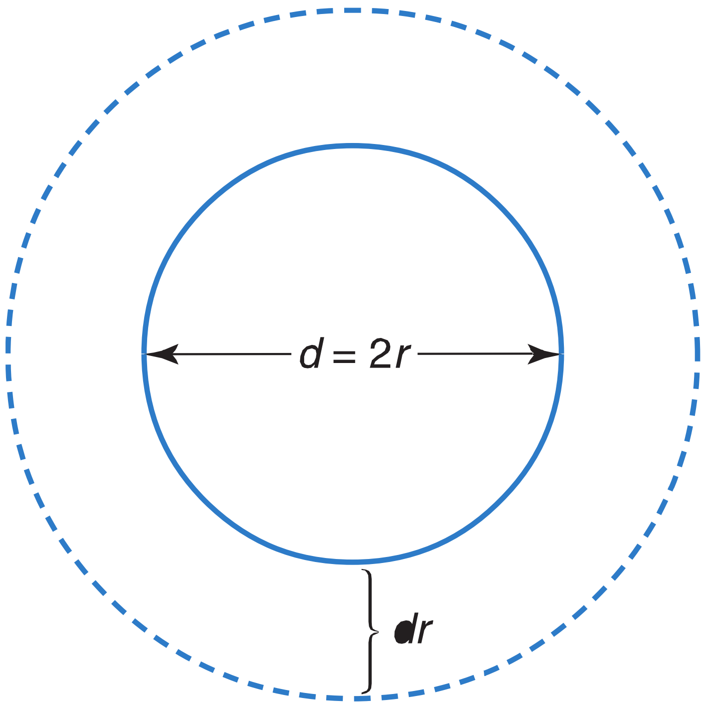

Fig. 2.4 • The reduction in surface area and volume during the dissolution of a spherical particle.

process progresses. (This effect is shown in Figure 30.7 and explained further in the associated discussion.)

Dispersibility of powdered solid in dissolution medium. If solid particles form cohered masses in the dissolution medium, then the surface area available for dissolution is reduced. This effect may be overcome by the addition of a wetting agent to improve the dispersion of the solid into primary powder particles.

Porosity of solid particles. Pores in some materials, particularly granulated ones, may be large enough to allow access of the dissolution medium and outward diffusion of dissolved solute molecules.

Solubility of solid in dissolution medium (C_S)

Temperature. Dissolution may be an exothermic or an endothermic process and so temperature changes will influence the energy balance and thus the energy available to promote dissolution.

Nature of dissolution medium. Factors such as solubility parameters, pH and presence of cosolvents will affect the rate of dissolution.

Molecular structure of solute. Factors such as the use of salts of either weakly acidic or weakly basic drugs, or esterification of neutral compounds, can influence solubility and dissolution rate.

Crystalline form of solid. The presence of polymorphs, hydrates, solvates or the amorphous form of the drug can all have an influence on dissolution rate.

Presence of other compounds. The common-ion effect, complex formation and the presence of solubilizing agents can affect the rate of dissolution.

Concentration of solute in solution at time t (C)

Volume of dissolution medium. If the volume of the dissolution medium is small, C can rapidly increase during dissolution and approach C_S. If the volume is large, then C may be negligible with respect to C_S and thus 'sink' conditions will operate. This can be controlled in vitro but must be taken into account in vivo as the volume of the stomach contents can vary greatly (hence the common instruction 'To be taken with a glass of water'). Also, the volume of the fluid in the rectum and vagina is small (see Chapter 42) and so this consideration can be important in drug delivery from suppositories and pessaries.

Any process that removes dissolved solute from the dissolution medium. For example, adsorption on to an insoluble adsorbent, partitioning into a second liquid that is immiscible with the dissolution medium, removal of solute by dialysis or by continuous replacement of solution by fresh dissolution medium can result in a decrease in C and thus an increased rate of dissolution.

Dissolution rate constant (k)

Thickness of the boundary layer. This is affected by the degree of agitation, which in turn depends on the speed of stirring or shaking, shape, size and position of stirrer, volume of dissolution medium, shape and size of container, and viscosity of dissolution medium.

Diffusion coefficient of solute in the dissolution medium. The diffusion coefficient of solute in the dissolution medium is affected by the viscosity of the dissolution medium, and the molecular characteristics and size of diffusing molecules.

It should be borne in mind that pharmaceutical scientists are often concerned with the rate of dissolution of a drug from a formulated product such as a tablet or a capsule, as well as with the dissolution rates of pure solids. In practice, the rate of dissolution can have either zero-order, first-order, second-order or cube-root kinetics. These are discussed later in the book when relevant to particular dosage forms. Later chapters in this book can also be consulted for information on the influence of