1 (corresponding to R_m values from $+\infty$ to $-\infty$, respectively) although in practice the measurable range is about 0.03 to 0.97, corresponding to R_m values of 1.5 to −1.5, respectively.

Addition of a co-solvent can be used to modulate the value of R_f obtained and the relationship is usually linear. This being so, it is possible to extrapolate to zero co-solvent and so calculate R_m in water.

Reverse-phase HPLC is an alternative, and widely used, technique for measurement of partition coefficients. The stationary phase comprises a non-polar compound (typically a C_{18} hydrocarbon) chemically bound to an inert, solid support medium (such as silica). It is possible to use water saturated with *n*-octanol as the mobile phase, and a stationary phase covered in *n*-octanol, but the eluting power is not strong, for the same reason noted above for TLC, and so to measure an acceptable range of partition coefficients it is necessary to change the volume ratio of mobile to stationary phase.

Because the hydrocarbon is bound to a solid substrate it cannot behave as a true liquid phase and so conceptually it is not clear whether the interaction between the solute and the stationary phase constitutes surface adsorption or true phase partitioning. While C_{18} hydrocarbons have been found to provide a better correlation to log*P* values, indicating that their greater reach from the solid surface of the support matrix means they behave more like a liquid phase, true partitioning is unlikely to occur.

Dissolution rate

Knowledge of solubility *per se* does not inform dissolution rate, since solubility is a position of equilibrium and not the speed at which it is attained. Thus, high aqueous solubility does not necessarily mean that a compound will exhibit satisfactory absorption. Absorption can be assumed to be unimpeded if a drug candidate has an intrinsic dissolution rate (IDR – see below) greater than 1 mg cm^{-2} min^{-1}.

Intrinsic dissolution rate

One assumption in the use of the Noyes and Whitney equation (described in Chapter 2, Eqns 2.3 and 2.4) is that the parameters of diffusion coefficient (D), the surface area of dissolving solid (A) and the thickness of the stationary solvent layer surrounding the dissolving solid (h) remain constant. Assuming a constant stirring speed and that the solution does not increase in viscosity as the solid dissolves, this is appropriate for D and h but A must always change as the solid dissolves (see Fig. 2.4). Also, if a tablet disintegrates, for instance, then A would increase rapidly at the start of dissolution before decreasing to zero, and there will be a concomitant effect on the dissolution rate.

If the sample is constructed such that A remains constant throughout dissolution, and sink conditions are maintained so that $(S_t - C) \approx S_t$ (see above), then the measured rate is called the *intrinsic dissolution rate* (IDR) (see also Chapter 2 and Eqn 2.6):

$$\mathrm{IDR} = KS_t \tag{23.25}$$

Wells (1988) suggests a method for measuring the IDR of a compound. A compact of the drug (300 mg) is prepared by compression (to 10 tonnes load) in an infrared punch and die set (13 mm diameter, corresponding to a surface area on the flat face of 1.33 cm^2). The metal surfaces of the punch and die should be pre-lubricated with a solution of stearic acid in chloroform (5% w/v). The compact is adhered to the holder of the rotating basket apparatus using low-melting paraffin wax. The compact is repeatedly dipped into the wax so that all sides are coated except the lower flat face (from which any residual wax should be removed with a scalpel blade). Dissolution is recorded while the disc is rotated (100 rpm) 20 mm from the bottom of a flat-bottomed dissolution vessel containing dissolution medium (1 L at 37 °C). The gradient of the dissolution line divided by the surface area of the compact gives the IDR.

IDR as a function of pH

Measurement of IDR as a function of either pH or ionic strength can give a good insight into the mechanism of drug release and the improvement in performance of salt forms, since, for weak acids, substitution of Equation 23.14 into Equation 23.25 yields:

$$\mathrm{IDR} = K(S_o[1 + \mathrm{antilog}(\mathrm{pH} - \mathrm{p}K_a)]) \tag{23.26}$$

And for weak bases substitution of Equation 23.15 into Equation 23.25 yields:

$$\mathrm{IDR} = K(S_o[1 + \mathrm{antilog}(\mathrm{p}K_a - \mathrm{pH})]) \tag{23.27}$$