the dissolution is said to be nonsink. While the use of the USP paddle dissolution apparatus is mandatory when developing a tablet, the rotating disc method has a great utility with regard to preformulation studies. The intrinsic dissolution rate is the dissolution rate of the compound under the condition of constant surface area. The rationale for the use of a compressed disc of pure material is that the intrinsic tendency of the test material to dissolve can be evaluated without formulation excipients.

Intrinsic dissolution rates of compounds obtained from rotating discs can be theoretically determined. Under hydrodynamic conditions, the intrinsic dissolution rate is usually proportional to the solubility of the solid. However, the dissolution rate obtained will depend on the rotation speed. Several modifications of rotating disc apparatus have been introduced to force zero intercepts. A disc is generally prepared by compressing about 200 mg of the candidate drug in a hydraulic press; the IR press often proves useful, as it gives a disc with a diameter of 1.3 cm. It should be noted that some compounds do not compress well and may exhibit elastic compression properties; that is, the disc may be very weak, rendering the experiment impossible. In addition to poor compression properties, another complication is that some compounds can undergo polymorphic transformations because of the application of pressure. This should therefore be borne in mind if there is insufficient compound to perform, for example, XRPD postcompaction.

If the disc has reasonable compression properties, it is then attached to a holder and set in motion in the dissolution medium (water, buffer, or simulated gastric fluid): we use a rotation speed of 100 rpm. A number of analytical techniques can be used to follow the dissolution process; however, UV–visible spectrophotometry and HPLC with fixed- or variable-wavelength detectors (or diode array) appear to be the most common. The UV system employs a flow through system and does not require much attention; however, if HPLC is used, then any aliquot taken should be replaced by an equal amount of solvent. The intrinsic dissolution rate is given by the slope of the linear portion of the concentration versus time curve, divided by the area of the disc, and has the units of mg/min cm^2.

6.9.12 High-Performance Liquid Chromatography

High-performance liquid chromatography is used to assess the degradation compounds in testing the stability of new drugs, since in these studies, the identification of degradation products is very important. Combined with mass spectrometer and the newer instrumentation, liquid chromatography/tandem mass spectroscopy (LC/MS/MS) and so on offer powerful tools for the elucidation of degradation mechanism.

Isocratic elution is often the most desirable method, as it does not require postequilibration phase for the next analysis; this can be an important consideration if a matrix of factors and excipients are studied for interaction. Gradient elution offers the advantage of sharper peaks, increased sensitivity, greater peak capacity, and selectivity (increased resolving power).

The type of detector to be used is usually dictated by the chemical structure of the compound under investigations. As most compounds of pharmaceutical interest contain aromatic rings, UV detection is the most common detection method. When using this technique, the most appropriate wavelength is selected from the UV spectrum