

arising from API deposition during the washing and drying steps. In fact, the requirement to prevent uncontrolled deposition of product dissolved in residual solvent during washing and drying means that the same approach to washing applies in either case. The drying process requires energy to provide the latent heat of vaporisation of the solvent which is evaporated. Delivery of this energy to the crystal surfaces from which solvent is to be evaporated without causing damage to the product crystals is one of the main challenges encountered in drying potentially heat sensitive APIs.

13.3 Filtration

A simple definition of filtration is the collection of particulate solids from suspension in a fluid as the fluid is driven through a porous medium. In this pharmaceutical application the valuable component is the crystalline drug substance and the fluid is the mother liquor solution from which the product has been crystallized. Classically the pharmaceutical industry employs dead end filtration in which the entire liquid volume is forced through the filter allowing all the particles above a collection threshold size to be retained. This collection threshold size is determined initially by the filter medium pore size but as a filter cake forms the collection threshold will be modified by the inter-particle path dimensions in the filter cake. This is determined by the product crystal size distribution and the filter cake structure. The process of dead end filtration is described in the equation first formalised by Darcy² which, in its most compact and widely used form, is shown in eqn (13.1).

$$\frac{t}{V} = \frac{\mu\alpha}{2\Delta P A^2} V + \frac{\mu R_m}{A\Delta P} \quad (13.1)$$

Here the duration of the filtration is expressed as the time, t , required to collect a volume of filtrate, V . Increasing values of t/V correspond to slower filtration rates, hence the viscosity of the solution being filtered, μ , the specific cake resistance, α , and the filter medium resistance, R_m are all in the numerator terms. The denominator terms which serve to increase the filtration rate are the pressure driving force, ΔP , and the filter area A . Filtration rate data can be collected relatively easily using a filter funnel, a calibrated filtrate receiver, a timer and a pressure controller. A suitable experimental arrangement for early development when API is in short supply is shown in Figure 13.2.

This is based on a Biotage Flash vac system in which the tube rack in the vacuum chamber has been modified to accommodate 50 mL measuring cylinders. Pressure control is provided by a Buchi vacuum controller. This design allows the experimentalist to charge a representative suspension sample to the filter tube, which is a syringe body, in the base of which a filter frit of known pore size has been positioned. When the desired pressure has been set in the vacuum chamber, filtration is started by opening a PTFE valve