where E is the energy required to achieve complete drying (kJ); $\Delta H_{\text{vap S1}}$, latent heat of vaporisation of solvent 1 (kJ mol^{-1}); LOD_{S1}, mass of solvent 1 evaporated (g); MW_{S1}, molecular weight of solvent 1; ΔC_{pS1}, heat capacity of solvent 1 (kJ mol^{-1} K^{-1}); ΔT, temperature change from input temp and drier operating temperature (K); M_{API}, mass of API; ΔC_{pAPI}, heat capacity of API (kJ mol^{-1} K^{-1}); MW_{API}, molecular mass of API.

Once the heating duty has been determined it is necessary to determine how the heat will be delivered. The two most widely used mechanisms of delivering heat during drying are provision of a heat transfer surface and appropriate agitation to ensure temperature uniformity, or flowing heated nitrogen through the drier. Obviously as the drier becomes larger the available surface area to volume ratio becomes less favourable, the extent to which this becomes a problem then depends on the selected equipment geometry. The heat capacity of dry nitrogen close to room temperature is 1.04 kJ kg^{-1} K^{-1} which limits the energy which can be delivered. To put this into context, the drying duty associated with the removal of typical organic solvents ranges from 500 to 1000 kJ kg^{-1} of solvent evaporated. Presuming an inlet nitrogen temperature of 60 °C and almost complete heat transfer from the nitrogen to the solvent in the filter cake, the volume of nitrogen required to remove 1 kg of solvent would be between 10 and 20 m^3.

13.5.2 Agitation

Agitation of the wet filter cake can cause “balling-up” which ultimately results in large agglomerates forming and may result in uneven impurity distribution. This problem is especially severe if agitation is applied around the critical solvent content (sometimes referred to as the sticky point); this point cannot be predicted but must be determined experimentally and is influenced by particle size distribution and solvent choice. A further consequence of agitation during drying is the potential for particle breakage; this may both reduce the mean particle size of the primary particles and produce fine particles which increase the product specific surface area resulting in impaired particle flow. There is also the possibility of introducing amorphous character through the breakage process which has the potential to reduce the stability of both the API and the final drug product.

13.5.3 Drying Kinetics

The drying process can be regarded as controlling temperature and heat flow to influence mass transport and evaporation. In most continuous dryers, particle movement is employed, *e.g.* fluidised bed, internal agitator/paddle/flights, to assist in maintaining a uniform product temperature, so