particle surfaces. A second consequence of this solvent transport mechanism is the tendency to form hardened surface layers because the vast majority of solvent evaporation takes place from the surface particle layers and any API dissolved in the residual solvent is deposited on the particles' surfaces and especially at points of contact. Both problems can be minimised by very effective washing such that virtually no impurity remains to be transported and by leaving the filter cake wet with a non-solvent such that there is nothing to deposit as the final wash solvent is evaporated; this is illustrated in Figure 13.11.

An alternative strategy is to agitate the filter cake during drying such that any impurities dissolved in the residual solvent are distributed evenly, and few strong inter particle bonds form as dissolved API is deposited by evaporation. Agitation also serves to aid heat transfer if drying is accomplished *via* contact with a heated surface. However, caution is needed as agitating the wet cake can promote granulation and lead to breakage of crystals with vulnerable crystal habits, especially needles.

13.5.1 Determining the Thermal Energy Required for Drying

Eqn (13.2) describes the energy needed to remove the solvent; if drying is isothermal then the second and third terms are zero.

$$E = \frac{\mathrm{LOD}_{S1} \cdot \Delta H_{\mathrm{vap}_{S1}}}{\mathrm{MW}_{S1}} + \frac{\Delta T \cdot M_{\mathrm{API}} \cdot \Delta C_{\mathrm{p}_{\mathrm{API}}}}{\mathrm{MW}_{\mathrm{API}}} + \frac{\Delta T \cdot \mathrm{LOD}_{S1} \cdot \Delta C_{\mathrm{p}_{S1}}}{\mathrm{MW}_{S1}} \tag{13.2}$$

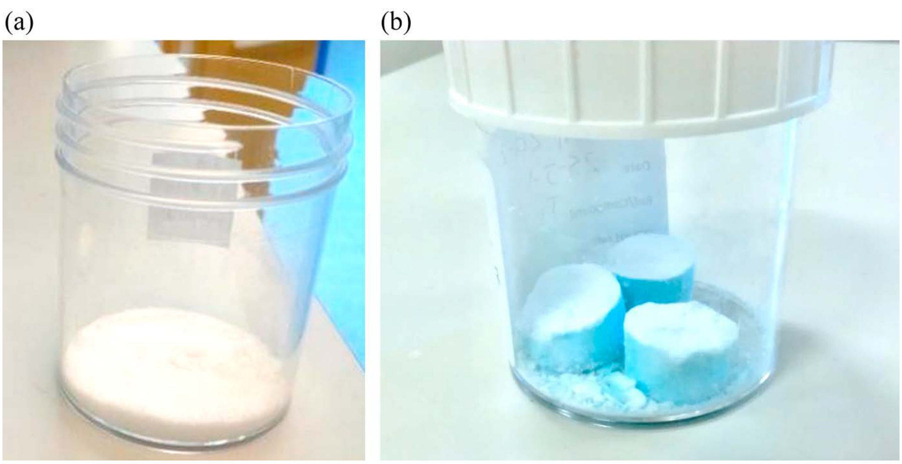

Figure 13.11 The effect of residual solvent on dry product attributes. (a) Material washed with a non-solvent and dried to deliver a free flowing powder (b) material dried with residual mother liquor including a trace of coloured impurity results in lump formation and inhomogeneous distribution of the impurity.