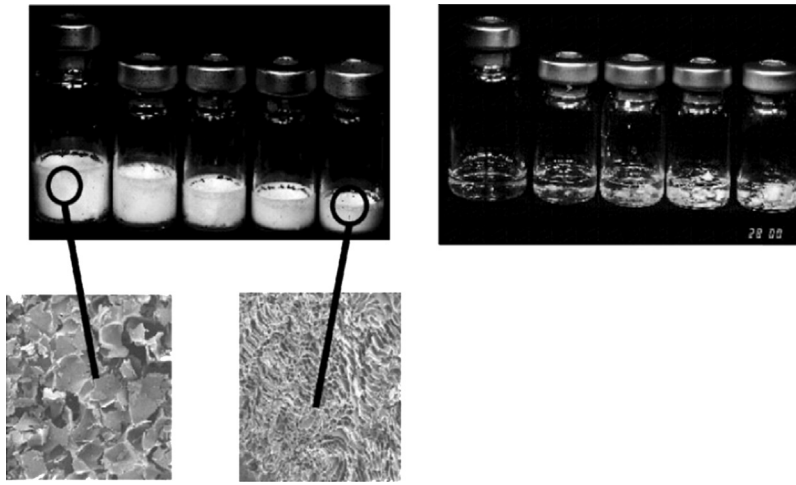

**Figure 7.6** Lyophilization of a mAb as a function of loading concentration. Upper left panel: Loading concentrations from left to right were 40, 60, 80, 100, and110 mg/mL, respectively, while maintaining the same total mass of mAb and excipients. Lower left panels: Scanning electron microscopy of lyophilized solid for the 40 and 110 mg/mL mAb loading concentrations. Right panel: 10 min after reconstitution of vials in the upper left panel to 125 mg/mL with sterile water for injection.
From Shire et al. (2004).

where $\eta$ is the suspension viscosity, $\eta_0$ the viscosity of the suspension vehicle, and $\varphi$ the volume fraction of solute (volume of solute/volume of solution).

Suspension of proteins should have viscosities that approach that of the diluent used for the suspension if the volume fraction of dispersed solute is low. As an example, crystallization of mAbs has been used to generate high-concentration suspensions, which generally have lower viscosity than the equivalent aqueous formulation (Figure 7.7) (although as will be discussed, appropriate selection of excipients can generate aqueous high concentration at low viscosity) (Yang et al., 2003). Suspensions have also been created using milled lyophilized powder (Chen et al., 2005), amorphous precipitates (Matheus, Friess, Schwartz, & Mahler, 2009), generation of excipient-free protein microspheres (Brown et al., 2006), and powders from spray drying (Bowen, Armstrong, & Maa, 2012; Dani, Platz, & Tzannis, 2007). In the recent study by Bowen et al., it was shown that suspensions of three mAbs in a low-viscosity oil, Miglyol® 840 ($\eta_0$ = ~9 mPa s), generally outperformed liquid formulations for injectability as assessed by glide force measurements despite higher viscosities when compared to equivalent mAb concentrations for liquid formulations. It was also emphasized that Einstein's equation (7.3) is valid only for dilute suspensions. An empirical equation relating suspension viscosity to powder concentration was derived and compared to a modified form of the Einstein equation. The latter was found to underestimate the empirical data. Another important finding was that the suspension viscosity was similar for all the mAbs studied although the liquid viscosity was very dependent on the mAb that was formulated.