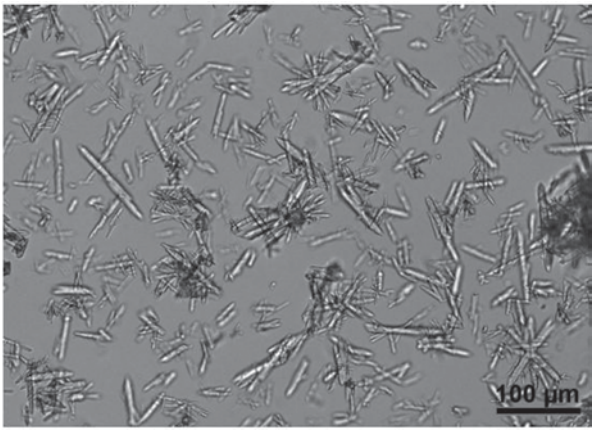

Fig. 10 Stirred-batch crystallization of mAb01 from pretreated harvest on the 1 L-scale (Experiment A). 2.2 g L^{-1} mAb01 in pretreated harvest; 2% w/v PEG 10000 added; TRIS base added to adjust the pH to 6.8. Microphotograph was taken after crystallization overnight at 10 °C. Robust rod-like crystals (the dark spots represent crystal agglomerates containing native antibody). *mAb* monoclonal antibodies, *w/v* weight/volume (Adapted with permission from [40])

similar microbatch experiments. The microbatch crystallization process was successfully scaled to 5 ml and ultimately to 100 ml in a stirred tank crystallizer (as described in previous chapter). Scale-up resulted in reproducible crystal morphologies, similar crystallization kinetics, and comparable crystallization yields.

Smejkal et al. describe a similar fast and scalable crystallization-based purification for a therapeutic IgG1 antibody [40]. While the purified IgG1 could be crystallized easily in microbatch experiments, the crystallization of IgG1 from clarified Chinese hamster ovary (CHO) cell culture harvest required a simple pretreatment. Stirred-batch crystallization of both the purified mAb01 and the pretreated harvest was scaled at 6-mL scale and 1-L scale, using stirred-batch crystallizers (as described in previous chapter). Figure 10 describes crystallization of mAb01 from pretreated harvest culture in stirred-batch crystallizer at 1 L scale.

The developed crystallization method resulted in high crystallization yield, high purity, and significant reduction in related impurities such as host cell protein and host cell DNA. The crystals were easily solubilized and recrystallizable without significantly affecting the biological activity of the therapeutic antibody. Based on the findings, the authors suggested that batch rystallization method could potentially replace protein A chromatography, a generally employed capture step in antibody purification.

Crystalline mAbs: High Concentration and Sustained Release Formulations As described previously, development of high-concentration mAb formulation remains a significantly challenging task due to high viscosity and related colloidal instability. Crystalline antibody suspensions are proposed as a drug-delivery alternative to high-viscosity solutions [4]. Besides reducing the viscosity, crystalline suspensions also offer the unique advantage of sustained release drug delivery. Yang et al. describe a successful application of small-volume, high-concentration crystalline antibody suspensions for subcutaneous delivery employing three commercial therapeutic antibodies rituximab, trastuzumab, and infliximab as examples [49]. The