vessels was fast, scalable, and reproducible. Hebel et al. describe the scale-up of protein crystallization in stirred crystallizers from a 5-ml scale onto geometrically similar stirred crystallizers at 100 mL and 1 L scale (stirred crystallizers as depicted in Fig. 4), using lysozyme and lipase as model proteins [21].

L-Methionine γ-Lyase

Takakura et al. describe industrial scale purification and bulk scale crystallization of L-methionine γ-lyase (METase) a pyridoxal 5′-phosphate-dependent enzyme with selective antitumor activity [46]. Bulk crystallization was employed as an initial capture and purification step for processing the crude enzyme preparation. Rod-shaped crystals (with a crystallization yield of 87%) were obtained in the presence of 9.0% polyethylene glycol 6000, 3.6% ammonium sulfate, and 0.18 M sodium chloride using a 100-L crystallizer (Fig. 5a). Repeated second and third crystallizations in the presence of polyethylene glycol 6000 and sodium chloride resulted in octahedral crystals (Fig. 5b).

The individual effects of PEG 6000, ammonium sulfate, and sodium chloride concentrations on the crystal purity and crystallization yield were evaluated on a small scale prior to bulk crystallization (Fig. 6). The crystal purity was assessed by measuring specific activity (U/mg) for the enzyme. As described in Fig. 6, each of the three components in crystallization affected the crystal purity and yield, the final composition of the crystallization recipe was optimized based on these results from

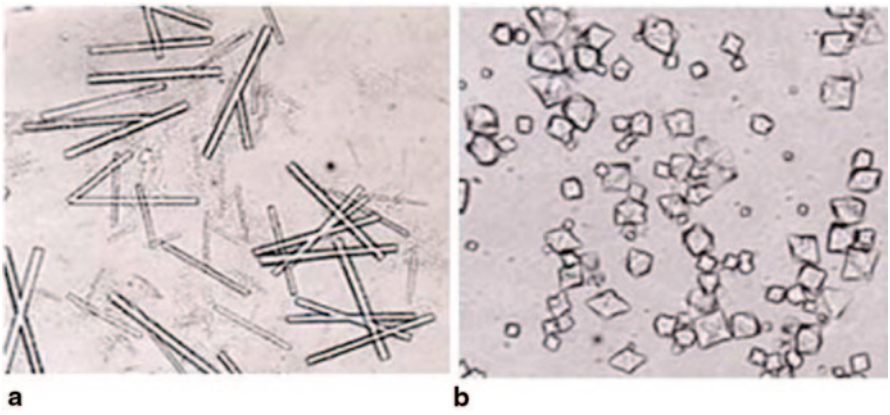

Fig. 5 Morphology of rod-shaped crystals (**a**) and octahedral-shaped crystals (**b**) of recombinant METase. **a** Rod-shaped crystals were obtained from the first crystallization in the presence of poly ethylene glycol (PEG) 6000, ammonium sulfate, and sodium chloride as precipitants. **b** Octahedral-shaped crystals were obtained from the second and third crystallizations in the presence of PEG 6000 and sodium chloride as precipitants. The bar shows 50 μm (Adapted with permission from [46])