crystallization conditions resulted in high yields, no detectable modifications in the protein properties, and complete retention of biological activity. The crystalline suspensions had significantly reduced viscosity, compared to similar concentration solutions. The crystalline suspension also demonstrated longer pharmacokinetic profile (sustained release) during in vivo evaluation. Using glucose oxidase and lipase as model proteins, Shenoy et al. describe the preparation of crystalline formulations [39]. Analytical characterization (using FTIR spectroscopy and size-exclusion chromatography) of the crystalline suspension suggested that such an approach generates more stable protein formulations.

Conclusions and Future Trends

Based on the examples discussed herein, undoubtedly crystallization and freeze-drying find applications in different stages of biopharmaceutical development such as, (i) capture or purification (e.g., enzymes, mAb, antibody fragments), (ii) polishing and finishing step for purified biologic (e.g., insulin, aprotinin), and (iii) high-concentration formulation development (e.g., high-concentration antibody formulation). Some of the interesting techniques such as developing high-concentration crystalline mAb formulations and the capture (purification) of antibodies by crystallization instead of a packed bed chromatography step, will definitely have widespread applications in the near future.

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