Control of Crystal Size in Cooling or Poor Solvent Crystallization

Hiroshi Ooshima*
Department of Applied Chemistry and Bioengineering, Graduate School of Engineering, Osaka City University
(ooshima@bioa.eng.osaka-cu.ac.jp*)

Crystal size is one of the most important characteristics of crystals to be controlled in industrial crystallization. There are some strategies for the control of crystal size. Most important thing is to homologize the timing of nucleation. If it is difficult, the second choice is to restrain the secondary nucleation and grow seed-crystals, for example, by programmed cooling of batch crystallizer (Mullin et al, Chem. Eng. Sci, 26, 369 (1997)) and the seed chart method (D. Jagadesh et al, J. Chem. Eng. Japan, 32, 514 (1999). However, we cannot always use seed-crystals. In particular, pharmaceutical companies do not hope to use seed-crystals to prevent the contamination. The third choice is to dissolve fine crystals by heating the solution on the way of crystallization.

Here, the author will discuss the relationship between the size control and the crystal nucleation in the crystallization without seed-crystals. The author shows that it is important to understand the solution structure in the control of crystal size. Furthermore, the author also shows that oiling out that is usually avoided in industrial crystallization is sometimes preferable for the size control.