

Operating Strategy for Improving Efficiency of Polymorph Productivity

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Polymorphism is the ability of a solid material to exist in more than one form. The organic substance with the different shapes has the different physical properties, thermodynamic properties, kinetic properties and mechanical properties and these properties affect bioavailability of drugs. In the existing industrial crystallization, two stage processes is required. First, the metastable form created by Ostwald's rule in initial crystallization is produced in bulk and then the metastable form is transformed to the stable form using recrystallization. That makes inefficient processes as a production of the stable form because of operating time and trouble of two step manufacturing. In this study, operating strategy is investigated to improve the existing process of L-histidine using drowning-out crystallization. In order that production of form B is excluded and growth of form A is only occurred, dynamic model is considered. Metastable limit of form B with nucleation time and growth rate of form A is focused to develop strategy of feeding rate. Using suggested optimal feeding rate, improvement of productivity for stable form A is demonstrated compared with existing crystallization.