

First, primary nucleation can be generated locally at the start of the tube. Second, continuous seeding can be used to prevent the nucleation process altogether.

1.3.2 Continuous Heterogeneous Crystallization on Excipient Surfaces

The direct crystallization of an API on a crystalline excipient surface is called “heteroepitaxy.” The heterosurface orders prenucleation aggregates, so nucleation becomes energetically favorable.^{86,87} In the crystallization process detailed in this example here (Figure. 1.6), the API (acetaminophen) nucleates and grows on an excipient surface (D-mannitol). The API-excipient system selection, induction time measurement, and molecular interaction modeling have been studied.⁸⁶⁻⁸⁹ The dynamic conditions of

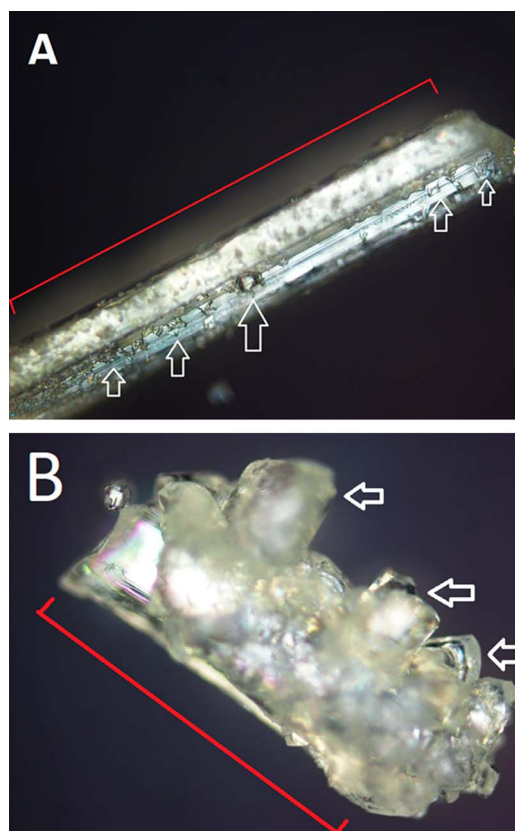


Figure 1.6 An example of direct nucleation and crystallization of a solute (acetaminophen here) on excipient (D-mannitol here) surface. (A) Nuclei are forming on the surface of the excipient. (B) Crystal growth. (Arrows show nuclei and crystals, line shows excipient.)