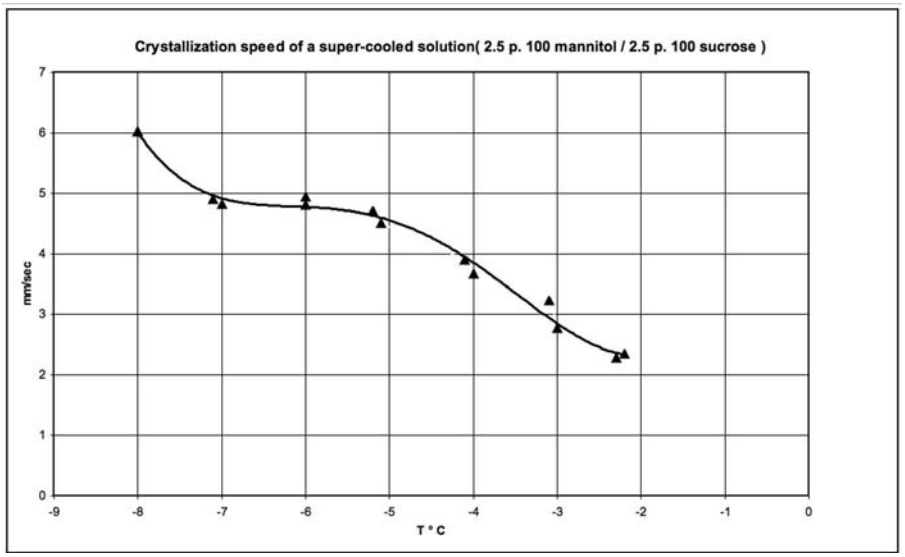

FIGURE 4 Crystallization velocity of a solution versus its degree of supercooling.

conveyor and frozen hard in a cold room. Then it is broken, ground or sliced, sifted, and finally fed into the freeze-drying plant.

In the preparation of many pharmaceuticals we know that some components in the formulation are not compatible together. For instance, if we mix acetyl salicylic acid with sodium bicarbonate in solution, there is an immediate reaction and a vigorous release of carbon dioxide. Nevertheless, it might be of interest to freeze-dry them together to have instant sparkling aspirin, but this is not possible, and the only way around this is to compact the products together in the dry state. The resulting tablet is not very stable and it takes a relatively long time to get back into solution.

Conversely, if such reactive substances are mixed together at low temperature after incorporation in a soft ice they will not react and the resulting paste can be molded in appropriate shapes and hardened by further cooling. The material can then be freeze-dried without difficulties. In that state, lyophilized aspirin, for instance, is perfectly stable and when water is added back it reconstitutes as a sparkling fluid in a few seconds because of its high porosity.

The "soft ice" technology is thus a very precious tool to prepare complex products, most often for oral route. Pure chemicals, drugs, vitamins, and mineral salts can be successfully freeze-dried in that way in rather elaborate formulations since it is possible to mix together "sherbets-lines" issued from different solutions and even add to the whole other solid ingredients as finely dispersed powders. The key to success in that process is a good control of the temperature of the icy paste, which is generally prepared in a cylindrical double-wall heat exchanger with a continuous scraped surface maintained at temperatures between $-4^{\circ}C$ and $-20^{\circ}C$ depending on the nature of the treated products. When the soft ice mixture is duly completed it can be molded by conventional equipment in plastic blisters and frozen hard in a blast tunnel.