



## **Freeze Drying of Co-Solvent Systems: Rationale, Opportunities, and Applications**

### **ABSTRACT:**

Co-solvents can be used during freeze-drying to optimize the freeze-drying cycle or to freeze-dry other compounds than usually used. A well known co-solvent that is suitable for freeze-drying due to its physico-chemical properties is tertiary butyl alcohol (TBA).

One advantage of TBA is that, due to its relatively high vapor pressure, it rapidly sublimates. The addition of TBA as co-solvent can therefore increase the drying rate of the product, which results in shorter freeze-drying cycles. Another advantage is that most lipophilic compounds can be dissolved in TBA. This could be used to prepare solid dispersion of a lipophilic drug incorporated in a hydrophilic carrier.

If one understands what happens during freeze-drying, within the solution to be freeze-dried, one can manipulate the process to obtain a product with the desired physico-chemical properties. It is for example common to perform freeze-drying at a relatively low temperature to prepare amorphous solid dispersions. An example that is less common, is modifying the freeze-drying cycle in such a way, an addition of a crystallization step, that drug nanocrystals can be prepared.