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ABSTRACT FORM

Title : **LYOPHILIZATION OPTIMIZATION USING DSC and MT-DSC**

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Aqueous formulation stability is a concern due to drug chemical degradation in solution and evolution in time. Lyophilization is often used to obtain physical and chemical stability. The material is first frozen, and then water concentration is reduced by sublimation and by desorption to obtain a dry product. The nature, time and expense of the lyophilization process are directly dependent on the chemical and physical properties of the formulation. Each lyophilized formulation has one or more active ingredient and stabilizing or bulking constituents. Their chemical nature and their concentration may vary.

Stabilizing or bulking components can be classified in two main families depending on their physical properties: ingredients crystallizing during freezing or staying in a glassy state. DSC or MT-DSC (for amorphous materials) provides useful information to optimize the initial freezing temperature and to ensure a complete frozen state and the lowest molecular mobility level of the matrix.

Stabilizing and bulking ingredients (glycine,maltose and trehalose) were characterized using DSC and MT-DSC and their state diagrams were obtained. They illustrate the two previously mentioned families : glycine shows an eutectic behavior and maltose freezes as a glassy matrix.

Trehalose has a more complex behavior closely dependent on its thermal history : slow cooling leads to crystalline phase, fast cooling to amorphous one.

The effect of small changes in the composition of the binary mixtures (solvent or active ingredient addition) was also studied. Major impacts on the thermal properties of the formulation and on the optimal lyophilization parameters were observed.