

# The persistence and crystallization behavior of atorvastatin calcium amorphous dispersions in polyvinylpyrrolidone

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## Abstract

The persistence of amorphous atorvastatin calcium has been studied as a function of the amorphization method, polymer content, and relative humidity during storage. For amorphization, ball milling, freeze drying, and spray drying have been used. Polyvinylpyrrolidone K40 (PVP) was mixed with atorvastatin in a wide range of concentrations and the resulting amorphous dispersions were subjected to storage conditions with different levels of relative humidity. The analysis of the glass transition temperature of the various samples demonstrates that interactions between atorvastatin calcium and PVP are unfavorable, leading to a destabilization of amorphous atorvastatin, which becomes therefore more prone to recrystallization. However, mixtures made with spray drying in methanol show an increased glass transition temperature and an increased stability against recrystallisation. PVP may act as a humidity reservoir providing water molecules to amorphous atorvastatin calcium and thus promoting crystallization of the hydrate form. For atorvastatin calcium, the most persistent amorphous sample appears to be that without PVP. It possesses a glass transition temperature as high as 143 °C and it remains amorphous for at least a year independent of the humidity level it is subjected to.