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Amorphous solid dispersions of APIs with crystallization inhibitors of different molecular weights

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A transformation of poorly water-soluble crystalline pharmaceuticals to the amorphous form is one of the most promising strategies to improve their oral bioavailability. Unfortunately, the amorphous drugs are usually thermodynamically unstable and quickly return to their crystalline form. A very promising way to enhance the physical stability of amorphous drugs is to prepare amorphous compositions of APIs with certain excipients which can be characterized by significantly different molecular weights, such as polymers, acetate saccharides and other APIs. We examine the effect of adding large molecular weight polymer polyvinylpyrrolidone (PVP K30) and the small molecular weight excipient octaacetylmaltose (acMAL) on the tendency to recrystallization of the amorphous celecoxib (CEL) in the amorphous Solid dispersions: CEL-PVP and CEL-acMAL. We found that acMAL is a better inhibitor of recrystallization of amorphous CEL than PVP K30 deep in the glassy state (T<T_g). In contrast, PVP K30 is a better crystallization inhibitor of CEL in the super cooled liquid state (at T>T_g) than acMal. The latter conclusion can be related to the slower crystallization times in the case of CEL+PVP as well as a strong antiplasticization effect of the added polymer on the super cooled CEL. However, the significantly different antiplasticization effects of PVP and acMal on super cooled CEL is not reflected in their ability to the physical stabilization of the drug in the glassy state. In the glassy state, both PVP and acMAL molecules form hydrogen bonds with CEL molecules, but acMal much more effectively suppresses some local molecular motions of CEL responsible for the drug devitrification.

Biography

Katarzyna Grzybowska has received her PhD degree in Physics at the University of Silesia in 2008. In 2012, she has completed a four-year Post doctorate in the research project "From Study of Molecular Dynamics in Amorphous Medicines at Ambient and Elevated Pressure is Novel Applications in Pharmacy" in the Institute of Physics at the University of Silesia. She is a co-author of more than 60 publications in the international peer reviewed journals from ISI list and two patents.

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