Poster

Ranolazine: crystal structure determination and investigation of its metastable polymorphs

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Ranolazine (RNL) is an anti-anginal drug widely used in treating cardiovascular diseases, which shows advantages over other anti-anginal agents because it exhibits an anti-ischemic effect [1,2]. Unfortunately, its bioavailability is limited by its low aqueous solubility [3]. Moreover, there is scarcity of scientific results regarding the solid-state forms of RNL. Within this framework, we investigated the polymorphism and the amorphization of RNL using both Single Crystal, Powder and Variable Temperature Powder X-ray Diffraction and micro- tomography on different RNL preparations. All these techniques are available at the CRIST - Crystallographic Service Centre of the University of Florence. Single crystals of RNL were produced by solvent evaporation from PEO-acetonitrile gel, allowing to solve the crystal structure for the first time. RNL crystallizes in the monoclinic system, space group $P2_1/n$, with one molecule of RNL in the asymmetric unit and four molecules of RNL in the unit cell. The analysis of the packing structure shows that two molecules of RNL are linked by a hydrogen bond forming a dimer at the center of the unit cell. RNL amorphous phases with T_g values lower than room temperature were obtained by cryo-milling and quench-cooling. New forms of RNL were identified by PXRD from the relaxation of the ranolazine amorphous phase produced by cryo-milling, which takes place within several hours after grinding. At room temperature, these metastable polymorphs relax to the lower energy polymorphI, which corresponds to the one obtained from SCXRD characterization. Finally, the thermal behavior of cryo-milled RNL samples was investigated by VT-XRPD experiments, which showed a partially amorphous material that increases crystallinity when subject to heating from 20 to 100 °C.

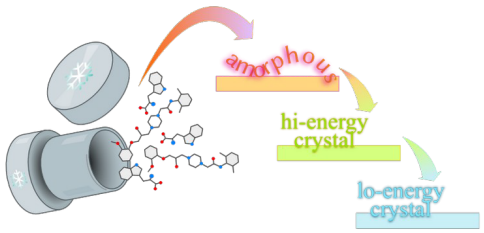

Figure 1. Relaxation process of RNL amorphous phase to lower energy polymorph I.

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