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Insight into the structure of liquid-crystalline itraconazole drug

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Nowadays, there is an increasing interest in the application of amorphous pharmaceutical formulations in tablet form since they exhibit better solubility and bioavailability than their crystalline counterparts. One of the very poorly soluble active pharmaceutical ingredients (APIs) is itraconazole (ITZ), which demonstrates superior antifungal activity. Moreover, ITZ is a well-known thermotropic liquid-crystalline (LC) compound. When cooled down from melt, ITZ exhibits transformation to the nematic and then to the smectic phase, which subsequently is trapped in the glass state at room temperature. Recently, we demonstrated that by cryo- milling it is possible to produce very stable solid ITZ particles with a lower degree of LC organization (nematic) compared to ordinary glass obtained by vitrification[1]. Importantly, the more disordered form resulted in better solubility in the conditions simulating gastrointestinal passage[1].

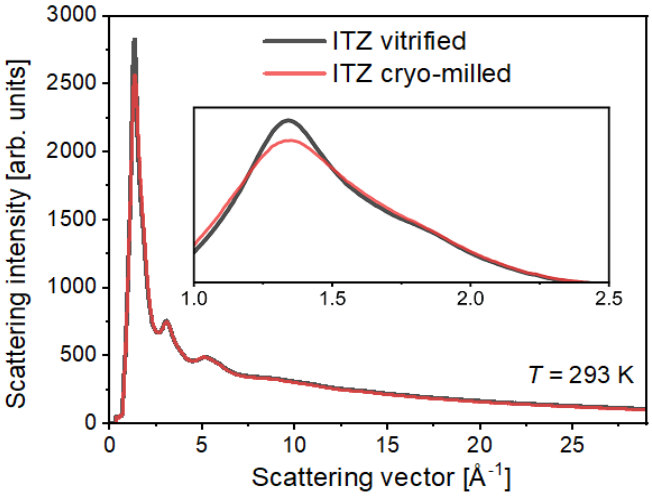

Figure 1. X-ray scattering (diffraction) data of the vitrified and cryo-milled ITZ collected using synchrotron radiation (ID22, ESRF).

In order to deepen the knowledge of the subtle differences in the local structure of non-crystalline, amorphous-like APIs, total X-ray scattering data collected using synchrotron sources may be used. Here, we will present the results of different X-ray scattering experiments and molecular dynamics simulations, which in combination allowed us to create coherent models of the atomic- scale structure of ITZ obtained using various methods: vitrification, cryo- milling, and solvation-evaporation.

The analysis of the obtained intermolecular structure factors and configurations changes the conventional thinking about the LC organization of molecules, which, in the case of the ITZ smectic glass, is difficult to distinguish from completely amorphous at first sight. Moreover, based on the analysis of the intramolecular structure factors, one may ask whether temperature-activated transitions between different diastereomers are possible.

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References

1. T. Lamrani, et al. J. Mol, Liq. 414 (2024) 126106.