Poster

Crystallization of molecular glass: from amorphous state to new polymorphic forms in the API sodium naproxen

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The solid form of an active pharmaceutical ingredient (API) is usually governing its material properties such as solubility or tableting characteristics. Several strategies have been put into place to improve solubility as this is often a major issue. Naproxen is a poorly soluble API, but its solubility can be improved by synthetizing corresponding sodium salt. Another alternative to improve solubility is to stabilize an amorphous state [1], however it has been shown that naproxen is a typical non glass former [2].

For ceramic materials, it has been demonstrated that crystallization from glass can be a successful approach [3] to stabilize new polymorphic forms of technological relevance. In this contribution, we have been applying a similar approach investigating sodium naproxen as an example. When heating up sodium naproxen above its melting point, various phases can be stabilized at room temperature depending on the heat treatment: a new polymorph, or a glass phase. This is in significant contrast to pure naproxen. We show in Fig. 1 the temperature dependence of this glass phase as function of temperature. Upon heating, the initial amorphous state (1) evolves towards a second amorphous state (2) before recrystallizing into previously unreported polymorphic forms of sodium naproxen (regions (3) and (4)). For instance, the crystal structure present in the region (4) can be stabilized at room temperature and varies from the initially reported crystal structure of sodium naproxen [4] only by the orientation of the methoxy group (Fig. 1 b).

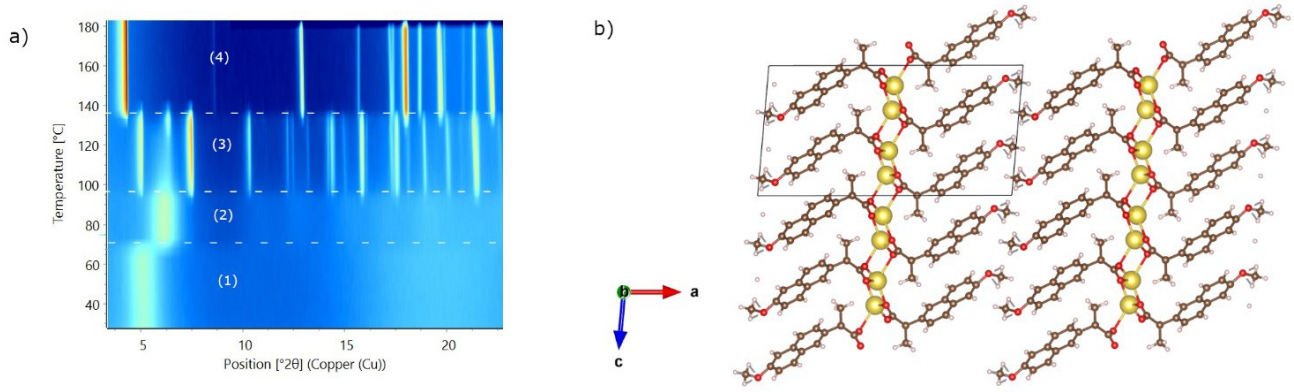

Figure 1. a) Isoline plot of the recrystallization of amorphous sodium naproxen as function of temperature and b) crystal structure of the new polymorph of sodium naproxen appearing at high temperature (section 4).

While molecular glasses are investigated to attempt stabilizing amorphous phases of APIs in the pharmaceutical industry, this work demonstrates their crystallization can be an alternative route for stabilization of new polymorphic forms of drug substances.

[1] Kalepu S, Nekkanti V. (2015) *Acta Pharmaceutica Sinica B*., **5**, 442.

[2] Wyttenbach, N., Kirchmeyer, W., Alsenz, J., Kuentz, M. (2016) *Mol. Pharmaceutics*, **13**, 241.

[3] Genevois**,** C., Bazzaoui, H., Boyer, M., Ory, S., Ledemi, Y., Messaddeq, Y., Pitcher, M. J., Allix, M. (2021) *Inorg. Chem.*, **60**, 12339.

[4] Kim, Y. B., Park, I Y, Lah, W. R. (1990), *Arch. Pharm. Res.*, **13**, 166.