

Poster Presentations

[MS24-P15] Screening of 6-propyl-2-thiouracil cocrystals.

Cristóbal Verdugo-Escamilla, Duane Choquesillo-Lazarte, Juan Manuel García-Ruíz.

Laboratorio de Estudios Cristalográficos, IACT, CSIC-UGR, 18100 Armilla, Granada, Spain.
E-mail: cverdugoe@iact.ugr-csic.es

The active pharmaceutical ingredient (API) 6-propyl-2-thiouracil, also known as propylthiouracil (PTU), is used for the treatment of the hyperthyroidism caused by Graves' disease [1] and its action mechanism is by decreasing the amount of thyroid hormone produced by the thyroid gland [2]. This API is used as a secondline treatment for patients who are intolerant to other therapies like methimazole [3]. The cocrystallization of PTU with pyrimidin-2-amine and N-(6-acetamidopyridin-2-yl)acetamide has been previously reported to study the relative stability of NH...O and N-H...S hydrogen bonds [4]. In this work, we report the cocrystallization of PTU with three different cocrystal formers such as resorcinol, hydroquinone and phloroglucinol, all of them having in common the presence of only hydroxyl groups in the benzene ring. In order to evaluate the propensity of the cocrystal formers to form PTU cocrystals, the software COSMOquick was used to calculate the excess enthalpy as parameter indicative of cocrystal formation propensity.

Therefore, it was developed a cocrystallization screening strategy in which slow evaporation solution experiments were performed by using a selection of different solvents that comprise a wide range of dielectric constants and functional groups. The solution screening was completed by liquid assisted grinding (LAG) experiments performed in a Retsch MM200 mill at 25 Hz. Six different cocrystal formers were selected as candidates for the cocrystallization screening attending to the excess enthalpy calculation for each of them and three different cocrystals were obtained. PTU-hydroquinone and PTU-

resorcinol cocrystals were obtained from solution experiments and their structure determined by single crystal X-ray diffraction (SCXRD). They were also characterized by powder X-ray diffraction (PXR), differential scanning calorimetry (DSC), and Raman spectroscopy. Single crystals of PTU-phloroglucinol cocrystal were not obtained due to the impossibility to recrystallize the polycrystalline material obtained from grinding experiments. Therefore, PTU-phloroglucinol cocrystal was only characterized by PXR, DSC and Raman spectroscopy. In this work, we have evidenced experimentally the ability of PTU to cocrystallize with hydroxyphenol derivatives, confirming in this way the results obtained from cocrystal propensity calculations.

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