New co-crystals of ketoconazole

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Ketoconazole is an oral antifungal agent with poor water-solubility and an erratic bioavailability which translates into an insufficient therapeutic window. Synthesis of co-crystals or salts is a promising pathway to mitigate this disadvantage, and also appropriate to produce newly species where the molecule of interest is kept intact preserving its pharmacological properties.[1]

There are different methods of synthesis of these multicomponent forms such as solution methods, mechanochemical methods or by using microwave radiation. However, different methods of preparation can lead to different compounds even if starting materials from identical batches are used. The assessment of the stability of a specific binary co-crystal or salt relative to its precursors, therefore, becomes of considerable importance.

In this work are presented three new cocrystals of ketoconazole with dicarboxilic acids as co-formers (**Figure 1**). Firstly, commercial samples purity was evaluated by High Performance Liquid Chromatography techniques coupled to the Mass Spectrometry (HPLC-MS). Then, cocrystallization was made through the different techniques referred above, like mechanochemistry, solution and microwave. The compounds obtained were characterized by X-ray diffraction (single crystal and powder diffraction), differential scanning calorimetry (DSC), thermogravimetry (TGA) and microscopy data (HSM). Crystallization of the new multicomponent forms was done by solvent evaporation.

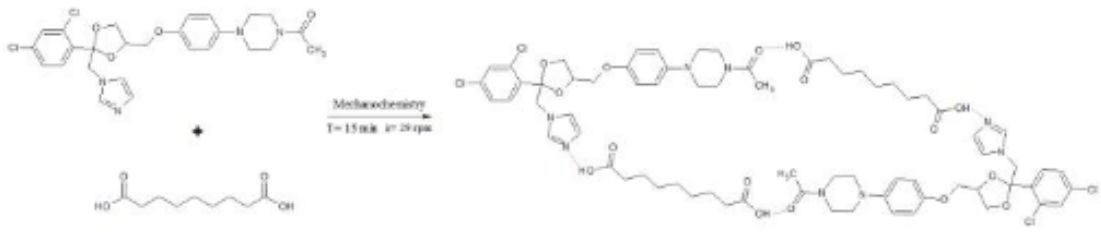

Figure 1: Scheme of the reaction of Ketoconazol with Azelaic Acid obtained by mechanochemistry.

Acknowledgements: This work was supported by Fundação para a Ciência e a Tecnologia (FCT), Portugal through Projects PTDC/QUI-OUT/28401/2017 (LISBOA-01-0145-FEDER-028401), UID/MULTI/00612/2013, and UID/QUI/00100/2013. A grant awarded by FCT to D. Silva (BL81/2019_IST-ID) was acknowledged.

References:

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