Crystallization Studies of Pharmaceutically Active Substance Apremilast

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X-ray crystallography is a widely used technique in pharmacy for drug design, development and, especially, for assignment of drug quality and detection of impurities. While X-ray diffraction pattern allows to distinguish different polymorphic forms, single crystal X-ray analysis is used to characterize molecule packing in a monocrystalline solid. Apremilast (S-enantiomer) is a pharmaceutically active compound applicable to a treatment of certain types of psoriasis and psoriatic arthritis for adult patients. To date, only X-ray crystallographic data of solvated forms of Apremilast monocrystals has been published in the scientific literature, whereas, for rac-Apremilast there is no data at all. The aim of this work was to find the most suitable method and solvent system to obtain both Apremilast and rac-Apremilast monocrystals in a solvent free form. We have succeeded in the growing of solvent free rac-Apremilast monocrystals by using a modified evaporation method with a binary solvent system containing ethanol and acetone in ratio 2:1. Interestingly, selective formation of racemic monocrystals was observed from enantiomerically rich sample (Apremilast, 86% ee) by employing the same method and solvents in various ratios. Without the above, we have obtained two different polymorphic forms of rac-Apremilast during recrystallization of the product after three step synthesis by using different temperature regimes. Observation was proved by difference in melting points and X-ray diffraction patterns of both samples. Based on our experimental results as well as literature, we can conclude that crystallization characteristics of Apremilast and rac-Apremilast differ. As a result, under our crystallization conditions only monocrystals of racemic compound can be obtained.

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