Activity report 2021

Project PD 45/2020

From amorphous to crystalline: in the quest for new pharmaceutical formulation, with improved stability of representative statin drugs (CryStatin)

Result of activity O1. 1.1 (Experimental reports (solubility profile for Pitavastatin))

(1 December 2021-10 December 2021)

Stage summary

In this phase of the project 24 solubility experiments were performed for the compound Pitavastatin, solubility in different solvents/solvent mixtures was estimated. X-ray Diffraction measurements were performed for 11 samples and the X-ray patterns were analysed.

After solubility experiments 12 solvents/solvent mixtures were identified in which Pitavastatin exhibits increased solubility, these solvents/solvent mixtures will be used for the design of co-crystallization experiments that will be performed in the next steps. After analysis of powder X-ray Diffraction data, were identified 3 solvents/solvent mixtures in which Pitavastatin is more crystalline. It was elaborated the project indicator Experimental reports (solubility profile for Pitavastatin) where all experimental data are detailed (Annex 1).

Content of the Scientific and Technical Report (STR)

1. Performance of Solubility Experiments for Pitavastatin
2. Measurements and analysis of X-ray Diffraction data for evaporated and powder samples
3. Results

In phase I of the project (1 December 2021 - 10 December 2021) the solubility profile of the compound Pitavastatin was studied using high-throughput experimental methodology implemented on the Crissy parallel crystallization platform. These experiments consisted in: weighing the starting compound, adding solvents in 2 steps of 1 ml, heating at 60°C for 30 min under stirring, cooling to 15°C, visual estimation of solubility after each step. The suspension samples were left at room temperature to evaporate, the solutions were stored at 4°C for 2 days (to obtain single crystals) and then, placed at room temperature to evaporate. After the experiments, it was found that Pitavastatin is soluble in 12 of the 24 solvents/solvent mixtures used.

The samples obtained as powder were analysed by Powder X-ray Diffraction, the measurements were carried out using Rigaku SmartLab Diffractometer. After comparing the 11 evaporated samples with Pitavastatin starting compound, a higher crystallinity is observed in the samples where the following solvent/mixtures of solvents were used: Pentanonitrile, 2-Methylpentane and Methanol: Water (8:2). The most crystalline sample was obtained in the solvent mixture Methanol : Water (8:2).

The results of the solubility experiments show a total of 12 solvents in which Pitavastatin is soluble and also 3 solvents/solvent mixtures which increase the crystallinity of Pitavastain. Using these three solvents, experiments will be carried out to obtain single crystals in order to determine the crystalline structure by X-ray Diffraction on single crystals.

Results

1. Experimental reports (solubility profile for Pitavastatin) - project indicator (Annex 1)

2. Preparation of the Scientific and Technical Report (STR)

Date	Project director
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