Dissolution and precipitation studies of carbamazepine cocrystals with small scale assays.

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Purpose: To better understand the dissolution properties and precipitation behaviour of carbamazepine cocrystals for the potential for oral administration based on a small scale dissolution assay.

Methods: Carbamazepine cocrystals with saccharin and nicotinamide as coformers were prepared with the sonic slurry method. Dissolution of the poorly soluble drug carbamazepine and the two cocrystals was studied with a small scale dissolution assay installed on a SiriusT3 instrument. Detection and quantitation of carbamazepine was performed by in-situ UV-spectroscopy using a fibre-optic dip-probe. Surface dissolution of a pressed pellet (3mm) was studied in 20mL of dissolution medium with sequential change of pH at four stages (pH1.8, pH3.9, pH5.4, pH7.3). Powder dissolution (2.6 mg) was studied in 2mL of dissolution medium at a constant pH (pH2).

Results: Dissolution profiles from the pellets of the drug and of the cocrystals show that a higher amount of dissolved carbamazepine is observed for the cocrystal samples compared to the carbamazepine sample. The powder dissolution of all samples under constant pH reveals that carbamazepine dissolves much more slowly from the carbamazepine sample than from the cocrystal samples and also provides information regarding the precipitation and kinetic solubility of the samples. A drop in the concentration of carbamazepine from the carbamazepine sample is observed after 1.5h, probably due to the formation of a less soluble carbamazepine polymorph. Precipitation of carbamazepine dissolved from the carbamazepine-saccharin cocrystal takes place earlier than from the carbamazepine sample. Dissolution of the carbamazepine-nicotinamide cocrystal is faster than the carbamazepine-saccharin cocrystal, and the solution becomes heavily turbid as the carbamazepine precipitates from solution.

Conclusion: The small scale dissolution assay provides useful information on the improved dissolution and the precipitation kinetics of carbamazepine from the cocrystal form. The type of coformer has a clear effect on the dissolution/precipitation behaviour of the carbamazepine cocrystals.