MS003.O04

Synergistic enhancement of tabletability and physicochemical properties through cocrystallization

Srinivasulu Aitipamula[1], Parijat Kanaujia[1]
[1]*Crystallization & Particle Sciences, Institute Of Chemical And Engineering Scien, Singapore, Singapore*
E-mail: srinivasulu_aitipamula@ices.a-star.edu.sg

Pharmaceutical cocrystals are defined as molecular complexes comprising an API and one or more pharmaceutically acceptable coformers (FDA-approved GRAS compounds), which are solids at room temperature [1]. Over the past two decades, interest in pharmaceutical cocrystals has increased tremendously in both industry and academia. This is primarily because physicochemical properties such as solubility, dissolution rate, tabletability, stability, etc. could be fine-tuned by choosing an appropriate coformer. However, barring a few bioavailability studies, the majority of the cocrystal research has been mainly focused on crystal engineering based design, preparation, characterization, and scale-up of cocrystals, but studies concerning formulation issues of cocrystals are seldom reported [2].

In a pursuit to discover novel solid forms of APIs, we have reported cocrystals of a number of APIs [3]. Crystal engineering principles have been effectively used to unravel these novel cocrystals. For a cocrystal to be marketable, they need to be converted to formulations. One of the fundamental aspects to be evaluated is the tabletability of the cocrystals. We have recently embarked on this task to understand the formulation issues of cocrystals and present results of our preliminary investigations on tablet formulations of a cocrystal hydrate which involves an antifungal drug, griseofulvin (GF) and an artificial sweetener, acesulfame. In particular, our findings on impact of two different excipients, namely lactose and dibasic calcium phosphate (DCP), on the properties of tablet formulations will be presented. We have previously demonstrated that the cocrystal, in its pure form, shows improved stability and solubility/dissolution rate of the parent GF [3]. In this study, two different prototype formulations of GF, cocrystal and the physical mixture were prepared, keeping all amounts of formulation ingredients constant, except lactose and DCP. Tablets were punched using FT-IR press and evaluated for their hardness, disintegration time, and dissolution rate. The results suggest that the tablets that contain the cocrystal and lactose offer better properties: hardness and disintegration time are much lower than the tablets made with pure GF, physical mixture, and their tablet formulations with DCP. Dissolution studies have revealed that both the cocrystal tablets with lactose and DCP show interesting dissolution profiles: while the cocrystal tablet with lactose showing the fastest initial dissolution, the cocrystal tablet with DCP shows highest supersaturation levels at 3 hrs. Stability of the tablets at accelerated condition (40 °C, 75 % relative humidity) proved satisfactory judging by the absence of dissociation of the cocrystal. Results of our studies dealing with powder flow and compaction properties of the cocrystal and its constituents will also be presented.

The presentation emphasizes the impact of excipients on the tabletability and physicochemical properties of a promising cocrystal which is essential for establishing true potential of cocrystals in drug development.

This work was supported by Science and Engineering Research Council of A*STAR, Singapore.
[1] Aitipamula, S. et al. (2012). Cryst. Growth Des. 12, 2147-2152.
[2] Childs, S. L. et al. (2012). Mol. Pharmaceutics, 10, 3112-3127.
[3] Aitipamula, S. et al. (2012). Cryst. Growth Des. 12, 5858-5863.
Keywords: Cocrystal, tabletability, formulation