Assessment of the stability of co-amorphous olanzapine in tablets

Nuno F. da Costa[1], João F. Pinto[1] and Ana I. Fernandes[2]

[1.] iMed.ULisboa, Faculdade de Farmácia, Universidade de Lisboa, Lisboa, Portugal; [2.] CiiEM − Centro de Investigação Interdisciplinar Egas Moniz, Instituto Universitário Egas Moniz, Monte de Caparica, Portugal.

aifernandes@egasmoniz.edu.pt

Introduction: Amorphous and co-amorphous (CAM) materials have been used in the last years as a strategy to overcome the low bioavailability of the majority (90%) of drugs due to low water solubility and low dissolution rates from solid dosage forms (1,2). Unit operations used to produce oral solid dosage forms impose stress conditions (*e.g.* pressure during tableting) on amorphous systems and can promote the recrystallization of the amorphous drug (3). This work presents new usages of spectroscopic based analytical methods and computational models to quantify the fraction of amorphous olanzapine (OLZ) in a formulation intended to produce immediate release OLZ tablets.

Materials and Methods: Near infrared (NIR) and Fourier-transform infrared (FTIR) spectroscopies were used to quantify the fraction of co-amorphous OLZ (30%) with saccharin (SAC; 18%) in formulations containing also calcium phosphate (27%), microcrystalline cellulose (20%) and povidone (5%). Tablets (250mg) were obtained using a universal testing machine fit with circular punches (7.5mm Ø), at a constant compression rate of 10mm/min (n=5). Different compression forces (8 and 25kN) and dwell times (DT; 0 and 20 min) were considered for the production of tablets. Evaluation of the impact of the compression conditions on the recrystallization of OLZ from a co-amorphous system was based on a computational model.

Results: Using a 2nd derivative filter to process both NIR and FTIR spectra, the quantification of amorphous olanzapine was possible with a root mean square error of calibration and prediction above 2% (Fig. 1). The method was further applied to evaluate the stability of co-amorphous systems after tableting, revealing that no significant recrystallization occurred, *i.e.* the co-amorphous were stable under the stress conditions applied.

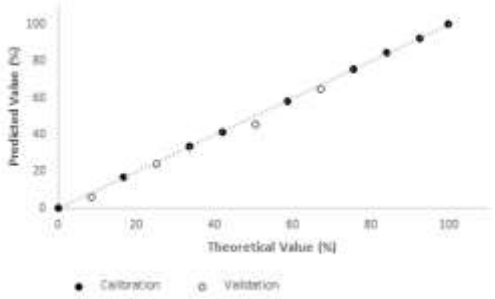

Figure 1- NIR calibration curve used to predict the amorphous fraction of OLZ.

ID	NIR	FTIR
CAM Physical Mixture	100	100
CAM 8kN 0DT	89	98
CAM 8kN 20DT	94	94
CAM 25kN 0DT	95	93
CAM 25kN 20DT	98	95

Table 1- Predicted fraction of amorphous OLZ by NIR and FTIR spectroscopy, in tablets prepared with the co-amorphous system.

Discussion and Conclusions: Using both NIR and FTIR spectroscopy it was possible to develop a methodology to monitor and quantify the conversion of the amorphous OLZ present in blends as a co-amorphous of OLZ:SAC. The models developed have also demonstrated that all tablets obtained were stable, since no recrystallization was observed.

References:

1. Skieneh J, Rohani S. Screening New Solid Forms of Pharmaceuticals to Enhance Solubility and Dissolution Rate. Austin Pharmacol Pharm. 2017;2(1):e1007.
2. Grohganz H, Löbmann K, Priemel P, Tarp Jensen K, Graeser K, Strachan C, et al. Amorphous drugs and dosage forms. J Drug Deliv Sci Technol. 2013;23(4):403–8.
3. Lenz E, Jensen KT, Blaabjerg LI, Knop K, Grohganz H, Löbmann K, et al. Solid-state properties and dissolution behaviour of tablets containing co-amorphous indomethacin-arginine. Eur J Pharm Biopharm. 2015;96:44–52.

Acknowledgements: Fundação para a Ciência e a Tecnologia (PTDC/CTM-BIO/3946/2014 and SFRH/BD/137080/2018) is acknowledged for funding.