COMPARISON OF THE AMORPHIZATION ABILITY OF TWO POLYMORPHIC FORMS OF OLANZAPINE

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INTRODUCTION

The production of amorphous and co-amorphous (CAM) materials has been used as a procedure to overcome the poor water solubility shown by most of the drugs currently under development (1). Ball milling has been considered to convert the crystalline state of a substance into its amorphous counterpart (2,3). At present, the impact of the initial polymorphic form of a drug substance on its final amorphous state upon milling, has not been clearly studied.

This work aims to compare the co-amorphization efficiency of two different polymorphic forms of olanzapine (OLZ; a BCS class II drug) using saccharin (SAC) as a co-former.

MATERIALS AND METHODS

Olanzapine Form I + **Olanzapine Form II** + **Saccharin**

Ball Milling

2.5g of 3.0mm balls

2 hours at 650 rpm

Differential Scanning Calorimetry

X-Ray Powder Diffraction

RESULTS AND DISCUSSION

The thermograms and the diffractograms obtained (Fig. 1 and Fig. 2) have shown a clear difference between the final products of the two polymorphic forms of olanzapine.

X-ray powder diffraction peaks were less intense for the product obtained using olanzapine form II as staring material. Furthermore, the peaks identified were more representative of saccharin, indicating that olanzapine was indeed mostly converted into the amorphous state.

On the other hand, when olanzapine form I was directly in ball milling, a richer diffractogram resulted, suggesting that a crystalline fraction of olanzapine remained in the particles' network of the final product and therefore olanzapine was not completely converted to the amorphous state.

The results were confirmed by differential scanning calorimetry, where it is possible to observe a melting band (T_m=151°C) in the diffraction pattern of the product obtained using the form I of olanzapine, which suggest the presence of a fraction of crystalline material. For the product obtained with form II of olanzapine, the melting band is not observed, which is in good agreement with the results provided by XRPD.

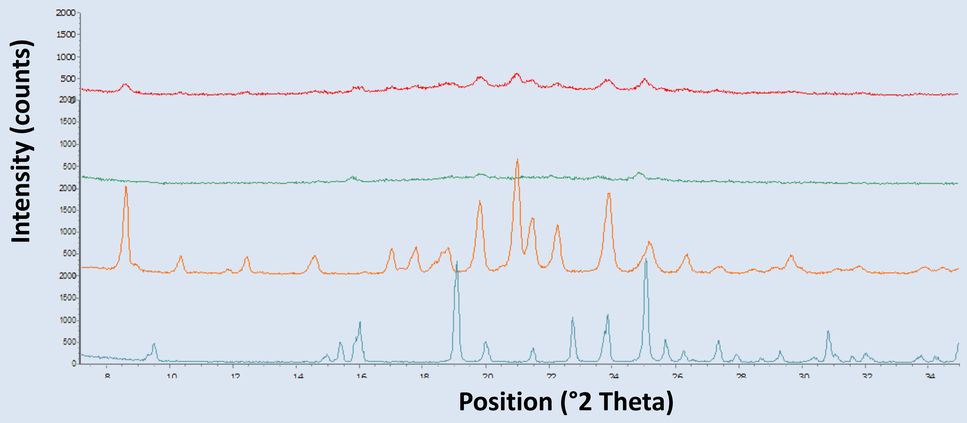

Fig. 1. X-ray powder diffraction of products obtained with olanzapine form I (red line) or form II (green line) and their comparison with the diffractograms of raw materials - olanzapine (orange) and saccharin (blue).

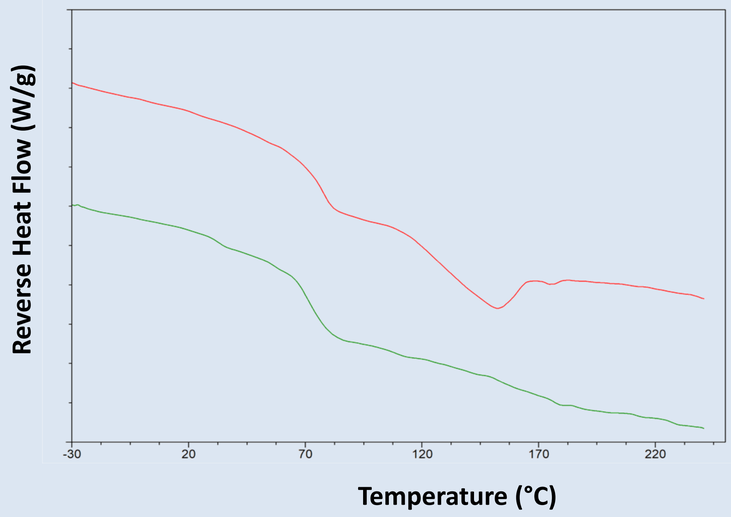

Fig. 2. Differential scanning calorimetry of products obtained with olanzapine form I (red line) or form II (green line).

CONCLUSIONS

The work has shown that the properties of the final products obtained by ball milling are dependent on the thermodynamic energy of the starting materials, in addition to the process parameters extensively studied in previous works.

Since OLZ form II has a higher thermodynamic energy than form I, it is not surprising that the former exhibits better amorphization ability. Thus, it is expected that either an increase on milling time, or milling speed, would enhance the co-amorphization of OLZ form I with SAC.

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