Synthesis and Characterization of Trans-Resveratrol Cocrystals

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The rise of antibiotics resistance is a global health threat in the 21st century, which is partially caused by the overuse of antibiotics in both humans and farm animals. It is estimated that 73% of worldwide antibiotics are used for livestock animals, such as pigs, cows and poultry, with pigs consuming the largest amount of antibiotics [1]. Plant extracts have recently gained traction as a potential functional alternative to antibiotics in livestock production [2]. The active ingredients are comprised of polysaccharides, polyphenols, alkaloids etc. Trans-Resveratrol (3,5,4′-trihydroxy-trans-stilbene) is a natural polyphenol which exhibits a range of useful biological properties, such as antioxidant, anticancer, antiangiogenic, cardioprotective and immunomodulatory activities. However, Resveratrol suffers from limited solubility and chemical stability, which prevents its widespread use.

Solid form modifications can be used to enhance desired properties of active pharmaceutical ingredients. Cocrystals formation represents a promising alternative to other solid form modifications (amorphization, polymorphs, *etc*) since it results in thermodynamically stable, crystalline compounds. Cocrystals exhibit unique physical properties, which can impact key pharmaceutical parameters, including storage stability, compressibility, density as well as dissolution rates and solubility, which are essential factors in achieving suitable bioavailability.

The aim of this study is the investigation of different synthesis pathways to obtaining a 1:1 (mol.) Resveratrol: Piperazine cocrystal, using methods amenable to large scale production. These methods include mechanochemical, ultrasound or microwave assisted synthesis.

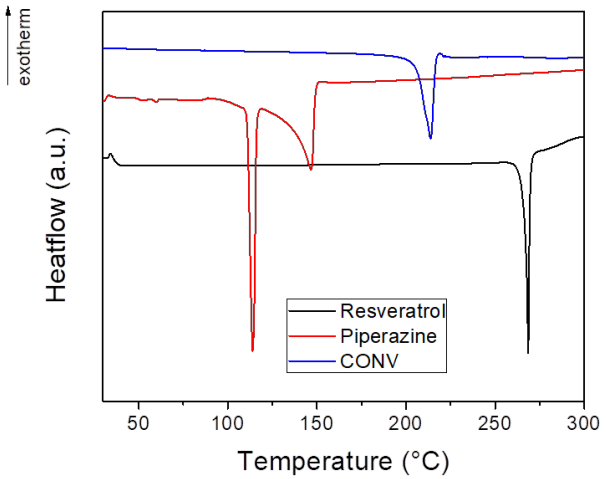

Fig. 1. DSC data of cocrystal and coformers.

Different synthesis conditions (the nature and amount of added solvent, reaction time and temperature) were investigated and their influence on the cocrystal phase and purity were determined, using thermal analysis (Fig. 1), X-ray powder diffraction and infrared spectroscopy methods. The solubility of the cocrystals obtained through different methods was assessed. Ethanol assisted mechanochemical synthesis, as well as microwave and ultrasound assisted methods provided the desired cocrystal phase with high purity and yield.

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References

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