Eutectic mixtures containing nevirapine: phase diagrams, solid-state characterization, and dissolution essays

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In the pharmaceutical area, some drugs exhibit physicochemical properties that adversely affect the formulation processes for bioavailability and effectiveness. Solid-state modifications can be used to improve the performance of the drugs. Studies have shown that among all possible modifications, multicomponent crystals, such as cocrystals and eutectic compositions, have been successfully used to improve the performance of certain drugs, including their solubility. Nevirapine (NVP) is an antiretroviral drug that presents low aqueous solubility, which directly impacts its bioavailability. The objective of this work was to study different nevirapine/coformer solid eutectic systems, define their phase diagrams and evaluate their dissolution properties. Caffeine (CAF) and theophylline (THEO) co-formers were chosen since they exhibit functional groups with possible interaction with NVP. Aiming to determine both temperature and eutectic composition, it was obtained phase and Tamman diagrams by using results of differential scanning calorimetry (DSC) analysis of the mixtures with different compositions (%w/w) of NEV–coformers. Powder X-ray diffraction (PXRD) and DSC were used to characterize the eutectic materials. To evaluate the impact of eutectic systems on dissolution properties, powder dissolution profiles and intrinsic dissolution rates of anhydrous NVP and eutectic systems NVP-CAF and NVP-THEO were determined using different dissolution media (0.1 M HCl, water, pH 1.2 and pH 6.8). Through the phase diagrams, the eutectic compositions were calculated from the interpolation of the curves obtained by linear regression. Thus, the eutectic composition of the NVP-CAF system was determined to be 31.44% of NVP and melting at 203.4 ºC, while in the NVP-THEO system, the eutectic was obtained in a composition of 70.15% NVP and melting 223.5 ºC. Tamman diagrams were generated from enthalpy values of the DSC curves obtained and the eutectic compositions were calculated again by using interpolation of the curves and linear regression. In this analysis, a eutectic composition of 29.13% of NVP was calculated for NVP-CAF, while a eutectic composition of 70.18% of NVP was calculated for NVP-THEO system. A comparative study between dissolution profiles and intrinsic dissolution rates in different dissolution medium demonstrated that there was a significant improvement in the NVP dissolution rate in both eutectic systems. NVP dissolved 16 times faster in the NVP-CAF sample, and 4 times faster in the NVP-THEO sample bout in an acid medium, compared to pure anhydrous NVP. In neutral medium, the dissolution profile of NVP was even more favorable in the same eutectic systems, showing that in a wide range of pH, the increase in dissolution is relevant. In addition, the intrinsic dissolution rate in the two eutectic systems was higher than that of anhydrous NVP in all dissolution medium used. The verification that these eutectic systems improve the dissolution kinetics behavior of these materials compared to pure NVP, opening an interesting perspective for future innovations and new medicines.