

Synthesis, thermoanalytical and spectroscopic study of norfloxacin-caffeine cocrystal

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Abstract

Norfloxacin-Caffeine cocrystal were synthesized by the technique of grinding-assisted solvent. Thermoanalytical and spectroscopic techniques were used to evaluate the synthesis and characterization of these compounds.

Introduction

A cocrystal is a multiple component crystal in which all components are solid under ambient conditions when in their pure form. These components co-exist in a stoichiometric ratio of a target molecule or ion and neutral molecule forming molecular cocrystal [1]. Increasingly cocrystals technology is becoming attractive to the pharmaceutical industry, especially in recent years, since these cocrystals can improve the physical and chemical properties of the active pharmaceutical compounds (API) [2]. The aim of this study was to obtain the cocrystal of norfloxacin antibiotic (fluoroquinolone), a drug that has a low solubility in water, with the cofomer caffeine, in order to improve its physical and chemical properties and perform spectroscopic and thermal characterization.

Results and discussion

The TG-DTA and DSC curves are shown in Fig. 1.

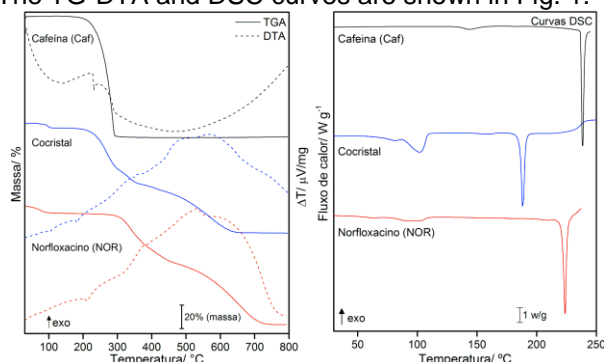


Figure 1. TG-DTA and DSC curves of the norfloxacin, cocrystal (API) and caffeine (coformer).

These curves show significant changes in thermal behavior of the blend as compared to the pure components (NOR and CAF). TG-DTA curves show that the thermal stability of the co-crystal was similar to that of caffeine and smaller than the antibiotic. Furthermore, the profile of thermal decomposition of the cocrystal have specific characteristics, as a greater number of mass loss steps and final

decomposition temperature (T_f) intermediate between the norfloxacin and the caffeine.

The DSC curve shows that the melting peak of the mixture occurs at lower temperature than the other pure components, suggesting weaker intermolecular interactions in the solid state.

Infrared spectra are shown in Fig. 2. These spectra suggest that there are different intermolecular interactions in the mixture (NOR-Caf) compared to pure constituents, since the profile bands above 2500 cm^{-1} are different, the band in 1728 cm^{-1} (NOR) is not observed or is overlying and some other bands located at smaller wavelengths are slightly displaced in the cocrystal.

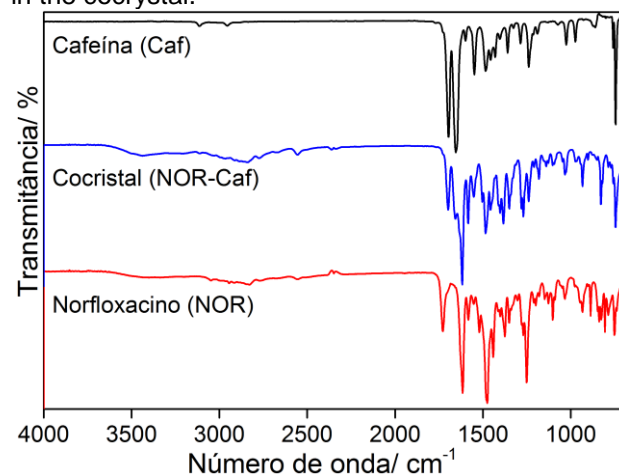


Figure 2. Infrared spectra of the components and blending.

Conclusion

The thermoanalytical and spectroscopic data suggest that NOR-Caf mixture is a cocrystal with molar ratio of 1:1 (NOR:CAF), since different thermal and spectroscopic properties were observed in the mixture (cocrystal).

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¹ Shan, N. e Zaworotko, M. J. Drug Discov Today 2008, 13, 440.

² Yamashita, H.; Hirakura, Y.; Yuda, M.; Teramura, T.; Terada, K. Pharm Res 2013, 30, 80.