Solid state properties of drugs for neglected diseases

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Introduction

In this work, the relevance of the knowledge of the physicochemical properties of the solids forms of active ingredients is discussed. As a case of study, the medicines applied in the treatment of filariasis and malaria are considered. Being classified as Neglected Diseases, these illness are endemic in South America and are the target of several public health programs. Thus, the success of such programs are highly correlated to the quality medicines.

Results and Discussion

One of the most relevant piece of information to provide an accurate description of the solids forms of an active ingredient are the corresponding crystalline structures. Thus, the knowledge of the molecular conformation and the intermolecular interaction cloud allow the understanding of several physicochemical properties. Let's take as first example diethylcarbamazine (DEC), the drug of choice for the treatment of filariasis, which is a parasitic and infectious tropical disease. Due to its low melting point (49 °C), DEC is usually formulated as a citrate, in which form the melting point increases up to 143 °C (Figure 1). As a pure base, DEC is bonded by very weak hydrogen bonds, but as a salt, critrate ions form a strongly bonded network in whose interstices DEC molecules are also strongly bonded. Thus, the new hydrogen bonds pattern is the key factor in the improving in the thermal stability of DEC.

However, not always is possible to determine the crystalline structure, or routine techniques are needed. Let's consider the artesunate-mefloquine hydrochloride (ASMQ) fixed-dose combination product developed by DNDi and Farmanguinhos treatment of malaria. In figure 2, the infrared spectra

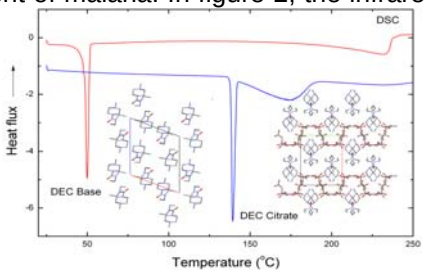

Figure 1. DSC thermograms and crystalline structures of DEC

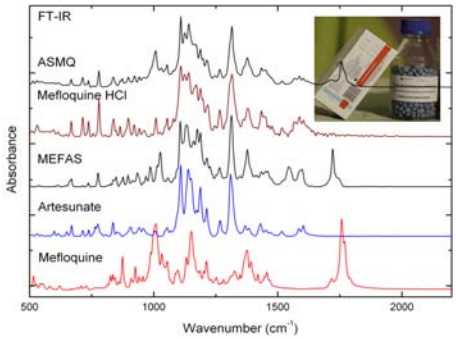

Figure 2. Infrared spectra of the tablets and individual components of ASMQ.

of tablets of this medicine and the individual components, providing a powerful tool for quality control. On the other hand, a new approach was proposed by combining mefloquine and artesunate in salt (MEFAS). The effect of the intermolecular interactions may be easily identified by comparing the infrared spectra of ASMQ and MEFAS. Furthermore, new physicochemical properties are observed, like an anomalous exothermic signal in the DSC thermogram, associated to a recrystallization process evidenced in the thermomicroscopy images (Figure 3).

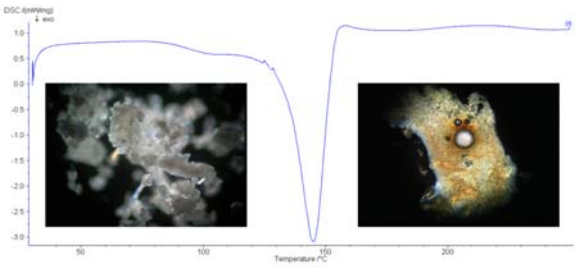

Figure 3. DSC thermogram of MEFAS

Conclusions

Physicochemical properties of are determinant factor to guarantee the quality of safety of solid formulations. The understanding of these properties are may provide alternative pathways for improving the efficacy of old and under development drugs.

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