Influence of the Pseudo-polimorphism in the Solid State Properties: diethylcarbamazine, an anti-filariasis drug.

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Introdução

Filariasis is an endemic disease caused by *spirunid nematodes*. It is prevalent in tropical regions of Asia, Africa, Central and South America, with 200 million of people infected worldwide. The most common type of filariasis is the lymphatic filariasis (LF), essentially caused by two thread-like parasitic filarial worms, *Wuchereria bancrofti* and *Brugia malayi*, both transmitted by mosquitoes bites[1]. The World Health Organization considers filariasis as one of the six potentially eradicable diseases[2]. In this way, the Global Programme for the Elimination of Lymphatic Filariasis aims to eliminate LF through time-limited mass drug administration programmes. The administration of diethylcarbamazine (*N,N*-Diethyl-4-methyl-1-piperazinecarboxamide, DEC), is used in the programme as the main strategy to eliminate LF[3]. Despite of its pharmaceutical importance no structural characterization of diethylcarbamazine has been published yet. In this paper we report a solid state analyze of the diethylcarbamazine and its citrate.

Resultados e Discussão

citrate (DEC-c). determined at room temperature (293K) (see Figure 1), crystallizes in the monoclinic space group $P2_1/c$, with an adopted chair conformation in the heterocyclic ring of the DEC molecule. The crystal packing is stabilized by the presence of one strong O-H…O intermolecular interaction between the DEC molecule and the citrate (O-O distance = 2.861(5) Å), and by two N-H…O Hydrogen bonds (N-O distance = 2.933 (5) Å and 2.797 (5) Å, respectively). The crystal interaction of DEC citrate forms intercalated layers of these two molecules in the packing, along *a*.

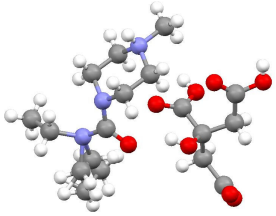

Figure 1. Asymmetric unit of Diethylcarbamazine citrate molecule.

The low temperature study of DEC-c, performed at 150K, show the presence of a phase transition and a slight, but notable, increase in the magnitude of the unit cell parameters, leading to changes in the structure of the DEC molecule, specially in the $O{=}CNC_2C_2$ group.).

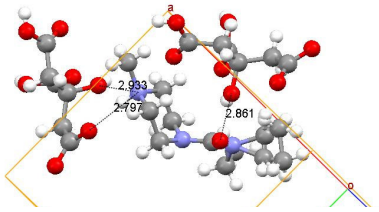

Figure 2. Hydrogen-bonds of the DEC citrate.

It is also interesting to notice that the lack of the intermolecular interactions lead to a very poor stability of the solid state form of the pure dietylcarbamazine compound (DEC). In this way the x-ray collection was performed just at 150K. Again the compound crystallize in a monoclinic space group. Nevertheless the DEC molecule suffers a very important conformational change .

Conclusões

It was noticed that the intermolecular packing of DEC is stabilized by the existence of hydrogen-bonds among the NH group and the two O of the citrate. These hydrogen bonds are also important in the solid state stability of the drug.

Agradecimentos

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