

Study in the Solid State, Framework Energy and Crystal Structure by X-Ray Diffraction Techniques of Cetirizine and Levocetirizine Dihydrochloride Used as an Antihistamines

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Cetirizine dihydrochloride and levocetirizine are antihistamines of second-generation that block histamine receptors H₁, are widely used to treat allergic symptoms. These compounds belong to the class of antihistamines piperazine type and like other second-generation antihistamines, are considered non-sedating [1]. The crystal structure of cetirizine dihydrochloride has been solved and refined using X-ray powder diffraction data and optimized using Density Functional Theory (DFT) techniques. The cetirizine dihydrochloride Fig. 1, crystallized in a monoclinic system and space group P2₁/n (N^o 14) with parameters $a=13,6663(3)$ Å, $b=7,0978(7)$ Å, $c=23,8311(1)$ Å, $\beta=102,488(3)^\circ$, $V=2251,06$ Å³ and $Z=4$. On the other hand, the levocetirizine dihydrochloride Fig. 1, crystallized in a monoclinic system and space group P2₁ (N^o 4) with parameters $a=13,5450(7)$ Å, $b=7,0719(9)$ Å, $c=24,0527(2)$ Å, $\beta=98,159(3)^\circ$, $V=2280,65$ Å³ and $Z=2$. In both crystalline structures there are multiple hydrogen bonds intra and inter molecular, π -interactions and hydrogen- π interactions. The molecular packing and crystal energy are dominated by Van der Waals attractions according to Hirshfeld surfaces. Finally, the crystal structure was optimized with DFT and all non-H bond distances and angles were subjected to restraints, based on a Mercury Mogul Geometry Check of each molecule.

A search in the *Cambridge Structural Database* (CSD) [2] confirmed the absence of reports for the crystal structure of cetirizine dihydrochloride and levocetirizine. However, there are several reports of cetirizine dihydrochloride and levocetirizine in the *PDF-4/Organics* database [3] contains four entries PDF 00-058-1973, 00-058-1974 and 00-058-1975, corresponding to unindexed patterns about cetirizine dihydrochloride, dextrocetirizine dihydrochloride and levocetirizine dihydrochloride, respectively; PDF 00-066-1627 corresponding an experimental pattern for cetirizine dihydrochloride, according to this report, it crystallizes in a monoclinic cell with parameters $a=24.1256(7)$ Å, $b=7.07588(7)$ Å, $c=13.5196(4)$ Å $\beta=98.0028(28)^\circ$ and $V=2285.45$ Å³ in space group P2₁/n (N^o14).

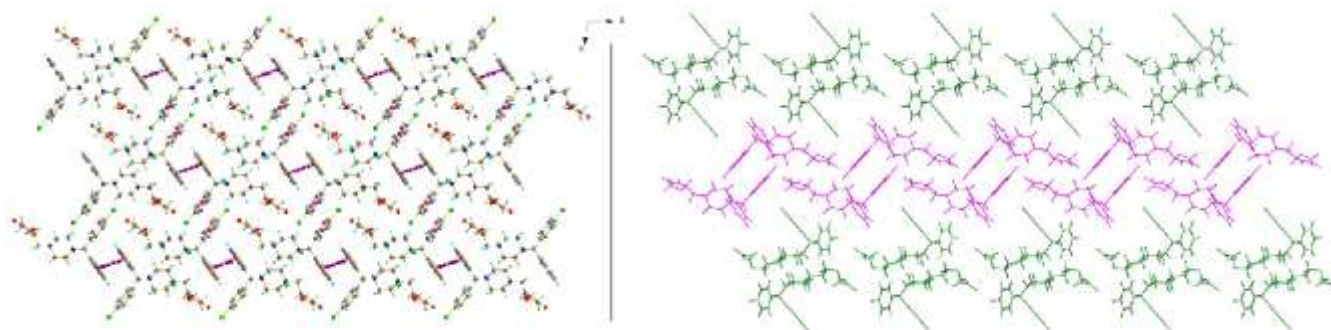


Figure 1. Cetirizine dihydrochloride crystal structure show π -interactions (left); Levocetirizine dihydrochloride crystal structure with two independent crystallographic molecules (right).

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[3] ICDD, PDF-4/Organics 2020 (database), edited by S. Kabekkodu, *International Centre for Diffraction Data*, Newtown Square, PA, USA.

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