

## THERMAL BEHAVIOUR OF AZITHROMYCIN MONOHYDRATE AND DIHYDRATE FORMS

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The *azalide* azithromycin, a half-synthetic macrolide from erythromycin A, and with higher antibiotic effect over erythromycin, can be crystallized in several solvents, giving rise to a large number of *pseudopolymorphs* (different solvates of the same chemical compound, azithromycin in our case), many of which are grouped into isostructural families, generally hosting water molecules in the crystallographic unit cell.

In the present work, we have analyzed the structural behaviour of two pseudopolymorphs of the azithromycin when they lose the solvent molecules under moderate heating. The studied crystals are the DiHydrate<sup>1</sup> (is the product actually marketed) and the MonoHydrate called *stable*<sup>2</sup> (referred to its hygroscopic character), containing one water molecule and one molecule of ethanol by molecule of azithromycin.

To study the transformations and the overall behaviour of the crystal when loss of solvent occurs, the samples were analyzed using DSC, thermogravimetric analysis and X-ray powder diffraction (within the relevant temperature range).

To probe the possibility of quantifying the amount of loose water in the dehydrate crystal by using only the information of the X-ray powder diffraction pattern, experimental patterns were obtained at different temperatures and compared with the theoretical patterns. The calculated diagrams were made up using different percentages of water in the crystal. The theoretical pattern calculations were made with the PoWdErCeLL program<sup>3</sup>. The results show the different behaviour of both hydrates, maintaining the crystal structure as the solvent loss occurs.

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