Ab-initio Structure Determination of two Kinds of Forma for Adrenal Cortical Hormone, Predonisolone

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Predonisolone is a very well known adrenal cortical hormone. It has been used as medicine almost for 40 years. Predonisolone has two different crystal forms and both of them are used as drug substances. At that time when Pledonisolone was approved, it was not thought that detailed crystal structure or polymorphism is so critical for medical use. But recently it has been recognized that crystal structure or polymorphism is very important for effectiveness and patents as drugs.

It is very important to know crystal structures from powder X-ray diffraction patterns because drug substances themselves are powder state in the production process. In this study, we show ab initio structure determination of two different crystal forms of Pledonisolone.

X-ray powder data are collected at BL02B2, SPring-8 in order to have better resolution. A program for ab-initio structure determination is developed based on genetic algorithm. It is found that one of polymorphism is monoclinic and the other is orthorhombic. After determining crystal structure, both of structures are refined by Rietveld method. R factor based on Bragg integrated intensities reached 4.78% for monoclinic form and 5.06% for orthorhombic form, respectively. These small factors guarantee that both of crystal forms of Predonisolone are determined successfully. There are two and four molecules in a unit cell for monoclinic and orthorhombic crystals, which are very consistent with cell volume.

Keywords: predonisolone, ab-initio structure determination, genetic algorythm