Poster Presentation

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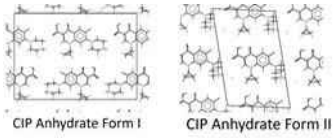
Dehydration mechanism of Ciprofloxacin Hydrochloride hydrate crystal

O. Putra[1], R. Toyoshima[1], S. Ibrahim[2], H. Uekusa[1]

[1]Tokyo Institute of Technology, Department of Chemistry and Materials Science, O-okayama, Meguro-ku, Tokyo, Japan, [2]Bandung Institute of Technology, School of Pharmacy, Pharmaceutical Chemistry Research Group, Bandung, Indonesia

Active pharmaceutical ingredients (APIs) often exist in different crystalline forms such as hydrate and polymorph, which show different pharmaceutically important physicochemical properties such as crystal color, solubility, stability, dissolution rate and bioavailability. Moreover, crystalline phase transformation is induced by environmental changes such as heating and humidity. Thus, mechanistic investigation based on crystal structures is essential. Ciprofloxacin Hydrochloride (CIP) is fluoroquinolone antimicrobials with potent activity against a broad spectrum of bacteria. From TG/DTA and XRD-DSC measurement, the sesqui-hydrate form dehydrates to anhydrate form I at 140 ºC and then transforms to another anhydrate form II at 172 ºC. The single crystals of sesqui-hydrate form and anhydrous II were obtained by recrystallization from water and methanol, respectively. However, anhydrate I could not be obtained as single crystal, so the powder crystal form was accomplished by dehydration of hydrate form at 140 ºC at vacuum heating condition, and the crystal structure was analyzed by ab-initio powder crystal structure analysis technique using synchrotron X-ray diffraction data. The crystal structure of anhydrous form I was partly related to the hydrate in the packing, i.e., both show one-dimensional chain and two-dimensional sheet structure. However, in anhydrous II, only one-dimensional chain structure was retained. Interestingly, the colors of powder crystal of hydrate and anhydrate I were white, meanwhile, anhydrate II appeared as yellow crystalline powder. The color changes may be explained from their molecular conformation . The torsion angle between flouroquinolone and piperazine of hydrate, anhydrate form I (white) and anhydrate form II (yellow) was 145.71º, 136.28º and 108.65º, respectively. Thus, the large difference in anhydrate II might affect the conjugation in aromatic group slightly and resulted in the color change.



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