

26G-ISMS17 **Atomic-Scale Investigation on Acetaminophen Crystals with Stable and Metastable Phases by Frequency Modulation Atomic Force Microscopy in Aqueous Solution**

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Selective crystallization methods of metastable phase of medicinal organic compounds have been being developed to improve bioavailability in pharmaceutical application. These crystals are often grown from liquid phase. Therefore, it is quite useful for acceleration of the development to understand atomic-scale processes at crystal-solution interfaces.

Frequency modulation atomic force microscopy (FM-AFM) is a powerful tool that can image surface structures with atomic resolution in liquid. FM-AFM has recently enabled us to visualize water molecules localized at solid-liquid interfaces by measuring 3D force distribution. The water distribution is called as hydration structure, which plays important roles in crystal growth. We have been investigating atomic-scale surface processes of acetaminophen (paracetamol) crystals with stable (Form I, monoclinic) and metastable (Form II, orthorhombic) phases by home-built atomic-resolution FM-AFM.

We succeeded in obtaining atomic resolution images of Form I and II by imaging during their dissolution in nearly-saturated solutions. This is the first demonstration of atomic resolution imaging of soluble meta- stable crystal. We also revealed subnanoscale hydration structures formed on the surfaces of Form I and II.