Variable humidity measurement of a drug substance using XRD-DSC and a humidity controller

Introduction

Some of the compounds that make up pharmaceuticals take water into the crystal structure and change to hydrates with humidification. There is a correlation between crystal structure and physical properties, so it is important to understand the phase transition behavior due to changes in humidity when controlling the quality of hydrates. By measuring the XRD of a crystal powder while humidifying, the structural changes associated with humidification can be examined. Here, we investigated the hydration behavior of a pharmaceutical drug substance using simultaneous XRD-DSC and a humidity controller.

Measurements and results

The antiallergic drug nedocromil sodium (NS) is known to exist in amorphous, anhydride, monohydrate and trihydrate forms. Figure 1 shows the results of XRD-DSC measurement of NS monohydrate using a humidity controller. The humidity of N2 gas was controlled from 27 °C, 5 %RH to 27 °C, 90 %RH at 20 %RH intervals using dedicated software. X-ray diffraction measurements were performed at 40 kV-50 mA at 10 °/min. The monohydrate changed to trihydrate with exotherm at 27 °C, 20 %RH. After that, even if the steam partial pressure was reduced, the trihydrate did not return to the original monohydrate within this time. By combining the XRD-DSC system with a humidity controller, variable humidity measurement at constant temperature and variable temperature measurement at constant humidity can be realized. As a result, hydration and structural changes due to humidity can be observed in situ.

Samples provided by: Dr. Katsuhide Terada, Toho University.

Recommended equipment and software

- Automated multipurpose X-ray diffractometer SmartLab + X-ray DSC + Humidity generator HUM-SL
- Integrated X-ray analysis software SmartLab Studio II (XRD-DSC plugin)

Fig. 1: XRD-DSC simultaneous measurement results of NS monohydrate using a humidity controller
XRD profile map (left), XRD profile (middle) and DSC chart (right)