

Identification of the crystal form of the active pharmaceutical ingredient in a tablet

—Non-destructive/transmission measurement using a convergent optical system—

Introduction

Many active pharmaceutical ingredients have multiple crystal forms, and it is known that solubility and bioavailability vary depending on the crystal form. In the drug manufacturing process, active ingredients may sometimes undergo a crystalline phase transition to another crystal form, due to factors such as heat, light, humidity or pressure, and there is a need to check what crystal form the ingredient is in, in its final product state. With optical systems employing the Bragg-Brentano focusing method, of the type generally used with powder X-ray diffractometry, measurement of the powdered sample is done with a reflection arrangement, but if a tablet is crushed into a powdered state, there are worries that transitions will occur due to the crushing, and it will be impossible to evaluate the original crystal form. In addition, if measurement is done with a reflection arrangement without crushing the tablet, it may be impossible to obtain internal information. Therefore, we analyzed a tablet non-destructively by using a convergent optical system enabling non-destructive/transmission measurement of tablets.

Measurements and results

The bronchodilator theophylline is known to have a monohydrate and anhydride as pseudo-polymorphs. Fig. 1 shows a comparison of the X-ray diffraction patterns of theophylline monohydrate powder (reference sample, bottom, black), theophylline anhydride powder (middle, blue), and the Theo-Dur tablet which is the tested sample (top, red). Due to matching at the peak angles indicated by the blue circles, it is evident that the tablet contains theophylline anhydride.

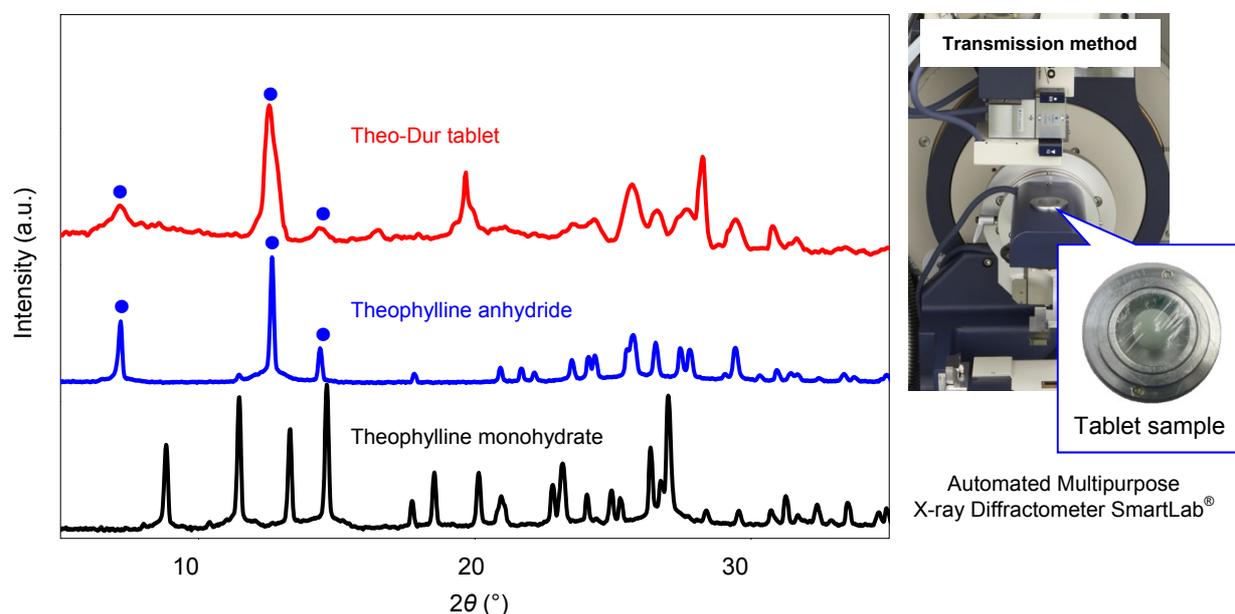


Fig. 1: Comparison of X-ray diffraction patterns of theophylline monohydrate powder, theophylline anhydride powder, and a Theo-Dur tablet

Recommended equipment and software

- ▶ Automated Multipurpose X-ray Diffractometer SmartLab® + Ellipsoidal multilayer X-ray mirror (CBO-E)
- ▶ Automatic 6 position sample changer with spinner ASC-6
- ▶ High-speed 1D detector D/teX Ultra