

**CHARACTERIZATION OF THE PHYSICAL FORM OF THE ACTIVE
PHARMACEUTICAL INGREDIENT IN INTACT FILM-COATED TABLETS
BY X-RAY POWDER DIFFRACTOMETRY**

Hiroyuki Yamada^{1,2}, Raj Suryanarayanan¹

¹Department of Pharmaceutics, University of Minnesota, Minneapolis, MN

²Mitsubishi Pharma Co., Kamisu, Japan.

Purpose. Characterize the physical form and estimate the content of the active pharmaceutical ingredient (API) in intact film-coated tablet by XRD.

Methods. Physical mixtures of each physical form of the API and placebo were used for baseline characterization. The film-coated tablets, which contained between 4 and 15% w/w API, were directly exposed to CuK α radiation in a microdiffractometer equipped with a 2-dimensional area detector. In this instrument, the microbeam can be focused on a small area of the convex surface of the intact tablets.

Results. Three anhydrous polymorphs (Forms I, II and III) and a hemihydrate (Form IV) of the API were obtained. The four forms were readily distinguished by their unique XRD patterns. In physical mixtures of each form with placebo, in spite of the presence of crystalline excipients, the API could be readily identified. Form C, used in the commercial formulation, exhibited unique peaks at 17.8° 2 θ . In the case of intact film-coated tablet, the coating material exhibited diffraction peaks, but these did not interfere with the characteristic peaks of API. In commercial formulations, the API content ranged from 5 to 20 mg per tablet. There was a directly correlation between the integrated intensity of the characteristic peaks of the API and the labeled drug content in the tablets.

Conclusion. The microdiffractometric method allowed the identification of the physical form of the API in intact film-coated tablets. Based on the intensity of the diffracted peaks, it was also possible to estimate the drug content. Since the technique is nondestructive, the same tablet can be repeatedly analyzed during conventional or accelerated stability studies.