ESTIMATION OF GRAIN SIZE IN PHARMACEUTICAL TABLETS BY TWO-DIMENSIONAL X-RAY DIFFRACTOMETRY.

Naveen K. Thakral[1,3] Seema Thakral[1,2] Raj Suryanarayanan[1]*

1. Department of Pharmaceutics, University of Minnesota, Minneapolis, Minnesota USA

2. Characterization Facility, University of Minnesota, Minneapolis, Minnesota USA

3. Presently at Upsher Smith Lab LLC, Minneapolis, Minnesota USA

Purpose: Particle size of the active pharmaceutical ingredient (API) is critical quality attribute as it can affect dissolution profile of a generic drug formulation in comparison to reference listed drug. It can influence the physicochemical, and more importantly, the biopharmaceutical properties of the solid dosage form. Though there are numerous methods for determining the particle size distribution of the 'as is' API, similar analyses in the final solid dosage form continues to be a challenge. Our objectives were to: (i) validate the method, based on γ-profile integration of Debye rings, for determining the average grain size in powders and tablets[1,2], and (ii) use the method to estimate the API grain size in a number of acetaminophen marketed tablets.

Method: Lactose monohydrate was used as the "in-house" standard and was used to set the instrument calibration factor. Two-dimensional XRD frames of samples were recorded using a 200 μm collimator (Microdiffractometer, Bruker). The γ-integration for various characteristic Debye rings in each frame was used to estimate the average grain size. Using sucrose as the model analyte, the method was validated for powders of known particle size distribution and their corresponding compacts. The technique was also used to estimate average grain size of acetaminophen in a number of marketed formulations.

Result: In the range of ~25 to 150 μm, sucrose grain size determined in the powder samples was in good agreement with the results from sieve analysis. For tablets, the effect of compression appeared to be highly dependent on the initial particle size. The average grain size of acetaminophen in the marketed formulations was either ~35 μm or ~80 μm. This type of information can be of immense value during pharmaceutical dosage form design and facilitate rational selection of the particle size of the formulation components.

Conclusion: The average grain size in powders and in intact tablets could be determined from the γ-profile integration of Debye rings.

References

1. He, B.B. Two-dimensional X-ray Diffraction, Wiley, 2009.

2. Bramble M.S., Flemming R.L., McCausland P.J.A., 45th Lunar and Planetary Science Conference 2014, 1658.