

Analysis of Pharmaceutical Powder Compaction and Active Pharmaceutical Gradient (API) Using Laboratory Small and Wide Angle X-Ray Scattering (SWAXS) Combined with Differential Scanning Calorimetry (DSC)

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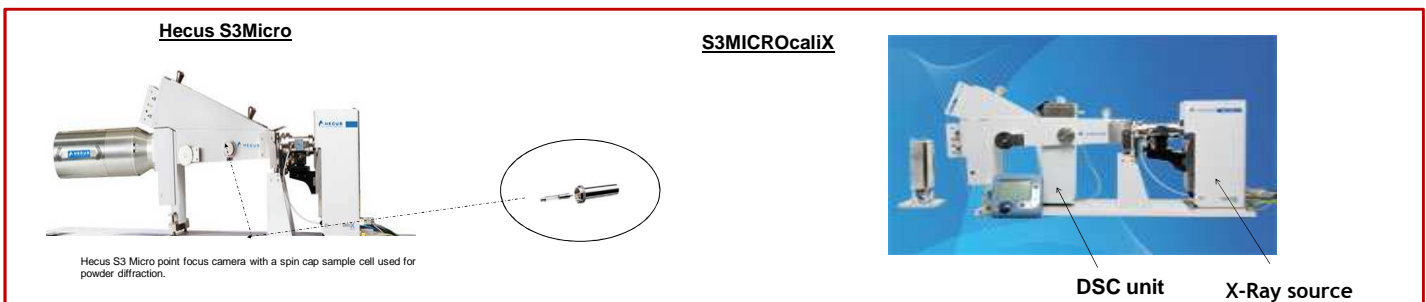
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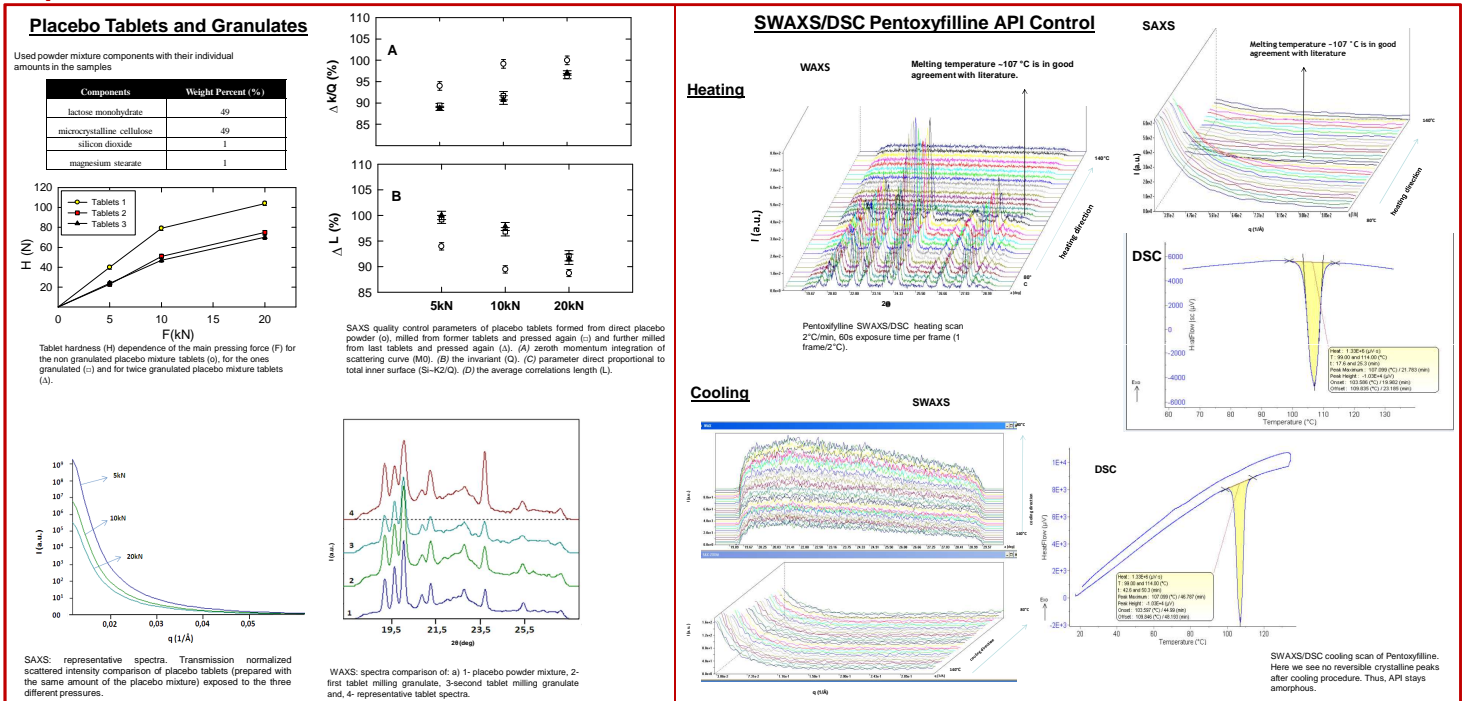
Introduction

First, we investigated the compaction behavior of the most typical pharmaceutical excipients mixture (placebo) containing lactose monohydrate (LM), microcrystalline cellulose (MCC), silicium dioxide (SiO₂) and magnesium stearate (MgSt) using combined small- and wide-angle X-ray scattering (SWAXS). In general, this method is becoming an increasingly important technique in pharmaceutical solid-state characterization^{1,2}. Issues, such as polymorphism in crystalline materials, stability and nanostructure of amorphous states, total inner surface in controlled-release formulations, stability and ageing formulations can be addressed using this technique. The information obtained using SAXS greatly expands the scope of conventional powder diffraction techniques. Particular advantageous is the simultaneous observation of nano scale (SAXS) and atomic scale (WAXS). Further method development is a direct coupling with differential scanning calorimetry (DSC). With the introduction of high-brilliance laboratory SWAXS systems (Hecus S3MICROpix and S3MICROcaliX) the analysis time has been greatly reduced, and hence the method can be applied to quality screening and process analytical technology (PAT). Furthermore, examples will be presented for technologically relevant systems, such as polymorphic forms of active ingredient pentoxifylline, compactness of granulate and amorphous formulations of their components. The results show that an analysis of robust SAXS parameters, such as total inner surface, scattering power intensity and average correlations length, can provide valuable information regarding granulate compactness and dissolution behavior in correlation with tablets hardness. Moreover, SWAXS/DSC analysis provides additional data concerning API thermal property and purity control.

Method and Instrumentation



Experiments and Results



Conclusion

The small-angle X-ray scattering (SAXS) results show a clear connection between the tablet's hardness and robust parameters, such as inner surface, total absolute scattering power, Porod exponent and correlations length. Better tablet compressibility correlates with lower tablet hardness due to a higher correlations length, lower total inner surface and lower true contact area. Thus, the method presents a potential tool for forecasting the tablets' compactness behavior using the SAXS analysis of corresponding output granulates. Simultaneously, wide-angle X-ray scattering (WAXS) does not affect the polymorphic state due to observed "fingerprints" of the material. Furthermore, a SWAXS/DSC coupling makes the analysis of nanostructural and calorimetric effects, phase transitions, reactions in solid powder possible in the course of a single experiment. Hence, it represents a good method for API quality and purity control.

References

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