ALL YOU NEED IS TWO TABLETS - HOW AXIAL RECOVERY IS THE KEY TO A PRECISE OUT-OF-DIE TABLET DENSITY PREDICTION

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Tablet density as a function of compaction pressure is valuable information during the development of a tablet formulation. However, getting a full out-of-die density profile is labour intensive and requires at least a few grams of material. During early development, material sparing methods are advantageous since even a few grams of active ingredients might not be available. This work introduces an easy to adopt method to predict an accurate full out-of-die density profile based on two tablets.

Two key observations that enable the prediction are: 1) in- die axial elastic recovery increases linearly with increasing compaction pressure and 2) the axial elastic recovery after ejection of a tablet is independent of compaction pressure (Figure 1A). Two tablets compacted at low and high pressures, respectively, are needed to establish the linear relationship and to identify the out of die elastic recovery. The two observations were confirmed using compaction data of 47 model powders collected in two laboratories using two different compaction simulators by four operators. These powders exhibit a wide range of compositions (common tablet excipients, binary mixtures, placebo formulations, and active tablet formulations) and mechanical properties (plastic, viscoelastic, and brittle). Based on these and by taking into consideration of the radial recovery, a full out-of-die density profile could be predicted. The predicted density profile is further corrected using the measured density of the two tablets to attain nearly perfect match between the predicted and experimental tablet density - pressure profiles (Figure 1B). The good accuracy of the predicted density profile makes it possible to predict the true density of a material and obtain a plasticity parameter by model fitting [1].

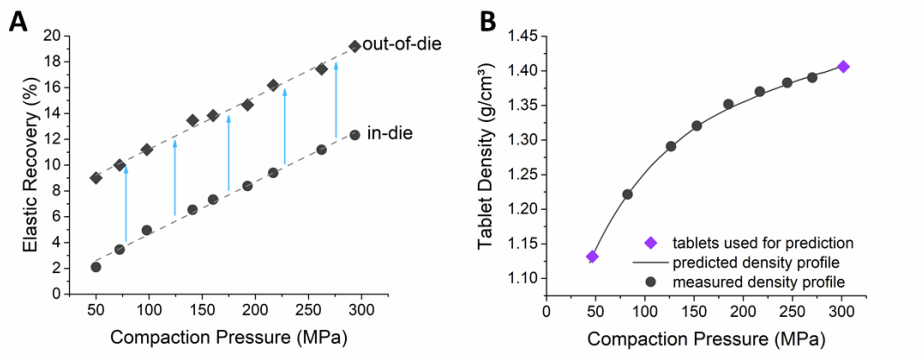

Figure 1. Example of lactose monohydrate A. axial elastic recovery in-die and out-of-die showing the compaction pressure independence of out-of-die elastic recovery. B. predicted versus measured density profile

[1] Sun CC. A novel method for deriving true density of pharmaceutical solids including hydrates and water-containing powders. J Pharm Sci. 2004; 93: 646–53.