34c Enhancing the Physical Stability of Tablets through Moisture Control across the Pharmaceutical Process

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Background: Crushing strength or hardness is a key attribute of pharmaceutical tablets. Ideally, formulations are designed to yield robust compressed tablets that retain their strength upon storage at elevated temperature and humidity. However, this is not always the case, and post manufacturing changes to tablet hardness are a concern as they can lead to product performance issues or consumer complaints. In this study, the ability of tablets to retain mechanical strength on storage was characterized as a function of equilibrium moisture content during processing steps leading up to and during storage immediately following tablet compression.

Experimental: A typical formulation comprised of microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, and a polymeric binder was granulated with water in a high shear mixer. The water was removed via fluid bed drying with the resulting dried granules milled, lubricated and compressed into tablets. This process train presents essentially one opportunity – fluid bed drying – to control the formulation's moisture content as mass transfer limitations across the bulk-stored material after the drying step minimize moisture control capabilities.

Results and Discussion: While granulation dried to low moisture levels (5-15% RH) yielded harder compressed tablets initially, once stored at elevated humidity levels of >60% RH, tablet hardness dropped by as much as 50% of the starting value. In contrast, compression of granulation dried to higher equilibrium moisture levels (35-50% RH) resulted in much less tablet softening when exposed to elevated humidity. Once all samples had equilibrated on storage, the tablets compressed from granulation at 35-50% RH had higher final hardness values than the material compressed from granulation initially at 5-15% RH. In general, changes to tablet hardness values were inversely proportional to changes in the tablet's equilibrium moisture content following compression. Additionally, the changes in equilibrium moisture content were found to impact tablet hardness via a combination of reversible and irreversible routes. It is believed that the irreversible route involves internal tablet defects created as a result of excipient swelling upon moisture uptake.

These studies demonstrate an advantage of stopping the fluid bed drying process at a steeper part of the drying curve as opposed to the more traditional approach of drying to a low moisture plateau. Furthermore, the studies highlight how careful moisture control across the granulation process train can enhance the physical stability of pharmaceutical tablets.