A Materials Science Approach to Bilayer Tablet Compaction

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Fixed dose combination products (FDC) consist of two or more active pharmaceutical ingredients (API) combined within a single dosage form. FDCs are becoming increasingly popular forms of treatment for several therapeutic areas because it offers convenience, a reduced dosing burden, and cost savings for patients. In many cases, when the APIs are chemically incompatible or multiple release strategies are desired, the dose must be formulated as a layered tablet. However, layered tablets pose unique development and manufacturing risks. A fine balance exists between maintaining sufficient physical separation between the layers to mitigate chemical incompatibilities and yet also maintain sufficient cohesion between the layers so that the tablet remains intact (i.e. avoid layer delamination) throughout the manufacturing process and product shelf life. Challenges during the manufacture of layered tablets can be difficult to resolve due to the limited mechanistic understanding of the compaction process. Thus, layered tablet formulations have been historically developed through trial-and-error, which requires significant resource investments, especially when considering that layered tablet production on a rotary press requires kilogram-quantities of materials.

In this work, a materials-science-based approach to bilayer compaction is utilized. Because failure of layered tablets typically occurs due to delamination at the interface, a fundamental appreciation of the governing mechanisms that impact interface strength is crucial in order to improve the overall mechanical integrity of that layered tablet. The authors leverage knowledge about the plastic/elastic properties of the materials of interest to predict the likelihood for that material combination to yield a feasible bilayer tablet. An empirical heuristic has been developed in which less than 20 g of material can be used to predict the feasibility for a particular material combination to result in successful bilayer tablets. Three case studies will be highlighted to illustrate the utility of this predictive tool to guide efficient formulation development of bilayer tablets. The case studies will focus on the ability of this tool to evaluate the following scenarios:

- Over-lubrication: Impact to bilayer tablet strength when the blend making up one of the layers is over-lubricated
- Change in wet-granulation conditions: Impact to bilayer tablet strength when granulation conditions for one of the layers is changed
- Change in excipient grades, i.e. particle size differences: Robustness of bilayer tablet strength in response to changing excipient grade, especially when different grades possess different particle size distributions