Interplay of API-API and API-Tablet Matrix Strength in Modulating Punch Sticking Kinetics

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Purpose: This research work focuses on the role of the relative bonding strength of API and tablet matrix on the punch sticking kinetics during tablet manufacturing. Punch sticking, i.e., powder adherence onto tooling, is one of the outstanding challenges in tablet manufacturing, which impacts economic and continuous production of tablets. The severity of sticking can be collectively demonstrated by the interplay of punch-API (F1, adhesive force), API-API (F2, cohesive force) and API-excipient (F3, adhesive force) interactions in a multi-component tablet formulation. Sticking occurs when F1 is greater than F2 and F3. F2 and F3 are expected to influence sticking propensity but their effects have not been studied in-depth. When a monolayer of API has already been formed on the punch face, sticking can increase in severity when F2 > F3. On the other hand, further transfer of API to punch ceases if F3 > F2. We hypothesize that severity of punch sticking can be modulated by controlling the interplay between F2 and F3 through varying nature of the excipient matrix.

Methods: The hypothesis was tested by studying the sticking kinetics of two APIs, Celecoxib (CEL) and Ibuprofen (IBN), that differ in their mechanical properties in four different tablet matrices with varying tensile strength (i.e., F3). Sticking propensity of these APIs in 20% loading was assessed in the presence of 80% Avicel PH102, PH105, hypromellose (K15M) and starch 1500 as excipients with 0.25% magnesium stearate as a lubricant. F3 was assessed from the net tablet tensile strength based on the proportions of different bonding interactions (API-API, API-excipient, excipient-excipient) in the tablet. The extent of sticking was assessed after 50 compactions at a speed of 25 ms. Two compaction pressures (150 MPa and 300 MPa) were employed to attain different F3 with the goal to further elucidate its effects on sticking.

Results: Sticking of CEL was higher than IBN due to the more plastic nature and greater cohesive strength (F2) of CEL (Fig. 1a), which occupied the whole punch surface while IBN did not. The F3 of excipient matrices (F3) followed the order: PH105 > PH102 > K15M > Starch 1500 matrices. Sticking of both CEL and IBN followed the reverse order, i.e., PH105 < PH102 < K15M < Starch 1500. A clear negative trend between F3 and sticking was observed for both CEL and IBN (Fig. 1b). These data support that greater F3 reduces sticking by virtue of securing the API particles in the tablet matrix (thus preventing transfer of API to the punch).

Conclusion: Severity of punch sticking of a given API can be overcome by suitable selection of excipients, preferably with those that lead to greater tablet tensile strength. When API is more plastic, sticking propensity is inherently high but can be controlled through stronger API-excipient bonding interaction that prevents further API transfer from tablet matrix to the already formed layer of API on the punch. A practical application of this work is that, for a given API, a simple solution to overcome severe punch sticking is to incorporate an excipient with better tabletability in the formulation.

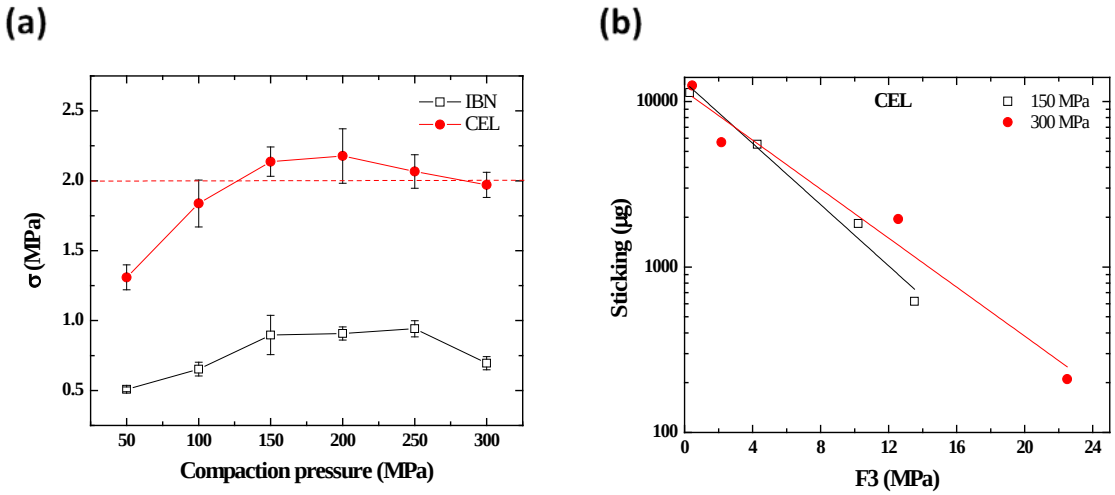

Fig. 1. (a) Cohesive strength of CEL and IBN at different compaction pressures, (b) relationship between sticking and F3 for CEL.