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Air Entrapment during Tablet Compression – Diagnosis and Impact on Tableting Performance Assessed with a Compaction Simulator

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PURPOSE

- Air entrapment during tablet compression can cause significant tablet defects.
- Highly plastic, low bulk density materials are prone to air entrapment.
- For these materials, deaeration of the powder bed prior to compression is essential to allow air to escape.
- Air entrapment may be difficult to diagnose if defects are internalized and not visually observed.
- In-die elastic recovery may be employed for diagnosing air entrapment related issues.

OBJECTIVES

To establish that in-die elastic recovery is an indicator for air entrapment propensity using a highly plastic material.

To demonstrate the effect of air entrapment on tablet strength.

METHODS

Materials

Celecoxib (CEL), a highly plastic, low bulk density crystalline active pharmaceutical ingredient, was used as received.

Methods

Tablets were prepared using a compaction simulator (Styl'One Evolution, MedelPharm, Beynost, France) using round, flat faced tooling with a diameter of 11.25 mm and a straight-bore die with an inner diameter of 11.28 mm. The simulator was operating at approximately 2.8 mm/s using a V-shaped profile.

Tablet porosity was determined from tablet dimensions measured after ejection and the true density of CEL. In-die elastic recovery was calculated from the tablet thickness at the highest pressure and the thickness after decompression. Plasticity was evaluated using the Heckel analysis, and mechanical strength was evaluated using a diametrical compression test on a texture analyzer.

RESULTS

Elastic recovery

- The in-die elastic recovery profile without precompression showed a sharp increase between 150 and 200 MPa (Figure 1, blue line), indicating air entrapment.
- A 10% precompression step, employed to deaerate the powder, eliminated the sharp jump in elastic recovery from 150 to 200 MPa (Figure 1, red line).
- Elastic recovery may be a valuable metric for diagnosing air entrapment in cases where no obvious defects are observed.

Impact on tablet mechanical properties

- Tablets made with precompression had a higher breaking force (Figure 2a) and lower porosities (Figure 2c) than those without.
- This indicates the presence of defects and a reduction in bonding area due to air entrapment without the deaeration step.
- The difference between breaking force and porosity with and without precompression are linearly related to compaction pressure, indicating that the presence of entrapped air is proportional to the applied pressure (Figures 2b,c).

Impact on plasticity

- in-die Heckel analysis, with and without precompression, showed no significant impact of entrapped air on P_y.
- Thus, entrapped air does not significantly influence the powder plasticity as quantified by the in-die Heckel analysis.

Condition	P_y (MPa)
No Precompression	78.2 (0.3)
10% Precompression	80.0 (0.9)

- The lack of impact on plasticity due to entrapped air is consistent with the significantly higher compressibility of air compared to solids.

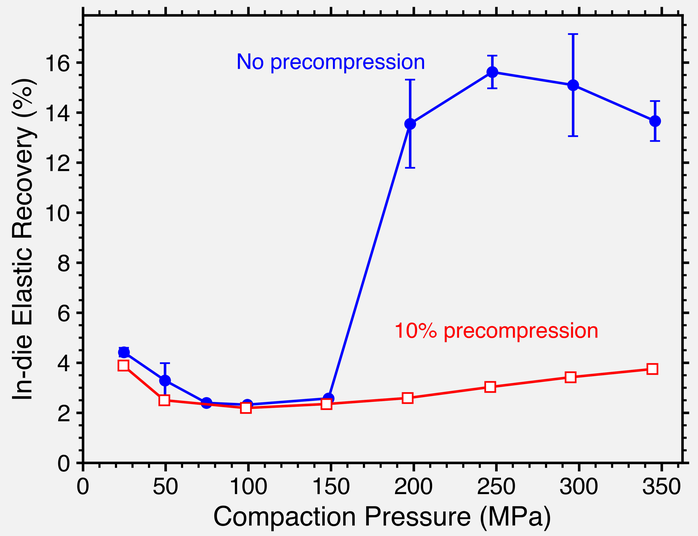

Figure 1: *In-die tablet elastic recovery of CEL with and without 10% precompression.*

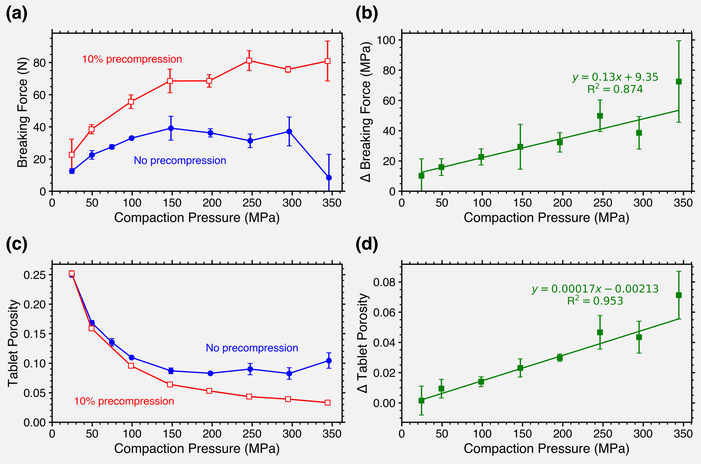

Figure 2. *(a) Tablet breaking force with and without 10% precompression, (b) absolute change in tablet breaking force as a result of precompression, (c) tablet porosity with and without precompression, and (d) absolute change in tablet porosity as a result of precompression as a function of compaction pressure.*

CONCLUSIONS

- Air entrapment was diagnosed using in-die elastic recovery profiles.
- Application of a precompression step effectively deaerated the powder and reduced in-die elastic recovery.
- Deareation by precompression effectively improved tablet breaking force and porosity.
  - The difference in tablet breaking force and porosity both linearly increased with compaction pressure.
- Powder plasticity quantified by the in-die Heckel analysis was not affected by air entrapment.

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