Oral solid dose

Predicting drug-loading limits in tablet formulations

Material characterization and predictive modeling helped determine the maximum feasible drug loading before tabletability risks emerge.

Development challenge

Formulating high-dose tablets can present significant challenges when the active pharmaceutical ingredient dominates blend behavior. High drug loading can reduce flowability, impair compression performance, and increase the risk of defects such as lamination or capping.

Traditional approaches often rely on extensive formulation experimentation to determine feasible drug loading levels.

Identifying critical percolation thresholds

To better understand the limits of drug loading, predictive modeling tools within the OSD Predict™ toolbox were used alongside material characterization techniques to evaluate formulation behavior for both the crystalline API and a spray-dried dispersion (SDD) form.

Material analysis showed that both forms of the compound exhibited low bulk density and cohesive powder behavior. Heckel analysis indicated limited bonding capacity and moderate strain-rate sensitivity, suggesting potential risks during tablet compression.

Modeling blend behavior

The analysis focused on identifying the critical percolation threshold, the point at which API concentration begins to dominate blend behavior and negatively affect tablet properties.

A power-law model was used to evaluate how particle size, morphology, and API-to-excipient ratios influence blend flowability and compression performance.

Development outcome

The study identified a critical percolation threshold of approximately 20% drug load for the crystalline API and 15% for the spray-dried dispersion.

Identifying these thresholds early helps formulation scientists define practical drug-loading limits, avoid compression failures, and reduce trial-and-error experimentation during tablet development

At a glance

Program focus

Determining maximum feasible API loading in tablet formulations while maintaining acceptable flowability and compression properties.

Methods used

Material characterization, Heckel analysis, compaction behavior evaluation, and predictive percolation modeling.

Formulation system studied

Binary blends of crystalline API and spray-dried dispersion (SDD) with Avicel® PH-102.

Key technical finding

Percolation thresholds were identified at ~20% drug load for crystalline API and ~15% for the SDD form, where blend behavior shifts significantly.

Development impact

Identification of drug-loading limits helped avoid formulation failure and reduced experimental screening during tablet development.

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