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Flexible Manufacturing with Starch-based Excipient Blends for Early-Stage Drug Product Development

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SUMMARY

Starch-based powder blends are gaining popularity in the pharmaceutical industry due to their inherent process flexibility and compatibility with different manufacturing techniques. In this study, we evaluated the performance of starch-based excipient blends in achieving process flexibility with four commonly used manufacturing techniques, including roller compaction, wet granulation, direct compression, and fluid bed granulation. We also evaluated the compressibility, compactibility, and tabletability of the powders made with these techniques, compressed using a Gamlen™ press. Our results show that the fluid bed process gave the strongest tablet blends, while the roller compaction technique gave the weakest tablet blends. These findings highlight the potential of starch-based excipients in providing flexibility in the manufacturing process for early-stage drug product development.

INTRODUCTION

Starch-based excipients have gained attention in early-stage drug product development due to their unique properties and process flexibility. Studies have demonstrated their use in various manufacturing techniques, such as roller compaction, wet granulation, direct compression, and fluid bed granulation (Svačinová, P et al., 2021). These excipients have been shown to improve the compressibility, tabletability, and strength of the final drug product. By conducting laboratory-based compaction analysis early within the formulation and process development may de-risk tablet development (Stewart, S et al, 2021).

MATERIALS AND METHODS

Starch 1500® and StarTab® were supplied by Colorcon Ltd, mannitol was obtained from Roquette, microcrystalline cellulose (MCC) was provided by IMCD Ltd, and magnesium carbonate (surrogate API) was procured from Scora S.A.S. Blends for direct compression and roller compaction were prepared by mixing the ingredients in a Turbula blender for 10 minutes. The granulation process utilized both fluid bed and high shear granulation techniques, involving the application of water and subsequent drying. The resulting granules/blends were lubricated with 0.5% w/w magnesium stearate and analysed for compaction using a Gamlen™ D-Series compaction analyser.

RESULTS AND DISCUSSION

Table 1 shows the formulations of multifunctional excipients like Starch 1500® and StarTab®, combined with plastically deforming MCC and brittle deforming mannitol. These excipient blends were selected to

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strike the right balance between tablet strength and disintegration, making them suitable for immediate-release drug products.

Table 1. *Composition of blends*

Formulation	Starch (%w/w)	MCC (%w/w)	Mannitol (%w/w)	$MgCO_3$ (%w/w)
Roller compaction	20.0[a]	49.5	20.0	10.0
Direct compression	20.0 [a]	49.5	20.0	10.0
High shear granulation	20.0 [b]	49.5	20.0	10.0
Fluid bed granulation	20.0 [b]	49.5	20.0	10.0

[a] refers to StarTab®, [b] referring to Starch 1500®.

Figure 1 displays tabletability profiles of different formulations from Table 1, produced using various manufacturing processes. The results show that fluidized bed granulation generated the strongest tablets (tensile strength ≥ 1.8 MPa) at all compaction pressures. Roller compaction produced weaker, yet acceptable tablets. Surprisingly, the wet-granulation process, intended to enhance tablet hardness, showed similar tabletability to the DC StarTab® blend. This suggests that high tensile strength tablets can be achieved using the direct compression grade of Starch (StarTab®).

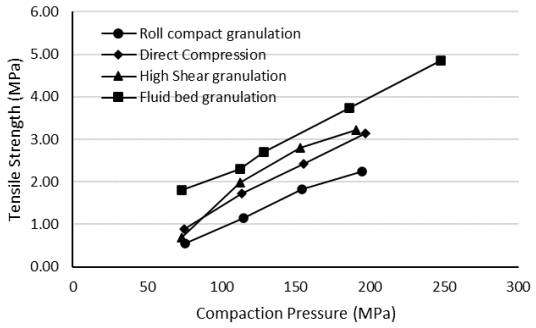

Fig. 1. *Tabletability profile of powder blends prepared using various manufacturing processes.*

Figure 2 presents compressibility profiles (compaction pressure vs solid fraction) of the different processes. The data shows that all combinations have a solid fraction of ≤0.9 at a nominal compression pressure of 200 MPa, indicating minimal risk of over compression. This finding is crucial as over compression can cause undesirable outcomes like capping and lamination. Figure 3 illustrates compactability profiles (solid fraction vs tensile strength) of the blends. The results indicate that the fluid bed granulation process generates the highest tensile strength at similar solid fraction levels. This is likely due to starch activation with water, which acts as a binder and increases compact hardness. Additionally, the fluid bed granulation process promotes granule formation and uniform mixing of excipients, resulting in a more homogenous blend and higher tensile strength.

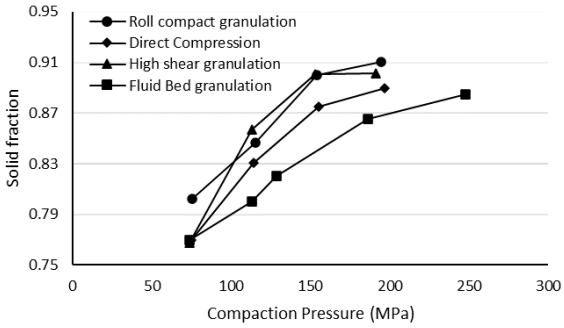

Fig. 2*. Compressibility profiles of powder blends.*

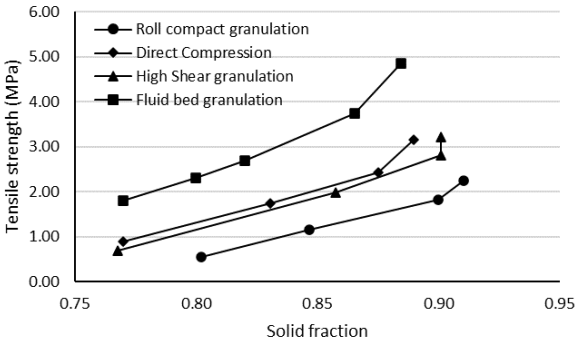

Fig. 3. *Compactibility profiles of powder blends.*

CONCLUSIONS

The study concludes that starch-based powder blends offer process flexibility and compatibility with different manufacturing techniques in the pharmaceutical industry. The results suggest that fluid bed granulation is a more suitable technique for achieving strong tablet blends compared to roller compaction.

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