Compression Profiles of a Directly Compressible Starch using Compaction Simulation and High-Speed Tablet Press

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Introduction

Starch based excipients are often used in solid oral formulations for their binder, filler or disintegrant properties. Maize starches are inert and stable with low water activity, making them the preferred choice for moisture management in solid oral dosage forms. These excipients are naturally derived, widely available, and well understood by formulators and regulators. Unmodified starch (native starch) is known to have poor flow and compressibility and hence, is not used as a primary filler for direct compression. The purpose of this study was to evaluate the compressibility and flow of a novel directly compressible starch (StarTab®) using compaction simulation and rotary tablet press.

Methods

StarTab® and native corn starch were evaluated for their powder flow characteristics using bulk and tapped density (Varian, USA), minimum orifice diameter and powder flow (Flodex, Hansen, USA), surface morphology via scanning electron microscopy (SEM) (Phenom, USA) and particle size distribution (Malvern, USA). Both materials were lubricated with 0.25% magnesium stearate and subjected to compaction evaluation using Stylcam® 100R rotary press simulator (Medel'Pharm, France); the equipment was fitted with 7 mm flat-faced tooling with an individual target tablet weight of 150 mg. The compression cycle followed a generic rotary press profile that corresponded to 7.5 – 30 mS dwell time. Measurements of punch displacement, compaction force (from which compaction pressure was calculated) and ejection force were determined using the Analis® software. True powder density was determined using Helium pycnometer (AccuPyc, Micromeritics, USA). Tensile strength, solid fraction and strain rate sensitivity were calculated using equation 1, 2 and 3 respectively (Table 1).[1] The values calculated were used to generate compressibility, compactibility and tabletability graphs; these were plotted based on Figure 1, using tensile strength, solid fraction and compaction pressure data.[1] Placebo tablets (400 mg weight each) of lubricated StarTab were compressed on lab scale single-rotary tablet press (4-station, Piccola B/D 370 press , USA) and production scale single-rotary tablet press (25-station, Manesty TPR 200Bosch, Germany). Powder paddle feeder was used on both rotary tablet presses. Tablet press parameters and set-up are listed in Table 2. All tablets were evaluated for tablet weight, hardness and thickness (Multicheck V, Erweka, Germany), friability (Varian, USA), and disintegration in 900mL of DI water at 37°C (Erweka ZT 224, Erweka, Germany).

Table 1. Equations

1	$\text{Tensile Strength } (\sigma) = \frac{2F}{\pi DH}$
2	$\text{Solid Fraction (SF)} = \frac{W}{\rho . V}$
3	$\text{Strain Rate Sensitivity } (\%) = \frac{Py1 - Py2}{Py2} \times 100$

where F, D, H, W and V are tablet hardness, diameter, thickness, weight and volume respectively; ρ is true density; Py1 is yield pressure at low dwell time and Py2 is yield pressure at high dwell time, which were calculated from slope of Heckel plot [4]

Figure 1. Compaction Terminology [1]

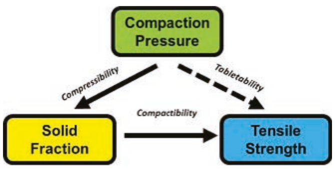


Table 2. Rotary Tablet Press Parameters

	Piccola	Manesty TPR 200	
Dwell time (mS)	24	18	7
Tooling type / size	B – tooling 10 mm round FF*	B – tooling 10.5 mm round SC^	B – tooling 10.5 mm round SC^
Press Speed (RPM)	50	40	92
Tablet per minute (TPM)	200	1000	2300
Tablet per hour (TPH)	12,000	60,000	138,000

** FF = flat-faced; 4 station; ^ SC = standard concave; **without or with 2 kN pre-compression force*

Results and Discussion

Powder Properties

Figure 2 compares the particle morphology of StarTab® to native corn starch. StarTab® particles have an optimized morphology, almost spherical in shape, which attributes to the material's excellent flow properties. When compared to native corn starch, StarTab® exhibited exceptional powder flow, demonstrated by compressibility index and Hausner ratio (Table 3).[2] Flodex minimum orifice diameter testing resulted with StarTab® flowing through the 4mm diameter (smallest orifice available). This suggests that StarTab® will provide good flow and a uniform tablet die fill during the tableting process.[3] StarTab® also has a mean particle size (d50) of approximately 90 micron; which is within range for most directly compressible excipients.

Figure 2. SEM Images (900x) of (A) Native Corn Starch and (B) StarTab®

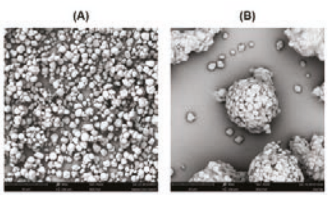


Table 3. Powder Flow Properties

Powder Flow Testing	StarTab®	Native Corn Starch
Bulk Density (g/mL)	0.57	0.51
Tapped Density (g/mL)	0.70	0.84
Hausner Ratio	1.22	1.65
Compressibility Index (%)	18.00	40.00
Flodex minimum orifice diameter (mm)	4	30
Flow rate from 4mm (g/min)	37.58	Did not flow
Particle size, d10 (µm)	36.90	9.49
Particle size, d50 (µm)	89.77	14.01
Particle size, d90 (µm)	171.37	20.59
Particle size, d4,3 (µm)	97.74	14.62

Compaction Simulation

When subjected to compaction simulation at different dwell times, StarTab® was compressible, forming compacts with greater than 0.8 (80%) solid fraction (Figure 3A). It also had superior tabletability and compactability in comparison to native corn starch.[5] StarTab® compacts were robust with tensile strengths above 2Mpa (Figure 3c). At all compaction pressures, high compactability was demonstrated with increasing compaction pressure. Heckel plot [4] was generated shorter dwell time of 10 mS and (Figure 4) shows that StarTab® primarily undergoes plastic deformation. Strain rate sensitivity was low for the product, with a calculated value of 3.4% (Table 4).

Figure 3. (A) Compressibility, (B) Compactability and (C) Tabletability Plots StarTab®

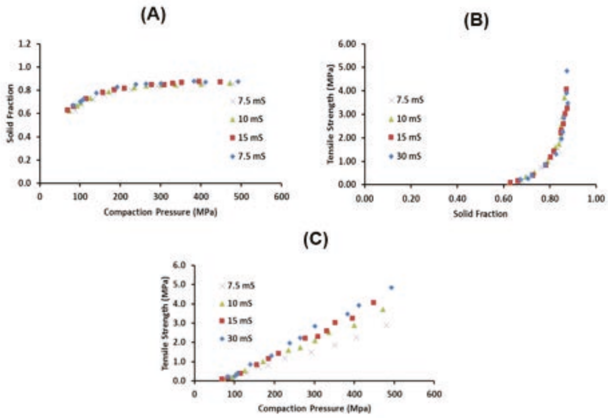
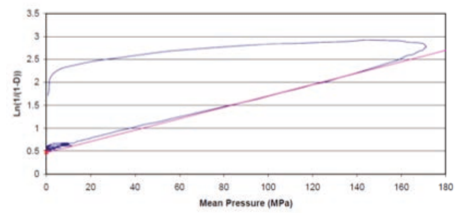


Figure 4. Heckel plot of StarTab Compacts Compressed at Increasing Compaction Pressure and at Dwell Time of 10 mS



Key: D = relative density

Table 4. Strain Rate Sensitivity (SRS) of Lubricated Blend of StarTab and Native Corn Starch

Material	Py1*	Py2**	% SRS
StarTab	81.3	84.2	3.4
Native Corn Starch	58.7	60.9	4.1

** Py1 = yield pressure at 10 mS dwell time*
***Py2 = yield pressure at 30 mS dwell time*

Rotary Tablet Compression

Individual lubricated blends of StarTab and native corn starch, were subjected to rotary tablet compression using powder paddle feeder to control powder flow. Native corn starch was incompressible due to poor flow and severe ratholing. Thus, no data was generated for this material. On the other hand, StarTab demonstrated excellent flow and compressibility on rotary tablet press at different dwell times, with uniform die fill, characterized by low variation in thickness (data not shown), weight and tensile strength of tablets (Figure 5A and 5B). StarTab tablets had low ejection force (between 0.2 to 0.4 kN), low friability of < 1 % (Figure 5C) and fast disintegration time in water of < 3 minutes (Figure 5D) irrespective of compression force. During high speed tableting, formulators often use pre-compression station set at up to 2 kN to allow air-escape from powder in die cavity before compression under main-compression station and avoid issues such as tablet capping and lamination. StarTab placebo tablets were compressed at very low dwell time (7 mS) with pre-compression force between 0 to 2 kN and then main compression force between 10 – 30 kN on Manesty TPR-200 single-rotary tablet press. Similar tablet compression profiles were obtained, indicating versatility of StarTab to perform similarly, confirming the high air permeability and low cohesivity of StarTab.[5] All the StarTab tablets produced in the study, were 'free' of any defects such as picking, sticking, capping or lamination. StarTab tablets show pH-independent disintegration in different buffers (Figure 6).

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Figure 5. Effect of Dwell Time and Compression Force on (A) Weight, (B) Hardness, (C) Friability and (D) Disintegration Time of StarTab Placebo Tablets

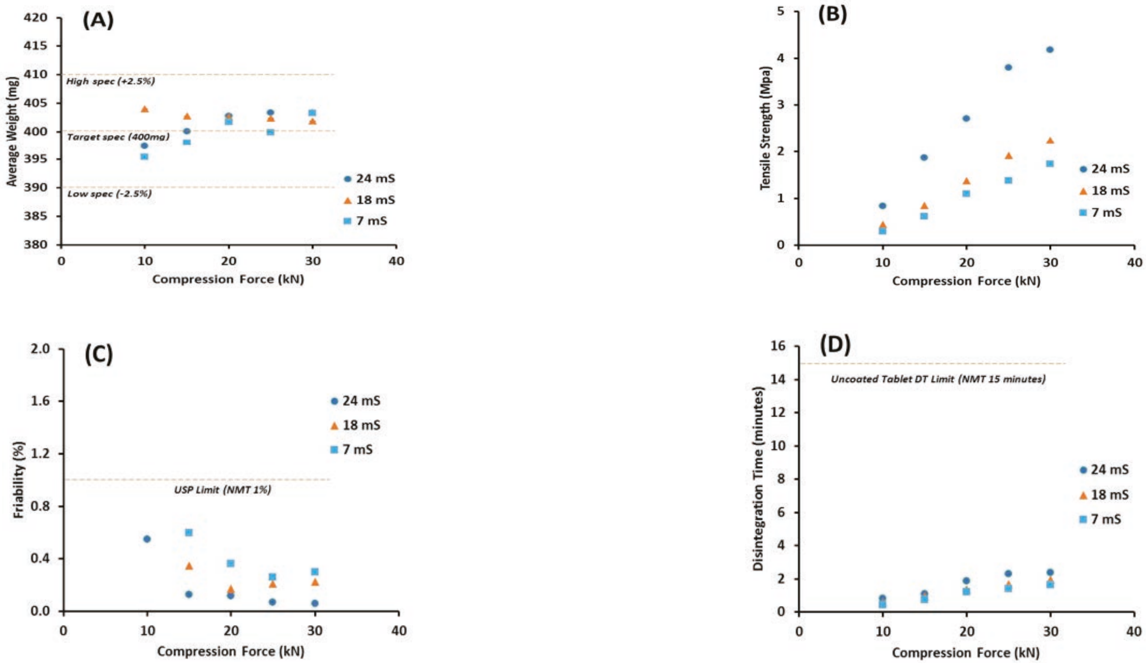
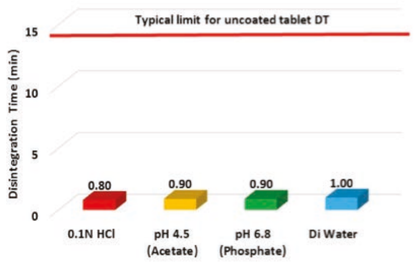


Figure 6. pH independent disintegration of StarTab® placebo tablets compressed at 15kN compression force



Conclusions

StarTab, directly compressible starch showed excellent powder flow and compression properties on compaction simulator and rotary tablet pres. StarTab placebo tablets also resulted in pH-independent disintegration within 3 minutes for tablets compressed between 10-30 kN compression force. This new excipient is also designed through particle optimization for high-speed tablet compression of tablets.

References

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