Development of High Dose Calcium Citrate Tablets Using a Novel Clean Label Lubricant

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Challenge

Calcium is known as an abrasive material when it comes to formulation development and tablet compression operation. Its daily recommended dose is approximately 1000 mg for adults[1].

Given its abrasive nature and requirement for a high dose, this study aims to develop a directly compressible formulation of high-loading calcium citrate (>95% w/w) using Nutracore™ Label Friendly Lubricant. Tablet film coating is desired for many reasons, including calcium tastemasking[2]. Therefore, tablet coating of the optimized formulation was investigated.

Method

Formulation Design and Tableting

High loading (>95% w/w) calcium citrate tablet was formulated using Cab-O-Sil M-5P as a glidant at 0.5% w/w and Nutracore or magnesium stearate as lubricants. Nutracore lubricant concentration was studied at 2, 3, and 4% w/w, and compared to a control formulation using magnesium stearate at 2% w/w. Furthermore, the effect of mixing time on tablet quality attributes was studied for the formulations with 2% w/w magnesium stearate at 3, 5 and 10 mins, and Nutracore lubricant at 3, 5, 10 and 20 mins.
Formulations were tableted using a Piccola B/D rotary press at 30 rpm turret speed with 12.5 x 25.0 mm modulated caplet tooling and compression force in the range of 20-45 kN.

Powder and Tablet Testing

Powder flow of selected formulations was determined using compressibility index. Tablet quality attributes were analyzed in terms of appearance, weight variation, tensile strength, friability and disintegration.

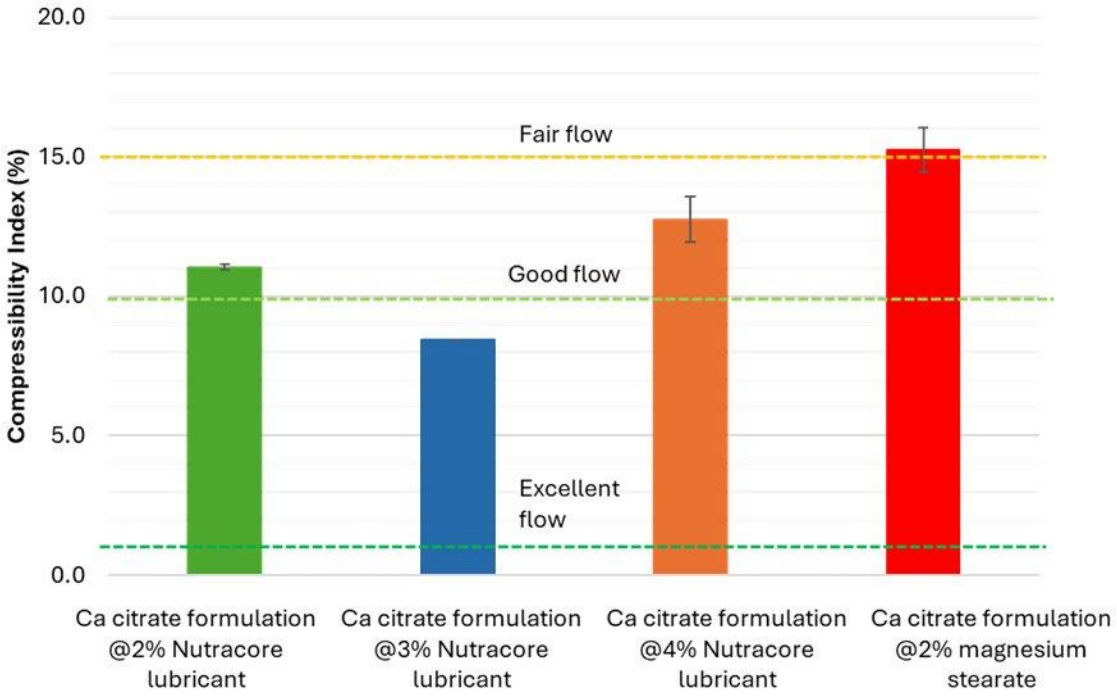
Tablet Film Coating

Hyperstart C2C, an online formulation tool, was used to recommend proper coating formulation as well as processing conditions. Optimized calcium citrate formulation using Nutracore were coated using Nutrafinish® Label-friendly coating at 3% weight gain in a 12” pan at a target product bed temperature of 45°C and 10 g/min spray rate.

Results

All formulations were manufactured successfully with Nutracore-based formulations at 2-4% lubricant having excellent to good powder flow compared to fair flow for magnesium stearate-based formulations as observed from Figure 1.

Figure 1. Compressibility Index of Calcium Citrate Formulations Using Nutracore Lubricant and Magnesium Stearate



The study on tablet formulations using Nutracore lubricant and magnesium stearate revealed significant differences in performance.

Tablets containing Nutracore lubricant exhibited acceptable appearance (Figure4), <1% w/w friability, and tensile strength of 1.69, 1.30, and 1.07 MPa at 40kN compression force for 2%, 3%, 4% w/w concentration respectively, as depicted in Figure 2, and acceptable ejection forces.

In contrast, calcium citrate tablets containing magnesium stearate showed lower tensile strength as shown in Figure 2, failed friability, and capped at compression forces >35 kN, with severe capping at even higher forces. Magnesium stearate was further tested at 1% that also failed due to capping even at lower compression forces (data not shown).

Disintegration time for tablets containing Nutracore at 2-4% w/w inclusion levels and compressed at 35-45 kN was less than 1 minute, meeting the USP monograph requirement of less than 15 minutes. Conversely, calcium citrate tablets containing magnesium stearate at 2% w/w inclusion level and 35 kN compression force failed disintegration criteria, requiring greater than 50minutes to disintegrate.

As expected, mixing time significantly impacted the robustness of tablets containing magnesium stearate, reducing tensile strength by almost 50% at 5and 10 minutes, as observed from Figure 3, with all tablets failing tensile strength targets and capped when noted. Nutracore-based blends at 2% w/w were less affected by mixing time, maintaining robust tensile strength (>1.2MPa) at >40 kN and friability <1% w/w, and disintegration time remained under 1 minute across all mixing times.

Coating operations of optimized calcium citrate tablets with 2% w/w Nutracore lubricant made at 3 minutes mixing time and 45 kN compression force resulted in tablets with acceptable appearance as observed in Figure 4, excellent tensile strength (3.0 MPa), and an acceptable disintegration time of 3.5 minutes.

Figure 2. Tabletability Profile of Calcium Citrate Using Nutracore Lubricant and Magnesium Stearate

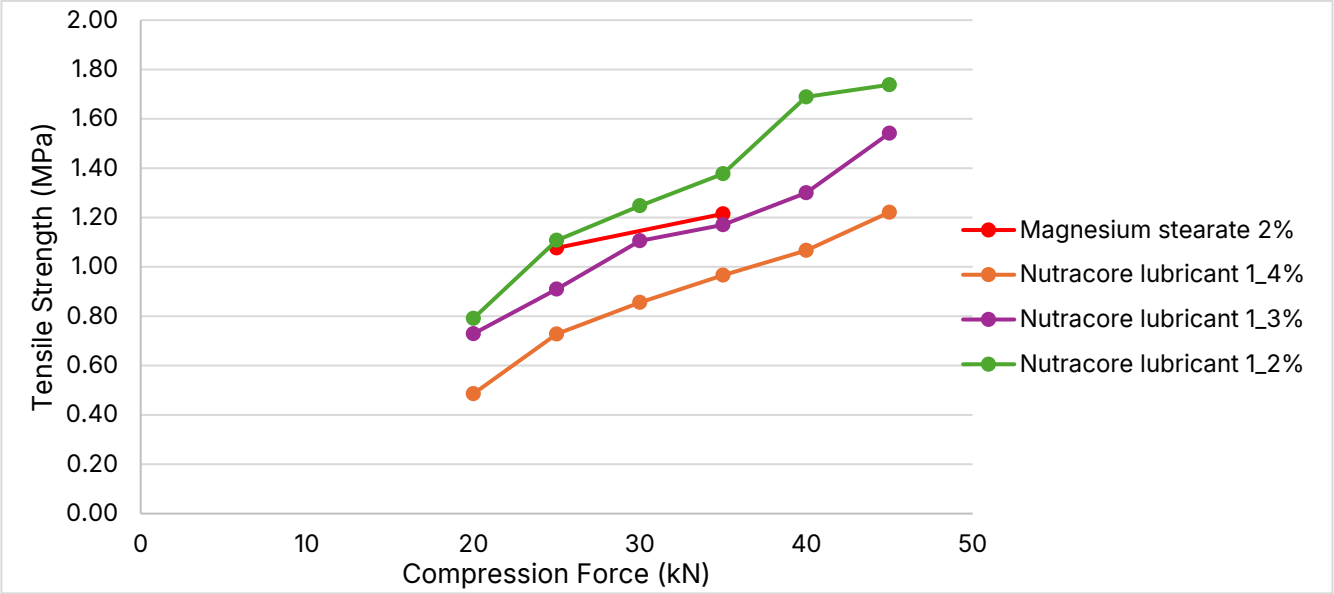
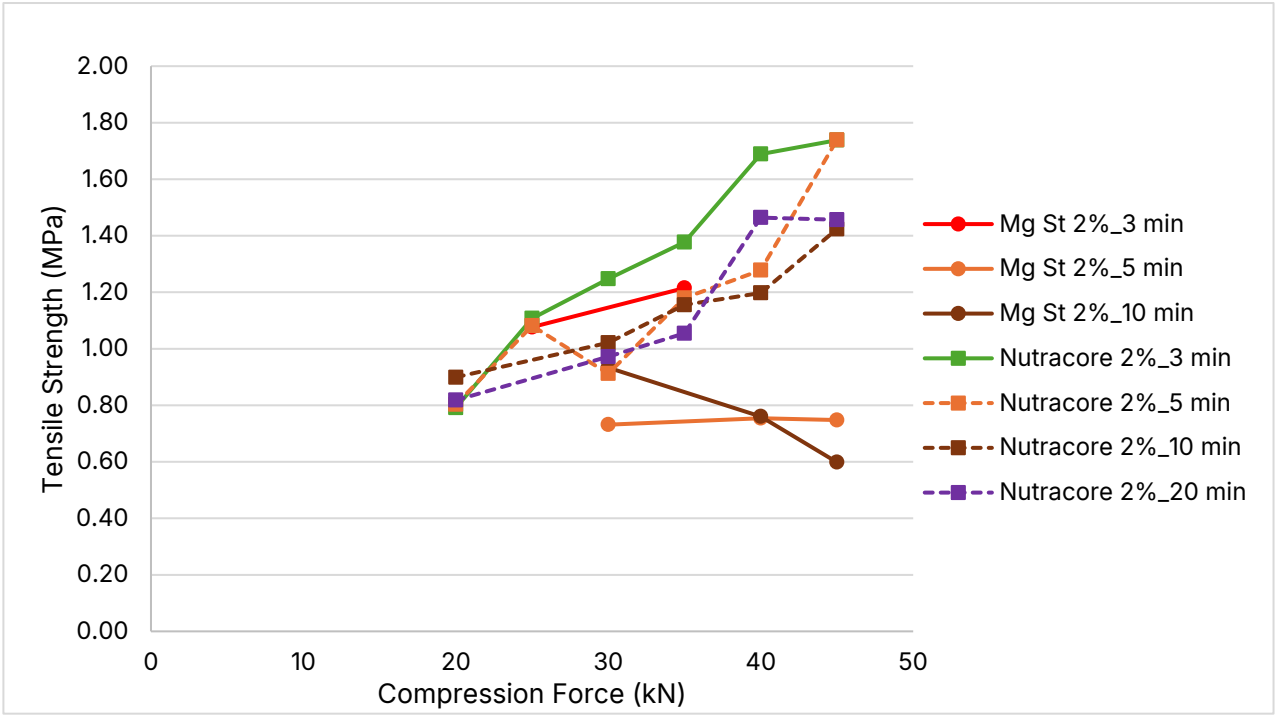


Figure 3. Impact of Mixing Time on Tabletability Profile of Calcium Citrate Using Nutracore and Magnesium Stearate



Conclusion

Nutracore™ Label Friendly Lubricant has proven to be a promising lubricant for producing robust, high-loading calcium citrate (>97% w/w) tablets, outperforming magnesium stearate. Nutracore-based tablets were less susceptible to over-lubrication issues compared to those with magnesium stearate. Additionally, film coating enhanced the tensile strength of the tablets without adversely affecting their disintegration time.

Figure 4. Tablet Appearance of Calcium Citrate Tablets Using 2%of Nutracore Lubricant; Both Uncoated (A) and Coated (B), and Magnesium Stearate, Zoomed Out (C) and Zoomed In (D).

References

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