Swift Single Step Scale up from Compaction Simulator to Production Rotary Press

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INTRODUCTION

The scale up process of tablets can be influenced by many factors that can occur during process development. The development can be highly catalyzed by compaction simulators, which allow for a single step scale up of tablet formulations by a concise simulation of the compaction of high throughput production presses [1]. The aim of this study was to perform a single step scale up with two tricalcium citrate formulations and a consecutive high speed performance test on a production rotary tablet press.

MATERIALS AND METHODS

Two qualities of Tricalcium citrate (TCC TB and TCC GN) were gifted by Jungbunzlauer Ladenburg GmbH (Ladenburg, Germany).

Compaction simulations were carried out on a STYL'One Evo (Evo) compaction simulator by Medelpharm (Beynost, France). A compaction on a KORSCH X 3 rotary press was simulated with the machine. A X 3 MFP rotary press manufactured by KORSCH AG (Berlin, Germany) was used for the performance tests (Figure 1). Oblong, biconvex, EU-B punches (17 mm x 8 mm) were used for both trials.

First the excipient blends were compacted on the Evo, where their compaction behavior was characterized using different main compaction forces. Afterwards, their behavior towards production speed increase was studied. Subsequently, the recipes with tabletting parameters for the transfer to the X 3 were created.

Resistance to crushing, weight and thickness measurements of the tablets were conducted on a P-Line tablet tester by Kraemer Elektronik GmbH (Darmstadt, Germany). Tensile strength for oblong tablet formats was calculated as suggested by Pitt et. al. [2].

Figure 1. KORSCH X 3 rotary press and STYL'One Evo compaction simulator

RESULTS

Both TCC qualities showed linear increases in tensile strength with increasing main compaction force during the simulations on the Evo as displayed in Figure 2.

Both TCC qualities showed a slight decrease of tensile strength when the simulated speed was increased (Figure 3).

The simulations suggested a very favorable compaction performance of the two TCC blends on the X 3 rotary press, if a constant die filling at high turret speed was possible.

On the X 3 both TCC qualities were adjusted to their maximum turret speed which was 80 rpm for TCC GN and 100 rpm for TCC TB. Both TCC qualities showed constant weight and tensile strength values for each sampling point (Figures 4 and 5), as well as constant compaction forces during (Figures 6 and 7).

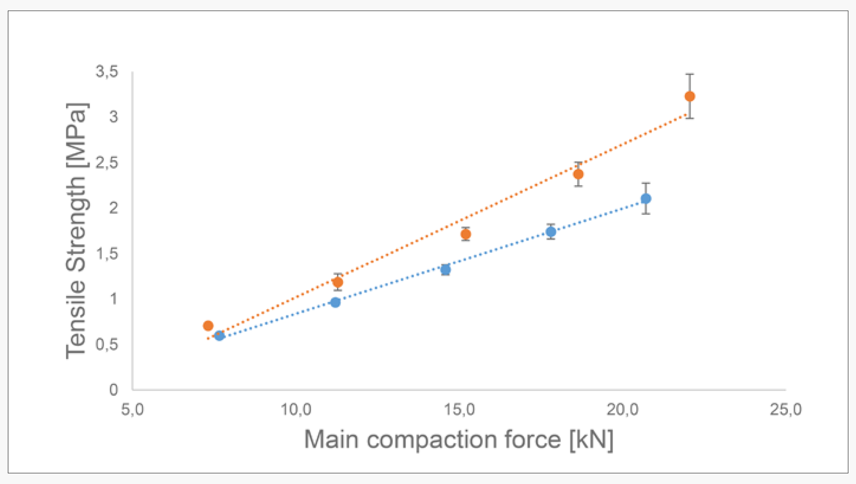

Figure 2. Main compaction force plots (n=10) simulated on a STYL'One Evo for TCC TB = orange and TCC GN= blue

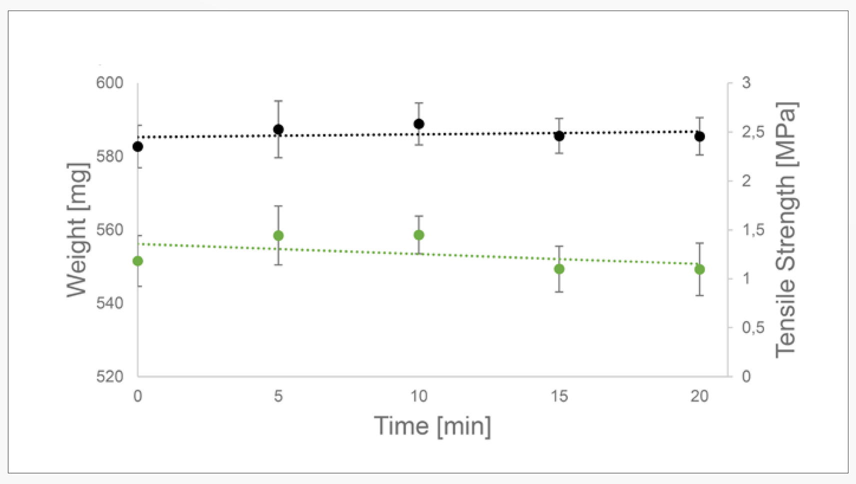

Figure 4. Performance test (n=20) for TCC TB on a KORSCH X 3 at 100 rpm. Green = Weight; Black = Tensile Strength

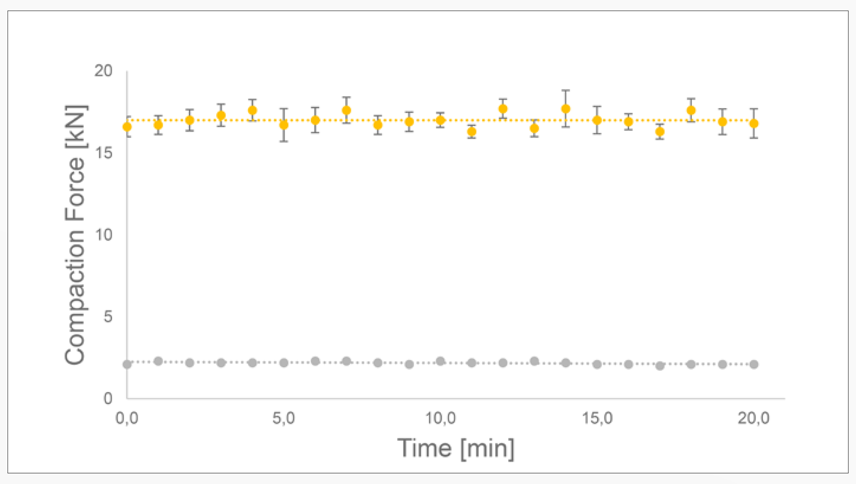

Figure 6. Compaction force measurements during the performance test for TCC TB on a KORSCH X 3 at 100 rpm. Gold = Main Compaction Force; Grey = Pre Compaction Force

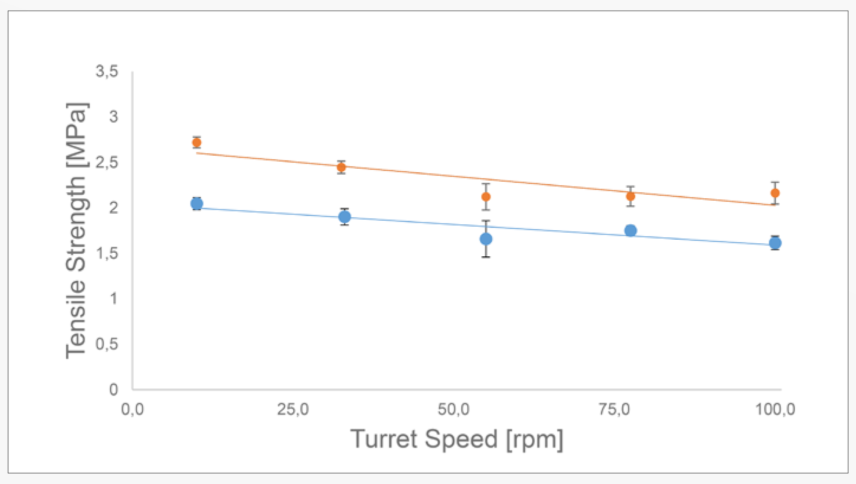

Figure 3. Turret speed plots (n=10) simulated on a STYL'One Evo for TCC TB = orange and TCC GN= blue

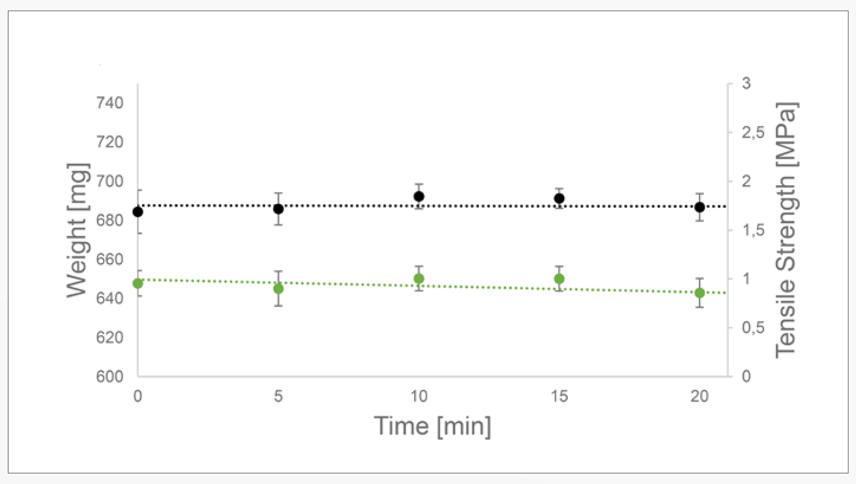

Figure 5. Performance test (n=20) for TCC GN on a KORSCH X 3 at 80 rpm. Green = Weight; Black = Tensile Strength

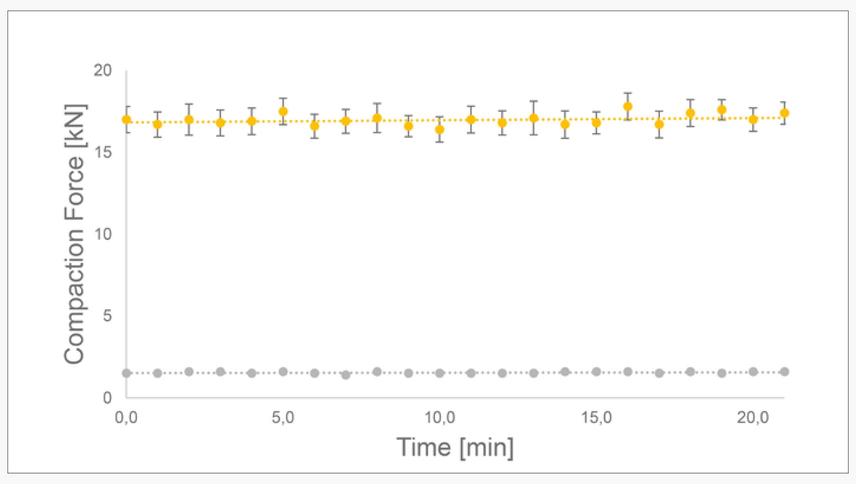

Figure 7. Compaction force measurements during the performance test for TCC GN on a KORSCH X 3 at 80 rpm. Gold = Main Compaction Force; Grey = Pre Compaction Force

CONCLUSION

A precise single step scale up of both excipients from compaction simulator to production rotary press was achieved in this study. With prior knowledge of the materials behavior towards compaction force and turret speed increase, the scale up was managed very quickly and with minimal material loss during adjustment of the X 3 machine parameters (Figures 2 and 3).

Both TCC qualities showed a linear increase of tensile strength in the investigated main compaction force range. Lower dwell times of increased turret velocities were also very well tolerated by both blends. This corresponds well with prior investigations, where TCC was classified as brittle [3].

On the rotary press both blends showed good flow capabilities. The dosing was monitored in process via main compaction force measurement as a surrogate (Figures 6 and 7), which ensured constant tablet weight and hardness over time with minimal deviations (Figures 4 and 5).

Further experiments with API loaded blends have to be executed, to further evaluate TCC as a suitable excipient for formulation development and tablet manufacturing. However, this study proves sound excipient characteristics of TCC, especially TCC TB, which showed more favorable compaction plots in the simulations and could facilitate a performance test at a higher turret speed.

REFERENCES

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