Employing Compaction Simulation to Support Development and Quality Prediction of Bilayer Tablets Produced in High-speed Manufacturing

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INTRODUCTION

A compaction simulator is an ideal tool for material characterization, tableting blend optimization, process troubleshooting, and predictive scale-up [1]. Furthermore, it simplifies the working procedures and reduces the amount of powder required during formulation development.

This tool is particularly useful in the development of complex drug products such as bi-layer tablets, which requires for a profound understanding of the tabletting process. For example, bi-layer tablet development requires investigation around both tablet strength and interfacial bonding [2].

To evaluate the predictive capabilities of a compaction simulator for bi-layer tablets, a formulation consisting of a brittle immediate and a plastic sustained release matrix layer was employed. The process parameters gained were transferred to a production scale rotary tablet press.

KORSCH X 3 MFP [KORSCH AG]

STYL'One Evolution [MEDELPHARM]

Breaking Strength Tester [KORSCH AG]

MATERIALS AND METHODS

Trade Name	Composition	Function
Kollidon® SR *(KD)* [BASF]	PVA/PVP	Matrix layer
Kollitab™ DC 87 L *(KT)* [BASF]	Lactose monohydrate, PEG-PVA, grafted copolymer, crospovidone, SSF	Immediate release layer

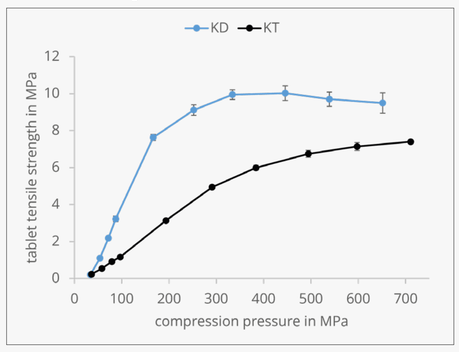
Comparison
- Power feeder with rectangular feeder paddle
- 9 mm flat punches
- (simulated) compression speed 40 rpm
- Pre-compression force 1 kN (15.7 MPa)
- Main-compression force 10 kN (157 MPa)
- KT 200 mg KD 150 mg layer weight

Material characterization
- V-shape profile 10 mm/sec
- Energy calculated from force-displacement profile

RESULTS

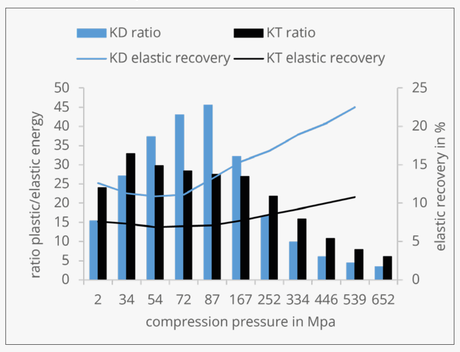
Material characterization

Tabletability



- KD: high tabletability at low pressures (steep increase), over-compression >300 MPa (plateau).
- KT: tensile strength less sensitive to changes in pressure, less sensitive >300 MPa, no over-compression
- Both materials reach tensile strength >1.7 MPa below 150 MPa

Elastic and plastic behavior

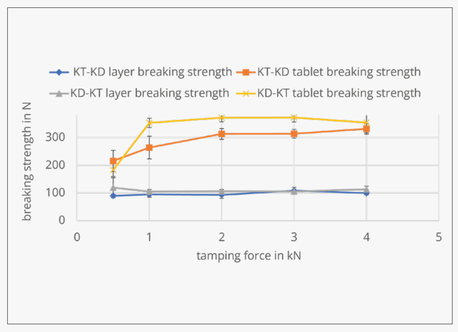


- KD develops higher elastic recovery values
- Between 54-167 MPa KD exhibits higher plastic to elastic ratio values than KT
- At low and high compression pressures KT has a more favorable plastic to elastic energy ratio

Compaction simulation

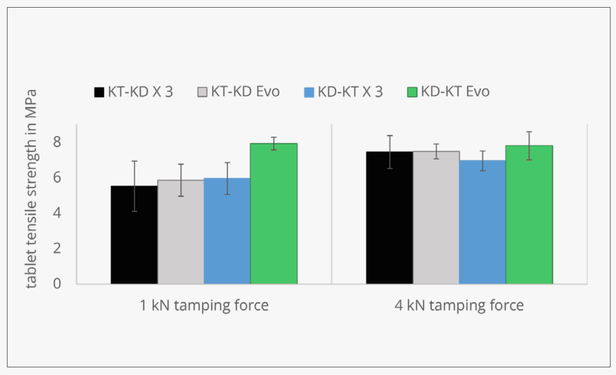
Filling
- Flowability of KT and KD on the first layer excellent
- Filling of dies on second layer with KD was just sufficient at high feeder paddle speeds (110 rpm/ and maximum 150 mg could be filled)

Influence of tamping pressure
- Layer breaking strength was measured with a custom adaption to Pharmatron MultiTest t50 G2
- Layer breaking strength was constant throughout the applied tamping forces
- Higher tablet breaking strength could be achieved with KD on first layer (1-3 kN tamping force)



Production Press vs. Compaction simulation

- Just minor adjustments in edge thickness and dosing had to be set to match the compression profiles
- The layer breaking strength for all layer combinations, applied tamping pressures and all press types was within a narrow range of 90 to 120 N
- KT on first layer
  - Tensile strength of produced tablets the same for production and simulation
- KD on first layer
  - Tablets produced by simulation higher tensile strength than on production press at low tamping pressure



CONCLUSION

- Kollitab™ DC 87 L as an all-in-one immediate release component has an excellent flowability.
- KT and KD form highly cohesive bi-layer tablets, with a robust performance even if changes in tamping pressure are applied.
- Employing the STYL'One Evolution supports product development of bi-layer tablets regarding layer position, maximum filling amount and tamping pressure selection.
- The production press X 3 could be set based on predicted values like target dosing deriving from STYL'One Evolution.
- Challenges during filling can be foreseen by simulation allowing for beneficial layer configuration.
- Depending on layer sequence, the tensile strength was not precisely transferable from simulation to production.

REFERENCES

1. Wünsch, I., et al. Scaling tableting processes from compaction simulator to rotary presses—Mind the sub-processes. Pharmaceutics, 2020, 12. Jg., Nr. 4, S. 310.
2. Singh, Abhay, et al. The Challenges of Producing Bi-layer Tablet: A Review. Journal of Drug Delivery and Therapeutics, 2021, 11. Jg., Nr. 4-S, S. 171-175