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Does Tabletability Really Improve With Decreased Diameters of Tablet Punches?

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INTRODUCTION

In 1989, Pich and Moest patented mini-tablets containing 99.5% pancreatin. In their investigations the same formulation should be tableted to 10 mm tablets, which failed however [1]. Lennartz and Mielck tableted paracetamol-lactose mixtures with 1.5, 2,3 and 5 mm punches and showed that the mini-tablets revealed higher mechanical stable [2]. In this study four different excipients should be investigated regarding their tabletability and compactability properties in dependence of the used punch size. Microcrystalline Cellulose (MCC) and lactose were chosen as frequently used excipients in tablet formulation. In addition functionalized isomalt and co-processed mannitol were used as novel excipients for direct compression. Aim of this study is to investigate, if the observations of Pich and Moest and Lennartz and Mielck were highly dependent on the used formulation, or if tablet properties are independent form the formulation but depend on the punch diameters. A more systematic and detailed study on this topic can be found in literature [3].

MATERIALS AND METHODS

MCC (Vivapur® 102, JRS Pharma), lactose monohydrate (Tablettose® 80, Meggle), co-processed mannitol (Ludiflash®, BASF) and functionalized isomalt (galenIQ™721, Beneo-Palatinit) were chosen as model excipients. Tablets were manufactured at five different tableting pressures on tablet press Styl'One Evolution (Medel'Pharm) and external lubrication with magnesium stearate (Parteck® LUB MST, Merck KGaA) or sodium stearyl fumarate (PRUV®, JRS Pharma). The mini-tablets (MT) were produced by manual die filling using 1 and 2 mm concave 19-tip tooling (Ritter-Pharma) and 3 mm concave 19-tip tooling (Natoli Engineering). For producing flat faced tablets, 8 mm (Ritter-Pharma) and 11.28 mm punches (Natoli Engineering) were used. Breaking force was determined using Texture Analyser TA.XT.plus (Stable Micro Systems) for MT and for 8 and 11.28 mm tablets SmartTest ST 50 (Sotax). Tensile strengths were calculated according to Fell and Newton [4]. Solid Fraction was calculated with the following equation $SF = \frac{\rho(tablet)}{\rho(powder)}$.

RESULTS AND DISCUSSION

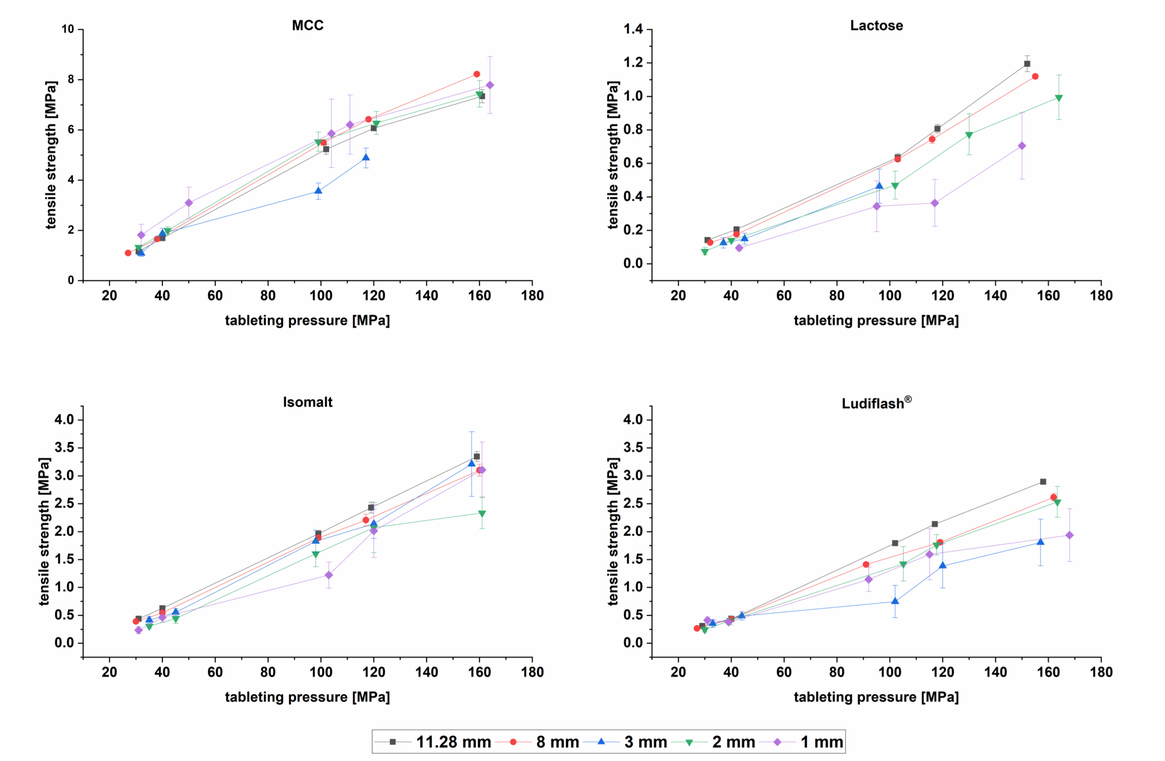

Figure 1. Tabletability plot of MCC, lactose, isomalt and Ludiflash®. n=10, mean ± CI (95 %)

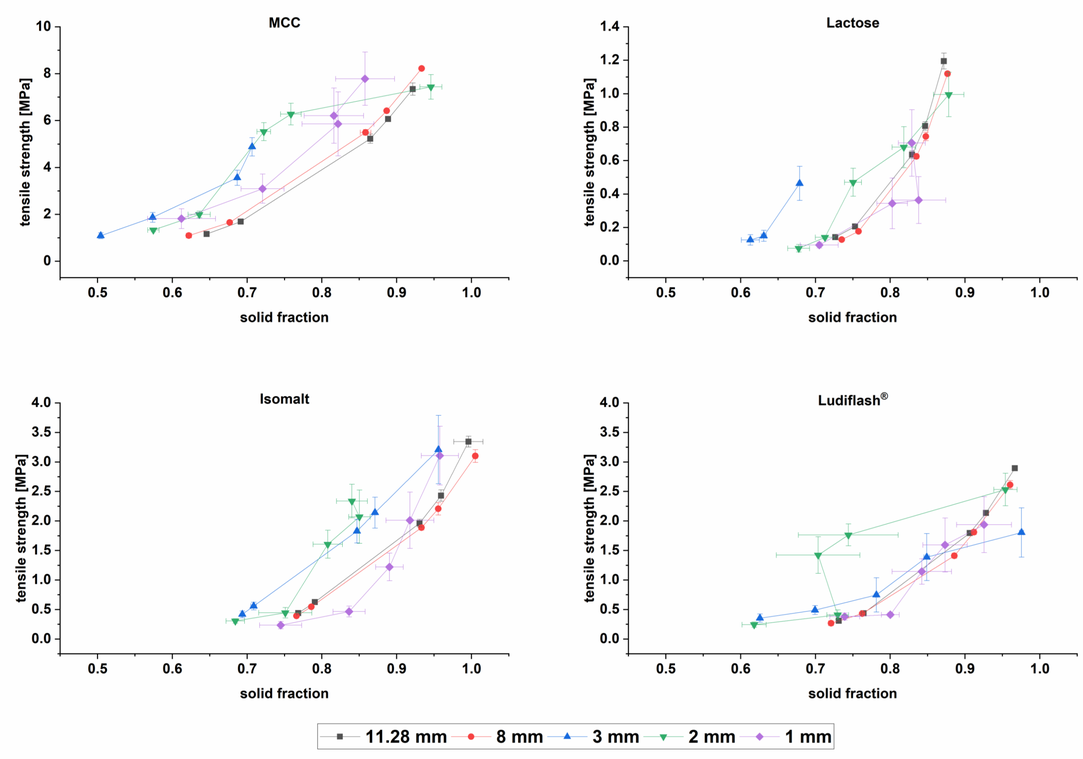

Figure 2. Compactibility plots of MCC, lactose, isomalt and Ludiflash®. n=10, mean ± CI (95 %)

The tabletability plot reveal that no significant improvements of tabletability could be achieved by reducing the tablet dimensions. Only for 1 mm MCC mini-tablets tabletability seems to be improved at lower tableting pressures compared to 8 or 11.28 mm tablets. Lactose shows the lowest TS in comparison to the other excipients. Only with conventionally sized tablets TS above 1 MPa are reached at the highest tableting pressures. 3 mm lactose mini-tablets could not be manufactured at higher tableting pressures as ejection forces above 1 kN were reached, despite of a sufficient lubrication.
The ready-to-use excipients isomalt and Ludiflash® show comparable tabletability plots. For both excipients TS between 1 and 2 MPa are reached at comparable tableting pressures. However, a better tabletability because of a smaller tablet size was neither found here.

Compactibility plots of the excipients shows in most cases a better compactibility towards mini-tablets in comparison to conventionally sized tablets. Higher TS are reached at comparable lower SF, when the tablet size is reduced by using 2 or 3 mm punches.
Obviously the SF could not be determined accurate for 1 mm mini-tablets, which is represented by the high scattering. Therefore the significance of the results is questionable.
It has to be mentioned that the data were obtained by tableting at targeted tableting pressures and not SF, which would explain the scattering of SF.
However, these results are coherent with data reported in various literature, where compactibility is also improved by reducing the tablet size.

CONCLUSION

This study shows that only compactibility is improved by reducing the tablet size, whereas tabletability is not. These findings are coherent with data from literature. Whether a formulation can be better manufactured seems to be linked more to the properties of the formulation itself, rather than to the dimension of the final dosage form.

References: [1] C.H. Pich and T. Moest; Magensaftresistent überzogene zylindrische Pankreatin-Mikrotabletten; EU Patent: 0 166 315 B1 (1989)
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[3] Lura et al. Tableting of mini-tablets in comparison with conventionally sized tablets: A comparison of tableting properties and tablet dimensions<; Int. J. Pharm X 2 (2020)
[4] J.T. Fell and J.M. Newton; Determination of tablet strength by diamteral compression test; J.Pharm. Sci 59:668-691 (1970)