The Effect of Tamping Force on Bi-Layer Tablet Robustness

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Introduction

Bi-layer tablets enable the combination of chemically incompatible Active Pharmaceutical Ingredients (API) in a single dosage form due to physical separation. They also offer the possibility to combine layers with different drug release profiles[1,2].
The adherence between the tablet layers influences the bi-layer tablets' quality. A common problem is layer-separation. Insufficient bonding capacity between the tablet layers leads to delamination[2]. Appropriate compression forces for the first and second layer during tableting are crucial in order to avoid separation of the two layers and to enable a high tablet quality[3,4].

Aim of the Study

The aim of this study was to analyse the effect of tamping force on the bi-layer tablet robustness. Appropriate tamping forces of < 1 kN and excessive tamping forces of 2 and 4 kN were chosen. Biplane bi-layer tablets were compared in terms of adherence between the two layers and crushing strength. In addition, the difference of appropriate and excessive tamping force was visualised by preparing cross sections of convex bi-layer tablets.

Material and Methods

Dibasic calcium phosphate dihydrate (EMCOMPRESS®), silicified microcrystalline cellulose (PROSOLV® SMCC 90) and sodium stearyl fumarate (PRUV®) were provided by JRS PHARMA GmbH & Co. KG (Rosenberg, Germany). Iron oxide, black, with a particle size < 150 µm was purchased from Merck KGaA (Darmstadt, Germany).

Formulations
The quantitative composition of the two formulations used for the production of the bi-layer tablets is shown in Table 1. Both formulations were blended for 3 min at 24 rpm using a freefall blender Brunimat Type Porta (Brunitec Suisse, Ermatingen, Switzerland).
Biplane bi-layer tablets consisted of 450 mg of formulation S and 600 mg of formulation D. For convex bi-layer tablets, 500 mg of formulation S and 700 mg of formulation D were used.

Ingredient	Formulation S	Formulation D
Dibasic Calcium Phosphate Dihydrate	–	99 %
Silicified Microcrystalline Cellulose	94 %	–
Iron Oxide, Black	5 %	–
Sodium Stearyl Fumarate	1 %	1 %

Tab. 1 Tested Formulations

Tableting
Both formulations were compacted into biplane bi-layer tablets with a diameter of 13 mm using the tablet press 1200i (Fette Compacting GmbH, Schwarzenbek, Germany). Tamping forces for the first layer were < 1 kN, 2 kN and 4 kN and compaction force for the second layer was 5 kN.
Additionally, convex bi-layer tablets with a diameter of 14 mm and a curvature radius of 14 mm were compressed using the tablet press EK0 (Korsch AG, Berlin, Germany). An appropriate tamping force and an excessive tamping force were applied to the first layer.

Functional Tablet Characteristics
Crushing strength was measured with model TBH 425 TD from Erweka GmbH (Langen, Germany). The force to separate the two tablet layers was analysed with the method "Tablet coating adhesion force" using a Texture Analyser TA.TX.plus from Winopal Forschungsbedarf GmbH (Elze, Germany). Biplane bi-layer tablets were fixed using superglue (Sekundenkleber blitzschnell PIPETTE was purchased from UHU GmbH & Co. KG, Bühl, Germany) both on upper and lower tablet surface. 4900 g were applied for 60 s with the upper punch, which was then lifted with a speed of 10 mm/s tearing the two layers apart.

Results and Discussion

Biplane Bi-Layer Tablets
Tablet Layer Separation
Adherence between the two tablet layers was found to depend on the applied tamping force. The lowest force to separate the two layers was analysed for tablets compressed with 4 kN tamping force.
If a tamping force of 2 kN was applied, a higher force was necessary to separate the bi-layer tablets at the layers' interface. Tablets compressed with an appropriate tamping force of < 1 kN could not be separated at the interface but broke within the layer consisting of the formulation D (Table 2).

Tamping Force	Formulation Used as First Layer	Force to Separate Tablet Layers [N]
< 1 kN	Formulation S	39.2*
	Formulation D	35.2*
2 kN	Formulation S	29.6
	Formulation D	26.5
4 kN	Formulation S	17.8
	Formulation D	20.3

* Tablets could not be separated between their two layers but broke within the layer of formulation D.

Tab. 2 Force to Separate Tablet Layers of Biplane Bi-Layer Tablets Depending on Applied Tamping Force and First Layer Composition

Tablet Hardness
When measured individually, the hardness of the first layer consisting of formulation S was found to be higher than for formulation D. This is due to the enhanced compressibility of silicified microcrystalline cellulose in comparison to dibasic calcium phosphate dihydrate. Similar tablet hardnesses were analysed for bi-layer tablets compressed with a final compression force of 5 kN independent of the tamping force (Table 3).

Tamping Force	Formulation of First Tablet Layer	Hardness of First Layer [N]	Tablet Hardness of Bi-Layer Tablet [N]
< 1 kN	Formulation S	7	160
	Formulation D	5	180
2 kN	Formulation S	78	172
	Formulation D	8	177
4 kN	Formulation S	123	169
	Formulation D	11	180

Tab. 3 Tablet Hardnesses of First Layer and of Bi-Layer Tablets Depending on the Tamping Force

Interestingly, layer adhesion and tablet hardness were not affected by the order in which the layers were compressed, i.e. whether formulation S or D was used as first layer.

Convex Bi-Layer Tablets
Cross Sections
The effect of tamping force was visualised by the cross section of convex bi-layer tablets. A horizontal line separated the tablet layers if an appropriate tamping force was applied (Figure 1 A and C). In contrast, the separation line between the layers was convex shaped if an excessive tamping force was applied (Figure 1 B and D). In each case, the black layer consists of formulation S and the white layer of formulation D.

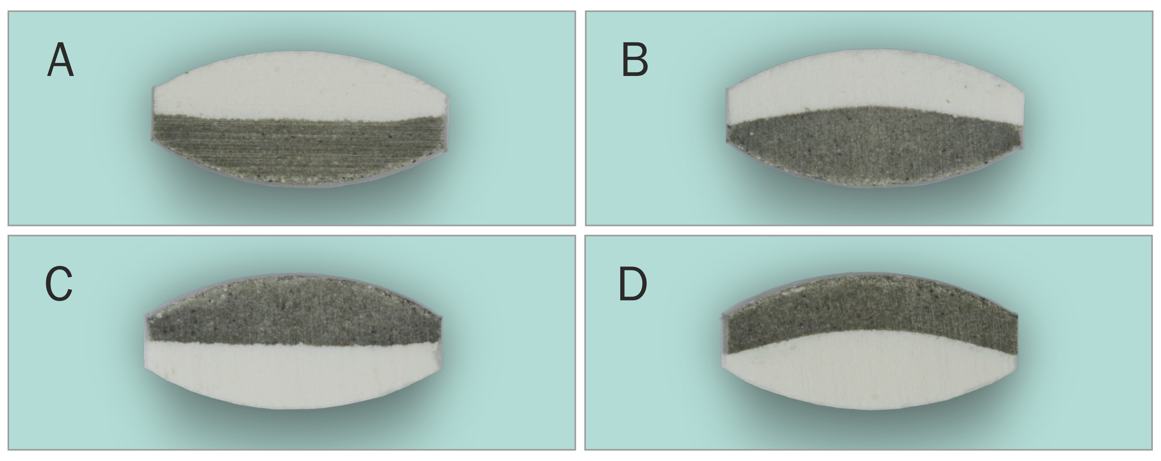

Fig. 1 Cross Sections of Convex Bi-Layer Tablets

Conclusion

The adherence between the tablet layers was analysed with a Texture Analyser, which measured the force needed to tear the layers apart. The tamping force influenced the bi-layer tablet robustness. Tablets compressed with an appropriate tamping force of < 1 kN were the most robust and could not be separated between their two layers whereas the lowest force to separate the layers was needed for tablets compressed with a tamping force of 4 kN. No differences in tablet hardness for bi-layer tablets compressed with different tamping forces could be seen indicating that this parameter in contrast to the tablet layer-separation is not suited for the analysis on the mechanical stability of bi-layer tablets.

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