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Short communication

Improved dissolution of immediate release tablets through optimization of compression force: The role of granule breakage

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Introduction

Tablet dissolution is influenced by multiple formulation and process parameters, including granulation conditions, moisture content, tablet hardness, and compression force (Augsburger & Hoag, 2008).

This study evaluated the impact of different compression forces on the dissolution performance of immediate release (IR) tablets as part of compression process optimization. Conventionally, higher compression forces are associated with increased tablet hardness, prolonged disintegration time, and consequently slower dissolution. Therefore, lower tablet hardness limits are often targeted to improve dissolution performance. However, this simplified relationship does not universally apply to all formulations, particularly for granulated systems where compression may alter granule structure (Adeleye, 2019).

Materials and methods

The IR tablets containing BCS class I API were produced by standard process of wet granulation. An optimization study of the compression process was performed using different compression forces and tableting speeds on a Fette tablet press. Tablets were tested for hardness, disintegration time, and dissolution. Tablet hardness was measured using a standard hardness tester. Disintegration time was determined according to the relevant pharmacopeial method. Dissolution testing was performed according to the approved method using the paddle apparatus, with evaluation at 15 minutes as Stage 1 acceptance criteria.

Results and discussion

During this study nine individual compression cases were evaluated. Compression force ranged from approximately 6.7 – 7.5 kN (low), 16-17 kN (medium) to 23-25.8 kN (high), combined with three different tableting speeds – 50 000 tbl/h (low), 87 000 tbl/h (intermediate) and 125 000 tbl/h (high). Optimal dissolution performance was observed in Case 2, where high compression force (25.8 kN) was applied in combination with a low tableting speed (50,000 tablets/h). Under these conditions, the average dissolution at 15 minutes was 89.09%, with a minimum value of 85.22% and a maximum of 93.52%.

Improved dissolution performance was consistently observed at higher compression forces, despite increased tablet hardness. In contrast, tablets produced at lower compression forces exhibited increased variability and a higher incidence of dissolution results below the specification limit

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(Case 3, 6.7 kN: average 82.31%, min 79.66%, max 88.99%; Case 4, 6.7 kN: average 83.99%, min 79.66%, max 87.13%).

This effect is result of compression-induced granule breakage. At higher compression forces, mechanical stress is applied to granules, leading to fragmentation of the granules (Jange et al., 2023). These fragmented granules and newly generated surfaces increase the effective surface area available for interaction with the dissolution medium, which results with enhanced liquid penetration into the tablet matrix. According to the results obtained during this study, granule disruption has a stronger effect on dissolution than the reduced porosity of more densely compressed (higher hardness) tablets. Furthermore, the improved dissolution observed at higher compression forces was more pronounced at lower tableting speeds. Reduced tableting speed likely allows for longer dwell time during compression, promoting more uniform stress distribution and more effective granule deformation and breakage. This combination of high compression force and sufficient dwell time may therefore play a critical role in achieving optimal tablet microstructure and dissolution performance.

Overall, the results indicate that tablet hardness by itself does not reliably predict dissolution performance. A better understanding of how the formulation responds to compression, especially granule behavior, is therefore important during process optimization (Jange et al., 2023).

The study also demonstrates that compression force and tableting speed should be evaluated together, rather than separately, to achieve consistent and reproducible dissolution results.

Conclusion

Although the initially defined target limits for tablet hardness were set at the lower specification limit (4-5 kP), where they were expected to have faster disintegration and consequently faster dissolution, the results demonstrated negative correlation, optimal dissolution was achieved at higher compression forces, corresponding to a tablet hardness range of 6-7 kP.

While higher compression force is generally associated with slower tablet dissolution due to increase hardness and reduced porosity, it can sometimes lead to faster dissolution, primarily, through the mechanism of granule breakage. A higher compression force of around 22 kN likely affects the internal structure of the tablet, leading to breakage of the granules and as a result, water/dissolution medium can penetrate the tablet more easily, which improves dissolution.

References

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