Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 155 - 156 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.075
Short communication

Effects of roll pressure during roller compaction on ribbon properties, granule characteristics and dissolution behavior of a BCS class IV drug product

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Introduction

Roller compaction is a dry granulation method used to enhance powder flow and compressibility without exposing materials to moisture or heat. A powder blend is compressed between two counter-rotating rolls to form a ribbon, which is then milled into granules. (Kleinebudde, 2004). BCS Class IV drugs exhibit poor solubility and poor permeability, making them sensitive to process-induced changes (Amidon et al., 1995). The aim of this study was to evaluate the effects of different roll pressure levels on the ribbon tensile strength, granule porosity and dissolution of the active substance from the film-coated tablets.

Materials and methods

Drug substance and formulation

A compaction-sensitive BCS Class IV drug substance, prone to increases in related substances and degradation products, was used. It was blended with appropriate excipients in fixed proportions, maintained constant across all batches, processed to film-coated tablets.

Roller compaction and granulation

Compaction was performed on a Chillsonator IR 220 roller compactor with fixed parameters: feeding screw rate:15 rpm, vertical pre-compression rate: 115 rpm, roll speed: 3 rpm. Roll pressure was varied at: low (5 bar), medium (10 bar), and high (15 bar) level. The roll-pressure range was intentionally narrow because the API exhibits high sensitivity to mechanical stress.

Ribbon characterization

The mechanical strength of the ribbons was evaluated by performing a three-point bending test using a Brookfield texture analyzer with an appropriate three-point bend fixture and blade. The obtained values for load force at fracture point, the fixture support span, sample width and thickness, was used to calculate the modulus of rupture for each sample (Lochan, 2024).

Granulate characterization

Porosity of granules was calculated using granule bulk density and skeletal density measured by Accupyc 1330 helium pycnometer. The obtained values for skeletal density were used for calculating the percent of pores in each sa(Web A. Paul, 2001).

Tableting and film coating

Using a rotary tablet press Korsch XL 100 the final blends were compressed into round, biconvex tablets at a target compression force of 6 kN, pre-compression force at 0.2 kN and speed of 20-30 rpm, identical for all batches. Tablets were coated in

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an Ohara LabCoat pan coater to a target weight gain identical across batches.

Dissolution testing

Dissolution testing performed according to Ph. Eur. 2.9.3 using USP Apparatus II (paddle) under identical conditions for every sample.

Results and discussion

Effect of roll pressure on ribbon tensile strength

Ribbon tensile strength increased with the increase of roll pressure, yielding values of 1.897 MPa, 2.832 MPa, and 8.166 MPa at low, medium, and high pressure levels, respectively. This positive relationship is expected because increasing roll pressure and increase in specific compaction force increases the extent of densification in the nip zone, promoting greater bond formation under higher compaction forces (Kleinebudde, 2004;). Consistent with this, increasing the roll pressure has been shown to produce harder/stronger ribbons.

Effect of roll pressure on granule porosity

Granule porosity decreased with increasing roll pressure: 67.4 %, 65.6 %, and 60.8 % at low, medium, and high pressure levels, respectively. Higher roll forces lead to greater densification, reduced pore volume and lower capillary networks leading to lower access for fluid penetration into the tablet and granules (Sun, 2010). In accordance to the results, increasing the roll pressure decreases the percentage of pores of the granules.

Effect of roll pressure on dissolution performance

The impact of roll pressure on dissolution was assessed via a bracketing strategy, with tests performed on batches manufactured at the minimum and maximum roll pressures. Across the entire dissolution profile, samples produced at 5 bar exhibited a faster dissolution than those produced at 15 bar, with the most pronounced difference at the early time points. Dissolution at 5 min was 56% at 5 bar versus 20% at 15 bar, and this difference persisted at 10 min (67% vs 48%) and 30 min (87% vs 77%). Although the profiles began to converge over time, material produced at the lower roll pressure achieved a higher extent of dissolution by 45 min (91% at 5 bar compared with 83% at 15 bar), indicating that increased roll pressure slows dissolution, particularly during the initial phase. Lower dissolution rate at higher pressures results from greater granule densification which reduces the surface area available for drug-solvent contact, limiting dissolution rate in accordance with the Noyes-Whitney equation. The sensitivity of the BCS Class IV drug underscores dissolution as the absorption rate-limiting step; given low intrinsic permeability, process-related changes in dissolution can directly compromise bioavailability. (Amidon et al., 1995).

Conclusion

Roll pressure during compaction significantly affects mechanical strength of ribbons, porosity of granules and in vitro dissolution. Higher roll pressures produced stronger, denser ribbons with reduced porosity, resulting in progressively lower drug release. The underlying mechanisms include reduced surface area, impaired liquid penetration, increased interparticle bonds and decreased tablet porosity after recompression. Careful optimization of roll pressure is therefore essential to maintain dissolution performance and insure appropriate bioavailability for BCS Class IV drug products.

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