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Short communication

Influence of intra- and extragranular excipient composition on dissolution and punch sticking in sildenafil film-coated tablets

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Introduction

Sildenafil citrate is a BCS Class II active substance, characterized by low aqueous solubility and high permeability, making the achievement of adequate and reproducible dissolution a central formulation challenge (Miranda et al., 2018).

The development of sildenafil 50 mg film-coated tablets was conducted using high shear wet granulation. This manufacturing technique promotes uniform drug distribution, improved compressibility, and consistent granule properties. However, the selection and proportion of intra- and extragranular excipients determine both the dissolution profile of the finished product and the tablet's mass tendency to stick to punch faces during compression.

Materials and methods

The active substance is micronized sildenafil citrate with a particle size d90 of less than 20µm from Amoli Organics. Excipients included: microcrystalline cellulose (MCC) (Vivapur® 101 and Vivapur® 102), calcium hydrogen phosphate, anhydrous (Emcompress® anhydrous) and croscarmellose sodium (Vivasol®) from JRS, calcium hydrogen phosphate, dihydrate (PharSQ® Fine D 14) from Budenheim, povidone (Kollidon® 30) from BASF, talc from Imerys Talc, magnesium stearate from Mosselman and hypromellose-based film coating system from Colorcon.

Method of production

Four batches were manufactured using high shear granulation. Each batch contained 70.24 mg sildenafil citrate with croscarmellose sodium, talc and magnesium stearate as a constant extragranular phase, and a film coating of 15 mg per tablet. The key variable across batches was the type and ratio of diluents and binders used in the intragranular phase.

Excipient variations

Batch 1 contained Vivapur 101 (26.5%) intragranularly, with Emcompress anhydrous (20.09%) and Vivapur 102 (18%) extragranularly. Batch 2 consisted of a higher level of Vivapur 101 (34.5%) intragranularly and calcium hydrogen phosphate, dihydrate (20.09%) also intragranularly, with Vivapur 102 (10%) extragranularly. Batch 3 employed a substantially higher intragranular MCC content (Vivapur 101, 44.5%) without any intragranular phosphate, and included Emcompress anhydrous (20.09%) extragranularly, with no extragranular Vivapur 102. Batch 4 represented the most distinct formulation: the intragranular phase contained Kollidon 30 (0.48%) as a binder without any MCC, while the extragranular phase comprised

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a high level of Vivapur 102 (44.02%) and Emcompress anhydrous (20.09%).

As shown above, MCC grade and intra- versus extragranular location, calcium hydrogen phosphate hydration state and location, and the presence of povidone all varied simultaneously across the four batches. Because there variables were not changed independently of one another, this study should therefore be regarded as an exploratory formulation comparison.

Evaluation parameters

Each batch was evaluated for assay, uniformity of dosage units, dissolution (0.1M HCl, pH 1.2, Ph. Eur. Apparatus II, minimum 75% (Q) at 30 min), tablet hardness, disintegration time, and sticking.

Results and discussion

All four batches met the dissolution specification, with drug release values of 93.52%, 92.44%, 90.36%, and 88.34% for batches 1, 2, 3, and 4, respectively. The use of micronized sildenafil citrate was a key factor for achieving these dissolution results since reduced particle size increases specific surface area available for wetting and drug release. Intragranular MCC generally contributed favorably to dissolution (>90%) in all batches produced. However, best dissolution results were seen when MCC was split intra- and extragranularly as in batch 1. A slightly decreased dissolution (90.36%) in batch 3 might be because of trapped API in the compact MCC granules. Batch 4, which lacked intragranular MCC showed the lowest dissolution (88.34%), suggesting that without the disintegrant-like functionality of MCC and with the strong binding capacity of povidone, drug release is compromised.

Sildenafil citrate is a weak base with reduced solubility at higher pH. Therefore, increasing the microenvironmental pH may potentially slow drug release. Calcium hydrogen phosphate anhydrous and its dihydrate form are both alkaline diluents, with a pH of approximately 7.0–8.0 in aqueous suspension. When used intragranularly, they are co-processed with the drug during granulation, resulting in intimate mixing at particle level, while when used extragranularly their contact is less intimate. Batches 1 and 2 exhibited comparable dissolution values. This suggests that under the investigated conditions, the intra- or extragranular location and hydration form of calcium hydrogen phosphate had no evident influence on sildenafil dissolution.

Regarding sticking to punches, batches 1 and 2 showed significant adhesion, likely due to the relatively lower intragranular MCC content and, in batch 2, the use of calcium hydrogen phosphate dihydrate, which may release moisture during compaction and promote surface tackiness. The lower MCC level in batch 1 may also have limited binding capacity, allowing the granulate to deform and adhere under compression. By contrast, batch 3, with the highest intragranular MCC level (44.5%), yielded a stable granulate with no sticking issues. This was also the case with batch 4 where the widely used povidone contributed to compact tablets.

Tablet hardness, disintegration (<1min), content uniformity and assay were acceptable across all batches and within acceptance limits.

Conclusion

The results indicate that the overall intragranular excipient composition is associated with both the dissolution performance and the compressibility behavior of sildenafil 50 mg film-coated tablets. Micronized sildenafil citrate provided the necessary surface area for dissolution, but the surrounding excipient matrix determined the extent of drug release. A high intragranular MCC content, as seen in batch 3, delivered the most favorable outcomes: satisfactory dissolution (> 90%) and no sticking to punches. The inclusion of calcium hydrogen phosphate dihydrate intragranularly (batch 2) was associated with compression problems and the exclusion of intragranular MCC with only povidone as a binder slightly decreased dissolution, but still produced robust tablets. These findings highlight the importance of balancing intragranular diluent and binder selection to achieve a robust, manufacturable tablet formulation.

References

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