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Short communication

Development of a robust and discriminatory dissolution method for Amlodipine/Atorvastatin 10mg/10mg film-coated tablets

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Introduction

The dissolution test is a highly significant in vitro test for characterizing the performance of pharmaceutical products. As a critical analytical tool, dissolution testing provides reliable insight into in vitro drug availability and prediction of in vivo performance, while also supporting formulation development, optimization and quality control by ensuring batch-to-batch consistency and identifying variables that may affect bioavailability (Barsagade et al., 2021).

The selection of dissolution test conditions is based on the physicochemical characteristics of the drug substance and physiological conditions after oral administration. In this context, Biopharmaceutical Classification System (BCS) plays a critical role in dissolution method development by linking solubility and permeability**.** Various experimental conditions, including rotation speeds, different apparatus and dissolution media, must be evaluated to develop a robust dissolution method with adequate discriminatory power (European Medicines Agency [EMA], 2017).

The test product, Amlodipine/Atorvastatin 10 mg/10 mg film-coated tablets is formulated as immediate release solid oral dosage form. According to BCS, atorvastatin calcium trihydrate is classified as Class II drug which possesses low solubility and high permeability. With pKa of ~4.5, atorvastatin calcium trihydrate exhibits pH-dependent solubility, showing enhanced solubility and rapid dissolution at intestinal pH (~6.5). In contrast, amlodipine besylate is classified as Class I drug, which possess high solubility and high permeability. With pKa of ~8.14, amlodipine besylate also exhibits pH-dependent solubility; however, it remains sufficiently soluble across a broad physiological pH range.

The aim of this study was to develop and optimize a robust and discriminatory dissolution method for both active substances, taking into account their different physicochemical and biopharmaceutical characteristics.

Materials and methods

Amlodipine besylate and Atorvastatin calcium trihydrate working standards were used, obtained from Alkaloid AD Skopje, North Macedonia. Potassium dihydrogen phosphate and sodium hydroxide were also supplied by Alkaloid AD Skopje, North Macedonia, while ammonium formate, formic acid, acetonitrile and methanol were purchased from Merck, Germany. All reagents used were of analytical grade.

The dissolution tests were performed on Agilent 708-DS dissolution apparatus. Samples were analyzed on Thermo Dionex 3000 HPLC system

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using a LiChrospher 60 RP-Select B column (125 mm x 4.0 mm i.d; 5 µm) maintained at 25°C. The mobile phase consisted of 0.01M ammonium formate buffer solution pH 2.5 and acetonitrile (50:50 *v/v*), with a flow rate 1.0 mL/min. Analytes were detected at 256 nm and the total run time was 6 minutes. 20 µL sample, maintained at an autosampler temperature of 25 °C, was injected into the HPLC system.

Based on FDA (U.S. Food and Drug Administration) recommendations, dissolution testing was performed using apparatus II in 900 mL phosphate buffer (pH 6.8) at 75 rpm. Dissolution profiles were obtained at time points 5, 10, 15, 20, 30 and 45 minutes; 30 minutes was chosen as dissolution endpoint.

Results and discussion

Influence of dissolution medium volume

The effect of dissolution medium volume was evaluated using 500 mL and 900 mL phosphate buffer (pH 6.8). In 500 mL, high variability (RSD > 18% for both active substances) was attributed to poor hydrodynamic conditions, which promoted coning and resulted in incomplete drug release at the endpoint (64% for amlodipine and 60% for atorvastatin). Therefore, 900 mL was selected as the most appropriate medium volume for dissolution testing.

Influence of rotation speed

Different paddle rotation speeds were evaluated at 50, 75 and 100 rpm. After 30 minutes, the results obtained at 50 rpm were below the target Q values for both components (56% for amlodipine and 47% for atorvastatin), with high variability (RSD > 13%), indicating incomplete release of both substances from tablets. Increasing the rotation speed to 75 rpm significantly improved drug release (94% and 93% for amlodipine and atorvastatin, respectively), with acceptable variability (RSD of 4.0% for amlodipine and 0.7% for atorvastatin). Although 100 rpm resulted in nearly complete dissolution (99% for amlodipine and 96% for atorvastatin), it likely reduced the discriminatory power of the method. Therefore, 75 rpm was considered as optimal, providing adequate dissolution and acceptable reproducibility.

Influence of different type apparatus

Additionally, apparatus I (basket) was evaluated at 100 rpm. Although comparable drug release profile was obtained, the paddle apparatus at moderate agitation provided more appropriate hydrodynamic conditions and better discriminatory ability. The higher agitation with baskets leads to excessively rapid dissolution, that potentially can mask formulation differences. Therefore, the paddle apparatus was selected as preferred method. In accordance with USP and BP monographs, PTFE-coated paddles were used to prevent degradation of amlodipine upon exposure to stainless steel.

Discriminatory properties of the dissolution method

The discriminatory capability of the method was confirmed using a formulation with modified excipient composition, which resulted in significantly reduced drug release at all evaluated time points for both active substances.

Conclusion

The results indicate that pH 6.8, together with selected method parameters (900 mL, 75 rpm, apparatus II) are reflective of the product characteristics and are able to distinguish differences in the formulation. The obtained results demonstrate that the developed method is robust, discriminatory and suitable for routine quality control.

References

Barsagade, P. et al., 2021. Review Article of Dissolution Test Method Development and Validation of Dosage Form by Using RP-HPLC. International Journal of Pharmaceutical Sciences Review and Research,70(1). https://doi.org/10.47583/ijpsrr.2021.v70i01.005

European Medicines Agency, 2017. Reflection paper on the dissolution specification for generic solid oral immediate release products with systemic action EMA/CHMP/CVMP/QWP/336031/2017

U.S. Food and Drug Administration. Dissolution methods database. https://www.fda.gov/drugs/drug-approvals-and-databases/dissolution-methods-database