Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 267 - 268 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.128
Short communication

Impact of excipient change with equivalent functionality on API extraction and its detection by a discriminatory HPLC method in prolonged-release tablets

Marija Velichkovska*, Marijana Bozinovska, Tina Achkoska, Oja Memed, Packa Antovska

Institute for Research and Development, Alkaloid AD-Skopje, Blv. Aleksandar Makedonski 12, 1000 Skopje, Macedonia

Introduction

Prolonged-release tablet formulations present specific analytical challenges due to their complex matrix structures and the presence of excipients that may influence drug release and extraction efficiency during sample preparation (Aulton and Taylor, 2018). Even minor modifications in excipient composition may significantly affect the interaction between the formulation matrix and the extraction medium, thereby impacting analytical performance (Snyder et al., 2010).

In this study, a comparative evaluation was performed between a reference product and two test formulations containing the same active pharmaceutical ingredient (API) but differing in excipient composition. The key difference between the formulations was the use of two lubricants with equivalent functionality: magnesium stearate and glyceryl behenate.

Although both excipients serve as lubricants, their physicochemical properties differ significantly, which may influence the extraction behavior of the API during sample preparation. Glyceryl behenate is a lipid-based excipient widely used as a lubricant and matrix-forming agent in modified-release formulations. Due to its hydrophobic nature, low aqueous solubility, and low density, it may float in the extraction medium and hinder proper wetting and dispersion of the formulation matrix (Rowe et al., 2009). As a result, incomplete extraction of the API and variability in assay results may occur.

The comparison of the two test formulations demonstrated that the change in lubricant significantly affected API extraction. Importantly, these differences were successfully detected using an existing HPLC method, indicating its discriminatory capability to capture formulation-related variations.

Therefore, the aim of this study was to evaluate the impact of excipient substitution with equivalent functionality on API extraction during sample preparation and to assess the ability of the applied HPLC method to discriminate between formulations with different lubricant characteristics.

Materials and methods

The study was performed on prolonged-release tablet formulations containing same API . The samples investigated included a reference product and two test formulations differing in excipient composition, specifically in the type of lubricant used. One test formulation contained magnesium stearate, while the other contained glyceryl behenate as a lubricant.

*marsova@alkaloid.com.mk

Sample preparation for HPLC assay was performed using a uniform analytical procedure applied to all three formulations. The process involved dispersion of the tablets in an appropriate solvent system, followed by mechanical agitation to ensure adequate matrix breakdown and API release.

All samples were analyzed using a validated HPLC method under standard chromatographic conditions. The method was applied without modification to all investigated formulations, enabling direct comparison of API extraction behavior and assessment of the impact of excipient composition.

Results and discussion

The comparative evaluation between the reference product and the two test formulations demonstrated a clear impact of excipient composition on API extraction. Although all formulations contained the same API as well as lubricants with equivalent functionality, significant differences in assay results were observed.

The test formulation containing magnesium stearate showed results comparable to the reference product, with consistent and satisfactory API recovery. This indicates that the extraction of the API under the applied conditions was efficient and not affected by the presence of this excipient.

In contrast, the test formulation containing glyceryl behenate exhibited insufficient extraction of the API, resulting in lower assay values. This difference can be attributed to the distinct physicochemical properties of glyceryl behenate. As a lipid-based and highly hydrophobic excipient with low aqueous solubility, it can hinder effective interaction between the extraction medium and the formulation matrix, thus limiting API release during sample preparation (Rowe et al., 2009).

Importantly, all formulations were analyzed using the same HPLC method under identical conditions. The method successfully detected the differences in API extraction between the two test formulations, indicating its sensitivity to formulation-related variations. These findings demonstrate that even minor changes in excipient composition, involving components with equivalent functional roles, can have a significant impact on API extraction.

At the same time, the ability of the applied HPLC method to capture these differences confirms its discriminatory capability.

Conclusion

The results of this study demonstrate that substitution of excipients with equivalent functionality, such as lubricants, can significantly influence the extraction of the active pharmaceutical ingredient in prolonged-release tablet formulations. While the formulation containing magnesium stearate showed comparable performance to the reference product, the formulation with glyceryl behenate exhibited insufficient API extraction.

The applied HPLC method successfully detected these differences, confirming its discriminatory capability toward formulation changes.

However, the observed extraction limitations in the formulation containing glyceryl behenate indicate that further optimization of the analytical procedure is necessary in order to ensure accurate and reliable assay results for formulations containing hydrophobic excipients.

References

Aulton, M.E., Taylor, K., 2018. Aulton's Pharmaceutics: The Design and Manufacture of Medicines, 5th ed. Elsevier, London.

Rowe, R.C. et al., 2009. Handbook of Pharmaceutical Excipients, 6th ed. Pharmaceutical Press, London.

Snyder, L.R., et al., 2010. Introduction to Modern Liquid Chromatography, 3rd ed. Wiley, Hoboken.