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Short communication

Comparative sustainability assessment of green HPLC method for cefalexin determination

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Introduction

The growing demand for sustainable analytical practices has driven significant interest in green analytical chemistry, aiming to minimize the environmental footprint, health risks, and operational costs associated with conventional laboratory methodologies. High-performance liquid chromatography (HPLC), one of the most widely used analytical techniques in pharmaceutical analysis, typically relies on hazardous organic solvents such as acetonitrile (ACN) and methanol (MeOH). These solvents are associated with toxicity, volatility, flammability, and the generation of hazardous waste, contributing to negative environmental and occupational health impacts.

In response to these challenges, alternative chromatographic approaches have been proposed, including the use of water-rich mobile phases and bio-renewable solvents. Dimethyl isosorbide (DMI), a solvent derived from renewable resources, represents a promising green alternative due to its favorable safety and environmental profile. Furthermore, chromatographic approaches aligned with per-aqueous liquid chromatography (PALC) principles emphasize the use of predominantly aqueous mobile phases to reduce hazardous solvent consumption.

The aim of this study was to assess the chromatographic performance, as well as the economic, health, and environmental impact of a green silica-based HPLC strategy for the quantification of cefalexin in pharmaceutical dosage forms (capsules and suspension), compared with a conventional in-house HPLC method.

Materials and methods

Conventional method

The conventional in-house HPLC-UV method was performed using an XTerra RP-18 column (150 mm × 4.6 mm, 5 μm) with a mobile phase consisting of pH 3.0 buffer, methanol, and acetonitrile (85:5:10, *v/v/v*). The flow rate was 1.0 mL/min, injection volume 20 μL, and detection was carried out at 254 nm under ambient temperature conditions.

Green method

The green HPLC-UV method, based on a silica column and a mobile phase of 0.5% acetic acid and dimethyl isosorbide (90:10, *v/v*), was previously developed and validated (Damjanoska et al., 2026).

Results and discussion

Chromatographic performance

The developed green method (Damjanoska et al., in press) showed improved chromatographic

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efficiency, with reduced retention time (5.5 *vs.* 6.9 min) and total runtime (8 min *vs*. 12 min), enabling higher throughput and lower solvent consumption. A significant increase in the number of theoretical plates (9126 *vs*. 3251) confirmed enhanced column performance. Although the retention factor decreased (1.9 *vs*. 3.2), it remained acceptable, while backpressure slightly increased (194 *vs*. 174 bar) but remained operationally manageable. Peak symmetry remained comparable (1.2 *vs*. 1.3), ensuring reliable analytical results.

Economic impact

The economic evaluation demonstrated a significant reduction in analytical costs when applying the green method. For both dosage forms (capsules and oral suspension), the total costs per analysis and on an annual level were reduced by about 70%, resulting in substantial overall cost savings. These findings highlight the strong economic advantage of replacing conventional solvent systems with the DMI-based mobile phase.

Health impact

From a health and safety perspective, replacing conventional solvents significantly reduces occupational exposure risks. Both ACN and MeOH, commonly used in HPLC, are hazardous: ACN is highly flammable and toxic upon inhalation, ingestion, or skin contact, while MeOH is also toxic and poses risks of systemic effects (Joshi and Adhikari, 2019). In contrast, DMI is not classified as a hazardous substance according to safety data sheets, minimizing risks during handling, storage, and accidental exposure (Damjanoska et al., 2025).

Thus, the green method improves laboratory safety, reduces reliance on strict protective measures related to toxic solvents, and enhances overall working conditions for analysts.

Environmental impact

The environmental benefits of the green method are primarily attributed to the mobile phase composition. The use of 90% aqueous components reduces the consumption of hazardous organic solvents and the generation of toxic waste.

This approach aligns with green chromatography strategies and PALC concepts, aiming to minimize the environmental impact of analytical procedures. Replacing ACN and MeOH with the bio-renewable solvent DMI further reduces volatile organic compounds emissions and improves sustainability.

Additionally, the shorter runtime of the green method contributes to lower energy consumption and improved overall resource efficiency.

Conclusion

The green silica-based HPLC-UV method using DMI as a bio-renewable solvent provides a reliable, efficient, and sustainable alternative to conventional chromatographic approaches for the determination of cephalexin in capsules and suspension as dosage forms. In addition to comparable or improved analytical performance, the method demonstrates significant economic benefits, with up to 70% reduction in cost per analysis, as well as substantial environmental advantages through reduced solvent consumption and hazardous waste generation. Importantly, the method also offers clear health and safety improvement, by minimizing exposure to toxic and flammable solvents. The successful application of identical chromatographic conditions for different formulations further emphasizes the robustness and versatility of the method, making it highly suitable for routine pharmaceutical quality control within the framework of green analytical chemistry.

References

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