Macedonian pharmaceutical bulletin, 69 (Suppl 1) 221 - 222 (2023)
Online ISSN 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2023.69.03.108
Short communication

Experience-based insights for switching to greener chromatographic methods

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Introduction

The concept of green chromatographic method development is a contemporary approach that is getting more and more attention for the past 15 years. Concerning the needs of drug quality control labs in the pharma industry, the greenness of the method is not decisive for method development, but the emphasis is put on the quality of the obtained chromatographic data. Ideally, the chromatographic method should be green and "equpitable" at the same time (Marcinkowska et al., 2019). The obstacles for green method development could be seen in lack of time for transfer of the established methods, need for well-trained personnel, but mostly because of insufficient confidence that the green method will provide same or better analytical results.

This article presents the experience-based insights from switching of conventional liquid chromatography (LC) methods to their green alternatives. The development of three ethanol (EtOH) based LC methods for determination of different active substances (APIs) is presented. The aim of this study is to show that green LC method development is not a laborious task, and what is more important, EtOH based methods could provide the same or even better performance in comparison to the conventional acetonitrile (ACN) based LC methods.

Materials and methods

The analysis was conducted on Agilent Technologies 1100 Liquid Chromatography System, equipped with photo-diode array detector. The reference standards of rivaroxaban and ibuprofen were obtained from EDQM.

1. Method for assay determination of rivaroxaban (RIV)

An XBridge (Waters) C18 column (250 x 4.6 mm; 5 µm) was used for the determination of RIV. The chromatographic conditions were the same as for the conventional method [Çelebier et al., 2013], except that in the mobile phase acetonitrile (CAN) was replaced with EtOH and the ratio of water and EtOH was 60:40 (%, v/v).

2. Method for impurity determination of RIV

The separation was carried out on an XBridge (Waters) C18 column (250 x 4.6 mm; 5 µm), under gradient elution as described in the Ph.Eur.11 monograph for Rivaroxaban tablets [European Pharmacopoeia 11]. The modification in the gradient mode of the conventional Ph.Eur method is that EtOH was used as organic eluent instead of ACN.

3. Method for assay determination of ibuprofen (IBU)

The analysis was conducted on BDS Hypersil C18 (Thermo Fisher Scientific) (250 x 4.6 mm; 5 µm). The mobile phase consisted of 0.5 mL phosphoric acid in 1000

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mL water and EtOH in ration 40:60 (%, v/v). The rest of the chromatographic conditions were the same as for the ACN based conventional method (Elias & Hilal, 2023).

Results and discussion

The most commonly used strategy for "greening" of the LC methods is to replace the toxic organic solvents with green ones. Considering that EtOH is the preferred green alternative solvent (Nakov et al., 2022), it was selected as an organic eluent during the green method development. As a starting point, the chromatographic conditions of the conventional LC methods for the APIs, were taken into account. The percentage of ACN in the stated conventional methods was replaced with EtOH, while the rest of the chromatographic conditions were kept the same or slightly adjusted. The chromatograms obtained with EtOH as an organic eluent for method 1 (assay determination of RIV), method 2 (impurity determination of RIV) and method 3 (assay determination of IBU) are presented in Fig.1a to Fig.1c, respectively.

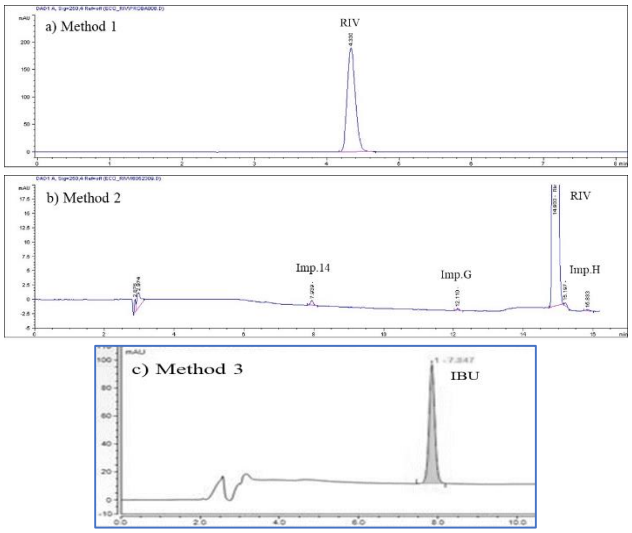

Fig. 1. Representative chromatograms: a) method 1, b) method 2 and c) method 3

The replacement of ACN with EtOH, in all three methods, didn't make disturbance of the critical chromatographic parameters and the proposed green methods fulfill the system suitability (SS) criteria (Table 1). The retention time (Rt) of APIs obtained with green methods were similar to the Rt obtained with the conventional ones: Rt 7.4 min for RIV in [Çelebier et al., 2013], Rt ~ 11 min for RIV in Ph.Eur. 11 and Rt 7.6 min for IBU in (Elias & Hilal, 2023). From a practical point of view, it is worth to mention that the column back-pressure in the methods was acceptable (below 300 bar).

Table 1. Results for system suitability parameters obtained with the ethanol based LC methods

Parameter of APIs	SS criteria	Method 1	Method 2	Method 3
Rt	/	4.3	14.9	7.8
As	0.8-1.8	1.2	1.1	1.0
N	>2000	7055	117745	14035
Rs	≥ 5.0	/	17.6(imp.G /RIV)	/

Conclusion

This research showed that switching from conventional to green LC methods could be easily accomplished. The replacement of ACN with EtOH in the mobile phase, even without additional adjustments, gives good starting chromatograms that fulfill the SS criteria. Hopefully this research could encourage more analysts to undertake the task of transfer of more conventional LC methods to green ones and alleviate the environmental burden on our planet without compromising the quality of analytical results.

Acknowledgements: This work was supported by the Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia (project code NIP.UKIM.22-23.19

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