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DEVELOPMENT AND VALIDATION OF SFC METHOD FOR DETERMINATION OF IMPURITIES IN ELVITEGRAVIR

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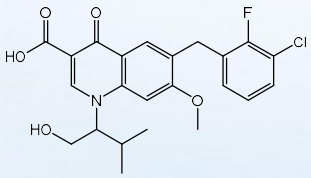
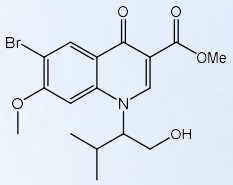
Introduction

Elvitegravir is a novel class of anti-retroviral agents that belongs to integrase strand transferase inhibitor, inhibits the integrase enzyme and prevents the virus replication [1]. In combination with other drugs, ELV is used to treat human immunodeficiency virus (HIV).

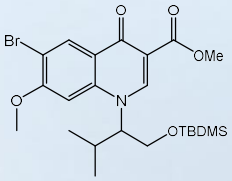
The chemical name of elvitegravir is 6(3-chloro-2-fluorobenzyl)-1-[(2S)-1-hydroxy-3-methylbutane-2-yl]-7-methoxy-4-oxo-1,4-dihzydroquinoline-3-carboxylic acid.



Elvitegravir



ELV Impurity 1



ELV Impurity 2

Figure 1: Chemical structure of elvitegravir and its related impurities.

Experimental

For the experiments an Agilent 1200 Infinity Series LC System and 1260 Infinity II SFC system (Agilent Technologies, Santa Clara, United States) was taken into service. Three different coulmns were used for method development. The column with the best separation of elvitegravir and related impurities was Lux Cellulose-3 250 x 4.6 mm, 5 µm. Run was isocratic, 12 min, with mobile phase containing 85% eluent A (CO_2) and 15% elunet B (MeOH, TFA, TEA). Temperature of column was 40°C.

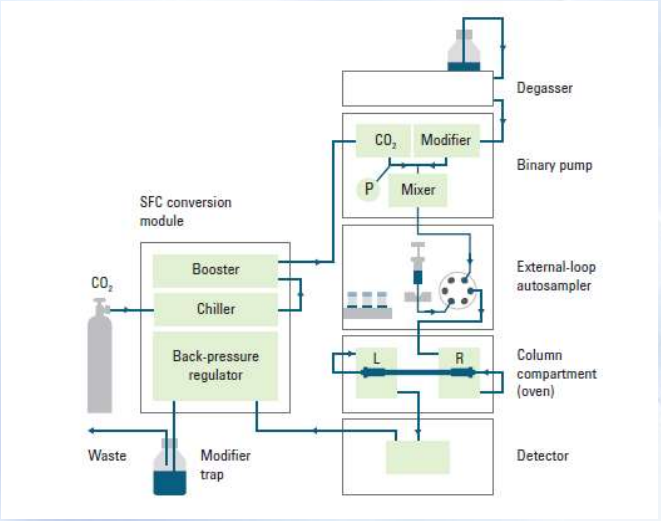


Figure 2: Schematic diagram of the Agilent analytical SFC system.

Results

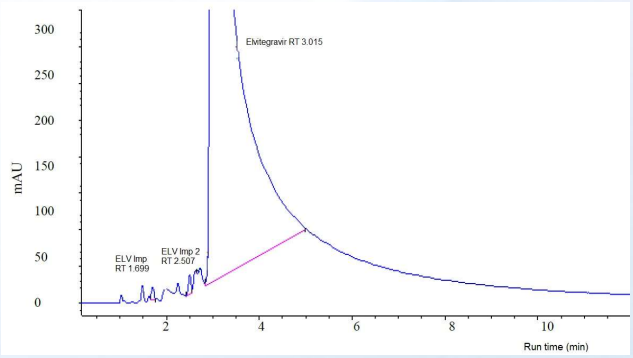


Figure 3: Chromatogram of elvitegravir and its related impurities at selected working condition.

Table 1: Method validation data

Parameter		ELV Imp 1	ELV Imp 2
LOD (µg/mL of nominal sample concentration)		4.5	4.5
LOQ (µg/mL of nominal sample concentration)		9	9
Average S/N value for LOQ (6 injections)		12	13
Correlation coefficient		0.9946	0.9984
Accuracy (Deviation from linearity %)	9 µg/mL (0.05%)	97.0	110.1
	30 µg/mL (0.15%)	100.7	112.0
	46 µg/mL (0.23%)	103.8	105.4
Repeatability (%RSD)	9 µg/mL (0.05%)	2.9	5.2
	30 µg/mL (0.15%)	3.5	2.6
	46 µg/mL (0.23%)	0.9	3.9

Conclusion

A fast and efficient supercritical fluid chromatography (SFC) method for the analysis of impurities in elvitegravir has been developed. The developed method has successfully separate main peak of Elvitegravir from related impurities and method was validated by determining the following validation parameters: specificity, limit of quantification, precision, linearity and accuracy [2,3].

References

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[2] Validation of analytical procedures ICHQ2 (R1). International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, 2015.
[3] A. Radić, Development and validation of supercritical fluid chromatography method for elvitegravir active pharmaceutical ingredient impurities determination, Diploma Thesis, Faculty of Science, Universitiy of Zagreb, Zagreb, 2019.