Optimization of an Electrolyte System for the Simultaneous Separation of Nelfinavir Mesylate and Two Impurities by MEKC

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Introduction

Nelfinavir mesylate is a drug used in the antiretroviral therapy[1]. With the expiration of the patent in 2014, it is important that other manufacturers to produce the drug, for that the treatment costs can be reduced. For this reason, a synthesis route for the drug was developed and in this route may be present as contaminants in the final product two impurities. This work developed and validated a method for the analysis of nelfinavir and its impurities by micellar electrokinetic chromatography (MEKC).

Results and Discussion

Taking into consideration the possible concomitant presence of the compounds of interest (Fig. 1) in the form of ions or neutral molecules across the pH range evaluated, according to the effective mobility curves, this work proposed a metodology by MEKC.

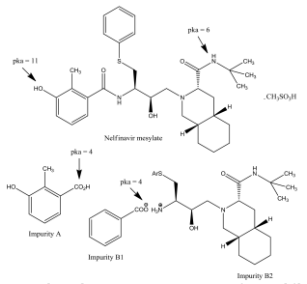

Figure 1. Chemical structures of nelfinavir mesylate and its impurities.

Then a mixed-level factorial design was performed, varying the composition of the electrolyte conductor (BGE), totaling 30 experiments (Table 1).

The electropherogram that provided better separation profile was achieved under the conditions of the experiment 26 (with SDS at lower level). So, a univariate test was performed in order to evaluate the SDS concentrations at levels lower than 10 mmol L^{-1}, i.e. 9 and 8 mmol L^{-1} and the best separation profile observed used 9 mmol L^{-1} of SDS in the BGE as shown in Fig. 2.

Other experimental conditions were: cartridge temperature, 20°C; injection, 50 mbar 3 s; voltage, +20 kV; λ, 200 nm; capillary, 50 µm x 48.5 cm (40.0 cm effective length).

Table 1. Matrix containing factors and levels.

Experiment	X_1	X_2	X_3	Experiment	X_1	X_2	X_3
1	-1	-1	-1	**16**	1	-1	-1
2	-1	-0.5	-1	**17**	1	-0.5	-1
3	-1	0	-1	**18**	1	0	-1
4	-1	0.5	-1	**19**	1	0.5	-1
5	-1	1	-1	**20**	1	1	-1
6	-1	-1	0	**21**	1	-1	0
7	-1	-0.5	0	**22**	1	-0.5	0
8	-1	0	0	**23**	1	0	0
9	-1	0.5	0	**24**	1	0.5	0
10	-1	1	0	**25**	1	1	0
11	-1	-1	1	**26**	1	-1	1
12	-1	-0.5	1	**27**	1	-0.5	1
13	-1	0	1	**28**	1	0	1
14	-1	0.5	1	**29**	1	0.5	1
15	-1	1	1	**30**	1	1	1

X_1 - TB (mmol L^{-1}): (−1) 15; (1) 25
X_2 - SDS (mmol L^{-1}): (−1) 10; (−0.5) 20; (0) 30; (0.5) 40; (1) 50
X_3 - MeOH (%, v/v): (−1) 0; (0) 5; (1) 10

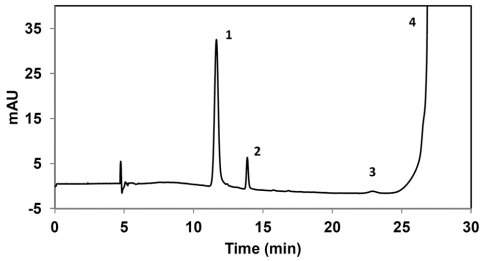

Figure 2. Electropherogram of standards containing 100 mg L^{-1} of impurities A and B; and 20000 mg L^{-1} of nelfinavir mesilate: (1) Impurity A (2) Impurity B1 (3) Impurity B2 (4) Nelfinavir mesylate.

Conclusions

The proposed methodology can be useful for the determination of the analytes in a synthesis monitoring process, raw materials and pharmaceutical formulations, as well as offering acceptable efficiency, LOQ, low solvent consumption (eco-friendly), small amount of sample and the use of non-specific columns as advantages.

Acknowledges

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[1] Souza, M. V. N. D; Almeida, M. V. D. *Quím. Nova* **2003**, 26, 366.