ISSN 0102-6593

caderno de farmácia

Órgão Oficial da Faculdade de Farmácia da Universidade Federal do Rio Grande do Sul
volume 26, Suplemento, 2010

DARIFENACIN HYDROBROMIDE TABLET STABILITY-INDICATOR HPLC METHOD DEVELOPMENT: CHEMOMETRICS APPROACH

Meneghini L.Z.[1*]; Codevilla C. F.[1]; Bergold A. M. [1]

[1]Laboratório de Química Farmacêutica, Faculdade de Farmácia, UFRGS
***Mestrando – Início: 2009/1**

Introduction: Several antimuscarinic drugs are on the market like darifenacin, a potent muscarinic receptor antagonist, available as its hydrobromide salt in Enablex®, an extended-release tablet which contains 7,5 mg or 15 mg of the drug. In the last years, the most important problem in liquid chromatography became the evaluation of analyte's chromatographic behavior and the optimization of chromatographic conditions. The statistical experimental designs are most widely used for this purpose in order to avoid too expensive and time-consuming trials.
Objective: For the present evaluation, a central composite design (*CCD*) has been applied to define optimal chromatographic conditions for the separation of darifenacin hydrobromide (Enablex®) and its oxidative product after forced degradation (hydrogen peroxide 10% v/v).
Materials and Methods: For the chemometrical evaluation was applied a rotable CCD with 2^3 full factorial design, ±1,681star design, and six replications in the central point. The factors were acetonitrile content, pH and column temperature; as dependent variables three responses (retention factor, resolution and Chromatographic Optimization Function-COF) were selected. Experimental design and data analysis were performed using Design-Expert® 7.0.0 (Stat–Ease Inc., Minneapolis). The plan of experiments for CCD is presented in Table 1.The chromatographic system consisted of Shimadzu HPLC with LC20A binary pump, SPD-AVvp UV/VIS detector, SIL 20-AC autosampler and CTO20A oven. The runs were performed on C8 column (5 mm x 2,0mm i.d. x 150mm) and 1,00ml/min flow rate.
Results and Discussion: Based on the performed experiments, coefficients were calculated characterizing the polynomes of second order and three-dimensional graphs were constructed as well. All the examined factors were identified as significant using ANOVA analysis. The mathematical model validity assumptions showed to be adequate for residual diagnostics, lack-of-fit, r^2, adjusted r^2, prediction r^2 and PRESS.
Conclusions: The optimal conditions determined by the response surface methodology were acetonitrile 28% (v/v) and pH 3.0 in the mobile phase, with the column temperature under room temperature (25°C).

Table 1. Central composite design domain.

	Levels		
Run	Acetonitrile	pH	Oven temperature
1	-1,000	-1,000	-1,000
2	1,000	-1,000	-1,000
3	-1,000	1,000	-1,000
4	1,000	1,000	-1,000
5	-1,000	-1,000	1,000
6	1,000	-1,000	1,000
7	-1,000	1,000	1,000
8	1,000	1,000	1,000
9	-1,681	0,000	0,000
10	1,681	0,000	0,000
11	0,000	-1,681	0,000
12	0,000	1,681	0,000
13	0,000	0,000	-1,681
14	0,000	0,000	1,681
15	0,000	0,000	0,000
16	0,000	0,000	0,000
17	0,000	0,000	0,000
18	0,000	0,000	0,000
19	0,000	0,000	0,000
20	0,000	0,000	0,000

Acknowldgements: Financial support from CNPq/Brazil and master scholarship from CAPES/Brazil.