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DEVELOPMENT OF A METHOD TO SIMULTANEOUS DETERMINATION OF DELAPRIL AND MANIDIPINE BY MICELLAR ELECTROKINETIC CHROMATOGRAPHY IN PHARMACEUTICAL FORMULATION

Todeschini V. [1*], Meira A. S. [1], Volpato N. M.[1]

[1]Laboratório de Controle de Qualidade Farmacêutico, Faculdade de Farmácia, UFRGS.
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Introduction: Delapril (DEL) is a non-sulfhydryl angiotensin converting enzyme inhibitor. It is an esterified pro-drug that is converted *in vivo* to its active metabolite. Manidipine (MAN) inhibits the calcium influx to the cell by antagonism on calcium channels. The association of active ingredients with complementary mechanisms of action produces a synergic antihypertensive effect, with a unique daily dose and more reduction in blood pressure, without mutual interference on the pharmacokinetic characteristics of the individual components.
Objective: The aim of the present work was to develop and validate a micellar electrokinetic chromatographic (MEKC) method for the analysis of DEL and MAN in tablets using an adequate substance as internal standard (IS).
Materials and Methods: CE experiments have been conducted in a capillary electrophoresis system (Agilent Technologies, model HP 3D CE, Palo Alto, CA, USA), equipped with a diode array UV detector and a temperature control device. Data acquisition and treatment software was supplied by the manufacturer (HP ChemStation, rev A.06.01). The capillary has been thermostated between 15 and 35 °C. Different sizes of an uncoated fused-silica capillary of 50 μm I.D. (Polymicro Technologies, Phoenix, AZ, USA) have been used (40, 56 and 72 cm effective length) to improve the separation of the drugs from their degraded products. Samples have been injected hydrodynamically by pressure of 50 mbar between 4 and 6 s and constant voltages between 15 and 30 kV have been applied. The influence of electrolyte (phosphate, tetraborate and borate), its molar concentration (15-75 mM) and pH (3.0-10.0) have been also evaluated, as well as the better internal standard to be used in all analysis.
Results and Discussion: Optimum results were obtained in a fused silica capillary with 72 cm of effective length, maintained at 35 °C, 25 mM borate buffer at pH 9.0 and 5 mM of anionic surfactant SDS. The applied voltage was 25 kV and the injection was performed using the hydrodynamic mode at 50 mbar for 5 s. The optimum detection wavelength chosen was 208 nm in order to favor the simultaneous quantification of DEL and MAN. The salicylic acid was selected as IS. The total running time was 14 minutes, with migration time of 6.6, 8.8 and 12.0 minutes for DEL, AS and MAN, respectively. The method was linear in the range of 15 – 150 μg/mL (r^2 = 0.9966) and 5 – 50 μg/mL (r^2 = 0.9985) for DEL and MAN, respectively, with suitable precision (RSD $\leq$ 1.87%) and accuracy (98.94% for DEL and 100.65% for MAN).
Conclusions: The methodology proved to be stability-indicating since good resolution was obtained between the two drugs, IS and their degraded products formed in stability studies (samples solutions subjecting to acidic, basic, oxidative and photolytic conditions). The analytical conditions were successfully validated according to the International Conference on Harmonization (ICH) guidelines by determination of the following parameters: specificity, linearity, precision, accuracy and robustness. In order to compare the results with well characterized procedure by LC method previously validate, the data obtained by the two methods will be statistically analyzed using ANOVA (α = 0.05).

References:
1. R. Fogari, *Clin. Ther.* **29**, supplement B (2007).
2. ICH. Harmonised tripartite guideline. Q2(R1). ICH Steering Committee. Commission of the European Communities, Geneva (2005).
3. M. L. Otero, *Vasc. Health Risk Manag.* **3**, 255-263 (2007).
4. G. A. Shabir, *J. Chromatogr.* A. **987**, 57-66 (2003).

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