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COUPLING SWEEPING-MICELLAR **ELECTROKINETIC** CHROMATOGRAPHY WITH TANDEM MASS SPECTROMETRY FOR THE THERAPEUTIC MONITORING OF BENZIMIDAZOLES IN ANIMAL URINE BY DILUTE AND SHOOT

Carmen Tejada-Casado, David Moreno-González, Monsalud del Olmo-Iruela, Ana M. García-Campaña, Francisco J. Lara



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ACCEPTED MANUSCRIPT

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Carmen Tejada-Casado, David Moreno-González, Monsalud del Olmo-Iruela, Ana M. García-Campaña, Francisco J. Lara*

Department of Analytical Chemistry, Faculty of Sciences, University of Granada, Av. Fuente Nueva s/n, E-18071 Granada, Spain

*Correspondence autor. Tel.: +34 958249510; fax: +34-958243326. frjlara@ugr.es

Abstract

A new method based on micellar electrokinetic chromatography-tandem mass spectrometry (MEKC-MS/MS) has been developed for the identification and simultaneous quantification of thirteen benzimidazoles in animal urine. In order to obtain an appropriate separation with the highest sensitivity, different electrophoretic parameters were evaluated. Under optimum conditions, the separation was performed using ammonium perfluorooctanoate as volatile surfactant and electrophoretic buffer (50 mM, pH 9). To increase the sensitivity, a stacking mode named sweeping was applied, using water as injection solvent at 50 mbar for 75 s, obtaining sensitivity enhancement factors from 50 to 181. The method was applied to different animal urine samples, including sheep, cow and goat. The sample treatment consisted of a 1:10 (v/v) dilution with water. Calibration using sheep urine samples can be used for both goat and cow urine samples with a relative bias below 25% and relative standard deviations lower than 8 %. The limits of detection were below 70 µg L⁻¹. As a result, the applicability of this rapid, simple, sensitive, and environmentally friendly method for therapeutic drug monitoring of benzimidazoles based on the analysis of animal urine has been demonstrated.

Keywords: animal urine, benzimidazoles, micellar electrokinetic chromatography, sweeping, tandem mass spectrometry, dilute and shoot.

1. Introduction

Therapeutic drug monitoring in veterinary medicine is a useful tool to assess when a treatment has attained therapeutic concentrations of a particular drug depending on the administered dose [1]. One of the main therapeutic drugs employed in veterinary medicine are benzimidazoles (BZs). These compounds are anthelmintic agents widely used in the prevention

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