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Analytical Methods

Analysis of potential adulteration in herbal medicines and dietary supplements for the weight control by capillary electrophoresis

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Abstract

Four different phytopharmaceutical dosage forms for use in weight control programs were analyzed. Two different ground herbal blends and their correspondent infusions, a capsule and a tincture were investigated for the presence of compounds used as adulterants in these products. A capillary electrophoresis (CE) method was developed and validated. The optimized experimental conditions were: BGE, sodium tetraborate buffer 20 mM, pH 9.2, voltage applied 30 kV, capillary temperature 25 °C, injection sample at 0.5 Psi during 5 s. Ephedrine, norephedrine, caffeine and furosemide were baseline separated in less than 7 min; the migration times were found to be 2.65, 2.90, 3.75 and 6.58 min, respectively. The analysis showed in sample 3 concentrations of 0.45 ± 0.03 mg g^{-1} (ephedrine), 0.33 ± 0.02 mg g^{-1} (norephedrine), 1.09 ± 0.41 mg g^{-1} (caffeine) and 0.80 ± 0.17 mg g^{-1} (furosemide). Caffeine content in samples 1, 2 and 4 was 0.61 ± 0.06 mg g^{-1}, 15.66 ± 1.05 mg g^{-1} and 2.27 ± 0.13 mg ml^{-1}, respectively. Linearity was obtained in the concentration range of 1–1000 μg ml^{-1}. Limits of detection (LOD) and quantification (LOQ) were determined as 0.42 μg ml^{-1} and 1.40 μg ml^{-1} (ephedrine), 0.47 μg ml^{-1} and 1.40 μg ml^{-1} (norephedrine), 0.12 μg ml^{-1} and 0.48 μg ml^{-1} (caffeine), 0.22 μg ml^{-1} and 0.73 μg ml^{-1} (furosemide).

The common constituents of the samples did not interfere with the potential adulterants. Repeatability was better than 0.24% RSD for the retention time and 1.43% for the peak area. Intermediate precision was tested by changing the capillary, the day of operation and the operator, in all the cases the %RSD was better than 3.06.

Keywords: Capillary electrophoresis; Adulterants; Dietary supplements; Quality control; Weight control drugs

1. Introduction

Numerous and different botanical products used for maintain and/or promote health are known as Botanical Health Products (BHP) (Bast et al., 2002). Several vegetal drugs and their derivatives (dietary supplements and phytopharmaceuticals) can be considered BHPs and, in contrast with the conventional drugs are perceived as non-toxic products with therapeutic activity (Bauer, 1998). These BHPs are widely consumed because of their pharmacological activity in weight control programs (Anonymous, 2005).

In order to increase the therapeutic effect of BHPs, it has been reported that pharmaceutical active principles are included in the formula of products marketed as 'herbal

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medicine' or 'dietary supplement' during the manufacturing process (Fugh-Berman & Ernst, 2001). When BHPs containing synthetic therapeutic drugs as adulterants are administered, pharmacokinetic and/or pharmacodynamic herb–drug interactions can occur (Fugh-Berman & Ernst, 2001). Adverse drug reactions and toxicity in heart, liver, blood, kidneys, central nervous system and skin and carcinogenesis have been reported (Bensoussan, Myers, Drew, Whyte, & Dawson, 2002; Ernst, 2000; Greensfelder, 2000; Kessler, 2000).

There are several pharmaceuticals active principles that have to be investigated like possible adulterants in products used in weigh control programs due to their potential toxic effects (anorexigens, diuretics, stimulants, laxative agents, etc.) (Bogusz, Al-Tufail, & Hassan, 2002).

Several analytical approaches were developed for adulterant determination in BHPs. A gas chromatography–mass spectrometry (GC–MS) method was applied to obtain an impurity profiling of ecstasy tablets seized in Hong Kong (Cheng, Chan, Chan, & Hung, 2006); two different high-performance liquid chromatography (HPLC) method were set up to verify the absence of hydroxyanthracene derivatives in commercial *Aloe vera* gel powders (Bozzi, Perrin, Austin, & Arce Vera, 2007) and to check components and purity in commercial saffron (Lozano, Castellar, Simancas, & Iborra, 1999). The use of capillary electrophoresis (CE) in BHP samples can have benefits in terms of low reagent and solvent consumption, simplicity and reduced time and cost of analysis (Sombra, Gómez, Olsina, Martínez, & Silva, 2005).

The present work consists in the development of a CE methodology and its application to the separation and determination of different active principles present as adulterants in weight control products. The potential adulterants studied show pharmacological properties corresponding with the claims of the analyzed remedies: caffeine (stimulant), furosemide (diuretic), norephedrine and ephedrine (stimulant, decongestant and anorexigen action); however, they can cause an unpredictable effect on the health of users.

2. Experimental

2.1. Instrumentation

The employed CE system consisted of a Beckman P/ACE MDQ instrument (Beckman Instruments, Inc., Fullerton, CA) equipped with a diode array detector and a data handling system comprising an IBM personal computer and P/ACE System MDQ Software. Detection was performed at 208 and 265 nm. The fused-silica capillaries were obtained from MicroSolv Technology Corporation and had the following dimensions: 60 cm total length, 50 cm effective length, 75 μm ID, 375 μm OD. The temperature of the capillary and the samples was maintained at 25 °C. The pH of the electrolytes was measured by an Orion 940 pHmeter equipped with a glass-combined electrode.

The studied compounds were purchased from Sigma–Aldrich Co. (St. Louis, MO), sodium tetraborate ($Na_2B_4O_7 \cdot 10H_2O$) was acquired from Mallinckrodt (St. Louis, USA). The water used in all studies was ultra-high-quality water obtained from a Barnstead Easy pure RF compact ultrapure water system. All other reagents and solvents were of analytical grade quality. All solutions were degassed by ultrasonication (Testlab, Argentina).

The electrolyte solution (background electrolyte, BGE) was prepared daily and filtered through a 0.45 μm Titan Syringe filters (Sri Inc., Eaton Town, NJ, USA). At the beginning of the day, the capillary was conditioned with 0.1 mol l^{-1} NaOH for 5 min, followed by water for 5 min, and then with running electrolyte for 10 min before sample injection. To achieve high reproducibility of migration times and to avoid solute adsorption, the capillary was washed between analyses with sodium hydroxide for 2 min, followed by water for 2 min, then equilibrated with the running buffer for 4 min. Samples were pressure-injected at the anodic side at 0.5 Psi for 5 s. A constant voltage (30 kV) was used for all the experiments.

2.2. Samples

Four different commercial products, BHPs, used in weight control programs were analyzed with the proposed methodology. The BHPs were: ground plant material containing *Marrubium vulgare* L., *Melissa officinalis* L., *Lippia fissicalyx* Tronc., *Maytenus ilicifolia* Reiss., *Prunus spinosa* L., *Hyssopus officinalis* L., *Equisetum arvense* L., *Cassia acutifolia* Delile y *Cassia angustifolia* Vahl., *Matricaria chamomilla* L. and *Fucus vesiculosus* L. as part of an herbal blend (sample 1); ground plant material containing *Ilex paraguariensis* St. Hil., *Fucus vesiculosus*, *Aloysia triphylla* L'Hér., *Camellia sinensis* L., *Equisetum arvense* L., *Minthostachys mollis* H.B.K. as part of an herbal blend (sample 2); a dietary supplement (capsule) claiming to contain *Garcinia cambogia* Desr. and *Centella asiatica* L. manufactured by "El Ceibo Laboratory" (San Luis, Argentina) (sample 3); a dietary supplement (tincture) claiming to contain *Fucus vesiculosus* L., *Hyssopus officinalis* L., *Equisetum arvense* L. and *Rhamnus purshiana* D.C L. manufactured by "El Ceibo Laboratory" (San Luis, Argentina) (sample 4). All the analyzed herbal products were taken randomly from drug shops and herbal markets in Argentina. These products were mainly from the central region of the country (four different batches) and were collected during 2004–2006.

2.3. Sample preparation

Samples consisted of both solid (ground plant material, capsule) and liquid (tincture) formulations. The water extracts (teas) of samples 1 and 2 were used for the examinations. The procedure adopted for the teas preparation