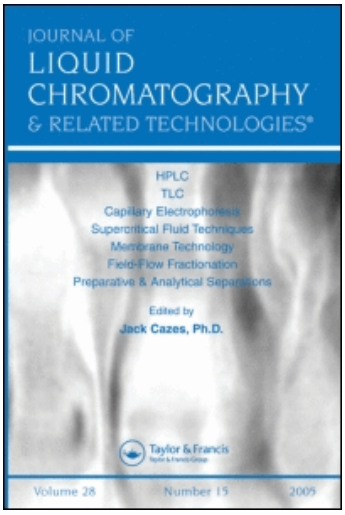

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Simultaneous Determination of Caffeine and Ergotamine in Pharmaceutical Dosage Formulation by Capillary Electrophoresis

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SIMULTANEOUS DETERMINATION OF CAFFEINE AND ERGOTAMINE IN PHARMACEUTICAL DOSAGE FORMULATION BY CAPILLARY ELECTROPHORESIS

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ABSTRACT

A method has been developed for the simultaneous assay of caffeine and ergotamine in the pharmaceutical dosage tablet formulations (Cafergot®) by capillary electrophoresis (CE). The analysis was accomplished by using 25 mM sodium phosphate buffer at pH 6.0 with UV detection at 214 nm. The mean recoveries were 98.9% ± 1.9% and 101% ± 1.03% for the analysis of caffeine and ergotamine respectively. Run time was less than six minutes for the analysis of the two active constituents in the tablets. There were no excipients interferences.

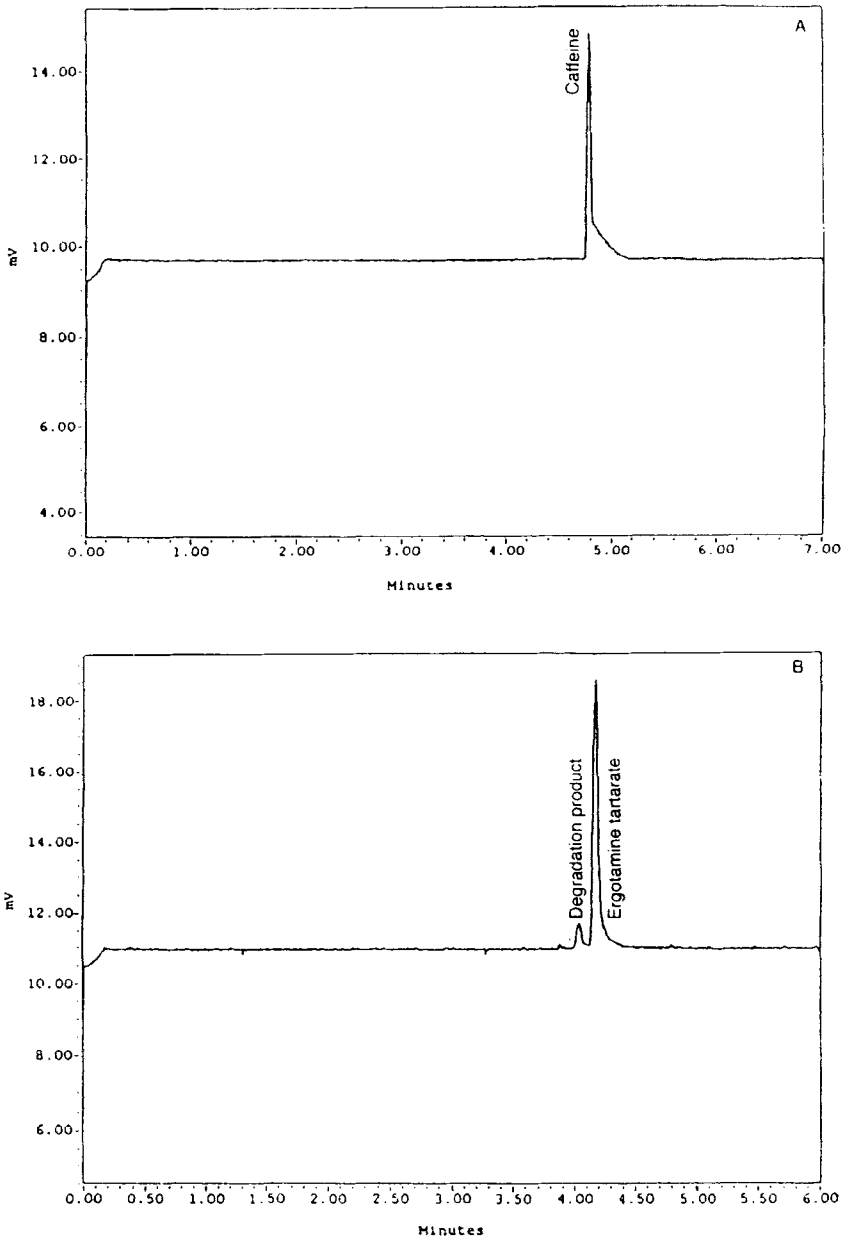
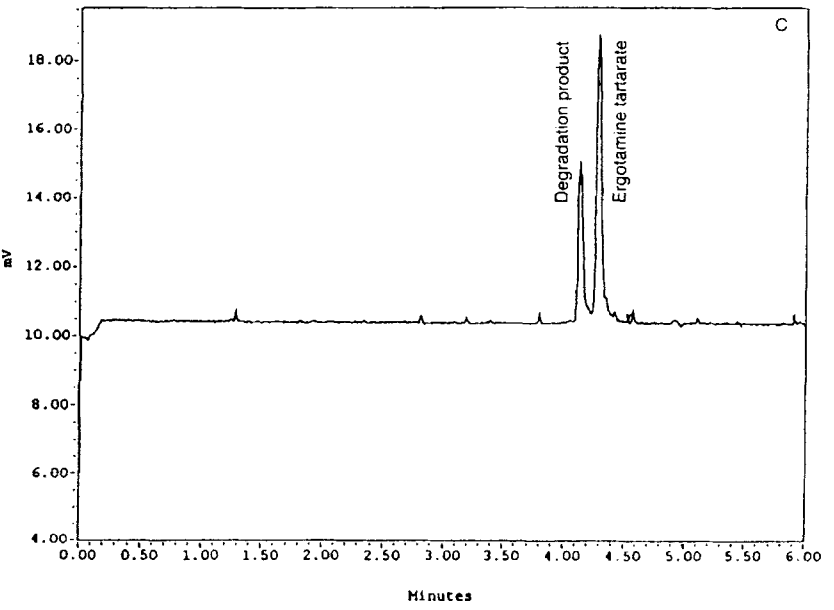


Figure 1. (above & right) Electropherogram of (A) caffeine (B) Fresh solution of ergotamine tartarate (C) Ergotamine tartarate solution after 24 hours.

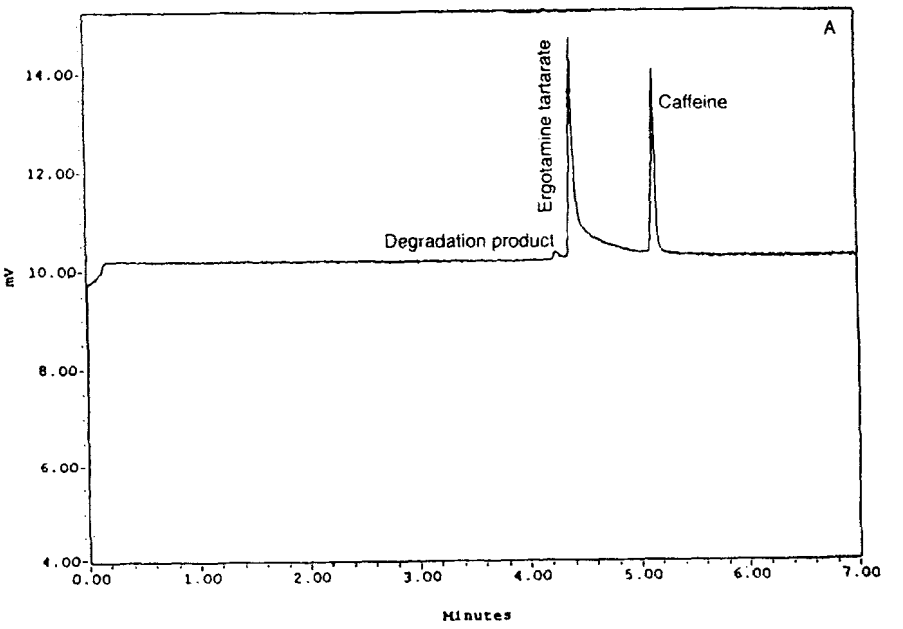


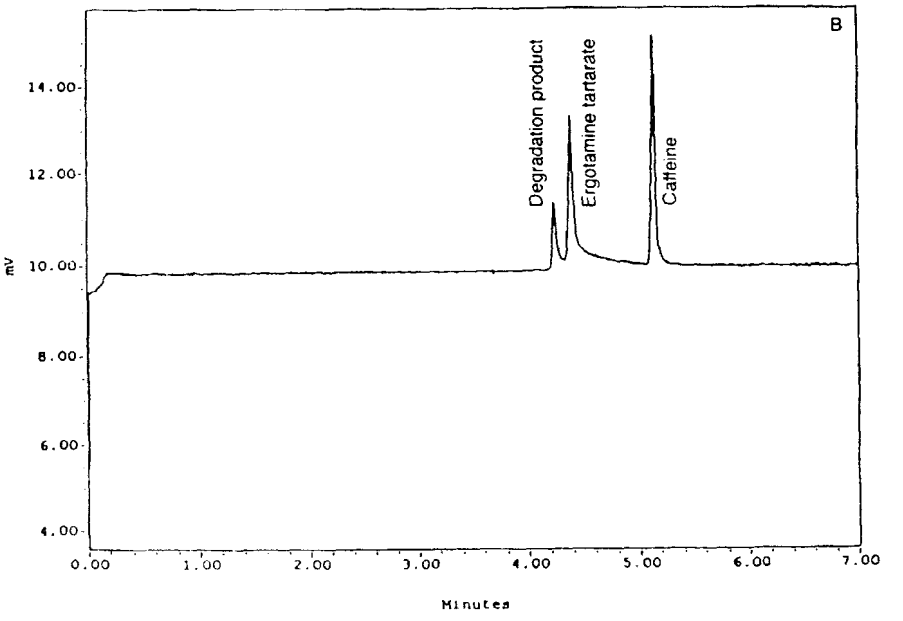
INTRODUCTION

Capillary electrophoresis (CE) has recently emerged as a powerful separation tool for the analysis of a wide variety of complex mixtures.[1] The characteristics of CE modality are reflected in its high separation efficiency, rapid analysis, small sample consumption. Direct detection of analytes and selectivity are remarkable and impressive, which make it very attractive for pharmaceutical analysis.

Ergotamine is considered to be one of the most effective drugs in the treatment of migraine and cluster headaches.[2, 3] A combination of ergotamine and caffeine is clinically used for the treatment of acute attacks of migraine. Saxena and De Deyn reviewed the use of this combination drug in treatment of migraine and its complications. [4]

Determination of ergotamine has been reported using high performance liquid chromatography[5]. Also its analysis in plasma by fluorescence detection[6] and by ion-pair chromatography were published.[7] The analytical profile of





caffeine was reviewed by Zubair et al[8] which include a compilation of the analytical methods reported in the literature for caffeine analysis. Furthermore, the analysis of caffeine content in various pharmaceutical formulations were also cited[9].

The purpose of this paper is to report, for the first time, a rapid and accurate capillary electrophoresis (CE) method for the simultaneous analysis of ergotamine and caffeine in the pharmaceutical tablet formulation.

EXPERIMENTAL

Chemicals

A standard of ergotamine tartarate was obtained from (GNF, GmbH, Berlin, Germany), caffeine and sodium phosphate were obtained from Sigma (St. Louis, MO, USA). High purity water was obtained from a Milli-Q Water System (Millipore, Bedford, MA). The pharmaceutical dosage forms of Carfergot® tablets (Sandoz Pharmaceuticals, Cambeley Surrey, UK) were purchased from local markets.

Apparatus

A Waters Quanta 4000E capillary electrophoresis system with positive power supply was used (Waters, Milford, MA, USA). The electrophoretic system was controlled by the Millennium 2010 Chromatography Manager (Waters) which was also used for data collection (5 points/sec.) and processing.

All analyses were performed on Accusep polyamide fused-silica capillaries (60 cm x 75 μm ID) obtained from Waters (Milford, MA, USA). The detector time constant was set at 0.3 seconds, all analyses were for 10 second injections, with hydrostatic mode and applied voltage of +20 KV at 30°C with detection at 214 nm.

Figure 2. (left) Electropherogram of caffeine and ergotamine tartarate after extraction from Cafergot® tablets. (A) Fresh solution (B) Solution after 24 hours.

Buffer and Solutions

A standard solution (500 μg/mL) of ergotamine tartarate and (100 μg/mL) of caffeine were prepared by dissolving in high purity water. For establishment of calibration curves of each, five concentrations of ergotamine tartarate in the range of 10-250 μg/mL and of caffeine in the range of 2.5-50 μg/mL were made in running buffer. The buffer used for CE analysis was 25 mM sodium phosphate at pH 6.0. Duplicate runs were made of all concentrations.

Sample Preparations

Two tablets of Cafergot® containing 2 mg of ergotamine tartarate and 200 mg of caffeine were accurately weighed and powdered. An aliquot portion of the powder containing an equivalent of 0.5 mg of ergotamine tartarate, and 50 mg of caffeine was diluted in 10 mL of sodium phosphate buffer and was shaken vigorously for 15 min. followed by centrifugation. An aliquot of the supernatant was then used for the determination of ergotamine tartarate. Further dilutions were made for caffeine determination in order to bring the peak area within scale.

RESULTS AND DISCUSSION

A rapid and simple capillary electrophoresis method has been achieved for the analysis of both ergotamine and caffeine as bulk drug and simultaneously in the pharmaceutical tablet form known as Cafergot®. Detection and separation of these two drugs was accomplished in less than 6 minutes. Retention time for caffeine and ergotamine tartarate as bulk drugs were 4.8 and 4.2 minutes, respectively (Figure 1 A & B).

An unknown peak was observed in the electropheragram of ergotamine tartarate which has a retention time of 4.1 minutes. This peak is believed to be a decomposition or degradation product as its size increases to reach about 50% of the ergotamine peak size within 24 hours (Figure 1 C). This requires the carrying out of the analysis of ergotamine in bulk form or in pharmaceutical tablets, as soon as possible, to avoid the formation of this decomposition product. Shown in Figure 2 A and B are the differences in the electropheragrams after 24 hours.

A regression analysis indicated a linear relationship between the peak area Y and the concentration X, over the range 10-250 μg/mL with correlation coefficient (r) of 0.997 and mean recovery of 101.9% ± 1.03% for ergotamine

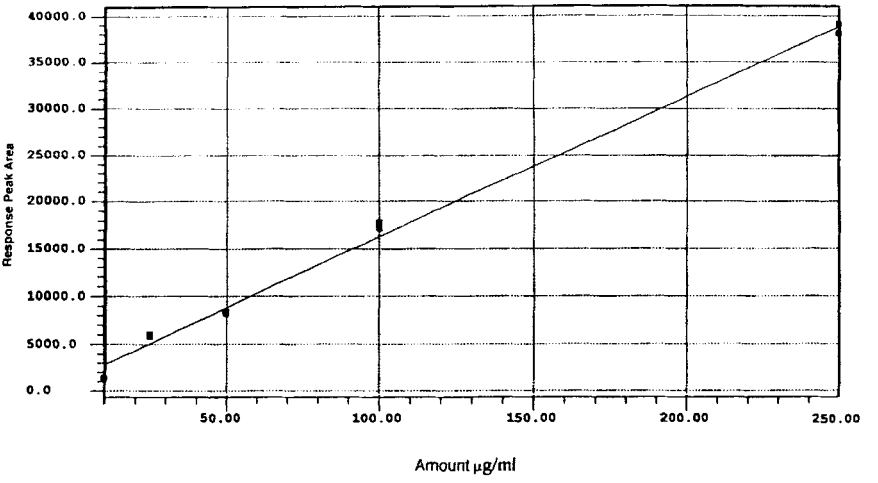


Figure 3. Calibration curve for ergotamine tartarate over the range of 10-250 µg/mL.

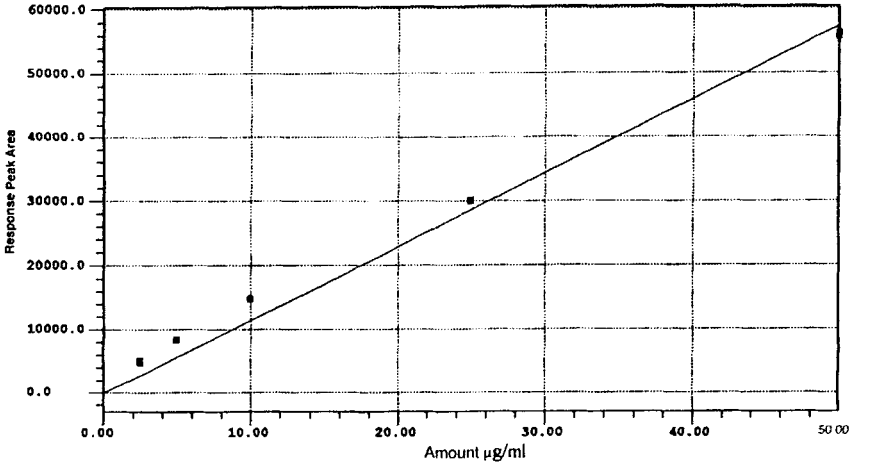


Figure 4. Calibration curve for caffeine over the range of 2.5-50 µg/mL.

tartarate as shown in Figure 3. The calibration curve for caffeine (Figure 4) was linear in the range of 2.5 - 50 μg/mL with correlation coefficient (r) of 0.993 and mean recovery of 98.9% ± 1.9% for caffeine.

The precision and accuracy of the method were verified by analysis of the samples after adding known concentrations of ergotamine tartarate and caffeine to the dosage forms. Tablet excipients did not interfere with the assay of the two drugs.

In summary, the method described permits a simultaneous determination of ergotamine tartarate and caffeine in bulk drug and pharmaceutical tablet forms by CE. This method is simple, rapid, specific and stability-indicating. The proposed method can be used for routine analysis of these drugs and can be used as an alternative tool for the drug quality control laboratories.

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