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Note

High-performance liquid chromatographic analysis of ephedrine in oily formulations

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Ephedrine, when used as nasal decongestant, is normally available in vegetable oil. A variety of methods for its analysis have been described[1–4], and extraction from oil is generally required leading to very long analysis times and poorly reproducible recovery from complex matrices. Among instrumental methods, the most successful has been ion-pair high-performance liquid chromatography (HPLC)[5]. However, since the use of counter ions usually shortens column life[6], a reversed-phase HPLC method without the addition of counter ion to the mobile phase is desirable.

The purpose of this study was to develop a simple procedure for the routine analysis of ephedrine in oily formulations, with minimum sample preparation and without addition of counter ions.

EXPERIMENTAL

Reagents

Ephedrine hydrochloride and procaine hydrochloride were obtained from Aldrich (Steinheim, F.R.G.). Acetonitrile was of HPLC grade (Chromasolv; Riedel de Haën, Hannover, F.R.G.) and water was distilled from glass apparatus and filtered through a 0.45-μm membrane filter (Type HA; Millipore, Bedford, MA, U.S.A.). All other reagents were reagent grade.

Chromatography

Analyses were performed on a 30 cm × 0.45 cm column prepacked with silica gel 60 C_8 from Riedel de Haën. The HPLC system consisted of a Model 6000 A pump, a Model U6K universal injector, a Lambda Max Model 480 ultraviolet detector and a Model 730 Data Module (Waters Assoc., Milford, MA, U.S.A.). The mobile phase was acetonitrile–0.01 *M* potassium dihydrogenphosphate (10:90) adjusted to pH 3.0 with 50% phosphoric acid. The flow-rate was 1 ml/min. UV detection was carried out at 214 nm (0.02 a.u.f.s.).

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Solutions

A stock solution of ephedrine hydrochloride (0.5 mg/ml) was prepared in 2-propanol. Procaine (internal standard) was dissolved in methanol to give a concentration of 1.0 mg/ml.

Sample preparation

An accurately weighed amount of sample (about 100 mg), equivalent to 0.5 mg of ephedrine hydrochloride, was transferred to a 50-ml volumetric flask. After addition of 1 ml of internal standard solution and 0.5 ml of acetic acid, the flask was filled with chloroform. Into a 15-ml tube were placed 5 ml of this solution and 5 ml of 0.1 *M* hydrochloric acid. After vortex mixing (2 min) and centrifugation (at 5000 *g*), the upper aqueous phase was separated and 10 μl were injected.

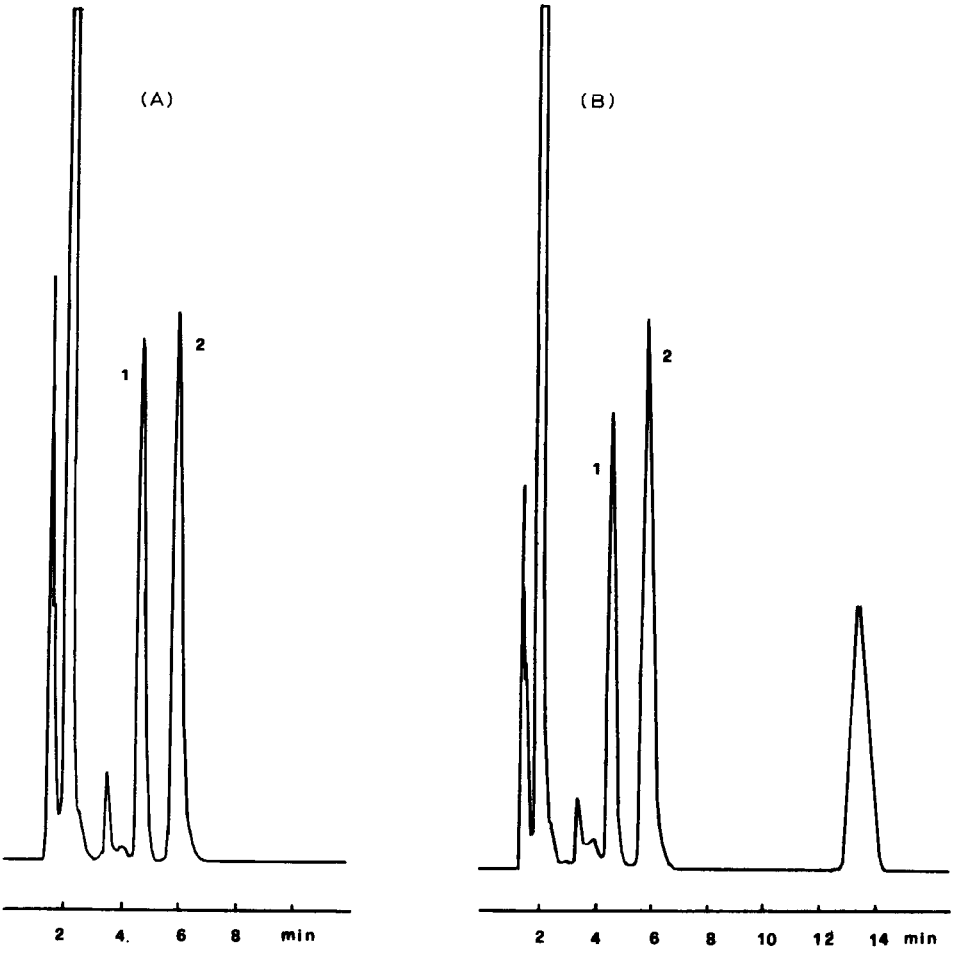

Fig. 1. Chromatograms of ephedrine hydrochloride and procaine hydrochloride standards (A) and of a commercial formulation (B). Peaks: 1 = ephedrine hydrochloride; 2 = procaine hydrochloride (I.S.) Eluent: acetonitrile–0.01 *M* potassium dihydrogenphosphate (10:90), pH = 3.0. Flow-rate = 1 ml/min. UV detection at 214 nm.

Recovery study

A mixture containing 0.5% ephedrine hydrochloride in vegetable oil was prepared and then treated as above.

Calibration curves

Into individual 50-ml volumetric flasks were placed 0.4–1.0 ml of ephedrine hydrochloride stock solution. A 1-ml volume of internal standard solution and 0.5 ml of acetic acid were added to each flask. After dilution to 50 ml in chloroform, 5 ml of each solution were treated as described in *Sample preparation.*

RESULTS AND DISCUSSION

A typical chromatogram of ephedrine and procaine hydrochloride standards and a commercial formulation is shown in Fig. 1. Complete baseline resolution was achieved and the standard deviation of the retention times was 1.5%.

Five ephedrine standards (0.2–0.5 mg) prepared in 2-propanol were processed as if they were in oil samples and analyzed. A correlation coefficient of 0.9982, a y intercept of 0.22, a slope of 28.32 and a standard error of 1.1% were calculated. These statistics indicate that the HPLC analysis gives a linear response in the range investigated, and a single determination may be used. The recovery of five ephedrine standards prepared in oil averaged 98 $\pm$ 0.3%. Three complete formulations were analyzed for their ephedrine contents on two consecutive days to check the assay reproducibility. These results were within the regulatory limits (90–110%), with good relative standard deviations (0.8%).

In conclusion, this HPLC procedure for the analysis of ephedrine present in oily solutions is rapid, specific and accurate.

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