EXPERIMENTAL[2]

Plant Material—The whole aerial parts and roots were collected during May, air dried in the shade, finally dried at 60° to a constant weight, and powdered so that all material passed a mesh not greater than 0.5 mm.

Extraction—Powdered plant material, 100 g, was moistened with 100 ml of 15% ammonia and stirred with 600 ml of chloroform at room temperature for 1 hr. The extraction was repeated four times. After evaporation of the solvent, the dark oily residue was extracted with 50 ml of 5% sulfuric acid. The solution was filtered and extracted with petroleum ether (3 × 20 ml) to remove the colored material.

The aqueous layer was made alkaline with 15% ammonia and extracted with chloroform (4 × 25 ml). After evaporation of the solvent, the dry residue (3.12 g) was subjected to preparative TLC on silica gel plates, using petroleum ether–chloroform–diethylamine (70:20:10) as the eluting solvent.

Dicentrine—The first major fraction was extracted with chloroform–methanol (85:15) and recrystallized from ethanol to give 1.24 g of I, mp 166–169° [lit. (8) mp 168–169°]; molecular weight by mass spectroscopy *m/e* 339; UV: λ_{max} (CH_3OH) 303 ($E^{1\%}_{1cm}$ 494) and 280 ($E^{1\%}_{1cm}$ 400) nm; IR (KBr): 1600, 1575, 1508, 1466, 1389, 1312, 1266, 1242, 1212, 1098, 1040, 955, 865, 838, and 769 cm^{-1}; NMR ($CDCl_3$): τ 7.46 (s, 3H, NCH_3), 6.1 (s, 6H, OCH_3), 4.0 (d, 2H, CH_2), 3.47 (s, 1H, aromatic), and 2.28 (s, 1H, aromatic)[3].

Anal.—Calc. for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.69; H, 6.30; N, 4.11.

Bulbocapnine—The second major fraction was extracted in a way similar to that used for dicentrine to give 0.89 g of II, mp 199–200° [lit. (11) mp 199°]; molecular weight by mass spectroscopy *m/e* 325; UV: λ_{max} (CH_3OH) 303 ($E^{1\%}_{1cm}$ 214), 275 ($E^{1\%}_{1cm}$ 370), and 268 ($E^{1\%}_{1cm}$ 432) nm; IR (KBr): 3175, 1645, 1618, 1515, 1488, 1466, 1404, 1299, 1235, 1136, 1082, 1062, 1033, 998, 959, 934, 853, 827, 806, and 735 cm^{-1}; NMR ($CDCl_3$): τ 7.44 (s, 3H, NCH_3), 6.1 (s, 3H, OCH_3), 3.97 (d, 2H, CH_2), 3.36 (s, 1H, aromatic), and 3.16 (s, 2H, aromatic)[4].

[2] Melting points were taken on a Kofler hot-stage microscope and are uncorrected. UV spectra were obtained on a Varian Techtron 635 instrument. IR spectra were recorded on a Leitz model III spectrograph. NMR spectra were obtained on a Varian T60A instrument, using tetramethylsilane as the internal standard. Mass spectra were recorded on a Varian Mat III spectrograph.

[3] NMR data were identical with those reported in the literature (9) for dicentrine.

[4] UV and NMR data were identical with those reported in the literature (10, 11) for bulbocapnine.

Anal.—Calc. for $C_{19}H_{19}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.69; H, 6.20; N, 4.23.

Salutaridine—The third fraction was extracted as already described and recrystallized from ether to give 0.05 g of III, mp 197–199° [lit. (4) mp 196–198°]. The isolated material was identical to an authentic sample of salutaridine according to melting-point, mixed-melting point, IR, UV, NMR, and mass spectroscopic analyses (4).

Anal.—Calc. for $C_{19}H_{21}NO_4$: C, 69.72; H, 6.42; N, 4.28. Found: C, 70.01; H, 6.43; N, 4.31.

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Simultaneous Quantitative GLC Determination of Chlorpheniramine Maleate and Phenylpropanolamine Hydrochloride in a Cold Tablet Preparation

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Abstract □ A GLC method was developed for the simultaneous determinations of chlorpheniramine maleate and phenylpropanolamine hydrochloride in a cold tablet preparation containing a large amount of aspirin. The method utilizes a solid sampling device to eliminate interference from solvent, and it is rapid and precise. The total analysis time is less than 1.5 hr, thereby permitting its use for quality control purposes.

Keyphrases □ Chlorpheniramine maleate—GLC analysis, commercial cold tablets □ Phenylpropanolamine hydrochloride—GLC analysis, commercial cold tablets □ GLC—analysis, simultaneous, chlorpheniramine maleate and phenylpropanolamine hydrochloride, commercial cold tablets □ Dosage forms—commercial cold tablets, simultaneous GLC analysis of chlorpheniramine maleate and phenylpropanolamine hydrochloride

Analyses of chlorpheniramine maleate and phenylpropanolamine hydrochloride have been performed in various formulations by several means. Partition (1, 2), ion-exchange (3), liquid (4), and gas (5) chromatography are among the forms applied to these analyses. The purpose of this study was to develop a rapid, precise, and simple method for the simultaneous determination of chlorpheniramine maleate and phenylpropanolamine

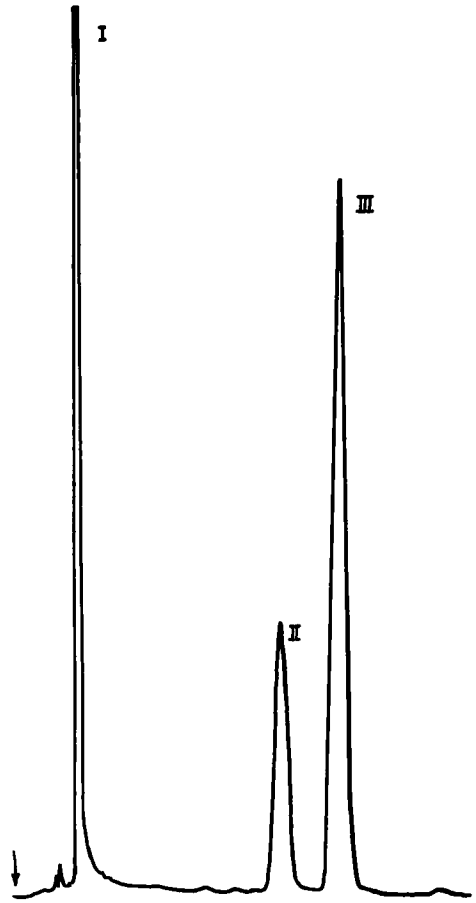

Figure 1—*Separation of phenylpropanolamine (I) and chlorpheniramine (II), using n-tetracosane (III) as an internal standard. Conditions are described in the text.*

hydrochloride in a cold tablet preparation containing a large amount of aspirin. The method is applicable to quality control procedures.

EXPERIMENTAL

Instrumentation—A gas chromatograph[1] fitted with a solid sampling device[2], was equipped with dual flame-ionization detectors. The column used was 1.8 m (6 ft) × 4 mm glass, packed with 3% OV-17 on 100–120-mesh Gas Chrom Q[3]. Helium was used as the carrier gas at a flow rate of 20 ml/min, and the air and hydrogen flows were set to maximize detector response. Temperatures were as follows: injector, 250°; column oven, 230°; and manifold, 250°. The signal was fed to a data processor[4], which calculated the results using the internal standard method.

Standard Solution[5]—Transfer 125.0 mg of reference phenylpropanolamine hydrochloride and 20.0 mg of reference chlorpheniramine maleate to the same 10-ml volumetric flask. Dissolve and dilute to volume with water.

Internal Standard Solution—Transfer 75.0 mg of reference *n*-tetracosane to a 25-ml volumetric flask. Dissolve and dilute to volume with chloroform.

Sample Preparation—Finely grind not less than 20 tablets and transfer a portion equivalent to two tablet weights to a 50-ml glass-stoppered centrifuge tube. Add 10.0 ml of chloroform and mix gently. Add 10 ml of 1 *N* sodium hydroxide, stopper, and shake vigorously for 1 min. Centrifuge to clarify the chloroform layer. Transfer 5.0 ml of the chloroform to a glass-stoppered test tube and evaporate just to dryness on a steam bath with the aid of a stream of air. Redissolve the residue in 1.0 ml of the internal standard solution.

Standard Preparation—Proceed as described for the sample preparation, substituting 2.0 ml of the standard solution for the ground tablet mixture.

Procedure—Transfer 2-μl portions[6] of the sample and standard preparations to separate aluminum capsules of the solid sampling device. Evaporate the chloroform and seal the capsules. Introduce the preparations into the gas chromatograph equilibrated at the given conditions.

The phenylpropanolamine elutes first at a retention time of 0.85 min, the chlorpheniramine next at 4.63 min, and the *n*-tetracosane last at 5.76 min (Fig. 1).

RESULTS AND DISCUSSION

Preliminary experimentation indicated that the solvent (chloroform) must be removed before the phenylpropanolamine content can be determined reproducibly. This step was accomplished through the use of the solid sampling device. No interference was noticed from aspirin in concentrations of 325 mg/tablet.

Verification tests, in triplicate, were run by two analysts on two separate samples of ground tablets. The results indicated amounts of 2.05 mg/tablet of chlorpheniramine maleate (label claim 2.0 mg/tablet) with a range of 2.02–2.08 mg/tablet and a *RSD* of ±1.2%. For the phenylpropanolamine hydrochloride, the value found was 12.22 mg/tablet (label claim 12.5 mg/tablet) with a range of 12.12–12.32 mg/tablet and a *RSD* of ±0.7%.

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[1] Perkin-Elmer model 900.
[2] Perkin-Elmer model MS-41.
[3] Supelco, Inc., Bellefonte, Pa.
[4] Perkin-Elmer PEP-1.
[5] All reference standards were obtained from Sterling Winthrop Research Institute, Rensselaer, N.Y.

[6] A Hamilton 25-μl syringe equipped with a repeating dispenser was used.