CAPSULES
preliminary notes and applications from Bioanalytical Systems, Inc.

Cough and Cold Remedies

Introduction

Most of the current cough and cold remedies contain various mixtures of the following compounds: acetaminophen, aspirin, brompheniramine maleate, caffeine, chlorpheniramine maleate, ephedrine, phenylpropanolamine hydrochloride and pseudoephedrine. The pharmacological action of these compounds varies widely as does their concentration within a remedy. A simple rapid means of detecting combinations of these compounds would be advantageous for batch analysis and quality assurance.

In spite of the differing chemical properties of these ingredients, this isocratic method allows the separation of up to five of these compounds in twenty minutes. An internal standard is used as a means of increasing precision.

Conditions

Liquid Chromatograph: BAS 400
Detector: BAS UV-8 at 254 nm
Temperature: 40°C; BAS LC22A/23B
Mobile Phase: 15% MeOH: 85% 0.01M $NH_4H_2PO_4$ (pH=2.3)
Stationary Phase: BAS Cyano (100 x 4.6 mm) 5µm
Flow: 1.5 mL/min
Injection Volume: 20 µL

Standard Preparation

The quantity of ingredients per dose in each remedy can range from 1 mg to 325 mg. Table 1 lists typical adult solid dosage levels. Brompheniramine maleate and chlorpheniramine maleate were prepared at 0.1 mg/mL. The rest of the ingredients, including the internal standard lidocaine, were prepared at 1 mg/mL. Acetonitrile was the solvent for acetaminophen. Aspirin was first dissolved in 20 mL acetonitrile and diluted to volume (100 mL) with deionized water. The remaining compounds are soluble in deionized water. The stock solutions were diluted to concentrations ranging from 75% to 150% of the manufacturers' labeled amounts. Phenylpropanolamine HCl was prepared at levels of 150%, 200% and 300%. One mL of diluted standard was mixed with 10 µL lidocaine prior to injection. Dextromethorphan HBr was not quantitated, but as can be seen, its separation can be achieved with this method.

Sample Preparation

Record the average weight of 1 tablet. Pulverize 20 tablets of the same lot. Weigh out 5% of the mass of 1 tablet and place in a 100 mL volumetric flask. Add 20 mL CH_3CN. After the sample is sufficiently dissolved, dilute to volume with deionized water. Filter the entire sample with Whatman #1 paper (11.0 cm). Mix 1 mL of filtered sample with 100 µL lidocaine.

Discussion

It is necessary for a change in detector sensitivity during the run. The gain is 1.0 AUFS initially. After the elution of lidocaine, the gain is changed to 0.01 AUFS. This allows for the detection of chlorpheniramine maleate, brompheniramine maleate, and dextromethorphan HBr (if desired) as they are present in such small amounts. Calibration curves were constructed plotting the peak height ratio vs. g injected for the compounds eluting before lidocaine. For those eluting after the internal standard, peak height was plotted vs. g injected. Correlation coefficients were calculated by linear regression for each compound. Refer to Figure 1.

Limitations

As mentioned earlier, up to five compounds can be quantitated in one chromatogram. Ephedrine could not be separated from its stereoisomer pseudoephedrine or from aspirin. Caffeine was separated from acetaminophen. Usually this does not present a problem due to the composition of the remedies.

Table 1

COMTREX TABLET: TYPICAL ADULT DOSAGE

325 mg	Acetaminophen
12.5 mg	Phenylpropanolamine HCl
2 mg	Chlorpheniramine Maleate
10 mg	Dextromethorophan HBR

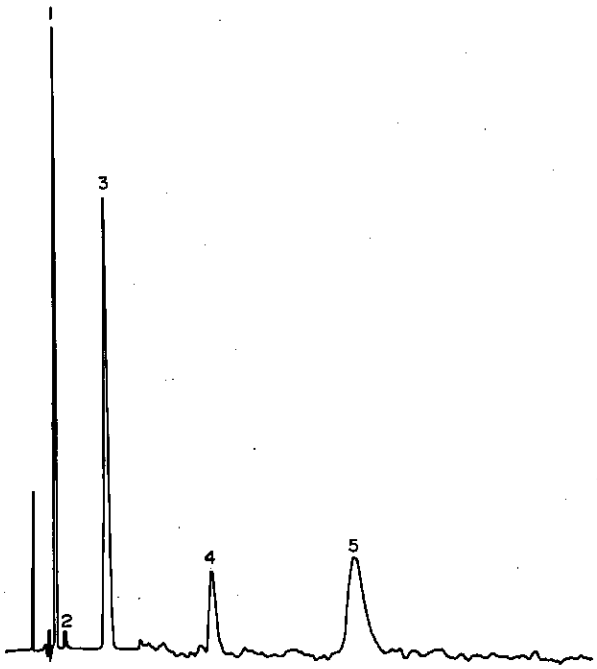

Figure 1. Separation of pharmaceuticals in a cold medication tablet. Conditions as per text. 1 = Acetaminophen, 2 = Phenylpropanolamine Hydrochloride, 3 = Lidocaine (internal standard), 4 = Chlorpheniramine Maleate, 5 = Dextromethorophan Hydrobromide.