

# Simultaneous Determination of Ethanol and Chloroform in Liquid Cough Preparations by Gas Chromatography

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A gas chromatographic procedure using a styrene-divinylbenzene polymer as column-packing material is described. The use of this column allows for the complete separation and simultaneous determination of ethanol and chloroform contained in liquid cough preparations.

THE WIDESPREAD current use of gas chromatography for the quantitative measurement of ethanol (1) and of chloroform (2) suggests that this approach would be desirable in the analytical examination of formulations containing both substances. In practice, however, important difficulties arise. The volume ratio of ethanol to chloroform is always large (e.g., 20 to 1). Response of a flame ionization detector is approximately 10 times greater to ethanol than it is to chloroform. With column materials available until recently, separation characteristics were such that chloroform showed up on the chromatogram as a very small peak on the tail of the ethanol peak. The contribution of ethanol peak tail area to the area under the chloroform peak was large enough to result in poor precision for the chloroform estimation. Recently, Hollis (3) introduced the use of a styrene-divinylbenzene polymer as a column-packing material. This material gives excellent separations of low molecular weight compounds with a minimum of tailing and permits column temperature programming with very low column bleed. A column packed with a styrene-divinylbenzene polymer<sup>1</sup> shows a complete separation of ethanol and chloroform. It has been found possible to measure 0.5% chloroform and 10% ethanol accurately and simultaneously in a cough syrup which also contains dextromethorphan hydrobromide, chlorpheniramine maleate, phenylephrine hydrochloride, glyceryl guaiacolate, glucose, and common preservative, sweetening, coloring, and flavoring agents.

## EXPERIMENTAL

An F and M model 609 instrument was set up as described in Fig. 1 with a glass wool plug inserted in the injection port. The column was a 6-mm. o.d. glass tube 4 ft. long packed with 80 to 120-mesh styrene-divinylbenzene polymer.

An ethanol-chloroform standard solution was prepared by accurately weighing 10.5 ml. of absolute ethanol and 0.55 ml. of chloroform into about 20 ml. of distilled water contained in a 100-ml. volumetric flask. The mixture was made to volume with distilled water and thoroughly mixed. An isopropanol-*n*-butanol internal standard solution was prepared by accurately weighing 11 ml. of isopropanol and 0.1 ml. of *n*-butanol into about 20 ml. of distilled water in a 100-ml. volumetric flask. This mixture was made to volume with distilled water and thoroughly mixed.

Detector response calibration factors were determined from a chromatogram obtained from a 3- $\mu$ l. injection of a solution prepared by mixing 10.0 ml. of the isopropanol-*n*-butanol internal standard

solution and 10.0 ml. of the ethanol-chloroform standard solution. The ethanol peak area was compared to the isopropanol peak area, and the chloroform peak area was compared to the *n*-butanol peak area. In the cough preparation already described, the amounts of chloroform and ethanol were determined from a chromatogram of a 3- $\mu$ l. aliquot of a mixture of 10.0 ml. of the cough syrup and 10.0 ml. of the isopropanol-*n*-butanol internal standard solution.

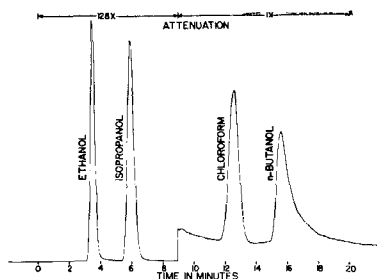


Fig. 1—Chromatogram of detector response calibration solution. Column temperature: 125° isothermally for 3 min., then programmed to 150° at a rate of 2.3° per minute. Injection port temperature = 125°. Helium carrier gas flow rate = 40 ml. per minute. Range = 10. Detector = flame ionization.

## DISCUSSION

The glass wool plug in the injection port retains sugars and other high boiling components. At injection port temperatures greater than 125°, spurious peaks are observed which presumably originate from the thermal decomposition of components. Results using this assay for determining the amounts of chloroform and ethanol in various cough medicines are shown in Table I.

TABLE I—RESULTS OF ASSAY

Cough Medicine Lot No.	Chloroform		Ethanol	
	% Theory	% Found	% Theory	% Found
Pn-N-7a	0.55	0.46	10.0	9.99
Pn-N-7b	0.55	0.54	10.0	9.94
Pn-N-33	0.56	0.49	10.0	10.22
Pn-N-48	0.56	0.55	10.0	9.85
Drm-D-159	0.56	0.55	10.0	10.0

## REFERENCES

- (1) Wesselman, H. J., *J. Am. Pharm. Assoc., Sci. Ed.*, **49**, 320(1960).
- (2) Brealey, L., Elvidge, D. A., and Proctor, K. A., *Analyst*, **84**, 221(1959).
- (3) Hollis, O. L., *Anal. Chem.*, **38**, 309(1966).

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