Gas Chromatographic Determination of Formaldehyde in Solution and High Purity Gas

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▶ **A quantitative procedure is described for determining formaldehyde either in solution or as a high purity gas. A new substrate, Ethofat 60/25, which elutes formaldehyde after water, yields symmetrical peaks for formaldehyde, water, and alcohols. The standard deviation of the method is ±0.34% with solutions containing 30% formaldehyde.**

FORMALDEHYDE is an important industrial chemical which has wide usage in both chemical and high polymer synthesis. It is available commercially as a 37% solution in a mixture of water and methanol (formalin) and as a 38% solution in water and butanol. It is also available from paraformaldehyde. There was a need for a rapid, direct method of analysis, specific for formaldehyde, in any of these compositions as either a liquid or gas. Gas chromatography provides such a method.

Several workers have reported separations of formaldehyde by gas chromatography (*2–4*). Among the more successful were Sandler and Strom (*4*) who used alkyl aryl sulfonates which they extracted from a commercial detergent and coated on either C-22 firebrick or on Fluoropak. They reported satisfactory separations and quantitative results. Although the chromatograms by either system showed tailing of both water and formaldehyde, quantitative results were achieved by these workers using Fluoropak as the solid support. McReynolds (*3*) reported separations on columns using sucrose octaacetate loaded on Celite which had been washed with acetic acid. However, he reported that methanol interfered with the elution of formaldehyde.

This work reports a new gas liquid chromatographic procedure to determine formaldehyde quantitatively. The system may be used with water–methanol solutions, water–butanol solutions, or on high purity gas streams. Symmetrical peaks are obtained for formaldehyde, water, and alcohols. Column life is extensive as indicated by a column which has been in nearly constant use for two years.

EXPERIMENTAL

Apparatus. A major portion of the work was done with an Aerograph Model A-100-C gas chromatograph. Selected portions of work were done on a modified Perkin-Elmer Model 154C gas chromatograph (*1*), a Consolidated Electrodynamics Corp. Model 201A gas chromatograph, and a dual column programmed temperature instrument constructed in this laboratory. The Perkin-Elmer instrument was equipped with a thermistor detector; the others used filaments.

Liquid samples were injected with a Hamilton Microliter syringe equipped with a Chaney Adapter. Inlet heaters were maintained at 200° C. Gas samples were added through an Aerograph heated gas sampling valve. The valve sample ports were enlarged to 0.064 inch to minimize pressure drop and to prevent plugging. The valve was equipped with an 18-ml. sample loop prepared from 1/8-inch o.d. copper tubing in a 2.5-inch coil mounted close to the body of the valve. The entire assembly was wrapped with insulation and maintained at 150° C. Feed lines from the formaldehyde gas generator were heat traced and maintained at about 135° C.

The columns were prepared from 5-meter lengths of 1/4-inch copper tubing, coiled, after packing, to fit the respective instruments. Solid supports investigated were Fluoropak 80 (Fluorocarbon Co.), Teflon 6 (E. I. du Pont de Nemours & Co.), Columnpak T (Fisher Scientific Co.), Chromosorb W (Johns-Manville Products Corp.), and Chromosorb W boiled for 1 hour in glacial acetic acid and water washed before coating.

The liquid phase used for the analysis was Ethofat 60/25, a polyoxyethylene monostearate containing an average of 15 ethylene oxide units. The material has an average molecular weight of 938. It was obtained from Armour Industrial Chemical Co. Other substrates investigated were *dl*-sorbitol, diethylene glycol, mannitol hexaacetate, sucrose octaacetate, Carbowax 6000, Apiezon N, and Lac 296 (polyethylene glycol succinate). All substrates were loaded to 10 wt. per cent on the fluorocarbon

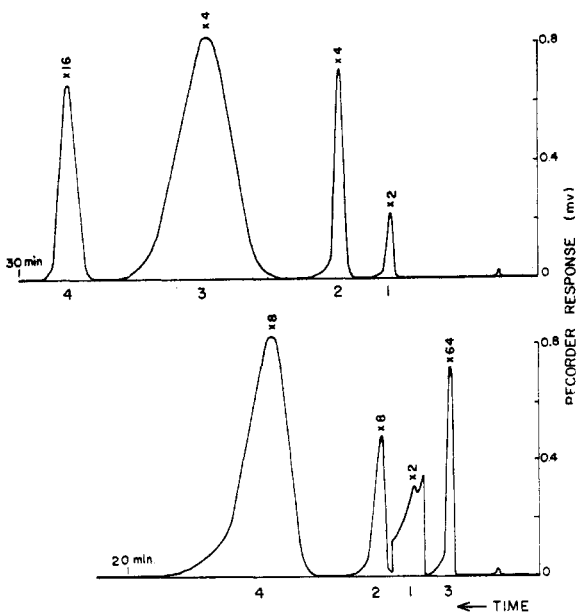

Figure 1. Comparison of Ethofat and sucrose octaacetate

Operating Conditions:
Top Chromatogram
Column: 5M Ethofat 60/25, 10 wt. % on Columnpak T
Temperature: Column 115° C. Injector 250° C.
Flow: 43 ml./min.
Bridge current: 230 ma.
Sample size: 5 μl.
Bottom Chromatogram
Column: Same as top but with sucrose octaacetate substrate
1. Methanol
2. Water
3. Formaldehyde
4. Butanol

Table I. Recovery Data from 18 Replicate Analyses of 2 Samples

Component	Added, %	Found, %
Methanol	10.9	10.8 ± 0.32
	8.9	8.7 ± 0.32
Water	47.2	47.2 ± 0.37
	38.6	38.3 ± 0.37
Formaldehyde	33.8	33.8 ± 0.34
	27.7	27.9 ± 0.34
Butanol	8.1	8.3 ± 0.40
	24.8	25.2 ± 0.40

supports and to 20 wt. per cent on the chromosorb supports.

Procedure. STANDARD SOLUTIONS. Calibration and test solutions were prepared from paraformaldehyde, from formalin, and from formalin plus butanol.

A formaldehyde standard solution containing 23.83% formaldehyde was prepared by boiling paraformaldehyde in distilled water. The solution was filtered and its formaldehyde content determined by the standard peroxide method (*5*). This solution was used to determine the sensitivity for formaldehyde.

Butanol–formaldehyde test solutions with concentrations shown in Table I were prepared by diluting previously analyzed formalin with butanol.

Formalin solutions used for the calibration were prepared by diluting previously analyzed formalin (*5*) with water.

A standard reference solution containing 15 wt. per cent methanol, 47.4 wt. per cent water, and 37.6 wt. per cent butanol was prepared for routine use as a reference.

ANALYSIS OF SOLUTIONS. Chromatograms of the test and of the reference solution were prepared at the operating conditions prescribed in Figure 1, and the areas of the peaks of interest were determined with a polar planimeter. The peak areas were corrected using Equation 1.

$$A_c = A_m \frac{S_o}{S_m} \qquad (1)$$

Where

A_c = corrected peak area
A_m = measured peak area
S_o = peak area of reference at time of calibration
S_m = peak area of reference at the time of analyses

Reference peak areas, S_o, for a 5-micron injection are given in Table II

Table II. Calibration Data

	S_o (cm.²)	m (cm.²/g. × 10^{-4})	b (cm.²)
Methanol	131.2	17.42	+7.65[a]
Water	402.5	19.63	−6.52
Formaldehyde	...	18.22	+3.37
Butanol	226.6	13.35	+3.07

[a] Use this correction when area is greater than 15 cm.² = 1% MeOH.

for methanol, water, and butanol. Each area may be used separately, and reasonable accuracy may be attained with a simplified procedure in which all peaks are normalized on the water peak.

The corrected areas were used to determine the mass, G, of each component in the test solution by Equation 2.

$$G = \frac{A_c - b}{m} \qquad (2)$$

Where

A_c = corrected peak area
b = intercept—determined at the time of calibrations (Table II)
m = slope of the calibration line (Table II)

For routine use the equations were combined and sample weight was introduced to produce Equation 3 which allows the calculation of the percentage of any component present, C.

$$C = \frac{\left(A_m \frac{S_o}{S_m} - b\right) 100}{mg} \qquad (3)$$

Where g = grams injected

Table I shows the recovery and the standard deviation from 18 replicate analyses of two samples of butanol–formaldehyde test solution.

ANALYSES OF HIGH PURITY GAS. Ethofat 60/25 was also used to analyze high purity formaldehyde gas streams. It provided a distinct advantage over other substrates because it eluted the major impurities before the formaldehyde peak and still provided a usable formaldehyde peak.

Formaldehyde was produced by heating paraformaldehyde to 150° to 175° C. in a glass generator. A 15- to 25-ml. per minute stream of argon swept the evolved gas into a heated gas sampling valve loop from which it was injected into the analytical column. A typical chromatogram of products from the degradation of paraformaldehyde is shown in Figure 2. (Sample composition was

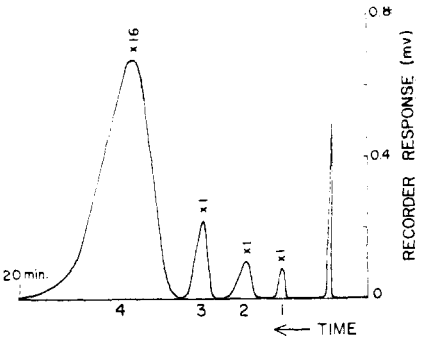

Figure 2. High purity formaldehyde

		% Composition
1.	Methyl Formate	0.08
2.	Methanol	0.27
3.	Water	0.41
4.	Formaldehyde	99.24

Initial peak is argon sweep gas

calculated from peak areas using appropriate calibration curves.) By decreasing sweep gas rate, samples containing as little as 0.007% water have been analyzed. The gas composition shown in Figure 2 was typical for the initial degradation of paraformaldehyde. As a given generator charge was depleted, it was necessary to raise the temperature to sustain the degradation rate, and with the increased temperature, impurities increased.

DISCUSSION

Calculation Procedure. While the calibration curve was suitable for formaldehyde analyses, the preferred technique in this laboratory was to use the slope intercept equation in conjunction with a reference solution. The standard reference solution was measured at the time of the initial formaldehyde calibration, and a formaldehyde-to-water instrument sensitivity ratio was determined. Once the ratio was established, the instru-

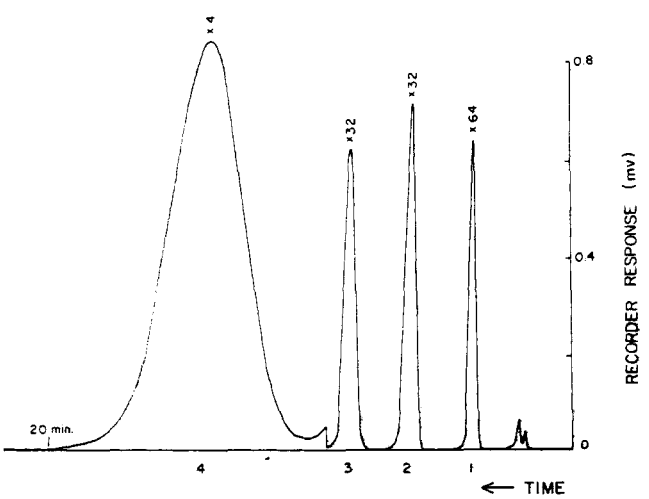

Figure 3. Separation of aldehydes on Ethofat 60/25

Operating conditions same as in Figure 1

1. Acetaldehyde
2. Methanol
3. Butyraldehyde
4. Formaldehyde

ment could be calibrated using the stable water alcohol solution. The ratio held for instruments other than the one on which the formaldehyde sensitivity was determined. The data shown in Table III, for example, were obtained on instruments calibrated with reference solution only. It appeared that the sensitivity ratio was virtually a constant for thermal detectors. The reference solution, used to correct day to day variations in sensitivity, allowed a single value to be used for the slope in the slope intercept equation.

Use of a reference standard is well known in mass spectrometry where a regular check of butane sensitivity is made to correct sensitivities to other components. The principle was employed here to allow the analyst to use an easily prepared stable calibration solution in place of one which was difficult to prepare and to maintain. During the initial phase of this work changes in sensitivity, particularly to formaldehyde, were observed, and frequent use of the reference solution was imperative. Preloading the column with several large (50 μl.) injections of formalin was necessary following periods of column purge to ensure stable sensitivities on successive runs. As the Fluoropak 80–Ethofat 60/25 column aged, sensitivity stabilized. In later work, Columnpak T or Teflon 6 was used as a solid support. These columns showed no need for preloading. Sensitivities were much more stable, and the reference solution was used less frequently. The reference solution did provide an excellent means for calibrating new instruments and enabled an analyst to use any of several instruments without developing and maintaining a calibration curve for each.

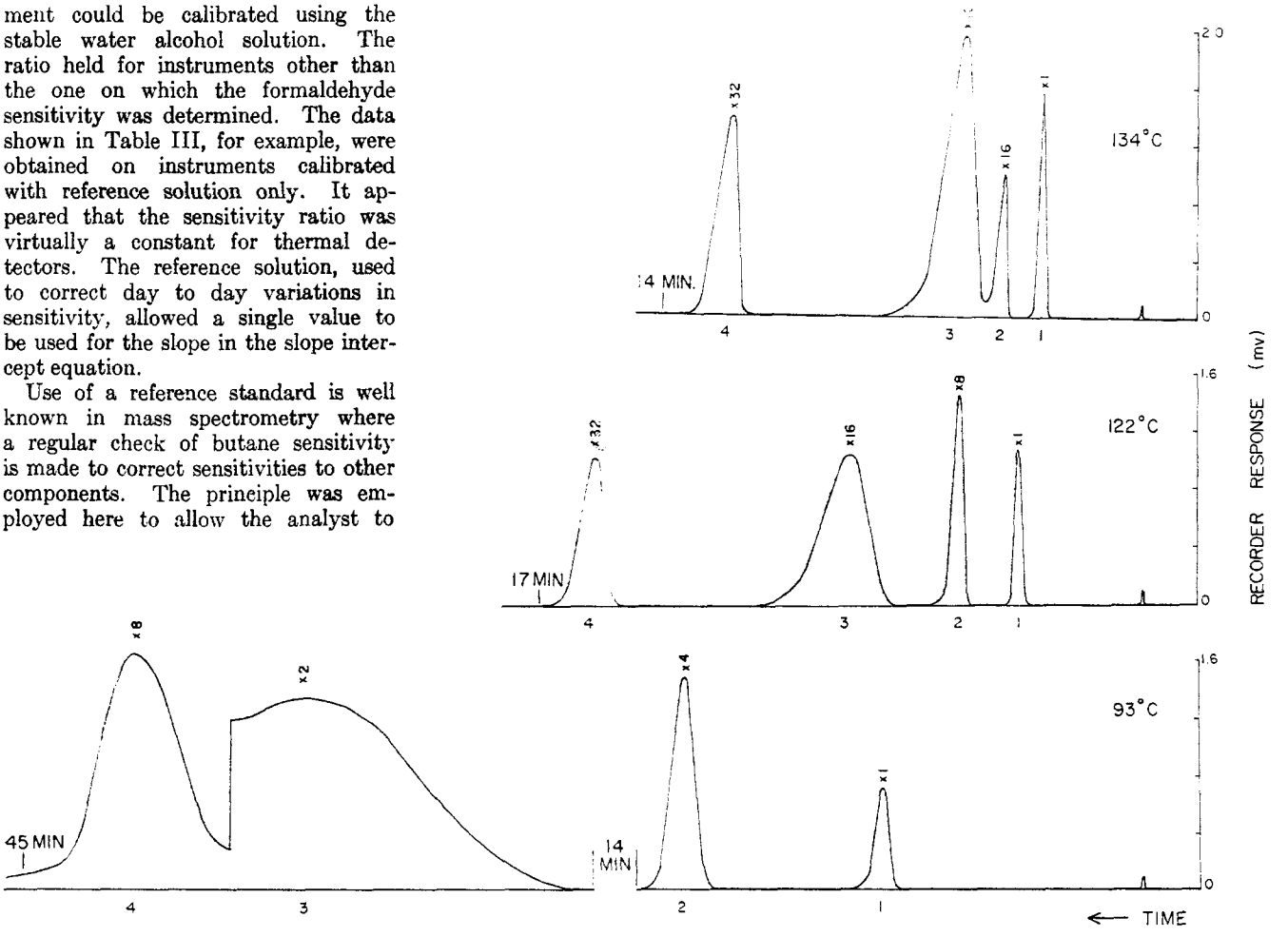

Figure 4. Effect of temperature on formaldehyde retention

Peak identities same as in Figure 1

Table III. Results from Instruments Calibrated with Reference Solution

Instrument	Per cent present: Methanol	Water	Formaldehyde
Consolidated Electrodynamics Corp.	8.5	54.7	36.8
Perkin-Elmer	8.9	54.8	36.3
Dual Column Instrument	8.9	54.4	36.7
Chemical Analysis	9.3	54.2	36.5

The intercepts shown in Table II deserve consideration. The positive intercepts for methanol, formaldehyde, and butanol result from sample not delivered by the plunger, but which flashed from the needle. The negative intercept shown for water is due to the difference between the amount of water flashed from the needle and the amount detained by the column. Although fluorocarbons are virtually inert, the water peak still tails slightly. The negative intercept therefore is caused by the longer retention of very low concentrations of water. This is indicated by a slight curvature of the calibration line for water indicating a nonlinear isotherm. The curvature was much more severe when chromasorb was used as a solid support.

The slope intercept equation was very desirable for use in the analysis of samples in the normal concentration range of formalin and butanol-form-

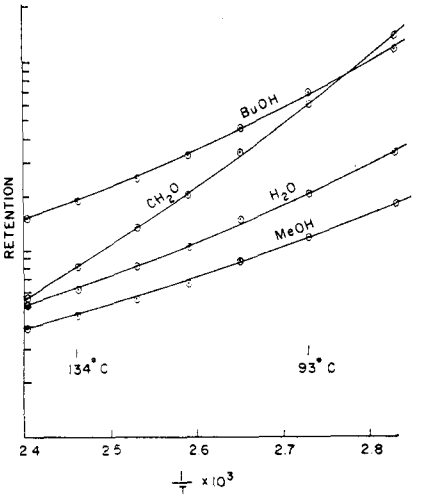

Figure 5. Effect of temperature on retention

aldehyde solution. When the concentration of any component approached the value of the intercept a separate calibration for that component was required.

Separation. Optimum separation of the components of formalin and butanol–formaldehyde solution was obtained with Ethofat 60/25 loaded on Columnpak T. Figure 1 shows a chromatogram of butanol–formaldehyde solution and the operating conditions at which the separation was made. Of the eight substrates investigated, only Ethofat 60/25 afforded complete resolution of all the components in butanol–formaldehyde solution and yielded symmetrical peaks for formaldehyde. Sucrose octaacetate produced reasonable peaks for formaldehyde as shown in the bottom chromatogram of Figure 1, but eluted methanol on the tail of the formaldehyde. Table IV shows the elution order of the components in butanol–formaldehyde solution from each of the eight substrates investigated. The components in parentheses were not resolved.

Ethofat 60/25 showed particularly

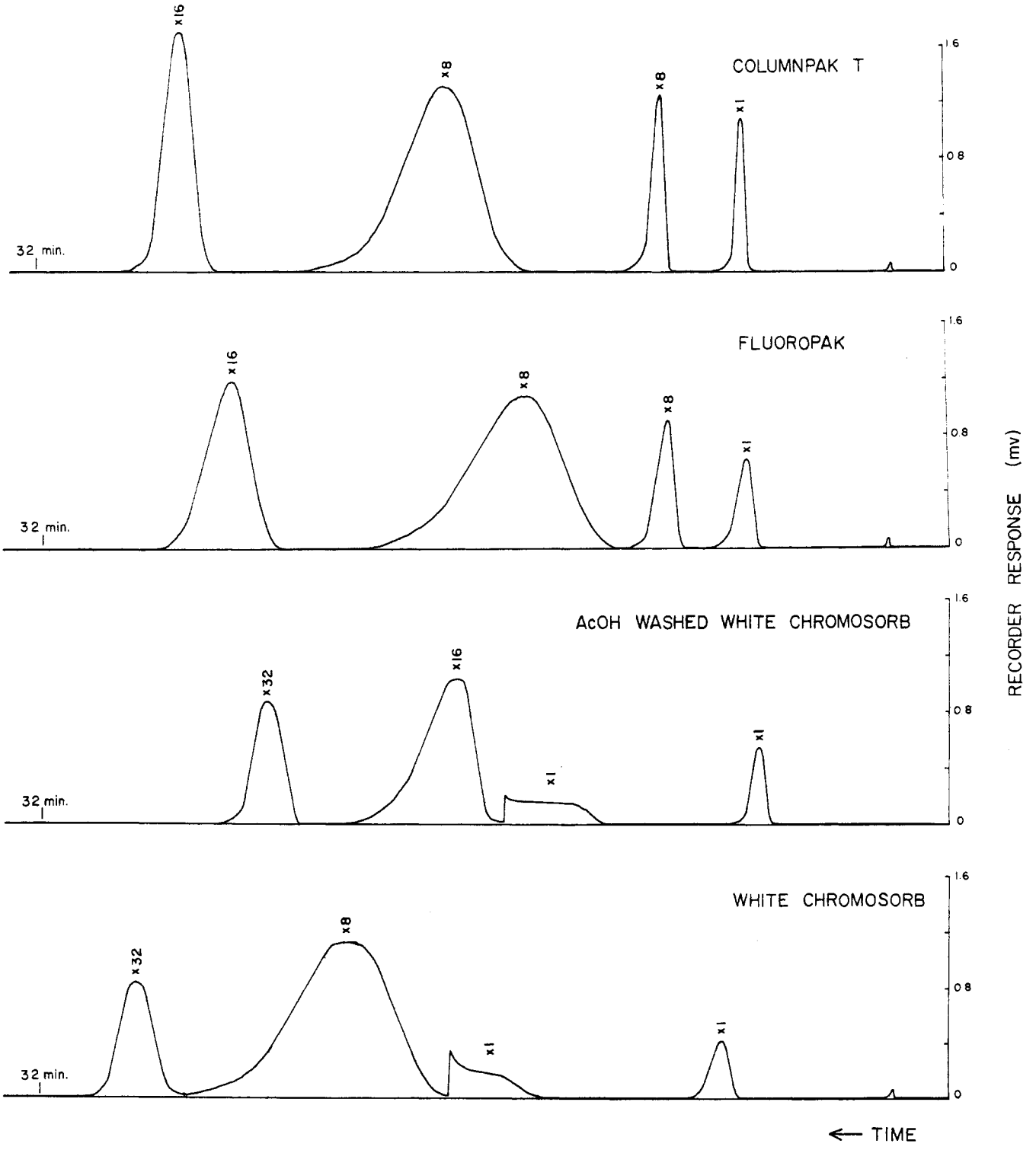

Figure 6. Comparison of solid supports for Ethofat 60/25

Peak identities same as in Figure 1

desirable properties in the analysis of formaldehyde. It afforded a complete separation of each of the components of butanol–formaldehyde solution and formalin. As shown in Figure 3, it separated higher aldehydes, eluting formaldehyde after the time for butyraldehyde. It was of particular interest that Ethofat 60/25 separated formaldehyde by a property other than solubility in the substrate. This was concluded because the formaldehyde peak was wider than the butanol peak which eluted after it. The performance of other substrates supported this conclusion. For example, formaldehyde was eluted from sorbitol after water in a broad peak. At 150° C. the formaldehyde peak was too broad to be used for direct analysis. The long retention was first attributed to the presence of hydroxyl groups present on both sorbitol and Ethofat 60/25. However, Carbowax 6000, which contains only secondary alcohol groups, eluted formaldehyde before methanol. It was then proposed that the unique retention of formaldehyde was due to the formation of a weak hemiacetal with the primary hydroxyl group on the substrate. The proposal was tested by comparing formaldehyde retention on diethylene glycol, hexane-1,6-diol, and 2-methyl pentane-2,4-diol. The two latter materials were not suitable for general use as substrates for formaldehyde analysis because of their high vapor pressures, but were chosen as available sources of primary and secondary alcohols, respectively. Formaldehyde was retained on diethylene glycol after water and butanol, although the separation from water was not complete. Formaldehyde eluted from the secondary alcohol before methanol but was retained by the primary diol. It was concluded from this work that the retention of formaldehyde on material containing primary hydroxyl groups was through the formation of an unstable hemiacetal.

Table IV. Elution Order for Several Substrates

Substrate	Elution Order[a]	Performance
Ethofat	M,W,F,B	Good
Sorbitol	(MB),W,F	Poor formaldehyde peak
Diethylene glycol	M,B,(WF)	High vapor pressure
Lac 296	F,M,W,B	Fair
Mannitol hexaacetate	F,M,(WB)	Anomalous
Sucrose octaacetate	F,M,W,B	Good
Carbowax 6000	F,M,W,B	Fair
Apiezon N	(FMW),B	Poor

[a] M = methanol, W = water, B = butanol, F = formaldehyde, ( ) includes peaks not resolved.

Influence of Temperature. Column temperature had a marked effect on the elution of formaldehyde from Ethofat 60/25. The separation was studied at seven different temperatures. Chromatograms of butanol–formaldehyde solutions obtained at three different column temperatures are shown in Figure 4. From a plot of log retention *vs.* $1/T$ as shown in Figure 5, it was determined that optimum separation was made at 118° C. However, satisfactory separations were made between 110° and 125° C.

Solid Supports. The effect of several solid supports on the separation of butanol–formaldehyde solution when using Ethofat 60/25 as the substrate is shown in Figure 6. Columnpak T produced the sharpest peaks for all components. The performance of Teflon 6, not shown on the figure, was between Columnpak T and Fluoropak 80. This work also demonstrated that acetylating the white chromosorb improved the formaldehyde and the alcohol peaks but did not improve the water peak. When water was present in the sample, Columnpak T was the preferred support.

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Purification of Vitamin A by Partition Chromatography in the Analysis of Pharmaceuticals and Margarine

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▶ **Partition chromatography was applied to the separation of vitamin A from various types of interference, such as oxidized vitamin A and vitamin E, commonly found in pharmaceuticals. Vitamin A was also separated from β-carotene and other interfering material found in margarine. Recovery of the vitamin was almost complete and the absorbance curves of the chromatographed samples resembled that of pure vitamin A. The column was easily prepared, required no standardization, could be used for successive samples, and made possible the application of the spectrophotometric method to samples which could not otherwise be assayed by this method.**

VITAMIN A is usually estimated in pharmaceuticals by the spectrophotometric method described in the USP **XVI** (*10*). Lehman *et al.* (*5*) pointed out the shortcomings of this method when applied to mixtures of *cis* and *trans* isomers, but for most samples it gave an accurate estimate of biological potency (*6*). Although no guidance on this matter was given in the USP method, it cannot be applied to samples with grossly distorted absorbance curves. The need for purification in such cases was recognized by the British Pharmacopoeia (*2*), but no procedure was recommended. The International Union of Pure and Applied Chemistry (I.U.P.A.C.), in a report of collaborative experiments (*1*), recommended that chromatography on alumina be used when the absorbance ratio, 300 mμ/325 mμ exceeded 0.730, and demonstrated the use of such a procedure in the purification of a