

# ANALYSIS OF GASES IN BLOOD WITH THE MASS SPECTROMETER. V. THE DETERMINATION OF CONCENTRATIONS OF CYCLOPROPANE IN BLOOD BY TOTAL EXTRACTION OF GASES\*†

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In the previous paper (1) a technic for the total extraction of gases from a sample of blood for the purpose of mass spectrometric analysis was described. The necessity for the adoption of this technic for gases entering into chemical combination with some element of the blood was explained. Gases entering only into physical solution in the blood may be partially extracted by equilibration at constant temperature. This method is dealt with in some detail in earlier papers describing analytic technics for ether and for nitrous oxide (2, 3). The equilibration method requires a knowledge of the distribution coefficient of the gases for which the analysis is being made. The technic of total extraction of gases just mentioned requires no knowledge of the solubility of the gases under consideration. This paper deals with the application of the total-extraction technic to analysis for cyclopropane in blood.

For details of the technic of total extraction of gases in the preparation of a sample of gases for analysis on the mass spectrometer the reader is referred to the previous paper dealing with carbon dioxide and oxygen (1). In brief, this method involves admission of the measured sample of blood to an evacuated system in which the blood may be dried quickly by application of gentle heat. The gases thus released with water vapor are moved to and fro through a calcium chloride absorber by alternate filling with mercury and emptying a tonometer of large volume. After the blood and gases released from it are completely dry, a measured amount of argon is admitted to, and mixed with, the sample of gas. A portion of the resulting mixture is then

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moved into a previously evacuated glass sample bulb suitable for transfer to the manifold of the mass spectrometer.

Analysis then proceeds in accordance with the principles set down in the previous papers (1, 2, 3) to determine the relative ratio between the abundance of cyclopropane and argon admitted to the mass spectrometer. This determination is made by suitable calculation after recording the voltage output of the mass peak 42 taken to represent cyclopropane (fig. 1) and the corrected voltage output of the mass 40 representing argon.¶

A constant  $k$  used in making the calculation is determined in the following manner: A carefully prepared known mixture of cyclopropane and argon is admitted to the mass spectrometer and the ratio

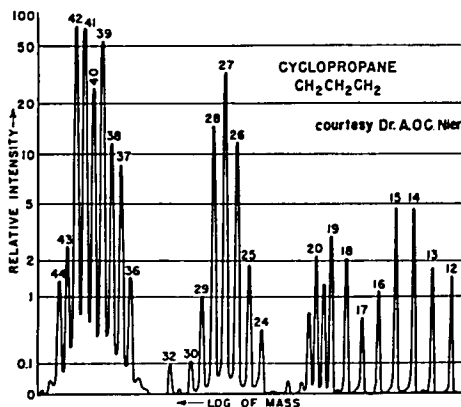


FIG. 1. Mass spectrum of cyclopropane. Peak 42 representing the ionized whole molecule was used to identify cyclopropane in these studies. The small contributions of cyclopropane to peaks 32 and 44 used for oxygen and carbon dioxide respectively and the large contribution to peak 40 used for argon should be noted.

of corrected voltages at peaks 42 and 40 is observed. This ratio of voltages bears a relationship to the ratio of volumes of these two gases and is determined by constant  $k$ . On comparison of several such mixtures,

$$\frac{\text{Vol } C_3H_6}{\text{Vol a}} = k \frac{V_{42}}{V_{40}}$$

this constant was determined accurately. Since it tended to change from day to day, a known mixture of the two gases was kept on hand

¶ The correction is required because of the substantial contribution of cyclopropane to mass 40. The amount of this contribution is calculated from the fixed and known 42/40 ratio of cyclopropane alone and the observed abundance of mass 42.

for frequent redetermination of this value. When the value  $k$  and the ratio of voltage of peak 42 ( $V_{42}$ ) to the corrected voltage of peak 40 ( $V_{40}$ ) is known, the amount of cyclopropane in the original sample may be determined as follows:

$$\text{Vol C}_3\text{H}_6 \text{ per 100 ml.} = \frac{kR \times \text{Vol a} \times 273.2 \times \text{BP} \times 100}{T \times 760 \times \text{Vol b}}$$

when:  $k = \text{constant}$

$$R = V_{42}/V_{40}$$

Vol a = volume of argon at temperature  $T$  (C.) and pressure BP (millimeters of mercury)

Vol b = volume of blood.

#### VALIDATION OF THE METHOD

In order to determine the limits of accuracy of the method, an apparatus was devised for the preparation of known concentrations of cyclopropane in blood. It was our object to prepare a sample of blood containing a known concentration of oxygen, carbon dioxide and a third gas; in this instance, cyclopropane. To this end blood was used in which the content of carbon dioxide had been previously determined by Van Slyke analysis. The problem then became one of adding known amounts of cyclopropane without loss of oxygen or carbon dioxide, or with loss or gain of a known quantity of these two gases. The apparatus used is illustrated in figure 2. Bulb  $F$  was filled with cyclopropane; bulb  $G$  with argon; both bulbs had been carefully calibrated. The temperature and pressure of the gas admitted were noted and it was possible to know the exact amount contained in the bulbs. Bulb  $B$  was filled with blood. Its volume had been previously calibrated. By means of leveling bulb  $D$ , mercury was held at the calibration line in the joint on the tube joining  $B$  and  $C$ . After the manifold joining different components of this system had been evacuated, cyclopropane was admitted by opening the stopcock on  $F$ . Blood was then pulled down into chamber  $C$  and stopcock  $a$  was turned to connect  $B$  with the manifold. Some of the cyclopropane was thus pulled into  $B$ . Stopcock  $a$  was then closed and the blood moved back and forth from  $B$  to  $C$  to facilitate solution of the cyclopropane. When sufficient absorption had taken place, stopcock  $a$  was opened and all the remaining gas was pushed back into the manifold. The sample of blood thus prepared was removed anaerobically through outlet  $A$  and stored for subsequent analysis. The argon  $G$  was then admitted to the manifold and mixed thoroughly with all of the remaining gas. This was accomplished by raising and lowering the mercury in chamber  $E$ . A sample of this mixture was drawn off through  $H$  into a gas sample bulb. The mixture contained a sample of the total remaining cyclopropane, argon and the nitrogen, carbon dioxide and oxygen which had come off of the blood during the mixing. The sample was then analyzed on the mass spectrometer for

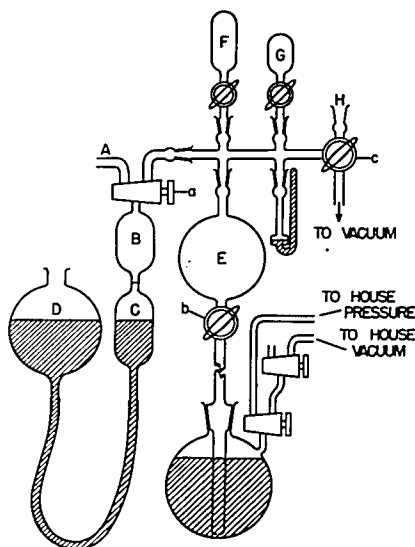


FIG. 2. Apparatus for preparation of blood samples containing a known amount of gas. *D*. The calibrated blood chamber. *F*. The calibrated bulb containing a known amount of gas to be added to the blood. *G*. The calibrated bulb containing a known amount of argon to be added to the remaining gas sample before analysis. *H*. Joint for attachment of gas sample bulb. See text for other details.

these components. Knowing the original amount of cyclopropane and the volume remaining after absorption and the volume of blood to which it was exposed, we could calculate the concentration of cyclopropane in the blood.\*

In a similar manner it was possible to calculate the remainder of the carbon dioxide or oxygen in the blood.

With the apparatus described, a total of thirty-nine samples of blood containing seven different concentrations of cyclopropane were an-

\* Let  $V_c$  = initial volume of cyclopropane contained in *F* (standard temperature and pressure).  $l_v$  = remaining cyclopropane after absorption (standard temperature and pressure).  $V_b$  = volume of blood used. Then:  $\frac{V_c - l_v}{V_b} \times 100$  = volume per cent cyclopropane in blood.

$l_v$  is calculated by the following formula:

$$l_v = V_a \times k \times R$$

when:  $V_a$  = volume of argon contained in *G*

$k$  = calibration constant described in another portion of this work

$R$  = 42/40 ratio as determined on mass spectrometer.

alyzed on the mass spectrometer by the technic described in this paper. The results of these analyses are shown in table 1.

It is probable that errors contributing to the differences shown in the table resulted from multiple transfers of the sample of blood from one syringe to another at various temperatures, and from the differences in pressure applied in the preparation of the samples of blood with known concentrations of cyclopropane. It is probable also that, in application of the analytical technic to samples of blood containing unknown quantities of gases, many of these sources of error would not be present. Therefore, we are of the opinion that in clinical use the accuracy of the method is substantially greater than that indicated in table 1. The mean standard deviation of the analyses in thirty-nine trials was  $\pm 4.2$  per cent. This degree of over-all consistency suggests that we must look to the method of known sample preparation for the

TABLE 1  
CYCLOPROPANE IN BLOOD

Calculated Concentration		Mass Spectrometric Analysis				
No. of Runs	Mean, Vol. Per Cent	No. of Runs	Mean, Vol. Per Cent	Per Cent Standard Deviation	Difference from Calculated Values	
					Vol. Per Cent	Per Cent RMS Difference
2	0.410	6	0.521	$\pm 7.2$	+0.111	$\pm 28.5$
2	2.93	4	3.25	$\pm 2.4$	+0.32	$\pm 11.3$
3	4.28	5	4.17	$\pm 4.2$	-0.11	$\pm 5.0$
2	7.11	6	6.33	$\pm 3.2$	-0.782	$\pm 11.4$
1	15.59	4	15.3	$\pm 2.0$	-0.29	$\pm 3.8$
4	22.23	6	21.43	$\pm 2.0$	-0.80	$\pm 4.6$
2	30.32	8	29.38	$\pm 7.3$	-0.94	$\pm 7.7$
Mean				$\pm 4.2$		$\pm 10.3$

major discrepancy indicated in the mean per cent root mean square (RMS) difference of  $\pm 10.3$ .

The analysis for carbon dioxide and oxygen follows the system outlined in the previous paper (1). Carbon dioxide is measured on the mass spectrometer as mass 44 and oxygen as mass 32. It may be noted from the mass spectrum of cyclopropane (fig. 1) that contributions by cyclopropane to peaks 44 and 32 are not significant, especially since peak 42 in actual samples is small as compared to that of oxygen and especially as compared to that of carbon dioxide. It is probable that some of the masses 44 and 32 in the mass spectrum of cyclopropane are contributed by contamination with air of the sample represented. In any event, these contributions have been ignored in analysis of samples since they contribute to the final result to an extent not greater than

0.5 per cent when cyclopropane is present at 10 volumes per cent in the analyzed sample.

### SUMMARY

The application of a technic for the total extraction of gases to the mass spectrometric analysis of samples of blood for cyclopropane is described. A method for the preparation of samples of blood containing known quantities of complex mixtures of gases is described. Application of this method is made in validating analysis of samples of blood. The evidence presented shows that simultaneous analysis for oxygen and carbon dioxide may be carried out in the presence of cyclopropane by use of this technic.

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