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APPLICATION OF THE METHOD OF CHROMATOGRAPHIC EQUILIBRATION TO AIR POLLUTION STUDIES

THE DETERMINATION OF MINUTE AMOUNTS OF HALOTHANE IN THE ATMOSPHERE OF AN OPERATING THEATRE

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SUMMARY

The method of chromatographic equilibration was applied to the determination of traces of halothane in the atmosphere of operating theatres. Apiezon K on Sterchamol and the porous polymers Porapak P and Q were employed as sampling tube packings, the detection being carried out with a flame ionisation detector. The relation for calculating the results contains a term allowing for the dead volume of the sampling tube. Under conditions of normal running in the theatres investigated, the concentrations of halothane found in the atmosphere varied between 10–50 p.p.m. When Porapak Q was used as the sampling tube packing, halothane concentrations down to 0.01 p.p.m. could be determined.

INTRODUCTION

Halothane (2-chloro-2-bromo-1,1,1-trifluoroethane) is used as an anaesthetic in surgery and is administered by inhalation. Some escape of halothane, to a lesser or larger degree, into the atmosphere of the operating theatre is possible when the usual method of application is used. It is therefore not surprising that many anaesthetists suffer from various malaises, such as headache, irritation, blockage, etc. These may be so marked as to impair the anaesthetist's working ability in some cases. At the present time, there are no objective data on a physiologically tolerable concentration of halothane in the atmosphere, and the threshold limit value has not yet been determined. The determination of trace amounts of halothane in the atmosphere is not very easy. Gas chromatography undoubtedly affords a suitable experimental approach to these problems, particularly with respect to the ease of separating halothane from other substances occurring in the atmosphere and the sensitivity of detection. There are several papers describing a gas chromatographic assay of the purity of halothane[1,2] and its content in respiratory mixtures, blood, and tissues[3–10]. The removal of halothane vapours from waste gases has also been described[11]. However, data on the determination of minute amounts of halothane in the atmo-

sphere of operating theatres are completely absent. By virtue of the information available it can be concluded that the mixtures analysed usually contained[6,9] 50–150 p.p.m. of halothane, the detection limit being about 1 p.p.m.

The constitution of halothane would suggest that a higher sensitivity of analysis could be obtained by using an electron capture detector[12] rather than a flame ionization one[13]. However, the higher sensitivity is impeded by a low stability of the electron capture detector if the electrodes are contaminated by large amounts of water vapour and oxygen[14] and by the limited linearity of the response to halothane[15].

We therefore used the method of chromatographic equilibration[16] which has previously been described and applied successfully in air pollution studies[17]. This method permits traces of halothane to be concentrated to a level which is easily perceptible, with analytical precision, by a flame ionization detector. The above concentration method is very expeditious and permits a sensitivity higher than that afforded by the electron capture detector, without encountering the problems incidental to the use of the latter in routine analysis.

As distinct from the original paper[16], a correction for the sampling-tube dead volume was introduced; this is of relevance in cases where the solute accumulation in the tube is relatively low. In order to attain a high degree of accumulation, porous polymers were tried out as the sampling tube packings.

EXPERIMENTAL

Sampling tube packings

Owing to the chemical nature of halothane and to its appreciably high volatility at room temperature, it is difficult to find a gas–liquid system which will have the property of good absorption of halothane and, at the same time, satisfactory thermal stability. Nevertheless, a gas–liquid system, with Apiezon K as the sorbent, has been used for actual analyses of the atmosphere of various operating theatres. In these cases, the concentration of halothane was usually quite sufficient for it to be determined conveniently even at the relatively low degree of accumulation afforded by the above system.

However, the gas–liquid system described above is unsatisfactory if halothane concentrations lower than 1 p.p.m. are to be determined. Therefore, gas–solid systems with the porous polymers Porapak P and Q as the sampling tube packings were tried out. The partition coefficients of halothane are much higher in these systems than in gas–Apiezon K, the adsorption isotherms being practically linear within relatively wide concentration limits. Both types of Porapak, like Apiezon K, are hydrophobic materials, so that one would not expect the results of the halothane determination to be affected by the humidity of the air.

The Porapaks intended as packings for the sampling tube were first packed into a column of the analytical gas chromatograph and kept for several hours under the carrier gas stream (nitrogen) at the temperature to be used later to accomplish the desorption of the halothane accumulated in the sampling tube (180° C), during which time halothane samples were repeatedly injected into the column and monitored for retention time. The latter decreased slightly at first and, after about half an hour, settled to a constant value. After carrying out the above conditioning procedure, the contents of the column were poured out and used for packing the sampling

tubes, thus precluding the possibility of changes in the tube-packing sorption capacity upon heating the tube repeatedly to the desorption temperature.

The sampling tubes proper were prepared from 1-ml tuberculin syringes, according to the procedure described earlier[16]. In the case of the Apiezon K packing (25 % by weight of Apiezon K on Sterchamol 0.20–0.25 mm; Associated Electrical Industries Ltd., Great Britain, and Sterchamol Werke, Dortmund, G.F.R., respectively), the length of the packing was about 5 cm, which represented about 0.45 g of material. In the work with the porous polymers, the tube packings amounted to about 0.1 g. The ends of the sampling tube were plugged with quartz-wool to keep the packing material in place. After insertion of an injection needle, the sampling tube served as a probe for introducing the desorbed halothane into the inlet port of the gas chromatograph.

Gas chromatographic analysis of the halothane trapped in the sampling tube

The chromatographic analyses were carried out on a Becker Multigraph 409 (Becker Delft, The Netherlands) with a flame ionisation detector. The column was of stainless steel, 1.5 m long and 3 mm I.D., packed with 7.15 g of 25 % by weight of Apiezon K on Sterchamol, 0.20–0.25 mm, and kept at a temperature of 80°C. The flow rates of the carrier gas, hydrogen and air were 0.47, 0.54, and 10 ml/sec, respectively. The arrangement employed in the work with the sampling tubes is shown in Fig. 1. The sampling valve installed ahead of the injection port was modified in

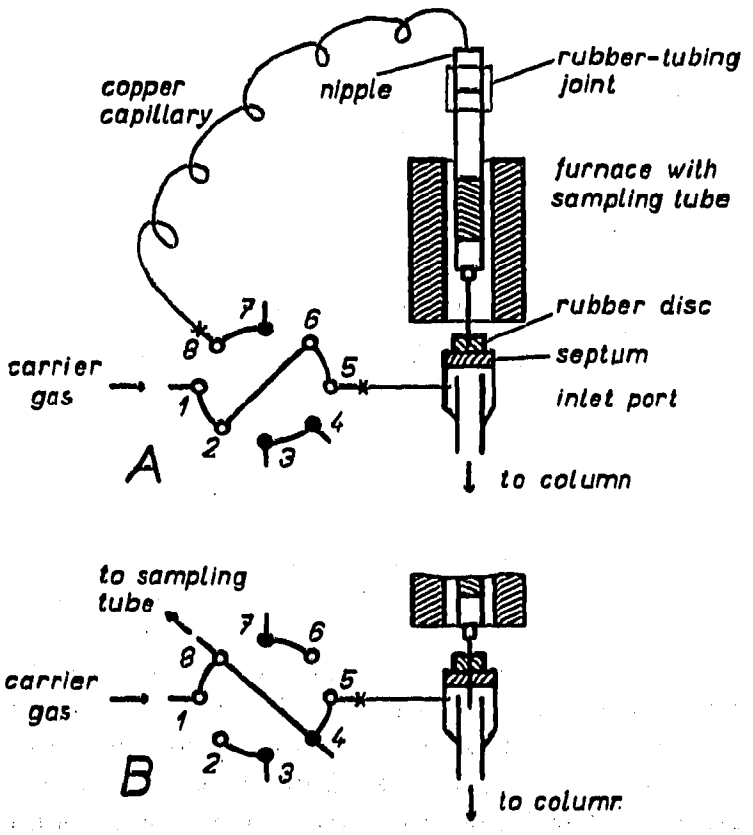

Fig. 1. Diagram of the switching arrangement and manipulation of the sampling tube. In the standard set-up, ports 7, 3, 8, and 4, serve as the sample inlet, sample vent, sampling-loop inlet, and sampling-loop outlet, respectively; in our experiments, the sampling loop was removed and ports 3, 4, and 7 were plugged.

a simple way so as to serve as a three-port stopcock routing the carrier gas from its source either directly into the column or, via the free port, into the atmosphere. When performing the analysis, the free port was connected by means of a copper capillary to the sampling tube. After connecting the saturated sampling tube (by a piece of rubber tubing) to the apparatus, the nozzle of the needle was closed by sticking a small silicone gum disc on it, after which the tube was inserted into a vertically situated electrical furnace positioned adjacent to the injection port of the gas chromatograph (Fig. 1A). After about 2-min heating (150°C with Apiezon K and 180°C with the porous polymers), the above-mentioned rubber disc was applied to the injection-port septum, whereupon the sampling-tube needle was inserted into the injection port and the stopcock turned into the position which allows the carrier gas to flow via the heated tube into the GC column (Fig. 1B). After about a 10-sec period, the stopcock was turned back into its initial position and the tube pulled out; under the above conditions, the retention time of halothane amounted to about 2.5 min. Fig. 2 shows a chromatogram obtained in one of the analyses.

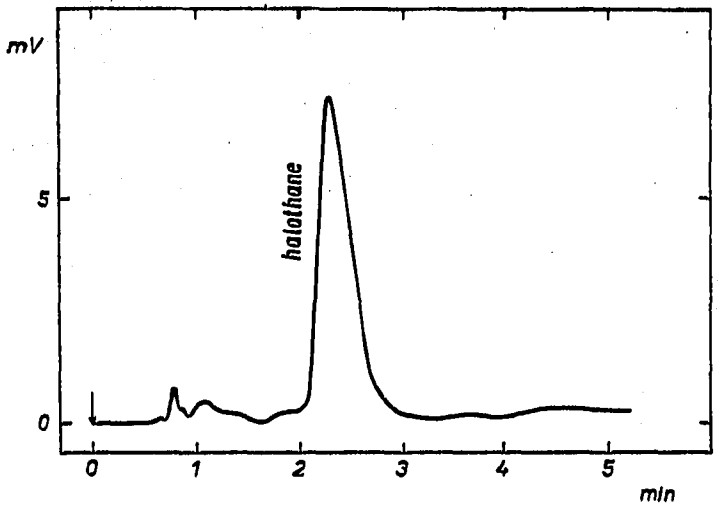

Fig. 2. Chromatogram obtained in an analysis of the air in an operating theatre. Apiezon K sampling tube; sensitivity attenuation, 1/100; Servogor RE 512 recorder, Goerz GmbH, Austria, set to a range of 10 mV. The halothane concentration in the air, as determined from the chromatogram, was 27 p.p.m.

METHOD

Principles and procedure

The gas to be analysed is drawn through a short tube containing a defined amount of chromatographic packing material until the concentrations of the impurity under determination in the gas and in the sorbent are in a state of equilibrium. Then the portion accumulated on the packing is desorbed by heating the tube to the predetermined temperature at which the entire solute can be flushed out of the tube by the carrier gas into the injection port of the gas chromatograph and determined by the method of direct calibration. The concentration of the substance in the air analysed can be calculated from the total amount of the substance trapped in the sampling tube, the amount of the sorbent, and the partition coefficient for the system at the temperature of sampling. The theory as well as instrumentation of the method have been described in detail earlier[10].

Calculation

The relation for calculating the concentration of the impurity in the gas from the data obtained by the above procedure can be derived directly from the definition of the specific retention volume[18]. It may easily be shown that the specific retention volume of a substance i, V_{gi}, is actually the partition coefficient defined by the relation:

$$V_{gi} = [w_i(S)/w_S]/[w_i(G)T/V_G 273] \quad (1)$$

where $w_i(S)/w_S$ denotes the concentration of substance i in the sorbent, which is equilibrated with the concentration of this substance in the gaseous phase, $w_i(G)/V_G$; the volume of the gaseous phase is reduced to a temperature of 0°C ($w_i(S)$ and w_S are the amount by weight of substance i in the sorbent and the amount by weight of the sorbent proper, $w_i(G)$ is the amount by weight of substance i in the gaseous phase, and V_G is the volume of the latter, respectively, T being the temperature of the column and/or the sampling tube).

Eqn. 1 relates the basic retention quantity, V_g, to an expression characterizing sorption equilibrium in a sorbent–solute-inert (carrier) gas system of any pattern. In elution chromatography (in a column), this equilibrium exists approximately in the centre of the chromatographic zone. When considering the sampling tube, $w_i(S)$, w_S, $w_i(G)$, and V_G are the weight of the substance entrapped in the sorbent of the tube the weight of the sorbent, the weight of the substance present in the dead volume of the tube, and the dead volume proper, respectively. In our case, the concentration $w_i(G)/V_G$ is of concern, and is given, according to eqn. 1, by:

$$w_i(G)/V_G = w_i(S)273/w_S V_{gi} T \quad (2)$$

Relation 2 was derived, in a somewhat different way, in the original paper on the method employed[16]. However, the use of the above relation implies the possibility of determining the concentration $w_i(S)/w_S$, which, strictly speaking, is impractical. Actually, the analysis of the desorbate from the tube always gives the sum of $w_i(S)$ and $w_i(G)$, which will be denoted as $w_i(SG)$. Since

$$w_i(S) = w_i(SG) - w_i(G) \quad (3)$$

while

$$w_i(G) = [w_i(G)/V_G]V_G \quad (4)$$

upon combining eqns. 2, 3, and 4 the following relation is obtained:

$$w_i(G)/V_G = [w_i(SG)273/w_S V_{gi} T]/[1 + (V_G 273/w_S V_{gi} T)] \quad (5)$$

The expression $V_G 273/w_S V_{gi} T$ represents the correction term for the dead volume of the tube. In systems with higher V_g values, the above correction may by neglected, whereupon eqn. 5 is transformed into eqn. 2 originally introduced. The value of V_G can be determined from the dead retention volume, by recalculating the latter so as to represent the actual amount of the packing in the tube, and from the geometry of the unfilled parts of the tube.

Determination of the substance trapped in the tube

The determination of the quantity $w_i(SG)$ may conveniently be carried out by the direct calibration of the instrument, using a solution of a suitable standard substance (s) of defined concentration. In the calibration chromatographic run, a chromatogram is obtained with a standard-substance peak of area A_s, which is given by the expression:

$$A_s = k f_{sr}^{w} c_s v_{(s)} \tag{6}$$

where k is an apparatus constant, f_{sr}^{w} denotes the relative weight-response factor of the standard substance, expressed with respect to a reference substance r, c_s is the concentration of the standard substance in the calibration solution, expressed as the amount by weight of the substance per unit volume of the solution, and $v_{(s)}$ is the volume of the calibration solution injected into the gas chromatograph. Analogously, the peak area of substance i in the chromatogram due to the material desorbed from the tube is given by:

$$A_i = k f_{ir}^{w} w_i(SG) \tag{7}$$

so that upon dividing eqn. 7 by eqn. 6 and carrying out the necessary rearrangement one obtains:

$$w_i(SG) = A_i f_{sr}^{w} c_s v_{(s)} / A_s f_{ir}^{w} \tag{8}$$

When the calibration is carried out with a solution of the substance identical to that under determination ($i = s$), the ratio f_{sr}^{w}/f_{ir}^{w} is obviously equal to unity.

RESULTS AND DISCUSSION

Specific retention volumes of halothane on the sorbents tested

The specific retention volumes at the temperature of sampling may be conveniently determined by virtue of the linear correlation of $\log V_g$ with the inverse of the absolute temperature. In all cases, the measurements of the V_g of halothane were carried out on columns packed with the material which was afterwards used as the packing for the sampling tubes. The measurements were carried out at several temperatures and the V_g values obtained (expressed in units of ml/g) were analysed, using the least squares method, to obtain empirical equations of the type $\log V_g = (A/T) - B$. The constants A and B, temperature limits (Δt) in which the V_g values were measured, and V_g values at 25°C (V_g^{25}) for the individual sorbents are summarized in Table I.

TABLE I

VALUES OF THE CONSTANTS A AND B IN THE EQUATION $\log V_g = (A/T) - B$ FOR THE SORBENTS EMPLOYED

Δt denotes the temperature interval over which the V_g values were measured. V_g^{25} is V_g value at 25°C.

Sorbent	*A*	*B*	*Δt (°C)*	V_g^{25} *(ml/g)*
Apiezon K	1403.5	2.55	30–80	145
Porapak P	2903.1	6.23	40–80	3 250
Porapak Q	2741.0	4.99	40–80	16 140

Concentration of halothane in the atmosphere of the operating theatres examined

The halothane content of the air in the theatres of five different surgical departments of a municipal hospital was determined under normal working conditions; aneasthesia was always carried out by a Vatra 5 apparatus, Chirana, N.E., Czechoslovakia. The flow rates of the respiratory mixture were controlled as required by the anaesthetist, so that the values for the flow rate quoted in Table II are of an indicative character only. The sampling was carried out at the following places: (a) at the venting valve of the anaesthetic machine, in the direction pointing towards the anaesthetist; (b) at the position of the anaesthetist (about 1 m away from the venting valve); (c) at the same place as quoted under (b), but 45 min after starting the anaesthesia. None of the theatres investigated was equipped with any arrangement for forced air exchange.

TABLE II

DATA ON THE CONDITIONS FOUND DURING ANAESTHESIA AND THE RESULTS OF THE ANALYSIS OF THE AIR FOR THE CONCENTRATION OF HALOTHANE

a, b, and c indicate the places of sampling (*cf.* the text).

Theatre no.	*Air temperature (°C)*	*Theatre size (m^3)*	*Respiratory mixture flow rate (l/min)*	*Halothane concentration in the respiratory mixture (vol. %)*	*Halothane concentration in the atmosphere (p.p.m.)*
1	25	300	3	1	(a) 31 (b) 10 (c) 25
2	24	400	7	1	(a) 50 (b) 7 (c) 27
3	26	800	6	1	(a) 46 (b) 5 (c) 12
4	29	200	3	1	(a) 36 (b) 23 (c) 29
5	28	150	3	1	(a) 33 (b) 12 (c) 24

It is apparent from eqn. 2 and the following ones that if V_g is expressed in ml/g and $w_l(S)$ and w_S in g, the concentration of halothane in the atmosphere will be expressed in units of g/ml. The conversion of the above units to those of p.p.m. can be carried out by use of the relation[19] (p.p.m.) = (g/ml)$10^{-9}RT/PM$ where R is the gas constant (1 atm/°K mole), T and P are the temperature and pressure of the air analysed (°K and atm), and M is the molecular weight of the substance under determination. Thus, for halothane (M = 197.4) at a temperature of 25 °C and pressure of 1 atm, 1 mg/m^3 = 0.124 p.p.m.

Sensitivity of analysis

The sensitivity of the flame ionisation detector towards halothane may be shown by determining its relative molar response, using a reference substance of known molar response. In our case, hexane was chosen as the reference substance (r), and the solvent was benzene. The relative molar response of a substance i, RMR_{ir}, is given by the relation $RMR_{ir} = (A_i/A_r)\,(x_r/x_i)$ where A_i/A_r is the ratio of the peak areas of substances i and r, and x_r/x_i that of the mole fractions of substances r and i in the solution. A value of 0.319 was found for the RMR_{ir} of halothane in this way. In flame ionisation detection, the RMR may be looked upon as the respective ratio of the sums of effective carbon atoms[20] in the molecules of substances i and r, $(\Sigma C_{ef})_i/(\Sigma C_{ef})_r$. Thus, the ΣC_{ef} of halothane is given by $(\Sigma C_{ef})_i = RMR_{ir}(\Sigma C_{ef})_r \equiv 6 \times 0.319 = 1.916$. Hence, the average effective-carbon value corresponding to one halogen (1 chlorine, 1 bromine, and 3 fluorines) is: $(1.916 - 2)/5 = -0.017$. It is apparent from the above result that the halogens in halothane have little effect on the sensitivity of the FID; and halothane behaves practically as ethane.

The amount of the substance entrapped in the tube corresponds roughly to the volume of air that would be necessary (as a carrier gas), under the conditions of sampling, to elute the substance from a column containing the same amount of the packing and having the same dead volume as the sampling tube. The above volume, V, is given by the relation $V = V_G + V_g w_S T/273$. The V_g of halothane at 25°C is 145 ml/g, the weight of Apiezon K in the tube was 0.11 g, and the dead volume of the tube was about 2 ml, so that the volume V amounted to about 20 ml. Hence, if the maximum volume of sample that can be injected directly into the gas chromatograph is 10 ml, the use of sampling tubes with Apiezon K permits the determination of halothane concentrations about half as high as those determinable by direct injection of the air to be analysed into the gas chromatograph. When Porapaks P and Q are employed as the sampling tube packings, it is possible to determine concentrations about 1/50 and 1/200 of those which can be determined by direct injection, respectively.

CONCLUSION

It can be concluded that the halothane concentrations currently occurring in the atmosphere of operating theatres may be conveniently determined by a method employing chromatographic equilibration and flame ionisation detection. When using Porapak Q as the sampling tube packing, concentrations of halothane down to 0.01 p.p.m. may be reliably determined. The results obtained indicate that the amounts of halothane inhaled by the anaesthetist and the medical personnel may be appreciably high, especially if the vapours of halothane are not drawn off from the room, and may cause physiological problems.

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