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Review

Gas chromatography in anaesthesia I. A brief review of analytical methods and gas chromatographic detector and column systems

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Abstract

Practical applications and relevant studies involving the anaesthetic gases, have been extensively described in the literature. Many eminent analytical methods have already been developed for medical practice where routine analysis of anaesthetics is frequently needed, particularly during anaesthesia, and in related and respiratory research programmes. The determination of halothane, isoflurane, enflurane and nitrous oxide concentrations from vaporizers, in exhaled and inhaled gas mixtures, in body fluids and tissues is necessary to control anaesthetic concentrations, and thus, the relevant and adverse effects successfully. Therefore, a literature review, with particular emphasis on gas chromatography would provide important information for investigators in the search for a suitable analytical method for the analysis of multi-component mixtures of anaesthetic gases.

Keywords: Anaesthetics

Contents

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1. Introduction

In general, frequency, urgency and accuracy have influenced the choice of the analytical method used for the analysis of the anaesthetic gases. Present methods may be classified into two main groups according to the fields where analysis is needed: those for use inside operating theatres in controlling of anaesthesia, and those for use outside the operating theatres for anaesthesia related research. These two main groups may also be divided into subgroups according to the nature of the samples and the type of the analysis needed. In each type of analysis various analytical methods can be used in the quantification of anaesthetics with respect to the level of concentration (high or low) and the physical state of the samples (gas or liquid) to be analysed.

2. Analysis required in operating theatres

Two main types of samples, gas and liquid (generally blood), are analysed in operating theatres to control the concentration of an anaesthetic during surgical operations. Gas samples may come from the delivered (inhaled) and/or exhaled gas mixtures while blood samples are taken directly from the anaesthetised patient [1,2].

During the course of a surgical operation analytical information is required immediately. For this reason physical methods of analysis are used on account of their rapid speed of response [3]. Nowadays, in operating theatres, where continuous monitoring is needed, automated techniques such as the Narko-Test gas monitor [4,5], UV gas monitors [6,7], infrared analysers [8], automated interferometers [9,10], mass spectrometers [11,12], the Datex Normac anaesthetic agent monitor [13,14], the Lamtec gas monitor [15] and Ohmeda Rascal II [16] etc., are mostly employed. Moreover, some vaporizers may be equipped with a built-in continuous gas monitoring device which utilises one of the above techniques. The advantages of the automated techniques, beside their immediate response, is that the result of the analysis can be displayed continuously on an output chart or digital device (monitor). Though these techniques are capable of measuring most of the substances encountered in the anaesthetic practice such as carbon dioxide, nitrous oxide and volatile anaesthetics, most of them can handle reliably only one component at a time. A list of the physical methods utilised in the analysis of anaesthetic gas components is given in Table 1.

Under certain circumstances, monitoring the blood concentration of anaesthetics provides more accurate information on the depth of the anaesthesia than monitoring the expired gas concentration from the patient [2]. Therefore, simultaneous determination of the volatile anaesthetics in liquid (blood) samples may also be needed periodically in operating theatres during surgery.

3. Analysis required in related research

In anaesthesia related research where continuous sampling is not needed, various methods such as refractometry [17], absorption and emission spectroscopy [18] and mass spectrometry [19] are employed in the determination of anaesthetic gases and vapours from different sources. Among them, gas chromatographic methods have been particularly popular for gas analysis. The great attraction of gas chromatography perhaps lies in its versatility, economy, simplicity and sensitivity, and the existence of, at least, one gas chromatograph in almost every research laboratory [20,21]. A limitation of the gas chromatograph lies in the fact that it needs to be fed with a series of samples and this limits its speed of analysis where continuous monitoring is needed.

The present gas chromatographic methods, given in the literature may be classified according to the source of the samples to be analysed. These samples may come from: (1) body fluids and tissues containing anaesthetics (usually low, in some cases trace, concentration analysis), (2) operating theatre atmosphere as pollutant (usually trace concentration analysis), (3) inspired or expired gas mixtures (high concentration analysis).

3.1. Methods for the analysis of body fluids and tissues containing anaesthetics

Although an alternative UV spectroscopic [22] and a high-performance liquid chromatographic (HPLC) method [23] have been suggested, gas chromatog-

Table 1
A list of the physical methods utilised in the analysis of anaesthetic gas components

Physical property	Bulk or individual	Components determined	Concentration range, (%)	Example type/make of instrument	Ref.
Solubility in stretched silicone rubber	Individual	N_2O and liquid anaesthetics	0–100 for N_2O; 0–3–4 for liquid anaesthetics	Narkotest anaesthetic gas monitor	[4,5]
UV absorption	Individual	halothane	0–5	UV halothane meters	[6,7]
Interference pattern of two gas samples	Bulk	O_2+N_2O and O_2+N_2O+liquid anaesthetics	0–100 for gases; 0–4 for liquid anaesthetics	Automated interferometers	[9,10]
Mass spectrometry	Individual	O_2, N_2, CO_2, N_2O, liquid anaesthetics	0–100 for N_2O; 0–2 for halothane	V.G. Micromass Q701B	[11,12]
IR absorption	Individual	liquid anaesthetics	0–5	Datex Normac anaesthetic agent monitor	[13,14]
Piezo electric crystal adsorption	Individual	liquid anaesthetics (N_2O and water interference)	0–5	Lamtec anaesthetic agent monitor	[15]
Raman scattering	Individual	O_2, N_2, CO_2,N_2O, liquid anaesthetics	0–100 for gases; 0–10 for liquid anaesthetics	Ohmeda Rascal II	[16]

raphy is widely utilised for the determination of the concentrations of anaesthetics in the analysis of liquid samples such as blood [24], urine [25], sperm [26] and solid tissues [27]. Gas chromatographic techniques produce reliable, fast, reproducible and accurate results in volatile liquid and gas anaesthetic analysis.

Four main sample handling techniques, associated with gas chromatography are generally employed. These use direct injection (for blood samples) [28,29], extraction with an organic solvent [24,27], the head space technique [2,30,31] and a heated removable sampling port (for solid tissues) [32]. The simplest technique, direct injection of test sample, introduces serious disadvantages such as contamination of the gas chromatographic system, and water vapour interference. Extraction with an organic solvent, despite requiring a smaller sample size (0.5–2 ml), is more complicated and large volumes of solvent injected cause either peak overlapping problems or can lead to swamping of the sensitive detector. Volatile anaesthetics can also be estimated in solid tissues by placing a sample in a heated sampling port at the column inlet. Since readings are available in 2–3 min it is invaluable when the results are required immediately [32]. With the head space technique, the test sample is equilibrated at a certain temperature with a gas phase and the concentration of the volatile anaesthetic in liquid sample derived from the gas phase equilibrium concentration. The most common method appearing in the literature on the analysis of blood samples is the head space technique on account of its rapid sample processing capability and its suitability for a direct determination of the partial pressure of anaesthetics in blood [2].

3.2. Methods for the analysis of anaesthetics as pollutant in operating theatre atmospheres

In the analysis of the low concentration samples, from operating theatre atmospheres, gas chromatography appears to fulfil all the criteria needed (e.g., it provides simple, versatile, inexpensive, rapid, etc., analyses) while offering adequate selectivity and sensitivity and being eminently suitable for the volatile nature of the components of interest [19]. Two types of sampling techniques associated with low-concentration samples are used in gas chromatographic analysis: integrated personal sampling (IPS) [33–36] and spot sampling techniques [37–42]. However integrated personal sampling technique was an uncommon method of measuring exposure to gases and vapours in pollution studies in the anaesthetic field [41] up to the early 70's. Extensive use of gas chromatography lead to smaller and simpler sample sizes to measure the average exposure over a period of hours. Two types of IPS are mainly used: the first type is dosimeters relying on diffusion of the pollutants on activated charcoal collection element [36], the second type passes the gas flow to be analysed into an adsorbent filled tube (cartridge) by using external power sources (e.g., pump). Generally activated charcoal and porous polymer beads are used as adsorbent material. The thermal stability, hydrophobic character, specific retention volume of the material play an important role in the choice of a suitable adsorbent. The largest specific retention volume indicates the largest sampling capacity. In a study, it was found that specific retention volumes of Porapak T>Porapak QS>Porapak Q>Chromosorb 101 and upper temperature limit of Chromosorb 101>Porapak QS=Porapak Q>Porapak T [34].

3.3. Methods suggested for the analysis of inhaled or exhaled gas mixtures

There are several techniques for measuring anaesthetic gas components at higher volume fractions. Mass spectrometry, infrared spectrophotometry and quartz crystal adsorption techniques, flueric respiratory and anaesthetic gas analyser (based on a resonant oscillator sensor) may be employed for analysing anaesthetic gases [43]. In general, inhaled or exhaled gas mixtures contain, in addition to the anaesthetic vapours, gaseous constituents such as air (oxygen), nitrous oxide and carbon dioxide. Therefore, their concentrations are also very important as a measure of the uptake of the anaesthetics, the depth of the anaesthesia and in related research. If all the components (gases and vapours) need to be detected, gas chromatography is extremely powerful for the separation and quantification of the components provided a suitable column and detection system is used. Gas chromatographic methods proposed for the analysis of the complex mixtures of anaesthetic gases [20,43–

48] involve complex column and detection combinations and injection techniques.

4. Detectors employed in the analysis of anaesthetic substances

The complexity of the mixtures to be analysed depends on the number of the components needed by anaesthetist during anaesthesia or in related research. Therefore, it can be a one-component mixture or a complex gas mixture which is likely to contain several of the following components: oxygen, nitrogen, carbon dioxide, nitrous oxide, halothane, isoflurane and enflurane. It is desirable that the composition of this mixture should be under the precise control of the anaesthetist and researchers have been devoted to improving methods of analysing gas mixtures which have anaesthetic importance.

The techniques, utilise physical properties, with the exception of mass spectrometry, and can handle the simultaneous determination of only one or two components at a time. If inorganic gases, besides liquid anaesthetics, are also needed in the gas chromatographic analysis, the detector system has to involve a thermal conductivity detector (thermistor or hot-wire TCD) due to its universal response to almost all substances and its very large linear dynamic range [32,49]. However, it is unsuitable for the detection of low concentrations because of its relatively poor sensitivity [50,51].

In contrast to this, in some studies the TCD was employed for low concentration detection of nitrous oxide as low as 1–25 ppm [40,52,53] and also in the analysis of whole blood [23]. As the thermal conductivity detector is a bulk property detector; decreasing the carrier gas flow-rate will increase the sensitivity as the solute is present at a higher concentration [54]. However, if the mixture contains components with longer retention times, such as volatile anaesthetics, a reasonable separation and analysis time cannot be sacrificed for the sake of sensitivity. Therefore the TCD is not commonly preferred for low concentration determinations.

ECD is extremely sensitive to compounds with halogen atoms and also to nitrous oxide. Because of the limited linear dynamic range of the ECD, it is generally employed for the determination of low concentrations of liquid anaesthetics and nitrous oxide. In the cases where the determination of the liquid anaesthetic is needed (e.g., In the analysis of blood and body fluids) the FID is commonly used [1,2,29,33–35,55,56] or if the analysis includes nitrous oxide the ECD alone may be chosen [20,25] or combination of these two detectors [41,48]. There are also some reports on the detection and quantification of nitrous oxide with FID [57]. In the great majority of the studies where only the determination of the volatile liquid anaesthetics is needed FID is used because of remarkably high sensitivity and large linear dynamic range with reasonable sample volume [58].

5. Column systems for the separation of the anaesthetic mixtures

There are hundreds of papers on the gas chromatographic separation and determination of anaesthetic components in which the column systems are suitable only for the analysis of one- or two-component mixtures (usually for liquid anaesthetics). The column packing materials employed could be classified into four main groups: (1) stationary phase coated columns (GLC), (2) solid adsorbent columns (mainly porous polymers) (GSC), (3) combined column systems (GLC–GSC), (4) capillary columns (CGC).

5.1. Stationary phase coated columns

Most of the columns employed in the separation of one or two component mixtures, in the past, involve a stationery phase coated on a support material (GLC). Commonly used stationery phases and column support materials are given in Table 2.

5.2. Solid adsorbent columns

Solid adsorbent columns (particularly porous polymers) are employed when the gas chromatographic separation involves a permanent gas and nitrous oxide with or without a liquid anaesthetic. Such columns used by the previous investigators in the analysis of anaesthetics are given in Table 3.

Table 2
Coated columns used in the gas chromatographic (GLC) analysis of anaesthetic components

Stationery phase	Support	Column length	Components determined [Ref.]
20% SE-30	Chromosorb W	2.0 m×4 mm and 1.83 m×3 mm, S.S.	Halothane, iso-octane [38] Halothane [58]
5% SE-30	Varaport 30	1.80 m×3 mm, S.S.	Air, heptane, enflurane [23]
3% SE-30	Diatomite CQ	1.5 m×6 mm, glass	CCl_4, chloroform, halothane [26]
8% SF-96	Chromosorb G	1.5 m×2 mm	Halothane, iso-octane [38]
25% DC-200	Celite 545	2.0 m×4 mm	Halothane, iso-octane [38]
5% Silicone oil (OV101)	Chromosorb W	3.0 m×2 mm and 2.0 m×4 mm, glass	Halothane [49] Halothane or isoflurane [29]
10% Silicone fluid C560	Universal support	5.0 m×6 mm, glass	Halothane, trichloroethylene [19]
15% FFAP	Diatomite C	2.0 m×4 mm, glass	CS_2, halothane, ethanol, propan-2-ol, toluene [36]
15% Apezon L	Chromosorb W HP	2.0 m×4 mm, glass	Halothane or isoflurane or enflurane [1] Halothane or isoflurane [2]
25% Apezon K	Sterchamol	1.5 m×3 mm, S.S.	Halothane [33]
20% Dimethylsulphoxide	SIL-O-CEL	6.0 m×6 mm	O_2, CO_2, N_2O [44]
15% Dinonylphthalate	Firebrick	0.6 m×6 mm	Halothane, ether, cyclopropane [44]

5.3. Combined column systems

In some studies, more than one column was employed for the separation and analysis of complex gas mixtures of anaesthetics. These mixtures which need complex column, detection and injection arrangements generally involve permanent gases, nitrous oxide and a volatile liquid anaesthetic. Since the separation of all the components at once is remarkably difficult, some special column lengths were inevitably employed to achieve satisfactory separations. The methods using combined column systems with different column packing materials and lengths are given in Table 4.

5.4. Capillary columns

Very few many gas chromatographic methods associated with a capillary column system were found for the separation and quantification of multicomponent mixtures of anaesthetics. Perhaps the reason is that separation of one or more components in anaesthetic mixtures other than the permanent gases could be accomplished on a simple laboratory-

Table 3
Solid adsorbent columns used in the analysis of anaesthetics

Column packing material	Column length	Components determined [Ref.]
Porapak Q	1.80 m×4 mm or 1.20 m×2.1 mm, glass or 3.66 m×3 mm, S.S.	N_2O [59] Dichloromethane, enflurane, halothane or N_2O, O_2 [25] N_2O, Freon-11, Freon-12, halothane [20] N_2O, C_2H_6, cyclopropane, acetone, ether, enflurane, halothane or O_2, SF_6, N_2 [48] Air, N_2O [53] Air, N_2O [60]
MS-5A	2.0 m×3 mm, S.S.	N_2O, C_2H_6, cyclopropane, acetone, ether, enflurane, halothane or O_2, SF_6, N_2 [48]
Porapak Q+MS-5A (mixed)	3.04 (2.75+0.29)m×4 mm, glass	Enflurane, halothane or ethanol, halothane [35]
Tide	0.50 m×6 mm	O_2, cyclopropane, fluomar, ether, halothane, CCl_3 anthrane, trilene [46]
Activated charcoal	1 m×5 mm	Air, N_2O [40]
Poropak P	2.5 m×3 mm, S.S.	Halothane [30]
Chromosorb 101	2.0 m, S.S.	Air, CO_2, N_2O, halothane or isoflurane or enflurane [62]

Table 4
Gas chromatographic methods using a combined column system

Stationary phase (column 1)	Solid adsorbent (column 2)	Components determined [Ref.]
15% F.F.A.P. on diatomaceous earth, 1.72 m	Carbosieve B, 2.13 m	Halothane, N_2O [42]
10% Silicone oil (OV101) on Chromosorb W, 2.13 m	Porapak Q, 3.0 m	Halothane or N_2O [41]
15% Kel-F oil 10 on Chromaton N-AW, 0.50 m	Porapak Q, 2.70 m	O_2, CO_2, N_2O [47]
0.1% SP1000 on Carbopack, 2.5 m	Porapak Q, 3.0 m	O_2, N_2O, halothane [43]
1–20% Dioctyl sebacate on firebrick 2–10% Dioctyl sebacate on silica gel	3-MS-5A	O_2, CO_2, halothane [45]
Chromosorb 101, 2 m (without coating)	Chromosorb 101, 2.0 m+2.0 m	Air, CO_2, N_2O, halothane or isoflurane or enflurane [62]

packed column instead of on an expensive and delicate capillary column. If the permanent gases must be determined in the mixture, complex column systems will be needed for an efficient separation. Because of the different physical and chemical properties of permanent gases and volatile liquid anaesthetics, effective separation of all the components may well be unsuccessful even with a long capillary column. Two published methods have been employed for the separation and detection of only one liquid anaesthetic component at a time. Imbriani et al. [25] used a cross-linked column 5% phenylmethylsilicone, 25 m×0.2 mm I.D., and isoflurane was detected from urine samples by employing a mass-selective detector. Targ et al. [61] analysed sevoflurane, isoflurane or halothane samples on a 5-μ-methylsilicone coated fused-silica column, 30 m×0.53 mm I.D., by using a FID detector.

6. Conclusion

This article is mainly designed to serve as a guide for those engaged in anaesthetic gas analysis by gas chromatography. One point that should be clear from this short review of a very broad topic is that there are many methods available for the analysis and separation of the anaesthetic gas mixtures varying from one component to multi-component mixtures (including light gases). It is important to remember, however, that not all of the methods may be applicable to all of the possible components of a mixture. In practical terms, the selection of a suitable method is often made on the basis of the nature of the samples and the number of the components to be analysed.

The report highlights that the length, number and type of the columns; temperature conditions and detector systems employed may vary according to the complexity and concentration level of the analysed mixtures. Although the field is now well established there is a room for improvements to simplify the column systems employed in the separations. Uyanık [62] has also introduced two new simple gas chromatographic methods based on commercially available solid adsorbent columns in conjunction with a TCD detection. In the first method, the separation of air, carbon dioxide, nitrous oxide and a liquid anaesthetic (halothane, isoflurane or enflurane) are achieved on a 2 m single column [Chromosorb 101, 80–100 mesh, 1/8 in. O.D. stainless steel (1 in.=2.54 cm)] with a temperature programme utilising room temperature. The second method is a dual column gas chromatographic method which uses both channels of TCD. Separation of the same mixtures are achieved on a 2 m (operated at 170°C) and 2 m+2 m (operated at room temperature) the same type of columns (Chromosorb 101, 80–100 mesh, 1/8 in. O.D. stainless steel). However, a researcher who needs to analyse a one component mixture of the liquid anaesthetics may use the coated column systems given in Table 2 provided they are already available in the laboratory. The solid adsorbent columns in Table 3 however, are more versatile and are capable of separating light gases. If a new purchase is necessary this type of column is preferable for the liquid anaesthetic analysis and future uses for light gases.

In addition to column systems, the chemical nature and concentration level of the analysed mixtures influence the choice of the detection systems to qualify and quantify the components. If the analysis

involves liquid anaesthetics at concentrations over 0.5% as well as light gases (air, carbon dioxide, nitrous oxide) a TCD should be used. For lower concentrations FID is preferable for the analysis of liquid anaesthetics excluding light gases. Since the linear dynamic range is limited the ECD may be employed in the low or trace concentration analysis of the anaesthetic components.

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References

[1] J. Flynn, J.D. O'Keeffe, S.W. Wren and M.I. Shanahan, Analyst, 114 (1989) 1207.
[2] J. Flynn, S. Masud, J.D. O'Keeffe, S.W. Wren and M.I. Shanahan, Analyst, 114 (1989) 1211.
[3] D.W. Hill, in R.P.W Scot (Editor), Gas Chromatography Edinburgh, Butterworths, London, 1960, p. 334.
[4] J.H. Lowe and K. Hagler, Anesthesiology, 34 (1971) 378.
[5] J.L. Velazquez, A. Feingold and P. Walther, Anesth. Analg., 56 (1977) 395.
[6] M.L. Tatnall, P.G. West and P. Morris, Br. J. Anaesth., 50 (1978) 617.
[7] K.V. Diprose, H.G. Epstein and L.R. Redman, Br. J. Anaesth., 52 (1980) 1155.
[8] E.S. Munson, L.M. Schick, J.C. Chapin, L.G. Kushins and A.A. Navarro, Anesthesiology, 51 (1979) 545.
[9] K.V. Diprose and L.R. Redman, Br. J. Anaesth., 50 (1978) 1155.
[10] B.R. Sugg, E. Palayiwa, W.L. Davies, R. Jackson, T. McGraghan, P. Shadbolt, S.J. Weller and C.E.V. Hahn, Br. J. Anaesth., 61 (1988) 484.
[11] J.M. Graham, B. Kay, W. Greer, J. Parkhouse and P.C.W. Beatty, Br. J. Anaesth., 52 (1980) 1055.
[12] M.G. Ozanne, W.G. Young, W.J. Mazzei and J.W. Severinghaus, Anesthesiology, 55 (1981) 62.
[13] N.P. Luff and D.C. White, Anaesthesia, 40 (1985) 555.
[14] A.D. Colquhoun, W.M. Gray and A.J. Asbury, Anaesthesia, 41 (1986) 198.
[15] S.J.E. Humphrey, N.P. Luff and D.C. White, Anaesthesia, 46 (1991) 478.
[16] G.G. Lockwood, M.J. Landon, M.K. Chakrabarti and J.G. Whitwam, Anaesthesia, 49 (1994) 44.
[17] W. Edmondson, Br. J. Anaest., 29 (1957) 570.
[18] A. Wald and V.D.B. Mazzia, N.Y. State J. Med., 2 (1965) 1858.
[19] W.O.M. Davis and A.A. Spence, Br. J. Anaesth., 51 (1979) 987.
[20] J.S. Robinson, J.M. Thompson, R.S. Barrat, R. Belcher and W.I. Stephen, Br. J. Anaesth., 48 (1976) 167.
[21] J.M. Thompson, W.I. Stephen and B. Sithamparanadarajah, Anal. Chim. Acta, 178 (1985) 341.
[22] J.J.T. Blanck and M. Thompson, Anesth. Analg., 59 (1980) 481.
[23] P.K. Janicki, W.A.R. Erskine and M.F.M. James, J. Chromatogr., 518 (1990) 250.
[24] M.S. Miller and A.J. Gandolfi, Anesthesiology, 51 (1979) 542.
[25] M. Imbriani, S. Ghittori, G. Pezzagno and E. Capodaglio, J. Toxicol. Environ. Health, 25 (1988) 393.
[26] O. Ladron De Guevara, A.A. Godoy and C. Cortinas De Nava, J. Chromatogr., 403 (1987) 350.
[27] P.R. Allot, A. Steward and W.W. Mapleson, Br. J. Anaesth., 43 (1971) 913.
[28] R. Douglas, D.W. Hill and D.G.L. Wood, Br. J. Anaesth., 42 (1970) 119.
[29] M.J. Cousins and R.I. Mazze, Anesthesiology, 36 (1972) 293.
[30] A.M. Zbinden, F.J. Frei, B. Funk, D.A. Thomson and D. Westenskow, Br. J. Anaesth., 57 (1985) 796.
[31] P. Koupil, J. Novak and J. Drozd, J. Chromatogr., 425 (1988) 99.
[32] D.W. Hill, Physics Applied to Anaesthesia, Butterworths, London, 4th ed., 1980.
[33] J. Gelbicova-Ruzickova, J. Novak and J. Janak, J. Chromatogr., 61 (1972) 15.
[34] M.M. Halliday and K.B. Carter, Br. J. Anaesth., 50 (1978) 1013.
[35] A.G.L. Burm and J. Spierdijk, Anesthesiology, 51 (1979) S355.
[36] M.M. Halliday and J. Anderson, Analyst, 105 (1980) 289.
[37] H.W. Linde and D.L. Bruce, Anesthesiology, 30 (1969) 363.
[38] B. Hallen, H. Ehrner-Samuel and M. Thomason, Acta Anaesth. Scand., 14 (1970) 17.
[39] L. Strunin, J.M. Strunin and C.C. Mallios, Br. Med. J., 4 (1973) 459.
[40] H. Yanagida, C. Kemi, K. Suva and H. Yamamura, Anesth. Analg., 53 (1974) 347.
[41] M.J. Davenport, M.J. Halsey, B. Wardley-Smith and B.M. Wright, Br. Med. J., November (1976) 1219.
[42] L.A. Salamonsen, W.J. Cole and R.F. Salamonsen, Br. J. Anaesth., 50 (1978) 221.
[43] H.M. Heise, Chromatographia, 23 (1987) 53.
[44] E.R. Adlard and D.W. Hill, Nature, 4730 (1960) 1045.
[45] K. Rehder, J. Forbes, O. Hessler and K. Gossmann, C.A., 65 (1966) 9317b.
[46] R.J. Leibrand, J. Gas Chromatogr., 5 (1967) 518.
[47] V. Patzelova, Chromatographia, 4 (1971) 174.
[48] R. Dueck, M. Rathbun and P.D. Wagner, Anesthesiology, 49 (1978) 31.

[49] I. MacDonald and J.E. MacKenzie, Br. J. Anaesth., 48 (1976) 519.
[50] J. Novak, Quantitative Analysis by Gas Chromatography (Chromatography, Science Series Vol. 5), Marcel Dekker, New York, NY, 1975.
[51] C.J. Cowper and A.J. DeRose, The Analysis of Gases by Gas Chromatography, Pergamon Press, UK, 1983.
[52] J.E. Cottrell, J. Chalon and H. Turndorf, Anesth. Analg., 56 (1977) 359.
[53] J.C. Austin, R. Shaw, D. Moyes and P.E. Cleaton-Jones, Br. J. Anaesth., 53 (1981) 997.
[54] M.D. LaHue, H.D. Axelrod and P. Lodge Jr., J. Chromatogr. Sci., 11 (1973) 585.
[55] P.R. Allot, A. Steward and W.W. Mapleson, Br. J. Anaesth., 43 (1971) 913.
[56] S. Kalman, M. Bengtsson and D. Lindmark, Acta Anaesth. Scand., 35 (1991) 190.
[57] P. Russev, T.A. Gough and C.J. Woollam, J. Chromatogr., 119 (1976) 461.
[58] C.D. Strout and M.L. Nahrwold, Br. J. Anaesth., 49 (1977) 722.
[59] R.J. Gardner, Ann. Occup. Hyg., 33 (1989) 159.
[60] J.C. Austin, R. Shaw, D. Moyes and P.E. Cleaton-Jones, Br. J. Anaesth., 50 (1978) 1109.
[61] A.G. Targ, N. Yasuda and E.I. Eger II, Anesth. Analg., 69 (1989) 218.
[62] A. Uyanık, An Investigation into the Preparation High-Pressure Behaviour and Stability of Pre-Mixed Volatile Liquid Anaesthetics in Entonox, PhD Thesis, Aberdeen University, Aberdeen, 1994.