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Gas Chromatography in the Low Concentration Determination of Nitrous Oxide and Volatile Anaesthetics

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A previously reported single-column gas chromatographic separation method was modified for dual-detection gas chromatography (TCD+FID) and evaluated for the low concentration analysis of volatile anaesthetics (halothane, isoflurane) and nitrous oxide. It was found that no serious problem occurs in the determination of volatile anaesthetics with FID (<10 ppm), but nitrous oxide introduces lack of sensitivity at lower concentrations with TCD (<40 ppm) in the described analysis method with a 0.25 ml sample loop.

Keywords: Gas chromatography, halothane, isoflurane, nitrous oxide.

Introduction

Anaesthetic pollution is of interest to people subject to low concentrations of all types of gases and volatile anaesthetic during occupational activities. The decrease in recent years in the number of relevant publications does not necessarily mean that pollution has gone away or that the problem has been solved. A number of coincidental factors have brought the matter back into consideration. Although some aspects of the hazardous effect of low-concentration exposure to anaesthetics have been satisfactorily explained, new questions have been raised[1]. Therefore, there is still a need for methods which will allow simultaneous analysis of volatile anaesthetic (halothane, isoflurane) and nitrous oxide from the operating theatre or intensive care unit, atmospheres or else at low concentration level. This type of analysis method is usually associated with gas chromatography[2–6]. However, the separation of multi-component mixtures (including light gases) is an important step in gas chromatography, as the remarkably different physical and chemical nature of the components makes the simultaneous detection of the anaesthetics studied more difficult after the separation. For example, the thermal conductivity detector (TCD) is known to be insufficiently sensitive for measurements of low concentrations[7–9]. The electron capture (ECD) and flame ionisation (FID) detection systems are much more sensitive to these components, but ECD is non-linear[2] and FID does not respond to nitrous oxide, and both types of detectors are of a destructive character, making a serial connection impossible[5]. To overcome this difficulty, a previously described gas chromatographic separation system[10] was modified for dual-detector gas chromatography in order to detect both inorganic gases (with TCD) and anaesthetic vapours (with FID) at low concentration levels.

Experimental

Gas Chromatography

A Perkin-Elmer F-30 dual column gas chromatograph equipped with a constant-current temperature-controlled hot-wire bridge TCD (Rhenium-Tungsten alloy) (GOW-MAC Instrument Co., USA) was connected in series to the FID detector port of a Perkin-Elmer F-33 gas chromatograph by a piece of stainless steel pipe to detect nitrous oxide by TCD, and volatile anaesthetics by FID. The length of the pipe was kept as short as possible and the pipe was insulated to prevent condensation during elution. A six-port gas switching valve (Perkin-Elmer) with a 0.25 ml sample loop and two stainless steel (2m, 1/8" o.d.) Chromosorb 101 (80-100 mesh) columns (Pierce & Warriner Ltd., England) were used as reference and working columns. The inlet pressure of helium was 40 psig (2.7 bar). Instrumental conditions are presented in Table 1.

Table 1. Conditions for the dual detection system gas chromatographic method

Detector	TCD	FID
Gas chromatograph	Perkin-Elmer F-30	Perkin-Elmer F-33
Injection temperature, °C	200	-
Detector temperature, °C	200	150
Filament temperature, °C	300	-
Carrier gas He inlet pressure, psig	40	-
Air inlet pressure, psig	-	21
Hydrogen inlet pressure, psig	-	20
Instrument attenuation	1	1
Instrument range	-	10
Oven temperature, °C	30-200	-
Working and reference column	Chromosorb 101	(detector only)

The output was fed to a Hewlett-Packard HP 3396-A integrator via a two-way switch to evaluate the responses of both detectors simultaneously. The separation of the anaesthetic was achieved by a fast temperature programme increasing from room temperature to 200° C by a nonlinear heating rate (achieved by shutting the oven door), as has been described previously[10]. A simple set-up of the combined gas chromatographic system used in the experiments is given in Figure 1. Mixtures used as the calibration standards in gas chromatography were prepared on gravimetric basis in aluminium cylinders (4.67 kg water capacity, Luxfer, Nottingham) in medical-quality air (BOC) at about 3.0 MPa pressure.

Results and Discussion

Low-concentration analysis of anaesthetic (halothane, isoflurane) and nitrous oxide from environmental samples (operating theatre or intensive care unit atmosphere) involves air at high proportions such as the atmospheric constituents (e.g. CO_2). These constituents must first be separated to quantify the peaks efficiently. While the concentration of the constituents is at percent level, the obtained retention times for air (29 sec), carbon dioxide (60 sec) and nitrous oxide (78 sec) result in excellent separation. But if the concentration of carbon dioxide and nitrous oxide is low and air is in high proportions, the peaks for carbon dioxide and nitrous oxide inevitably appear on the tail of a large air (N_2+O_2) peak (see Figure 2). However, the chromatography remains and the peak for atmospheric carbon dioxide that appears in the real

sample analysis does not interfere with the analyses and integrating eligible tail peaks can be achieved by a computing integrator automatically without any problem.

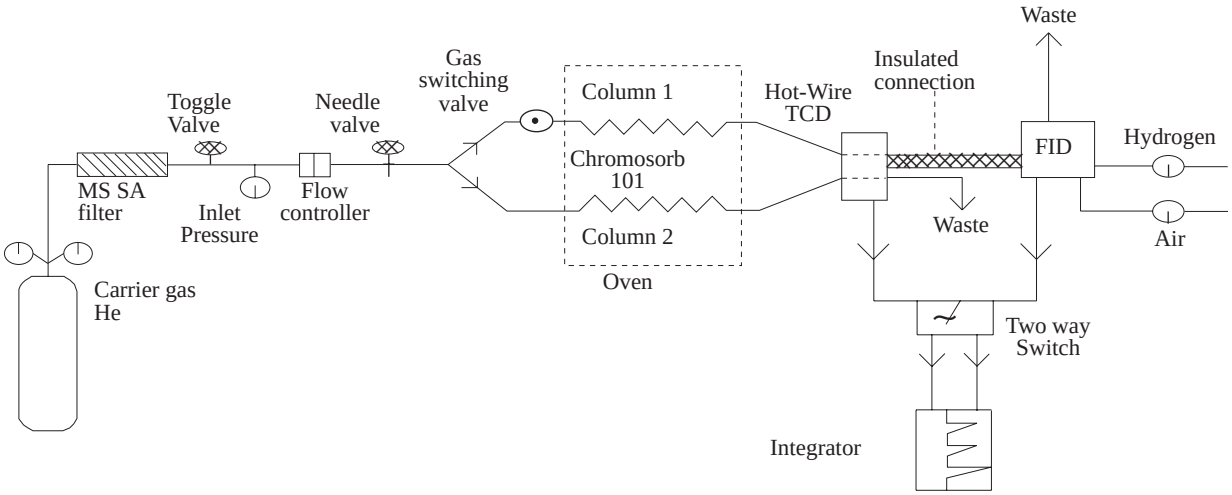

Figure 1. Simple set-up of the combined dual detector gas chromatographic system used in the experiments

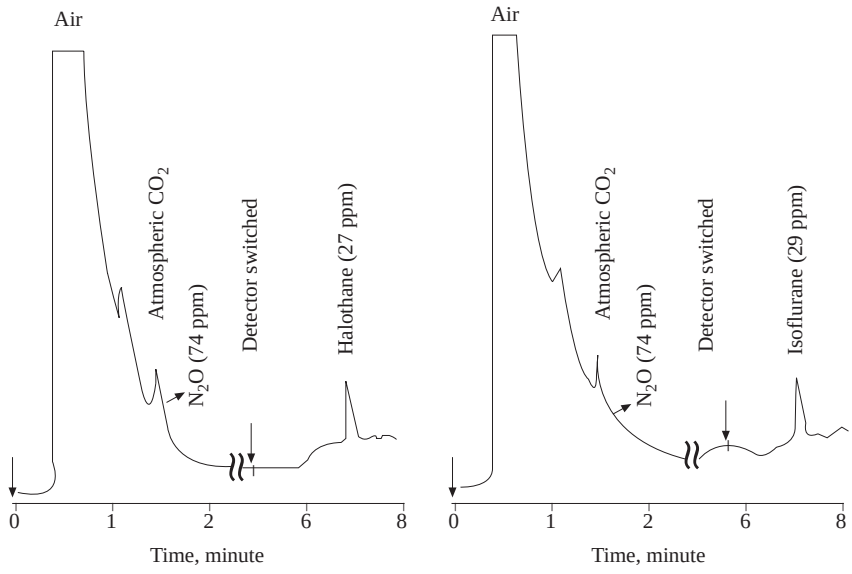

Figure 2. Gas chromatographic separation and detection of atmospheric carbon dioxide, nitrous oxide and a) halothane, b) isoflurane in air

FID produces linear responses for halothane (r=0.998, y=1193x-2901, Limit of detection = 4.15 ppm; Repeatability = 1.04%) and for isoflurane (r=0.999, y=1174x+1213, Limit of detection = 1.07 ppm; Repeatability = 3.05 %) and also the TCD produces linear responses for nitrous oxide (r=0.999, y=25.1x-239.1, Limit of detection = 40 ppm; Repeatability = 7.34 %). Repeatability (within-run precission) of each substance was tested by using single gravimetrically prepared cylinder mixtures of halothane (45 ppm), isoflurane (40 ppm) and nitrous oxide (50 ppm). In each determination sequence, each test mixture was introduced at least ten times in the same day and the coefficient of variation was calculated. Since the same mixtures were used by a fixed loop (0.25 ml), the presented repeatability errors represent the inherent

variability of the instruments and also reflect the magnitude of the integration error. The repeatability error for nitrous oxide, found to be greater than those of halothane and isoflurane, was possibly due to the integration error of its relatively smaller peaks. Yet FID produces very sensitive responses to liquid anaesthetic, and the peaks were larger for halothane and isoflurane.

However the limit of detection for nitrous oxide was found to be around 40 ppm with a 0.25 ml sample loop in the experiments, some reports present in the literature on the TCD quantification of lower concentrations[3,6,11]. At the concentrations lower than 40 ppm the peak for nitrous oxide appears on the chromatograms, but peak quantification by the integrator cannot succeed automatically. If the manually measured peak heights are used instead of peak areas, this detection limit could be brought as low as 10 ppm. Preparing the calibration standards in He (the carrier gas) rather than in air also eliminates the air peak appearing on the chromatograms (see Figure 3) and lowers the detection limit of nitrous oxide, but brings a big systematic error on the results of the air involved real sample analysis. On the other hand, using a larger sample loop (e.g. 1-10 ml) would also increase the peak size, but injecting larger volumes causes peak broadening, which makes separation and quantitative evaluation of the components more difficult.

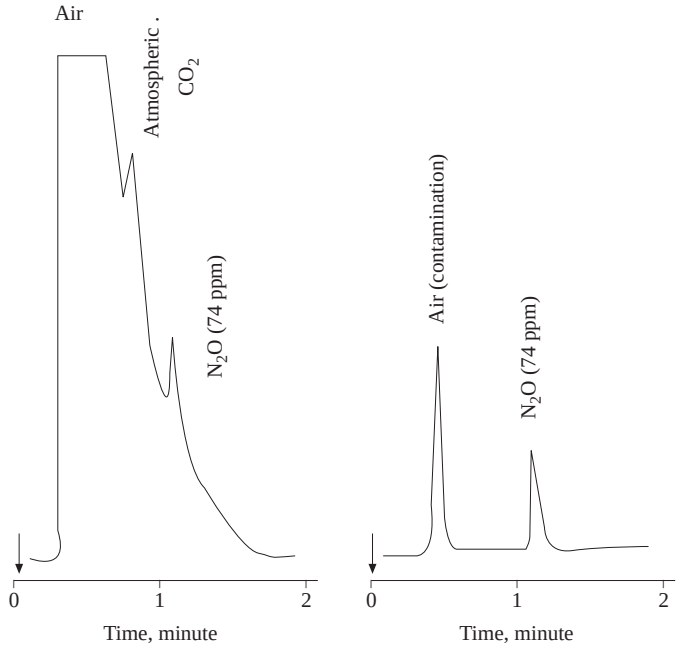

Figure 3. Comparison of the gas chromatographic separation and detection of nitrous oxide with TCD a) in air, b) in He.

The method described here did not succeed the quantitative determination of nitrous oxide automatically at concentrations lower than 40 ppm with smaller loop (0.25 ml). Since the operating theatre, intensive care unit, etc. level of nitrous oxide is usually found (and expected) higher than this concentration, the method can still be utilised for the monitoring of medical environments. Manual peak height measurements also lower the detection limits and allow the method to be used for lower concentration determination. Further experiments showed that quantitative analysis of nitrous oxide at low concentration levels was not straightforward and it may not be achieved by gas chromatograply without difficulty. In light of the discussion above, it could be concluded that the connection of FID with the previous column system makes the method useful for low concentration measurements of halothane and nitrous oxide in the clinical and chemical research level for routine uses. The method described is rapid and easy to use and the main

advantage is that two instruments can be connected or separated in minutes by disconnecting the pipe into their original position without any damage.

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