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The determination of residual ethylene oxide and halogenated hydrocarbon propellants in sterilized plastics

B. WARREN

Abbott Laboratories Ltd, Queenborough, Kent, U.K.

A specific and sensitive method is described for the determination of residual ethylene oxide, dichlorodifluoromethane and trichlorofluoromethane in sterilized plastic surgical equipment. Residues are isolated from the plastics by high vacuum distillation and analysed by gas chromatography using an exponential dilution apparatus, to avoid the use of solvents. Under the conditions specified, a lower limit of 1 ppm of each component could be detected in blood giving sets of which the main plastics material was PVC. The rate of loss of each component has been studied, to indicate the necessary holding time of the material before it can be considered safe to use.

Undesirable reactions *in vivo* have been reported from the use of surgical equipment sterilized with and containing residues of ethylene oxide (Freeman & Barwell, 1960; Clarke, Davidson & Johnson, 1966). There is thus a need for a specific and sensitive method for the determination of ethylene oxide. Many commercial sterilizing gases also contain halogenated hydrocarbon propellants but as yet no residue study has been made on these.

Chemical methods proposed for residual ethylene oxide (Gunther, 1951; Critchfield & Johnson, 1957; Belman, 1963; Sawicki, Stanley & Pfaff, 1963) either suffer from lack of sensitivity and specificity or require rigorous control of experimental technique. None is adaptable to propellant determination. Gas chromatography has also been used but the methods proposed (Kulkarni, Bartak & others, 1968; Ben-Yehoshua & Krinsky, 1968; Mokeeva & Tsarfin, 1968) suffer from the difficulties associated with leaching or solution of the plastic in a suitable solvent before analysis.

This investigation has been made to determine concomitantly the rate of loss of ethylene oxide and propellants from sterilized plastic materials, so that the storage times necessary to reduce their concentration to an insignificant level may be predicted. To achieve this it was necessary to develop a method which would be adaptable to a wide range of sample sizes, eliminate the use of solvents for residue removal and preferably be capable of application to the control analysis of purchased supplies of sterilizing gas mixtures.

METHODS

The method is based on distillation under high vacuum with a distillate trap cooled in liquid nitrogen. The volatile components in the plastic are thus removed in under 30 min and trapped without the use of a solvent. They are then expanded into an evacuated "exponential gas dilution" vessel (Lovelock, 1961) and raised to atmospheric pressure. The contents of the vessel are then diluted exponentially

and samples analysed by gas chromatography at timed intervals. The peak height-time plot is compared with individual standard dilution plots of ethylene oxide, and propellants diluted in the same way. From a comparison of the time taken for sample and standard to reach an equivalent peak height using the same gas chromatography amplifier sensitivity setting, the initial concentration of residues in the plastic can be calculated.

Extraction technique

Using the apparatus shown in Fig. 1 the residues are extracted as follows: (*a*) Weigh the complete plastic sample and place in test tube A: open tap 1 to connect test tube to trapping coil. (*b*) Cool the trapping coil in liquid nitrogen and apply vacuum source (0·1 mm) to outlet (x) of tap 2. (*c*) Heat the test tube containing the sample to 130° (30 min). (*d*) Isolate trapping coil with tap 1. (*e*) With taps 3 and 4 closed to isolate the exponential dilution vessel, adjust tap 2 to evacuate this vessel. (*f*) Adjust tap 2 to connect the trapping coil to the dilution vessel isolating the vacuum source. (*g*) Replace the liquid nitrogen bath with a water bath at about 60° and allow the volatile condensate in the trap to expand into the dilution vessel. (*h*) Using tap 1 allow pressure in the dilution vessel to return to atmospheric or other fixed pressure, then close tap 1. (*i*) Isolate dilution vessel with tap 2.

At this stage the dilution vessel contains in the gaseous state and at the predetermined pressure, the volatile components from the plastic. Exponential dilution and subsequent gas chromatographic analysis may then be carried out as follows: (*k*) Simultaneously open tap 3 and connect the nitrogen inlet to the dilution vessel by

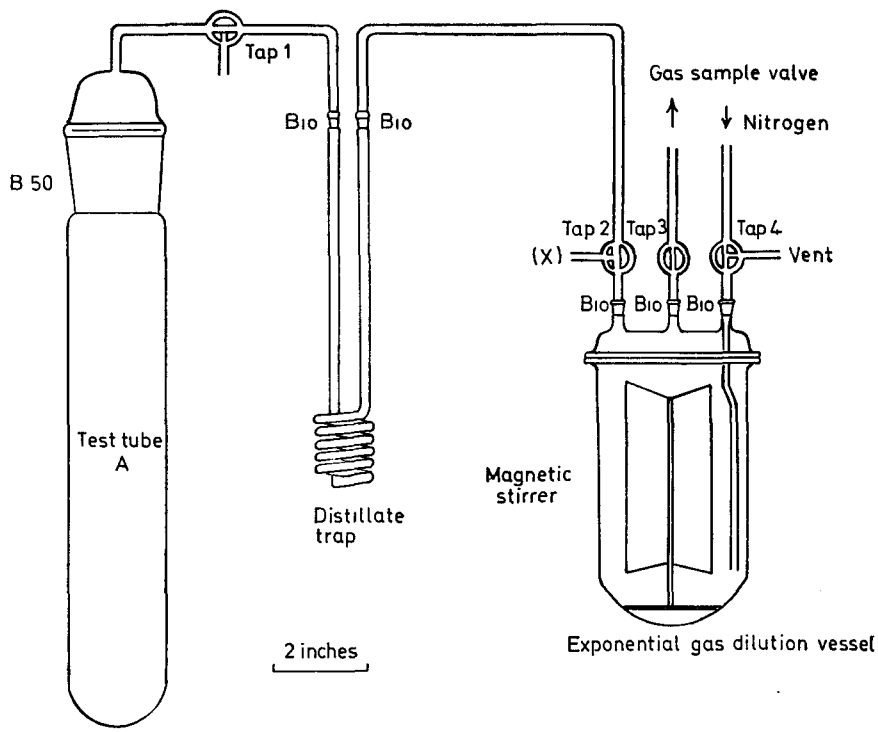

FIG. 1. Extraction apparatus (see text for description).

tap 4. (*l*) Sample the dilution vessel effluent at timed intervals with a gas sampling valve attached to the gas chromatograph. (*m*) Record peak heights, time of injection and sensitivity setting for each peak.

Standardization

Known concentrations of the individual standards are prepared in an exponential dilution vessel either by volume or by weight. Although standards may be prepared by volume using gas-tight syringes, correction must be made for deviation from N.T.P. Standards prepared by weight are more convenient but their initial preparation requires careful experimental technique. Individual components are sealed into preweighed lengths of capillary tubing cooled in liquid nitrogen and reweighed. The weighed tube is then placed in a sampling tube, and the exponential dilution flask evacuated. The sealed capillary is broken in a suitable manner, allowing the sample to vaporize into the dilution vessel, which is then raised to atmospheric pressure.

Calculation

Lovelock (1961) and Williams & Winefordner (1966) have previously demonstrated the exponential dilution of permanent gases in the type of dilution vessel used. The dilution follows the relation:

$$C = C_0 \exp -\frac{Ut}{V} \quad \text{or} \quad 2{\cdot}303 \log C = 2{\cdot}303 \log C_0 - \frac{Ut}{V}$$

where V = volume of flask (cc). U = flow rate of diluting gas (cc/min). t = time (min). C_0 = initial concentration of sample gas. C = concentration at any time t. Therefore a plot of C versus time will give a slope of $-U/V$ and intercept of $2{\cdot}303 \log C_0$.

Since the major contribution to non linearity in the system probably comes from the gas chromatographic detector response and amplifier, it is preferable to compare the times taken for sample and standard to reach an equivalent peak height on identical amplifier sensitivity ranges. Then for both sample and standard, equation (1) applies.

$$\log_e C = \log_e C_0 - \frac{Ut}{V} \qquad \ldots \quad \ldots \quad \ldots \quad (1)$$

When peak heights for both sample (sm) and standard (Std) are equal, then

$$\log_e C_0\,(\text{sm}) - \frac{Ut}{V}(\text{sm}) = \log_e C_0\,(\text{std}) - \frac{Ut}{V}(\text{std})$$

$$\therefore \log_e C_0\,(\text{sm}) = \log_e C_0\,(\text{std}) - \frac{U}{V}(t_{\text{std}} - t_{\text{sm}})$$

or

$$\log_{10} C_0\,(\text{sm}) = \log_{10} C_0\,(\text{std}) - \frac{U(t_{\text{std}} - t_{\text{sm}})}{2{\cdot}303\ V} \qquad \ldots \quad \ldots \quad (2)$$

From equation (2), it is possible to calculate the initial concentration of 'residual' gas in the dilution vessel and hence the amount present in the original plastic sample.

Equipment. Pye 104 gas chromatograph equipped with flame ionization detector. 5 ft × 4 mm i.d. glass column packed with Phasepak Q (Phase Separations Ltd); column temperature: 150° isothermal; carrier gas: nitrogen 80 ml/min; sample injection: Pye gas sampling valve fitted with 0·14 ml sample loop.

Reagents. Ethylene oxide supplied by BDH. Dichlorodifluoromethane and trichlorofluoromethane supplied by ICI.

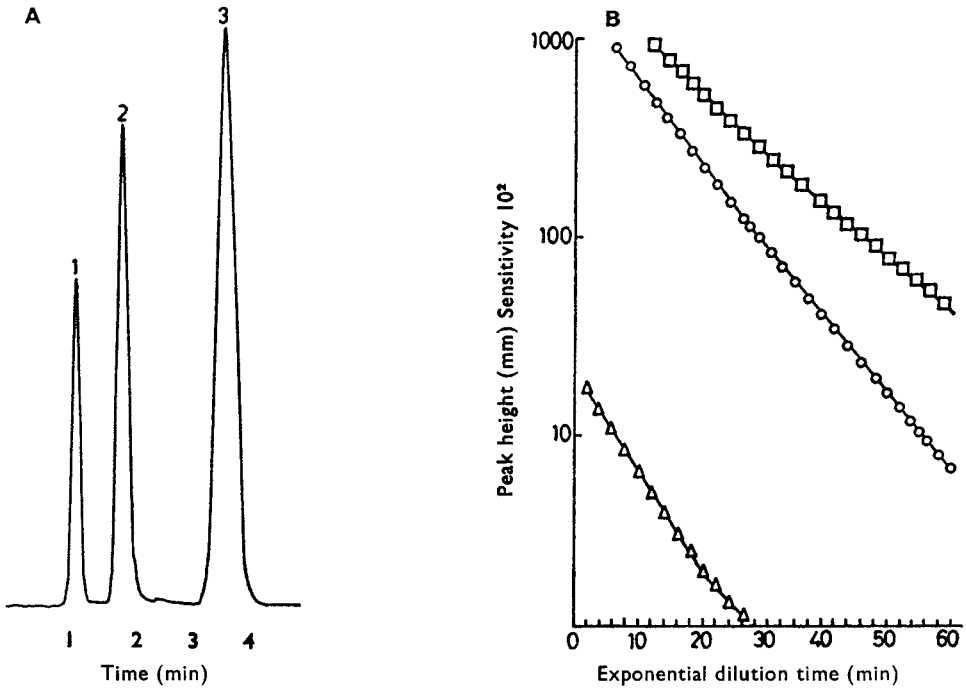

FIG. 2. A. A typical gas chromatographic separation of dichlorodifluoromethane (1), ethylene oxide (2), and trichlorofluoromethane (3).

B. Graph of log peak heights against time. △ Trichlorofluoromethane. □ Dichlorodifluoromethane. ○ Ethylene oxide.

RESULTS

Separation of propellants and ethylene oxide

Fig. 2A shows the separation achieved under the conditions stated. A porous polymer column with no liquid phase was chosen for this separation to achieve greater stability on high sensitivity; different conditions may be necessary for other propellants.

Linearity of the gas chromatographic system to exponential dilution

The complete amplifier range was checked for response to ethylene oxide, dichlorodifluoromethane and trichlorofluoromethane during exponential dilution from 0·33% v/v to the minimum detectable level. The graph of log peak height *vs* time shows a series of straight lines for each range step on the amplifier; Fig. 2B shows a typical example. When the amplifier range is changed the slope of this line changes to a new value. Hence, it is important to measure peak heights of sample and standard on identical ranges.

Effect of extraction time and temperature

Treatment at 130° (30 min) was found satisfactory for distillation of ethylene oxide and propellants from the PVC of blood transfusion equipment. Temperatures in excess of 150° tended to cause pyrolysis of the PVC leading to numerous additional chromatographic peaks.

Study of residue content of sterilized equipment

Samples of the blood transfusion equipment sterilized in a 200 ft^3 water jacketed sterilizer, were stored at room temperature under normal warehouse conditions and examined periodically by this technique to determine the rate of loss of ethylene oxide and propellants. The sterilization cycle was at 135° F ± 5° F. The chamber pressure was reduced by 12·77 p.s.i. and the chamber humidified for 1 h at a relative humidity in the range 50–65%. The sterilizing gas consisting of ethylene oxide 11% w/w, dichlorodifluoromethane 35% w/w and trichlorofluoromethane 54% w/w was then admitted to a pressure of 14 p.s.i. and maintained for 5 h, after which an air flushing cycle of 2 h was used before removal of samples.

The blood giving sets consisted mainly of PVC with some parts in high and low density polyethylene, nylon, polycarbonate, modified acrylics and latex rubber. The sets were stored in their normal cardboard trays and sleeves. No plastic covering is used in this packaging. For each estimation a complete blood set weighing about 40 g was extracted. Fig. 3 shows the residue levels obtained over 42 days. After this period the levels of ethylene oxide and dichlorodifluoromethane fell below 1 ppm whereas trichlorofluoromethane was still present to the extent of about 5 ppm.

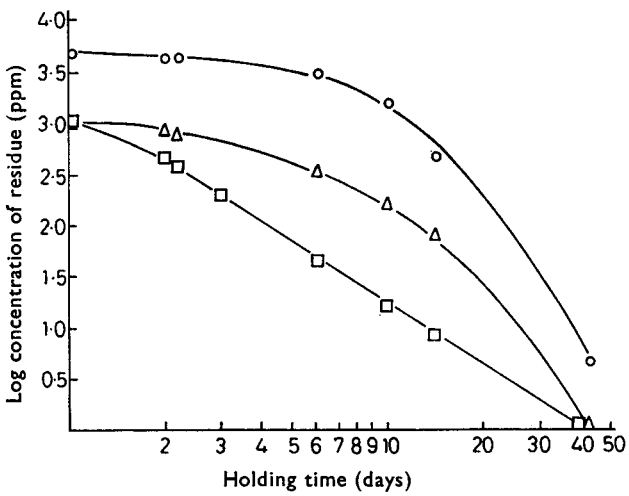

FIG. 3. Residue concentration with holding time of plastic blood giving sets. ○ Trichlorofluoromethane. △ Dichlorodifluoromethane. □ Ethylene oxide.

DISCUSSION

The use of vacuum distillation for removal of residues in an analysis of this kind has many advantages over solution techniques which require solvents of high purity and suffer severe limitations in the sample to solvent ratios that can be used. The use of an exponential dilution system enables a number of chromatograms to be

obtained from a single sample so that suitable sensitivity settings can be obtained as the dilution proceeds. Extension of this method to the analysis of sterilizing gas mixtures can be made by sealing samples of the liquified mixture into capillaries as detailed under the section on standardization. An exponential dilution plot of the constituents of this mixture can then be compared to standard dilution plots. With little modification the method may be used for other volatile residues or extended below the lower limit of 1 ppm described in this paper.

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