CASE REPORT

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Fatality Due to Recreational Use of Chlorodifluoromethane and Chloropentafluoroethane

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ABSTRACT: Reports on fatalities of chlorofluorocarbons usually involve chlorotrifluoroethane, trichlorofluoromethane, dichlorodifluoromethane or chlorodifluoromethane, where analysis was done using packed column gas chromatography. In this case a death was caused by an azeotropic mixture of chlorodifluoromethane and chloropentafluoroethane, a combination that has not previously been reported in the forensic literature. This report details the analysis using mass selective detection employing capillary gas chromatography columns currently used in many toxicology laboratories.

Postmortem toxicology revealed blood concentrations of chlorodifluoromethane and chloropentafluoroethane of 71 mg/L and 0.30 mg/L, respectively. Brain, liver, and lung concentrations of chlorodifluoromethane were (mg/kg) 2.8, 4.4, and 1.6, respectively. Brain, liver, and lung concentrations of chloropentafluoroethane were (mg/kg) 0.80, 0.80, and 0.11, respectively. The victim's blood contained 5.5 mg/L caffeine. Lidocaine, used in resuscitation attempts, was also present in the victim's blood. No other alkali-extractable drugs or volatile alcohols were detected in the victim's blood. The cause of death was acute respiratory arrest due to chlorofluorocarbon inhalation.

KEYWORDS: toxicology, Freon, fatality, overdose, gas chromatography, mass spectrometry, chlorodifluoromethane, chloropentafluoroethane

A 22-year-old white man was found coughing and wheezing by roommates in his apartment with large cans of freon nearby. The victim had a past history of abusing freons, one can of freon (Genetron 502) near the victim was empty and the other was partially full (with a hose for venting the freon still attached). The patient arrived at the emergency room in ventricular fibrillation, which progressed to a flat line EKG. Resuscitation attempts failed and the victim was pronounced dead in the emergency room

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approximately 1 h after being found by roommates. A medicolegal autopsy was performed the following morning (14 h postmortem).

Autopsy revealed slight suffusion of the face and scattered, small, red abrasions of the face, left forearm, right shoulder, and right thumb. These injuries were all superficial and there were no lethal internal or external injuries identified. There was severe, acute pulmonary edema and congestion with copious bloody froth present in the tracheobronchial tree. The hyperemia of the tracheal mucosa indicated some pulmonary insult such as inhalation of a pulmonary irritant. There were no congenital anomalies and no cardiac disease present. The brain was unremarkable and there was no gross evidence of infection in any organ.

Postmortem toxicology revealed the presence of chlorodifluoromethane and chloropentafluoroethane in the blood, liver, lung, and brain of the victim. The quantitative results of chlorofluorocarbons in the decedent's blood and tissue are shown in Table 1. These concentrations are in the range of fluorocarbons reported in previous cases of freon overdoses (Table 2). The blood also contained 5.5 mg/L caffeine. Lidocaine, which was used in resuscitation attempts, was also present in the blood. No other alkali-extractable drugs were detected in the victim's blood. Blood and urine were negative for ethanol, methanol, and isopropanol. The cause of death was acute respiratory arrest due to freon inhalation.

Standard Preparation

Commercial grade Genetron (Allied Signal Chemical Co., 99.999%) was used in this case report. Genetron 502 (a gas at room temperature and pressure) consists of 48.8% chlorodifluoromethane (boiling pt = −40.8°C) and 51.2% chloropentafluoroethane (boiling pt = −37.77°C).

TABLE 1—*Concentrations of chlorodifluoromethane and chloropentafluoroethane in the decedent.*

Specimen	$[C_2ClF_5]$	$[CHClF_2]$
Blood	0.30 mg/L	71 mg/L
Brain	0.80 mg/kg	2.8 mg/kg
Liver	0.80 mg/kg	4.4 mg/kg
Lung	0.11 mg/kg	1.6 mg/kg

TABLE 2—*Concentrations of chlorofluorocarbons in previously reported cases. Tissue concentrations are listed in mg/kg. Blood concentrations are listed in mg/L except noted cases (*), which are listed as mg/kg.*

Chlorofluorocarbon	Blood	Brain	Liver	Lung	Reference
Chlorodifluoromethane	286*	282	294	75	#6
Chlorodifluoromethane	538*	414	381	80	#6
Trichlorofluoromethane	32	61	45	32	#4
Dichlorodifluoromethane	3.2	4.5	3.9	3.2	#4
Dichlorodifluoromethane	1.2*	3.5	23	94	#5
Trichlorofluoromethane	0.6*	0.5	2.9	35	#5
Trichlorotrifluoroethane	—	—	—	0.05	#14
Trichlorotrifluoroethane	—	—	—	1.00	#14
Trichlorotrifluoroethane	—	—	—	0.05	#14

A methanolic standard of the freons was prepared by adding 1 mL of methanol to a 2 mL vial. This vial was then sealed with a teflon-lined cap and weighed. A 20 mL sealed vial that had previously been purged (at room temperature and atmospheric pressure) with Genetron 502 served as the analytical standard. 300 μl of the gas sample was taken from the 20 mL vial and added to the 2 mL vial containing 1 mL of methanol. The 2 mL vial containing the methanol was reweighed and the amount of freon added was calculated by subtracting the weight before adding the freon. The vial containing the methanol and freons was gently shaken and left at room temperature for 2 h. After the 2 h equilibration period the partition coefficient of the freon between the methanol and air above the methanol, was calculated by injecting equal volumes of each into the gas chromatograph/mass spectrometer (GC/MS) and determining peak areas of the two components. By knowing the volume of the standard container, the volume of methanol, the air to methanol ratio of the freons, and the weight of freons added, the concentration of freons in the methanol was calculated. Methanolic portions of this standard were added to blank tissues to make up standard curves for quantitative purposes.

Due to the high concentration of chlorodifluoromethane in the blood of the victim, blood standards were made by adding the freon gas mixture, Genetron 502, directly to preweighed vials and determining the amount of freon added by weight. These samples were gently shaken and allowed to equilibrate for 2 h before injection into the GC/MS.

GC/MS

Initial analysis revealed that the components of interest, chloropentafluoroethane and chlorodifluoromethane, were not separated on a 100% methylsilicone column (12 m by 0.25 mm by 0.25 μm) so a second polyethyleneglycol column (15 m by 0.25 mm by 0.25 μm) was added in series to the first column with a 0.25 mm glass connector.

The GC oven temperature initially was 35°C for 2 min and then was ramped to 45°C at 20°C/min where the temperature program was terminated. Total elution time was 3

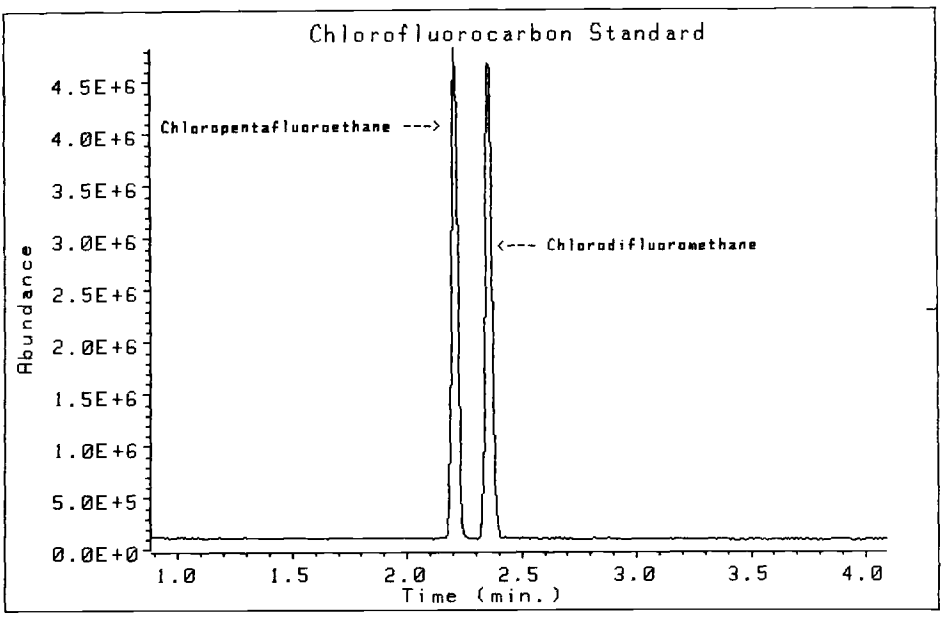
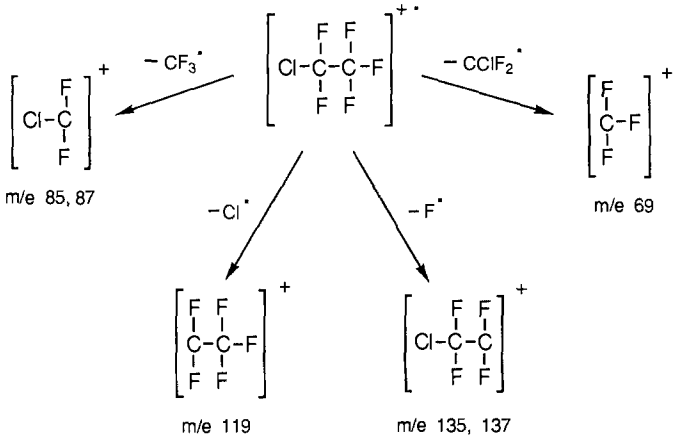


FIG. 1—*Chromatography showing resolution of chloropentafluoroethane (2.21 min) and chlorodifluoromethane (2.35 min).*

min. The injection port temperature was 150°C and the transfer line was 280°C. The GC (Hewlett Packard, GC Model 5890) was operated in the split mode (split = 25:1) with a column head pressure of 5 psi.

The mass spectrometer (Hewlett Packard, mass selective dector model 5970) was operated in electron impact mode and was tuned daily using AUTOTUNE parameters. The ionization potential was 70 electron volts. The mass spectrometer source temperature was maintained at 220°C. For quantitative purposes the MS was operated in the selected ion monitoring mode (SIM). A dwell time of 100 milliseconds was used in scanning the following ions 51, 67, 69, 85, 119, and 135. Chlorofluorocarbons were quantitated using peak areas.

The chromatography of a standard containing the chlorofluorocarbons is shown in Fig. 1. Chloropentafluoroethane eluted at 2.21 min and chlorodifluoromethane eluted second at 2.35 min. The mass spectra and proposed fragmentation pathways of chloropentafluoroethane and chlorodifluoromethane are shown in Fig. 2 and Fig 3 respectively. The fragmentation pathways are consistent with previous reports of similar fluorocarbons [2,3].



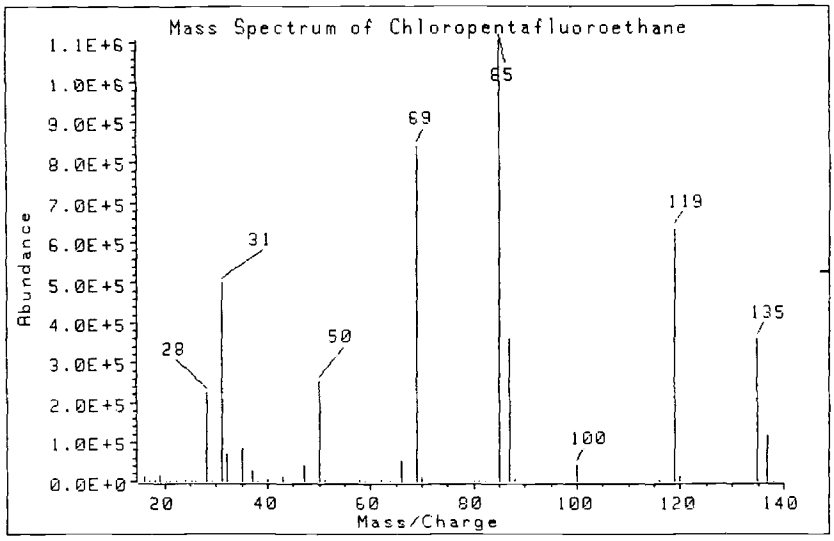
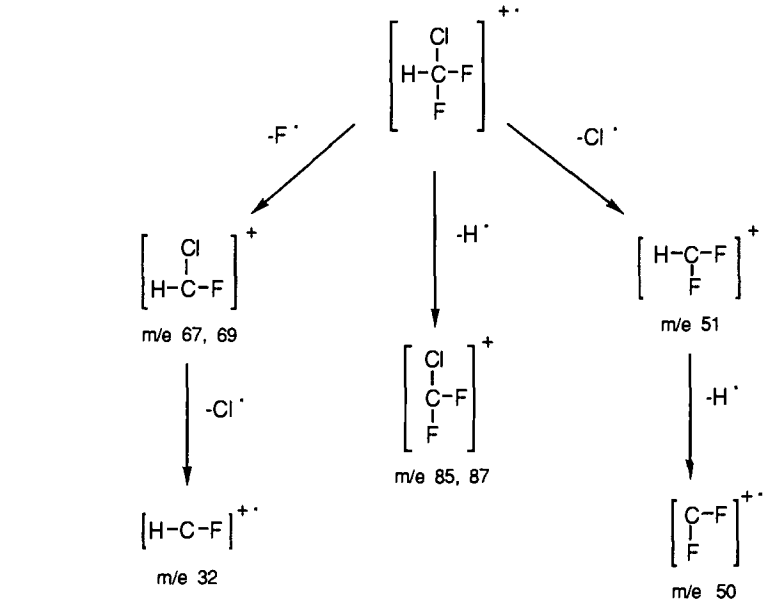


FIG. 2—*Proposed fragmentation pathway and mass spectrum of chloropentafluoroethane.*

Blood and Tissue

Blood and tissue concentrations of the chlorofluorocarbons were quantitated using a slightly modified version of the Chiou and Niazi method [*1*].

Blood was submitted in 16 mL screw cap tubes containing 120 mg sodium fluoride and 45 mg potassium oxalate. Blood was kept at 5°C from time of autopsy until time of analysis (35 days). At the time of analysis 5 mL of blood was added to a 20 mL vial that was sealed with a butyl rubber stopper and a crimp-top seal. Blood samples were gently shaken and allowed to equilibrate at room temperature for 1 h. After equilibration 5 μl of the headspace was introduced into the GC/MS using a gas tight syringe.



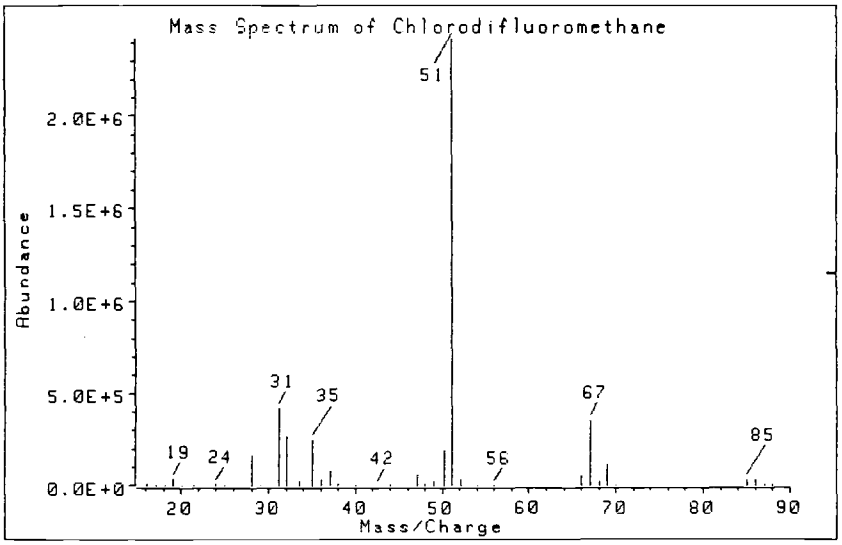


FIG. 3—*Proposed fragmentation pathway and mass spectrum of chlorodifluoromethane.*

Tissue samples were placed in 20 mL crimp-top sealed vials at the time of autopsy and stored at −5°C until time of analysis (35 days). At the time of analysis samples were allowed to equilibrate for 1 h at room temperature, after equilibration 50 μl of the headspace was introduced into the GC/MS. This analysis revealed that the concentration of fluorocarbons in the tissue samples were less than that of blood. To ensure that the fluorocarbons in the tissues were reaching equilibration with the headspace, 10 g of tissue was homogenized with 10 mL of water. Then, 10 g of the homogenate was added to a 20 mL vial, which was sealed and allowed to equilibrate for 1 h before analysis. After equilibration, 50 μl of the headspace above the tissue homogenate was introduced into the GC/MS using a gas tight syringe. The results before and after homogenization were similar suggesting that the fluorocarbons in the tissues were reaching equilibration with the headspace.

Discussion

The interpretation of postmortem blood and tissue concentrations of a gaseous component following administration of an unknown quantity under uncontrolled conditions is difficult. Because the suspected source of chlorofluorocarbons in this case is about a 50:50 mixture of chlorofluorocarbons, the tissue ratios of these compounds might be expected to be near unity. Chlorofluorocarbons do have different pharmacokinetics, which could help explain the observed differences [*7*]. Another possible explanation is that the less polar chloropentafluoroethane had a greater vapor pressure in alveolar blood. This would help explain the preferential removal of this compound especially since vigorous resuscitation was attempted. Previous reports on fatalities involving trichlorofluoromethane and dichlorodifluoromethane generally have reported the highest concentrations of chlorofluorocarbons in heart and lung tissue as compared with blood [*4,5*]. In a case report of three fatalities involving chlorodifluoromethane, blood, brain, lung, and liver concentrations were similar [*6*]. In this study the highest concentrations were found in the blood of the victim. The resuscitation attempts probably explain why the lung concentrations of chlorofluorocarbons were less than the blood concentrations in this case.

Chlorofluorocarbons are toxic to cardiac tissue. In addition to negative inotropic effects, they disrupt sinoatrial rhythm, atrioventricular conduction and may cause ventricular arrhythmias [*8,9*]. These effects have been apparent despite adequate oxygenation and seem to require the presence of epinephrine [*10*]. It has been suggested that fluorocarbons do not sensitize the myocardium to endogenous neurotransmitters, but that they have a depressant effect on sinoatrial, atrioventricular and ventricular conduction systems, allowing other ectopic foci to cause arrhythmias [*9*].

Caffeine can also cause arrhythmias and the presence of caffeine in the present case should not be overlooked. The concentration of caffeine in the decedent's blood is in the same range as volunteers who ingested 120 to 300 mg of caffeine as a single dose and is close to the mean peak concentration after consumption of two cups of strong coffee [*11,12*]. The identification of caffeine in the present case is also important because caffeine is known to increase circulating concentrations of epinephrine in humans [*13*].

Chlorofluorocarbon mixtures have a greater than additive effect on arrhythmia production as compared with exposure to a single agent [*9*]. In this case, the decedent was exposing himself to chlorofluorocarbons while also consuming caffeine. This combination may have increased his chance of having a fatal arrhythmia secondary to development of ectopic foci, potentiated by the epinephrine increase due to the caffeine.

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