6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring bromomethane in environmental media and in biological samples. The intent is not to provide an exhaustive list of analytical methods that could be used to detect and quantify bromomethane. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used to detect bromomethane in environmental samples are the methods approved by federal agencies such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that refine previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

As a volatile material, bromomethane is readily determined by gas chromatographic analysis. The selectivity and sensitivity of detection are increased by the use of an electron capture detector or a halide-specific detector, both of which are very sensitive for organohalides such as bromomethane. Specificity in detection is achieved with mass spectrometric detectors.

6.1 BIOLOGICAL MATERIALS

Bromomethane may be isolated from biological materials either by extraction into an organic solvent, or simply by collecting headspace vapors. Table 6-1 summarizes several methods used by researchers for measuring parent bromomethane in blood or tissues. Detection limits are sufficiently low that levels in blood or tissue associated with health effects can easily be measured. However, as discussed in Section 2.3.4, parent bromomethane is cleared from blood and tissues quite rapidly, so detection of bromomethane exposure in humans is typically performed by measuring serum bromide levels instead. Several methods for measuring bromide ion in serum are also presented in Table 6-1. These methods are also sufficiently sensitive that detection limits (0.5-2.5 ppm) are lower than typical levels of bromide in serum of unexposed people (5-15 ppm), and increases due to bromomethane exposure can easily be measured (Alexeeff and Kilgore 1983).

6.2 ENVIRONMENTAL SAMPLES

Collection of bromomethane from environmental samples is nearly always achieved by trapping on a solid sorbent such as activated charcoal. For air samples, this is done simply by drawing the air through the sorbent. For water, soil, or solid wastes, bromomethane is purged from the sample by flushing with an inert gas, and this is then passed through the sorbent. Desorption may be achieved by extraction in a convenient solvent, or by heating. Table 6-2 summarizes a number of methods that have been developed for measuring bromomethane in various types of environmental media. In all cases, detection limits are much lower than levels of health concern.

TABLE 6-1. Analytical Methods for Determining Bromomethane in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Bromomethane					
Blood, tissue	Purge with inert gas, trap on Tenax® GC, desorb thermally[a]	GC/MS	3 ng/mL blood 6 ng/mL tissue	No data	Pellizzari et al. 1985
Blood, tissue, adipose	Homogenize in toluene, centrifuge, inject supernatant fluid	GC/ECD	1 ng/g	100	Honma et al. 1985
Food	Collect headspace vapor	HRGC	0.4 ppb	No data	DeVries et al. 1985
Grain	Extract with acetone, collect headspace vapor from acetone extract	GC	<1 mg/kg	91.3±3	Scudamore 1985
Bromide					
Blood plasma	Collect headspace vapor of HBr from plasma treated with dimethyl sulfate at 85°C	HRGC	<0.5 µg/mL bromide	97.3±6.3 at 5 µg/mL	Yamano et al. 1987
Tissues	Extract in 18% trichloroacetic acid; derivatize to 1,2-dibromo-cylcohexanone	GC/ECD	2.5 µg/g	17	Honma et al. 1985
Serum, urine	Digest in KOH. Convert to bromate, then to tetrabromorosaniline	Colorimetric (570 nm)	1 µg/mL	100±1	Hunter 1955

[a]Method for the determination of volatile halocarbons in blood and tissue adaptable to bromomethane determination.

ECD = electron capture detector; GC = gas chromatography; HRGC = high-resolution gas chromatography; MS = mass spectrometry

TABLE 6-2. Analytical Methods for Determining Bromomethane in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Sorption by activated carbon, desorption by carbon disulfide	GC/FID	<20 mg/m^3	No data	Mackenzie Peers 1985
Air	Sorption by HBr-treated activated carbon, desorption with carbon disulfide	GC/ECD	0.2 ppm	No data	LeFevre et al. 1989
Air	Retention by activated carbon, removal as headspace gas	GC/ECD	2 µg/m^3	37-91	Woodrow et al. 1988
Exhaust gas	Collect on Tenax® GC, desorb	GC/MWP	<90 µg/m^3	No data	Baumann and Heumann 1987
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/HSD	Approx. 0.5 µg/L	No data	APHA 1985a
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/MS	<1 µg/L	96±11	APHA 1985b
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/HSD	0.01 µg/L	90-110±10[a]	EPA 1988d
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	HRGC/HSD	0.01-0.05 µg/L	97±4	EPA 1988e
Water	Purge with inert gas, trap on sorbent trap, desorb thermally	HRGC/MS	0.11 µg/L	95±8	EPA 1988g
Wastewater	Purge with inert gas, trap on sorbent trap, desorb thermally	GC/MS	No data	88±23	EPA 1982b
Solid waste	Purge by helium, collect on solid, thermally desorb	GC/MS	10 µg/kg	111±48 at 37.2 µg/L	EPA 1986c

[a]Value for similar volatile organohalide compounds in air, not determined directly for bromomethane.

ECD = electron capture detector; FID = flame ionization detector; GC = gas chromatography; HRGC = high-resolution gas chromatography; HSD = haldie specific detector; MS = mass spectrometry; MWP = microwave plasma

6.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of bromomethane is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of bromomethane.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met, would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.3.1 Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Exposure to bromomethane may be evaluated by measuring parent bromomethane, serum bromide, or methylated adducts. Existing methods can measure parent bromomethane in blood or expired air with excellent sensitivity (Honma et al. 1985; Pellizzari et al. 1985; Woodrow et al. 1988), but this is rarely done because bromomethane is cleared so quickly. Several sensitive methods exist for measuring serum bromide (Honma et al. 1985; Hunter 1955; Yamano et al. 1987), and this is the most common means for evaluating exposure. However, increased bromide is not specific for bromomethane exposure, and levels may vary widely between individuals. No routine methods have been established for measuring methyl adducts in DNA or protein (except those involving ^{14}C-labeled bromomethane). Efforts to develop sensitive and specific immunoassays for these adducts would be valuable, since levels of these adducts may be directly proportional to tissue damage. In addition, combination of a method for detecting methyl adducts with a test for increased serum bromide would increase specificity in bromomethane exposure estimates.

The characteristic markers of effect in people exposed to high levels of bromomethane are lung irritation, renal shut-down, and central nervous system injury (Clarke et al. 1945; O'Neal 1987; Prain and Smith 1952). In people exposed to low levels, only the neurological effects can be detected (Anger et al. 1986; Kishi et al. 1988; Verberk et al. 1979). Other than standard clinical neurological or neurobehavior tests, no specific biomarkers of bromomethane effects are known. Since parameters measured in these tests are highly variable among individuals, these tests are neither specific nor particularly sensitive. Efforts to identify and develop a more specific and objective biomarker of exposure would be valuable in evaluating the health significance of exposures that might occur in the environment or near waste sites.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. The medium of main concern for human exposure to bromomethane is air. Trace levels may occur in water or soil, but human exposures from these sources are not expected to be large enough to be of concern except in rare situations. Existing analytical methods can measure bromomethane in air (LeFevre et al. 1989; Mackenzie Peers 1985; Woodrow et al. 1988) and other environmental media (APHA 1985a, 1985b; EPA 1982b, 1986c, 1988d, 1988e, 19883) at levels considerably below those of health concern. The accuracy and precision of the methods are established, and adequate specificity may be achieved by use of mass spectrophotometric detectors. Nevertheless, further efforts to improve accuracy and ease of sample isolation and transfer to the analytical instrument would be helpful.

6.3.2 On-going Studies

The Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control, is developing methods for the analysis of bromomethane and other volatile organic compounds in blood. These methods use purge and trap methodology and magnetic mass spectrometry which gives detection limits in the low parts per trillion range.

Research is underway at the Cooperative Institute for Research in Environmental Sciences (CIRES) at the University of Colorado, Boulder, to improve methods of analysis for bromomethane and related compounds in environmental samples.

Examination of the literature suggests that studies are in progress to improve means for determining bromomethane, its metabolites, and related compounds in biological samples and environmental media. For example, a "Master Analytical Scheme" is being developed for organic compounds in water (Michael et al. 1988), which includes bromomethane as an analyte. The overall goal is to detect and quantitatively measure organic compounds at 0.1 μg/L in drinking water, 1 μg/L in surface waters, and 10 μg/L in effluent waters. Improvements continue to be made in chromatographic separation and detection. Problems associated with the collection of bromomethane on a sorbent trap, followed by thermal desorption may be overcome with direct purging to a capillary column with whole column cryotrapping (Pankow and Rosen 1988). Current research activities in supercritical fluid extraction (King 1989) and supercritical fluid chromatography (Smith 1988) include organohalide analytes such as bromomethane in biological samples and environmental media.