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6.1 BIOLOGICAL MATERIALS

No methods were located that are routinely used for the detection of BCEE in biological materials. Norpoth et al. (1986) reported a method for measuring thiodiglycolic acid (the principal animal metabolite of BCEE) in the urine of rats. This method employed an ion exchange isolation of TDGA followed by gas chromatographic analysis using a flame ionization detector. Sensitivity was not reported, but the method was able to detect a two-fold increase in thiodiglycolic acid (TDGA) excretion (from 0.37 to 0.72 μmo1/24 hours) resulting from an 8-hour exposure to 10 ppm BCEE.

6.2 ENVIRONMENTAL SAMPLES

BCEE in environmental samples is most commonly determined by gas chromatography with a halogen-specific detector (GC/HSD) (Dressman et al. 1977; EPA 1982a), gas chromatography/mass spectrometry (GC/MS) (EPA 1986a), or capillary column gas chromatography/Fourier transform infrared (GC/FT-IR) spectrometry (EPA 1986c).

The determination of BCEE in air requires passing the air samples through a sorbent, followed by elution of adsorbed BCEE from the sorbent and gas chromatographic measurement. Coconut shell charcoal is the favored sorbent, carbon disulfide is used for elution, and gas chromatography is employed for analysis (NIOSH 1984).

The EPA has developed a method of analysis specifically for haloethers in water (EPA 1982a). These compounds include bis(2-chloroethyl), bis(2-chloroisopropyl), 4-chlorophenol phenyl, and 4-bromophenol phenyl ethers, and bis(2-chloroethoxy) methane. The analysis involves an extraction into dichloromethane solvent, concentration by evaporation with exchange to hexane, and Florisil cleanup prior to gas chromatographic measurement. Other standard EPA methods are adapted to the determination of BCEE in wastes.

If BCEE is identified in a sample by a GC procedure other than GC-MS, it is important to confirm the identification by a second method. For example, in a survey of water samples from 113 cities, 44 samples were tentatively found to contain BCEE. Reanalysis of these samples (either by using a different GC column, or by separating interfering components with Florisil prior to GC analysis) indicated that only 13 of the 44 tentatively-identified samples actually contained BCEE (Dressman et al. 1977). Thus, false positive results are likely if confirmatory tests are not performed.

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Methods for the determination of BCEE in environmental samples are summarized in Table 6-1.

6.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, 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 BCEE is available. Where adequate information is not available, ATSDR, in cooperation with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine these health effects (and techniques for developing methods to determine such health effects). The following discussion highlights the availability, or absence, of exposure and toxicity information applicable to human health assessment. A statement of the relevance of identified data needs is also included. In a separate effort, ATSDR, in collaboration with NTP and EPA, will prioritize data needs across chemicals that have been profiled.

6.3.1 Data Needs

Methods for Determining Parent Compound and Metabolites in Biological Materials. Since there are no standard methods for analysis of BCEE in biological materials, development of such methods would be useful. The properties of this compound suggest that it should be amenable to determination in biological samples. It is a relatively high-boiling liquid (178°C) with a low log octanol/water partition coefficient, extractable from water into dichloromethane, relatively stable to hydrolysis, and easily measured by gas chromatography. The high boiling temperature suggests that purge-and-trap and headspace techniques may not be readily applicable to the determination of BCEE in biological samples, but techniques based upon solvent extraction should work well.

Norpoth et al. (1986) reported a method for measuring TDGA in urine. Although this is the principal animal metabolite of BCEE, it occurs naturally in the urine of control animals and is also formed by metabolism of other chemicals. For these reasons, it would be helpful to develop methods for the detection and quantification of urinary metabolites that are unique to BCEE, such as N-acetyl-S-[2-(chloroethoxy)ethyl] cysteine or 2-chloroethoxyacetic acid.

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TABLE 6-1. Analytical Methods for BCEE in Environmental Media

Sample type	Extraction/cleanup	Detection	Limit of Detection	References
Air	Absorb on charcoal, desorb with carbon disulfide	GC	1 $\mu g/m^3$	Berck 1965
Air	Absorb on coconut shell charcoal, elute with carbon disulfide	GC/FID	0.01 mg/ sample	NIOSH 1984
Soil/sediment	Extraction and cleanup	GC/MS	1 mg/kg	EPA 1986a
Solid wastes	Extraction and cleanup	GC/MS	1-200 mg/kg	EPA 1986a
Soil/sediment	Extraction and cleanup	CCGC/MS	1 mg/kg	EPA 1986b
Solid Wastes	Extraction and cleanup	CCGC/MS	1-200 mg/kg	EPA 1986b
Water	Extract with ethyl ether/hexane; concentrate by evaporation; separate interfering compounds using Florisil	GC/HSD	0.005 µg/L	Dressman et al. 1977
Water	Extract with dichloromethane, exchange to hexane, Florisil cleanup	GC/HSD	0.3 µg/L	EPA 1982a
Water	Extract with dichloromethane, concentrate by evaporation	GC/MS	5.7 µg/L	EPA 1982b
Water	Extract with dichloromethane, dry, concentrate by evaporation	GC/IDMS	10 µg/L	EPA 1984
Environmental samples, waste water	Extract with dichloromethane, concentrate by evaporation	GC/FT-IR	35 µg/L	EPA 1986c, Gurka et al. 1987

Abbreviations: GC, gas chromatography; FID, flame ionization detector; MS, mass spectrometry; CCGC, capillary column gas chromatography; HSD, halide specific detector; IDMS, isotope dilution mass spectrometry; FT-IR, fourier transform infrared spectrometry.

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Methods for Biomarkers of Exposure. No routine tests for biomarkers of exposure to BCEE were located. Using radioactively labeled BCEE, Gwinner et al. (1983) reported incorporation of label into cellular proteins of animals exposed to BCEE. Studies to determine if this is due to protein adduct formation would be valuable. If so, immunological assays might be developed to detect such adducts formed from reaction of unlabeled BCEE with proteins such as albumin or hemoglobin. Gwinner et al. (1983) did not detect label in DNA or RNA from animals exposed to BCEE, suggesting that adduct formation with these macromolecules might not be a sensitive biomarker of exposure.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Although methods exist for the determination of BCEE in environmental samples, detection limits (see Table 6-1) are not adequate to measure BCEE in water or air at the concentrations estimated to correspond to the 10^{-6} risk level for cancer (0.03 ppb in water, 0.003 $\mu g/m^3$ in air). Consequently, improvements in sensitivity would be helpful. The problem of high humidity interfering with the collection of BCEE from air (lowered breakthrough volume) should also be addressed.

6.3.2 Ongoing Studies

Supercritical fluid extraction/chromatography and immunoassay are two areas of intense current activity from which substantial advances in the determination of BCEE and metabolites in biological samples can be anticipated. The two techniques are complementary in that supercritical fluid extraction is especially promising for the removal of analytes from sample material (Hawthorne 1988) while immunoassay is very selective and sensitive (Vanderlaan et al. 1988).

An especially promising approach to the determination of BCEE in biological samples is supercritical fluid extraction coupled with supercritical fluid chromatography. This combination has been described for the determination of sulfonylurea herbicides and their metabolites in complex matrices, including soil, plant materials, and cell culture medium (McNally and Wheeler 1988). The approach described in this work should be applicable to BCEE.

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Thermospray techniques interfaced with mass spectrometry, with or without high performance liquid chromatographic separation, are proving useful for the determination of thermally labile compounds (as are some toxicant metabolites), and should be applicable to the determination of BCEE and its metabolites in biological materials (Korfmacher et al. 1987; Betowski et al. 1987).

The EPA is funding an ongoing effort to develop a master analytical scheme for organic compounds in water (Michael et al. 1988). The overall goal is the development of a technology capable of detecting and quantifying organic compounds at 0.1 μg/L in drinking water, 1 μg/L in surface waters, and 10 μg/L in effluent waters. Analytes are to include numerous semivolatile compounds and some compounds that are only semisoluble in water, as well as volatile compounds. A comprehensive review of the literature leading to these efforts has been published (Pellizzari et al. 1985). It may be anticipated that improved methods for the determination of BCEE in environmental samples will be developed as part of this effort.

The current high level of activity in supercritical fluid extraction of solid and semisolid samples should yield improved recoveries and sensitivities for the determination of BCEE in solid wastes, and the compound should be amenable to supercritical fluid chromatographic analysis. Immunoassay analysis (Vanderlaan et al. 1988) is an area of intense current activity from which substantial advances in the determination of BCEE in environmental samples can be anticipated.