$CH_2(C_6H_4NH_2)_2$ MW: 198.27 CAS: 101-77-9 RTECS: BY5425000

METHOD: 5029, Issue 2 **EVALUATION: PARTIAL** **Issue 1: 15 August 1990**
Issue 2: 15 August 1994

OSHA : no PEL
NIOSH: lowest feasible; carcinogen
ACGIH: 0.1 ppm (skin); suspected human carcinogen
(1 ppm = 8.11 mg/m^3 @ NTP)

PROPERTIES: solid; MP 92 °C; BP 399 °C;
VP 0.2 x 10^{-7} kPa (1.5 x 10^{-7} mm Hg)
@ 25 °C

SYNONYMS: p,p'-diaminodiphenylmethane; MDA.

SAMPLING

SAMPLER: FILTER
(acid-treated glass fiber, 37-mm)

FLOW RATE: 1 to 2 L/min

VOL-MIN: 10 L @ 0.1 ppm
-MAX: 1000 L

SHIPMENT: transfer filter to glass vial; extract with 4 mL 0.1 N methanolic KOH before shipping

SAMPLE STABILITY: stable at least 60 days @ 20 °C [1]

FIELD BLANKS: 2 to 10 field blanks per set

MEDIA BLANKS: at least 3 per set

ACCURACY

RANGE STUDIED: not studied

BIAS: not determined

OVERALL PRECISION ($\hat{S}_{rT}$): not determined

ACCURACY: not determined

MEASUREMENT

TECHNIQUE: HPLC, UV AND ELECTROCHEMICAL DETECTION

ANALYTE: 4,4'-methylenedianiline (MDA)

EXTRACTION: 0.1 N KOH In methanol

INJECTION VOLUME: 25 µL

MOBILE PHASE: 0.1 N sodium acetate in 30% acetonitrile/70% H_2O @ 1 mL/min

COLUMN: C_{18} column, 4-µm particle size

DETECTOR: UV, 245 nm; electrochemical (ECHD), glassy carbon electrode at +0.75 to +0.85 V vs. Ag/AgCl electrode

CALIBRATION: MDA in 0.1 N methanolic KOH

RANGE: UV: 0.3 to 5 µg per sample [1]
ECHD: 0.025 to 0.5 µg per sample [1]

ESTIMATED LOD: 0.12 to 1.2 µg per sample [4]

PRECISION ($\bar{S}_r$): 0.027

ESTIMATED LOD: UV: 0.12 µg per sample
ECHD: 0.007 µg per sample [1]

APPLICABILITY: The working range is 0.025 ppb to 1.2 ppm (0.0002 to 10 mg/m^3) for a 100-L air sample, and the method is applicable to STEL measurements. The method is specific for MDA and the use of UV and electrochemical detectors in serie s gives greater reliability to the analysis, and allows a wide measurement range. The method has been applied to wipe samp les.

INTERFERENCES: 4,4'-Diphenylmethane diisocyanate (MDI) will interfere owing to its conversion to MDA on the acid-treated glass fiber filter. Other aromatic amines do not interfere.

OTHER METHODS: Methods with acetylation, and the determination of the acetic anhydride derivative of MDA either by HPLC/UV [2] or by GC/EC (OSHA Method 57) [3] have been reported.

REAGENTS:

1. 4,4'-Methylenedianiline (MDA),* reagent grade.
2. Acetonitrile, distilled in glass.
3. Water, deionized.
4. Sodium acetate, reagent grade.
5. HPLC Mobile Phase: 0.1 N sodium acetate in 30% acetonitrile/70% water.
6. Methanol, distilled in glass.
7. Potassium hydroxide, reagent grade.
8. Calibration stock solution,* 1.0 µg/µL. Dissolve 0.01 g MDA in 10 mL 0.1 N methanolic KOH.
9. Extraction solution: 0.1 N potassium hydroxide in methanol.
10. Sulfuric acid solution: 0.26 N in water. Add, with caution, 1.5 mL concentrated sulfuric acid to deionized water and dilute to 200 mL.

* See SPECIAL PRECAUTIONS.

EQUIPMENT:

1. Sampler: filter, acid-treated glass fiber (Gelman AE or equivalent), with a paper O-ring, in a 37-mm polystyrene 3-piece cassette. NOTE: Prepare filter by adding 0.5 mL 0.26 N sulfuric acid to glass fiber filter on a glass tray. Heat for 1 hour at 100 °C. Load the filter, backed by a paper O-ring, into a cassette and seal with shrink band to enable open-face sampling.
2. Personal sampling pump, 1 to 2 L/min, with flexible tubing.
3. High performance liquid chromatograph (HPLC), with UV detector, 245-nm, and an electrochemical detector, glassy carbon electrode operated at +0.75 to +0.85V with reference to silver/silver chloride reference electrode, oxidative mode.
4. Wipe Tabs (Whatman Smear Tabs or equivalent).
5. Sample filter apparatus: 0.45-µm, PTFE.
6. Syringe, 10-mL, disposable.
7. Vials, glass, scintillation, 20-mL, with PTFE-lined caps.
8. Syringes, microliter, readable to 0.1-µL.
9. Pipets, 2-, 4-, and 10-mL.
10. Tweezers.
11. Ultrasonic water bath.
12. Gauze Pad (Johnson Gauze sponges 2x2, 12 ply or equivalent).

SPECIAL PRECAUTIONS: 4,4'-Methylenedianiline is a potential human carcinogen [4,5]. Avoid contact with acid and base solutions. Handle the acid-treated filters with care.

SAMPLING:

1. Calibrate each personal sampling pump with a representative sampler in line.
2. Remove the front piece and rear plug immediately before sampling. Attach sampler to personal sampling pump with flexible tubing.
3. Sample open-faced at an accurately controlled flow rate between 1 and 2 L/min for a sample volume of 10 to 1000 L.
4. Within 4 hours of completion of sampling, transfer the filter with tweezers to a glass vial. Discard the paper O-ring. Add 4.0 mL 0.1 N methanolic KOH.
   NOTE: Wipe sampling and skin pad instructions:
   a. Identify surfaces to be wiped, usually a 100-cm^2 area.
   b. Add wetting agent (isopropanol) if needed and wipe in square pattern.
   c. Place in 20-mL scintillation vial.
   d. If wetting agent was used, allow the solvent to evaporate.
   e. Add 0.1 N methanolic KOH to vial (10 mL for gauze pads, 2 mL for smear tabs).
5. Pack securely for shipment. Include appropriate number of blanks in the shipment.

SAMPLE PREPARATION:

6. Agitate the samples for 1 hour in an ultrasonic water bath.
7. Filter the sample solution through a 0.45-µm PTFE filter and a disposable syringe into a clean vial.

CALIBRATION AND QUALITY CONTROL:

8. Calibrate daily with at least six working standards over the range of interest.
   a. Make serial dilutions as needed to obtain MDA concentrations in the range 0.025 to 1 µg/mL.
   b. Analyze together with samples and blanks (steps 11 through 13).
   c. Prepare a calibration graph (peak area vs. concentration of MDA, µg per sample) for each detector (UV and ECHD).
9. Determine the recovery at least once for each lot of filters used for sampling in the range of interest. Prepare six filters at each of three concentration levels plus three media blanks.
   a. Add known amounts of MDA in methanol to the filters, using a microliter syringe.
   b. Cover filters. Allow to stand overnight for solvent evaporation.
   c. Extract with 4.0 mL extracting solutions, prepare samples (steps 6 and 7) and analyze (steps 11 through 13) together with standards and blanks.
   d. Determine recovery (R). Construct a graph of R vs. µg MDA recovered.
10. Analyze three quality control blind spikes and three analyst spikes to ensure that the calibration graph and recovery graph are in control.

MEASUREMENT:

11. Set liquid chromatograph to manufacturer's recommendations and parameters given on page 5029-1.
12. Inject sample aliquot manually or with autosampler.
13. Measure peak areas for UV and ECHD responses.

CALCULATIONS:

14. Determine the mass, µg (corrected for recovery) of MDA found on the sample filter (W) and in the average blank filter (B).
15. Calculate concentration (C) of MDA in the air volume sampled, V (L):

$$C = \frac{(W - B)}{V}, \text{ mg/m}^3.$$

EVALUATION OF METHOD:

A calibration curve for the UV absorption detector was constructed from 8 standards over the range 0.03 µg/mL to 1.22 µg/mL [1]. The curve was linear over this region and the LOD was determined to be 0.03 µg/mL. A calibration curve for the ECHD over the range 0.001 µg/mL to 0.12 µg/mL was linear and the LOD was determined to be 0.002 µg/mL. Test samples were prepared by spiking acid-impregnated filters with known amounts of MDA from a solution in methanol. Samples were prepared in triplicate at levels between 0.009 µg per filter and 3.7 µg per filter. (See Table 1 for results):

a. To evaluate extraction efficiency, the filters were analyzed immediately.

b. To assess storage stability, spiked filters were stored in glass scintillation vials for 1 month prior to analysis.
c. To investigate the stability of MDA on the filter during sampling, spiked filters were attached to a sampling pump and 1000 L of laboratory air was drawn through them at 2.5 L/min before analysis.

Table 1: Average Percent Recovery (n=3) of 4,4'-Methylenedianiline From Filter Media

Spiked Amount (µg)	Extraction Efficiency (S.D.) (%)	Storage Stability[a] (%)	Sampling Stability (%)
3.71	94.5 (0.8)	94.4 (1.0)	94.4 (1.0)
1.80	91.3 (0.2)	91.1 (0.4)	90.8 (1.7)
0.93	85.9 (0.8)	86.4 (0.9)	85.5 (0.4)
0.37	84.8 (0.9)	86.0 (0.7)	84.9 (1.0)
0.09	82.0 (2.7)	82.0 (3.8)	77.0 (3.5)
0.037	80.0 (4.1)	83.0 (4.1)	77.0 (3.1)

[a] - Stored in glass scintillation vial for 1 month.

Nine spiked filters were prepared independently and submitted for analysis as a single blind test. Recoveries were 80 to 95% when spiked with 0.012 to 1.2 µg per filter.

During method ruggedization, recoveries were observed to drop significantly during shipment in cassettes. The reason has not been determined but stability has been achieved by field extraction of the filter with methanolic KOH. Solutions and extracted filters were prepared, shipped, stored for 60 days, and analyzed. The data are shown in Table 2.

Table 2: Stability of Extracted Filter Solutions

Spiked Amount (µg)	N	% Recovery (S.D.)
9.9	4	92.1 (0.017)
5.1	4	90.4 (0.042)
1.0	4	100.0 (0.050)
0.0	2	NA

WIPE SAMPLING-This analytical method was used to analyze environmental samples collected on gauze pads and smear tabs. MDA was spiked onto acid-treated gauze pads, plain gauze pads, and smear tabs at 92, 9.2, and 0.92 µg per sample. Sets of each concentration were extracted immediately after allowing the spiking solution to evaporate, one day, one week, and one month after spiking. The extraction solution consisted of 10 mL 0.1 N methanolic KOH for the gauze pads and 2 mL for the smear tabs. The best recovery was obtained when the media were extracted immediately after the methanol evaporated. The same-day samples were reanalyzed at various times to determine if MDA would react with the medium when in solution. Recoveries are given in Table 3.

Table 3: Recoveries of MDA from Gauze Pads and Smear Tabs

Samples & Loading	Average Recovered after			
	0 day	1 day	7 days	30 days
Acid-treated Gauze Pads				
9.3 µg	96	89	87	86
0.93 µg	98	90	86	85
0.09 µg	97	85	85	87
Untreated Gauze Pad				
9.3 µg	97	73	70	53
0.93 µg	98	70	63	46
0.09 µg	93	62	60	55
Smear Tab				
9.3 µg	93	64	53	51
0.93 µg	87	62	48	46
0.09 µg	85	56	44	42
Solutions				
9.3 µg	98	97	98	96
0.93 µg	95	96	95	97
0.09 µg	98	97	94	98

MDA was extracted with greater than 90% extraction efficiency from all the media tested. The extraction efficiency did not decrease when the analyte was isolated from the media by extraction or media elimination. However, upon evaporation of the solvent from the spikes, the MDA begins to react with the media and loss of MDA begins immediately. This is shown by the decrease in recovery and the appearance of a yellow discoloration of the white medium. Although the recovery stabilizes, the addition of sulfuric acid to the pads does not prevent the loss of about 7% of the analyte during the first day. Addition of the 0.1 N methanolic KOH serves as an efficient stabilizer when added to the sample with no recovery loss. The improved recovery following field extraction, the imprecise mode of treated media preparation, and safety considerations of using acid-treated media for wipe samples were factors in using field extraction for surface and dermal samples.

REFERENCES:

[1] Neumeister, C. E. Method Development for 4,4'-Methylenedianiline, Sequence #4752, NIOSH/MRSB, Cincinnati, OH., (NIOSH, unpublished, November 20, 1986).
[2] Anderson, C. C. and E. C. Gunderson, Methods Validation Study of High Performance Liquid Chromatographic Technique for Determining the MPDA and MDA Content of Air samples, SRI International, Menlo Park, CA (1986).
[3] Elskamp, C. J. Method 57 (4,4'-Methylenedianiline), Organic Methods Evaluation Branch, OSHA Analytical Laboratory, Salt Lake City, UT (1986).
[4] Federal Register 29, Part 2, CFR Parts 1910 and 1926 (May 12, 1989).
[5] NIOSH Current Intelligence Bulletin #47, 4,4'-Methylenedianiline (MDA), U. S. Dept. of Health and Human Services (NIOSH) Publication No. 86-115 (1986).

METHOD WRITTEN BY:

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