

4,4'-Methylenedianiline (MDA)



Method no.: 57

Matrix: Air

Target concentration: 1 ppb (8.1 $\mu\text{g}/\text{m}^3$)

Procedure: Samples are collected by drawing known volumes of air through sulfuric acid-treated glass fiber filters. Before submitting the samples to the laboratory, each filter is transferred to separate glass vials containing 2 mL of deionized water. Analysis is performed by analyzing the heptafluorobutyric acid anhydride derivative of MDA by gas chromatography using an electron capture detector.

Recommended air volume and sampling rate: 100 L at 1 L/min

Reliable quantitation limit: 10 ppt (81 ng/m^3)

Standard error of estimate at the target concentration: (Figure 4.4.2.) 9.7%

Status of method: Evaluated method. This method has been subjected to the established evaluation procedures of the Organic Methods Evaluation Branch.

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1. General Discussion

1.1. Background

1.1.1. History

There are several procedures in the literature for the determination of MDA in air. These include collection on silica gel coated with diethylamine and analysis by high-performance liquid chromatography (Ref. 5.1.), collection in an impinger solution of ethanolic potassium hydroxide and analysis by high-performance liquid chromatography (Ref. 5.2.), and collection in an impinger containing dilute hydrochloric acid and analysis of the heptafluorobutyric acid anhydride (HFAA) derivative by gas chromatography (GC) (Ref. 5.3.). NIOSH has proposed a procedure which involves collection on glass fiber filters acidified with sulfuric acid and analysis by high-performance liquid chromatography of acetylated MDA (Ref. 5.4.).

Since impinger solutions are inconvenient to use in the field and silica gel tubes may not efficiently collect aerosols or dusts, the NIOSH filter method was evaluated. The analytical portion of this method was considered to have inadequate sensitivity for a target concentration of 1 ppb. Thus, the analysis scheme was modified to GC analysis of the HFAA derivative of MDA using an electron capture detector. To enhance stability of collected samples, the method was further modified by requiring that the filters be transferred to vials containing deionized water before shipment to the laboratory for analysis.

Note: As a consequence of later evaluation tests done for toluidine, this method has been updated. The sampling device now consists of two acid-treated glass fiber filters assembled in a three-piece cassette instead of a single acid-treated filter with a support pad in a two-piece cassette. Not only does this device offer several advantages as listed in the toluidine method, it is now the common sampler for several aromatic amines.

1.1.2. Toxic effects (This section is for information only and should not be taken as the basis of OSHA policy.)

A bioassay study conducted by the National Toxicology Program indicated that the dihydrochloride salt of MDA is carcinogenic in both sexes of rats and mice. MDA significantly increased the incidence of cancer of the liver, thyroid gland, and hematopoietic system. There were also several other very rare tumors found. (Ref. 5.5.)

Currently there is no OSHA PEL for MDA. Since there is strong evidence that MDA causes cancer (Ref. 5.5.), a target concentration of 1 ppb was chosen for this evaluation.

1.1.3. Potential workplace exposure (Ref. 5.6.)

MDA is produced commercially by the acid catalyzed condensation reaction between aniline and formaldehyde. It is mainly used as an intermediate for production of isocyanates, which in turn are used to make polyurethane foams, elastomers, coatings, spandex, etc. Only a small amount of MDA is actually isolated for production of isocyanates.

MDA is produced only by one company in the United States for sale purposes. The major application of isolated MDA is as an epoxy curative. It is also used in the preparation of high performance wire coatings (formed by reacting with trimellitic anhydride). Other uses include an antioxidant in rubber; a corrosion preventative for iron under highly acidic conditions; an antioxidant in lubricating oils; and an intermediate for dyes.

1.1.4. Physical properties (Ref. 5.6.)

molecular weight:	198.3
boiling range at 35 mm Hg:	262-268°C
freezing point:	89.0°C
color:	light brown crystals (oxidizes slowly in air resulting in darker color)
specific gravity at 100°/4°C:	1.056
flash point:	221.1°C
odor:	faint amine-like
synonyms:	p,p'-methylenedianiline; methylenedianiline;

4,4'-diaminodiphenylmethane; dianilinomethane;
bis(4-aminophenyl)methane; 4,4'-methylenedianiline;
4,4'-methylenediphenylamine; MDA; DADPM; DAPM
structural formula: Figure 1.1.4.

1.2. Limit defining parameters (The analyte air concentrations listed throughout this method are based on an air volume of 100 L and a toluene extraction volume of 2.0 mL. Air concentrations listed in ppb and ppt are referenced to 25°C and 760 mm Hg. Although the derivative of MDA is analyzed, the equivalent mass of MDA is listed throughout the method.)

1.2.1. Detection limit of the analytical procedure

The detection limit of the analytical procedure is 3.2 pg per injection. This is the amount of analyte which gives a measurable response with the amounts of interferences present in analytical standards. (Section 4.1.)

1.2.2. Detection limit of the overall procedure

The detection limit of the overall procedure is 8.1 ng per sample (10 ppt or 81 ng/m³). This is the amount of MDA that can be spiked on a sample filter that when extracted, after 100 L of humid air were drawn through it, gives a measurable response in the presence of trace interferences. (Section 4.2.)

1.2.3. Reliable quantitation limit

The reliable quantitation limit is 8.1 ng per sample (10 ppt or 81 ng/m³). This is the smallest amount of MDA which can be quantitated within the requirements of a recovery of at least 75% and a precision (± 1.96 SD) of $\pm 25\%$ or better. (Section 4.2.)

The reliable quantitation limit and detection limits reported in the method are based upon optimization of the instrument for the smallest possible amount of analyte. When the target concentration of an analyte is exceptionally higher than these limits, they may not be attainable at the routine operating parameters.

1.2.4. Sensitivity

The sensitivity of the analytical procedure over a concentration range representing 0.5 to 2 times the target concentration based on the recommended air volume is 699,800 area units per $\mu\text{g}/\text{sample}$. This is determined by the slope of the calibration curve. (Section 4.3.) The sensitivity will vary with the particular instrument used in the analysis.

1.2.5. Recovery

The recovery of MDA from samples used in a 15-day storage test remained above 79% when the samples were stored in a closed drawer at ambient temperatures of 20 to 25°C. (Section 4.4.) The recovery of MDA from the collection medium during storage must be 75% or greater.

1.2.6. Precision (analytical method only)

The pooled coefficient of variation obtained from replicate determinations of analytical standards at 0.5, 1, and 2 times the target concentration is 0.030. (Section 4.3.)

1.2.7. Precision (overall procedure)

The precision at the 95% confidence level for the 15-day storage test is $\pm 18.9\%$. (Section 4.4.) This includes an additional $\pm 5\%$ for sampling error. The overall procedure must provide results at the target concentration that are $\pm 25\%$ or better at the 95% confidence level.

1.2.8. Reproducibility

Six samples, spiked by liquid injection, and a draft copy of this procedure were given to a chemist unassociated with this evaluation. The samples were analyzed after 0.5 days of storage at 2°C. The average recovery was 88.5% with a standard deviation of 7.3%. (Section 4.5.)

1.3. Advantages

- 1.3.1. The acid-treated filter provides a convenient method for sampling.
- 1.3.2. The analysis is rapid, sensitive, and precise.
- 1.3.3. Samples are stable, even at ambient temperatures.

1.4. Disadvantages

- 1.4.1. Sample filters must be transferred to vials containing water before being submitted to the laboratory for analysis.
- 1.4.2. Methylene bisphenyl isocyanate (MDI) appears to be a positive interference.

2. Sampling Procedure

2.1. Apparatus

- 2.1.1. Samples are collected by use of a personal sampling pump that can be calibrated within $\pm 5\%$ of the recommended flow rate with the sampling filter in line.
- 2.1.2. Samples are collected closed-face using a sampling device consisting of two sulfuric-acid treated 37-mm Gelman type A/E glass fiber filters contained in a three-piece cassette. The filters are prepared by soaking each filter with 0.5 mL of 0.26 N sulfuric acid. (0.26 N Sulfuric acid can be prepared by diluting 1.5 mL of 36 N sulfuric acid to 200 mL with deionized water.) The filters are dried in an oven at 100°C for 1 h and then assembled into three-piece 37-mm polystyrene cassettes without support pads. The front filter is separated from the back filter by a polystyrene spacer. The cassettes are sealed with shrink bands and the ends are plugged with plastic plugs.
- 2.1.3. After sampling, the filters are carefully removed from the cassettes and individually transferred to small vials containing approximately 2 mL of deionized water. The vials must be tightly sealed. The water can be added before or after the filters are transferred. The vials must be sealable and capable of holding at least 7 mL of liquid. Small glass scintillation vials with caps containing Teflon liners are recommended.

2.2. Reagents

Deionized water is needed for addition to the vials in 2.1.3.

2.3. Sampling technique

- 2.3.1. Immediately before sampling, remove the plastic plugs from the filter cassettes. (closed-face sampling)
- 2.3.2. Attach the cassette to the sampling pump with flexible tubing and place the cassette in the employee's breathing zone.
- 2.3.3. After sampling, seal the cassettes with plastic plugs until the filters are transferred to the vials containing deionized water.
- 2.3.4. At some convenient time within 10 h of sampling, transfer the sample filters to vials as in Section 2.1.3.
- 2.3.5. Seal the small vials lengthwise with OSHA Form 21.
- 2.3.6. Submit at least one blank filter with each sample set. Blanks should be handled in the same manner as samples, but no air is drawn through them.
- 2.3.7. Record sample volumes (in liters of air) for each sample, along with any potential interferences.

2.4. Retention efficiency

A retention efficiency study was performed by drawing 100 L of air (80% relative humidity) at 1 L/min through sample filters that had been spiked with 0.814 µg of MDA. Blank acid-treated filters were used as backups in each cassette. The top filters were found to have an average of 91.8% of the spiked amount. There was no MDA found on the bottom filters, so the amount lost was probably due to the slight instability of the MDA salt. (Section 4.6.)

2.5. Extraction efficiency

2.5.1. The average extraction efficiency for six filters spiked at the target concentration is 99.6%. (Section 4.7.)

2.5.2. The stability of extracted and derivatized samples was verified by reanalyzing the above six samples the next day using fresh standards. The average extraction efficiency for the reanalyzed samples is 98.7%. (Section 4.7.)

2.6. Recommended air volume and sampling rate

2.6.1. The recommended air volume is 100 L.

2.6.2. The recommended sampling rate is 1 L/min.

2.7. Interferences (sampling)

2.7.1. MDI appears to be a positive interference. It was found that when MDI was spiked onto an acid-treated filter, it was partially converted to MDA after humid air was drawn through it.

2.7.2. Suspected interferences should be reported to the laboratory with submitted samples.

2.8. Safety precautions (sampling)

2.8.1. Attach the sampling equipment to the employees so that it will not interfere with work performance or safety.

2.8.2. Follow all safety procedures that apply to the work area being sampled.

3. Analytical Procedure

3.1. Apparatus

3.1.1. A GC equipped with an electron capture detector. For this evaluation a Tracor 222 Gas Chromatograph equipped with a Nickel 63 High Temperature Electron Capture Detector and a Linearizer was used.

3.1.2. A GC column capable of separating the MDA derivative from the solvent and interferences. A 6-ft × 2-mm i.d. glass column packed with 3% OV-101 coated on 100/120 Gas Chrom Q was used in this evaluation.

3.1.3. An electronic integrator or some other suitable means of measuring peak areas or heights.

3.1.4. Small resealable vials with Teflon-lined caps capable of holding 4 mL.

3.1.5. A dispenser or pipet for toluene capable of delivering 2.0 mL.

3.1.6. Pipets (or repipets with plastic or Teflon tips) capable of delivering 1 mL for the sodium hydroxide and buffer solutions.

3.1.7. A repipet capable of delivering 25 µL of HFAA.

3.1.8. Syringes for preparation of standards and injection of standards and samples into a GC.

3.1.9. Volumetric flasks and pipets to dilute the pure MDA in preparation of standards.

3.1.10. Disposable pipets to transfer the toluene layers after the samples are extracted.

3.2. Reagents

- 3.2.1. 0.5 N NaOH prepared from reagent grade NaOH.
- 3.2.2. Toluene, pesticide grade. Burdick and Jackson distilled in glass toluene was used.
- 3.2.3. Heptafluorobutyric acid anhydride (HFAA). HFAA from Pierce Chemical Company was used.
- 3.2.4. Phosphate buffer (pH 7.0), prepared from 136 g of potassium dihydrogen phosphate and 1 L of deionized water. The pH is adjusted to 7.0 with saturated sodium hydroxide solution.
- 3.2.5. 4,4'-Methylenedianiline (MDA), reagent grade.

3.3. Standard preparation

- 3.3.1. Concentrated stock standards are prepared by diluting pure MDA with toluene. Analytical standards are prepared by injecting microliter amounts of diluted stock standards into vials that contain 2.0 mL of toluene.
- 3.3.2. Twenty-five microliters of HFAA is added to each vial and the vials are capped and shaken for 10 s.
- 3.3.3. After 10 min, 1 mL of buffer is added to each vial.
- 3.3.4. The vials are recapped and shaken for 10 s.
- 3.3.5. After allowing the layers to separate, aliquots of the toluene (upper) layers are removed with a syringe and analyzed by GC.
- 3.3.6. Analytical standard concentrations should bracket sample concentrations. Thus, if samples fall out of the range of prepared standards, additional standards must be prepared to ascertain detector response.

3.4. Sample preparation

- 3.4.1. The sample filters are received in vials containing deionized water.
- 3.4.2. One milliliter of 0.5 N NaOH and 2.0 mL of toluene are added to each vial.
- 3.4.3. The vials are recapped and shaken for 10 min.
- 3.4.4. After allowing the layers to separate, approximately 1-mL aliquots of the toluene (upper) layers are transferred to separate vials with clean disposable pipets.
- 3.4.5. The toluene layers are treated and analyzed as in sections 3.3.2. through 3.3.5.

3.5. Analysis

3.5.1. GC conditions

zone temperatures:	220°C (column) 235°C (injector) 335°C (detector)
gas flows, Ar/CH ₄ (95/5):	28 mL/min (column) 40 mL/min (purge)
injection volume:	5.0 µL
column:	6 ft × 2-mm i.d. glass, 3% OV-101 on 100/120 Gas Chrom Q
retention time:	3.5 min (MDA derivative)
chromatogram:	Section 4.8.

- 3.5.2. Peak areas or heights are measured by an integrator or other suitable means.

3.5.3. A calibration curve is constructed by plotting response (peak areas or heights) of standard injections versus μg of MDA per sample. Sample concentrations must be bracketed by standards.

3.6. Interferences (analytical)

3.6.1. Any compound that gives an electron capture detector response and has the same general retention time as the HFAA derivative of MDA is a potential interference. Suspected interferences reported to the laboratory with submitted samples by the industrial hygienist must be considered before samples are derivatized.

3.6.2. GC parameters may be changed to possibly circumvent interferences.

3.6.3. Retention time on a single column is not considered proof of chemical identity. Analyte identity should be confirmed by GC/MS if possible.

3.7. Calculations

The analyte concentration for samples is obtained from the calibration curve in terms of micrograms of MDA per sample. The extraction efficiency is 100%. If any MDA is found on the blank, that amount is subtracted from the sample amounts. The air concentrations are calculated using the following formulae:

$$\frac{\mu\text{g}}{\text{m}^3} = \frac{(\mu\text{g of MDA per sample}) \times 1000}{(\text{liters of air sampled})}$$
$$\text{ppb} = \frac{(\frac{\mu\text{g}}{\text{m}^3})(24.46)}{198.3} = (\frac{\mu\text{g}}{\text{m}^3})(0.1233)$$

where 24.46 = molar volume (liters) at 25°C and 760 mm Hg
198.3 = molecular weight of MDA

3.8. Safety precautions (analytical)

3.8.1. Avoid skin contact and inhalation of all chemicals.

3.8.2. Restrict the use of all chemicals to a fume hood if possible.

3.8.3. Wear safety glasses and a lab coat at all times while in the lab area.

4. Backup Data

4.1. Detection limit of the analytical procedure

The injection volume listed in the analytical procedure (5.0 μL) was used in the determination of the detection limit of the analytical procedure. The detection limit of 3.2 pg was determined by analyzing a dilute standard equivalent to 1.3 ng of MDA per sample. This amount was judged to give a measurable response since the conventional means of determining the detection limit based on 5 times the baseline noise was not possible because of interfering peaks. Shown in Figure 4.1. is a chromatogram of this analysis.

4.2. Detection limit of the overall procedure and reliable quantitation limit data

The detection limit of the overall procedure is normally determined by analyzing filters spiked with a loading equivalent to the detection limit of the analytical procedure plus the amount expected to be lost due to incomplete recovery. Since there are more analytical interferences found in samples than standards, a larger amount of MDA had to be spiked onto the filters in order to obtain a measurable amount of derivative. Samples were prepared by injecting 8.1 ng of MDA onto six filters. This is equivalent to 10 ppt or 81 ng/m^3 for 100-L air samples. The samples were analyzed after 100 L of air at 80% relative humidity had been drawn through them. Since the recovery was near 100% at this level, the reliable quantitation limit was taken to be the same as the detection limit of the overall procedure.

Table 4.2.
Detection Limit of the Overall
Procedure and Reliable Quantitation Limit Data

sample no.	% recovery	statistics
1	90.1	
2	93.4	
3	87.9	$\bar{X} = 90.3$
4	91.1	SD = 1.9
5	90.4	1.96 SD = 3.7
6	88.8	

4.3. Sensitivity and Precision (analytical method only)

The sensitivity and precision of the analytical procedure were determined from multiple injections of analytical standards. These data are given in Table 4.3. and Figure 4.3.

Table 4.3.
Sensitivity and Precision Data

x target conc.	0.5x	1x	2x
$\mu\text{g}/\text{sample}$	0.407	0.814	1.627
ppb	0.50	1.00	2.01
area	286134	549995	1162300
counts	286479	549924	1134140
	290451	530925	1126760
	282307	511480	1198810
	281069	568540	1192670
	285986	560580	1089170
\bar{X}	285404	545241	1150640
SD	3343	20820	42057
CV	0.012	0.038	0.037
$\overline{CV} = 0.030$	Response = 699800 area units per $\mu\text{g}/\text{sample}$		

4.4. Storage test

Storage samples were generated by spiking 36 filters with 3.6 μL of 0.226 $\mu\text{g}/\mu\text{L}$ MDA (0.814 μg). Thirty liters of 80% relative humidity air were then drawn through each filter. Within 1 h, the filters were transferred to scintillation vials, each containing 2 mL of deionized water. Six samples were analyzed immediately, fifteen were stored in a refrigerator at 2°C, and fifteen were stored in a closed drawer at ambient temperature. Six samples, three from refrigerated and three from ambient storage, were analyzed in 3-day intervals over a period of 15 days. The results are given in Table 4.4. and Figures 4.4.1. and 4.4.2.

Table 4.4.
Storage Tests

storage time (days)	% recovery					
	(refrigerated)			(ambient)		
0	89.6	92.3	104.4	89.6	92.3	104.4
0	103.6	107.8	103.3	103.6	107.8	103.3
3	96.1	90.5	90.8	90.0	85.6	92.9
6	76.1	90.2	99.1	80.2	82.0	73.7
9	82.7	81.9	89.4	82.7	--	74.1
12	87.9	92.2	97.5	84.5	85.3	81.4
15	94.4	93.9	97.5	88.6	77.0	92.2

4.5. Reproducibility data

Six samples were prepared by injecting microliter quantities of an MDA standard onto acid-treated filters. The samples were analyzed by a chemist unassociated with this evaluation. The results are given in Table 4.5.

Table 4.5.
Reproducibility

sample no.	µg found	µg expected	% found
1	1.20	1.36	88.2
2	0.44	0.45	97.8
3	0.55	0.68	80.9
4	1.09	1.36	80.1
5	0.60	0.68	88.2
6	0.43	0.45	95.6
			$\bar{X} = 88.5$
			SD = 7.3

4.6 Retention efficiency data

Six filters were liquid spiked with 0.814 µg of MDA. The filters were assembled into cassettes using acid-treated filters instead of backup pads. The filters were analyzed after 100 L of humid air (80% relative humidity) had been drawn through them at 1 L/min. There was no MDA found on any of the backup filters. The results for the spiked filters are given in Table 4.6.

Table 4.6.
Retention Efficiency Data

sample no.	µg found	% found
1	0.744	91.4
2	0.774	95.1
3	0.721	88.6
4	0.746	91.6
5	0.747	91.8
6	0.750	92.1
		$\bar{X} = 91.8$

4.7. Extraction efficiency data

Six sample filters were each spiked with 0.814 µg of MDA and analyzed to determine the extraction efficiency. To determine the stability of extracted and derivatized samples, these same six samples were reanalyzed with fresh standards after 24 h.

Table 4.7.
Extraction Efficiency Data

sample no.	% extracted	reanalyzed after 24 h
1	102.8	102.3
2	100.5	99.6
3	94.4	96.3
4	99.2	101.9
5	103.2	98.3
6	97.2	93.6
\bar{x}	99.6	98.7

4.8. Chromatogram

A chromatogram is shown in Figure 4.8. The chromatogram is from a 5.0-µL injection of a standard equivalent to 0.814 µg per sample. This concentration is equal to 1.0 ppb for a 100-L air sample.

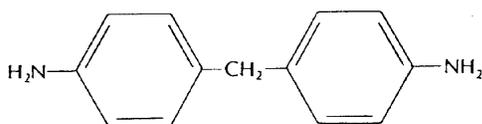


Figure 1.1.4. Structural formula of 4,4'-methylenedianiline.

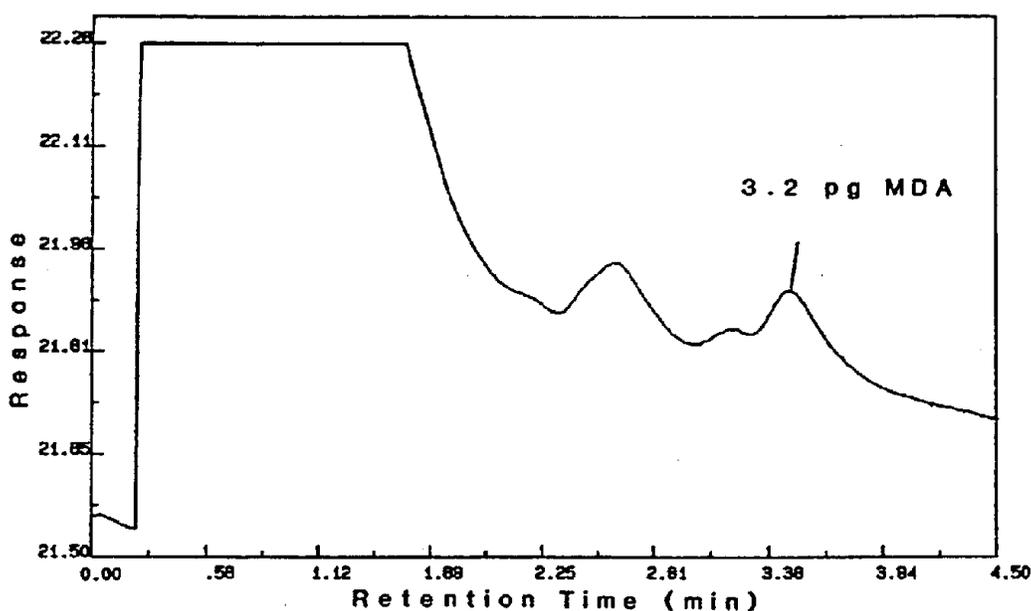


Figure 4.1. Detection limit chromatogram.

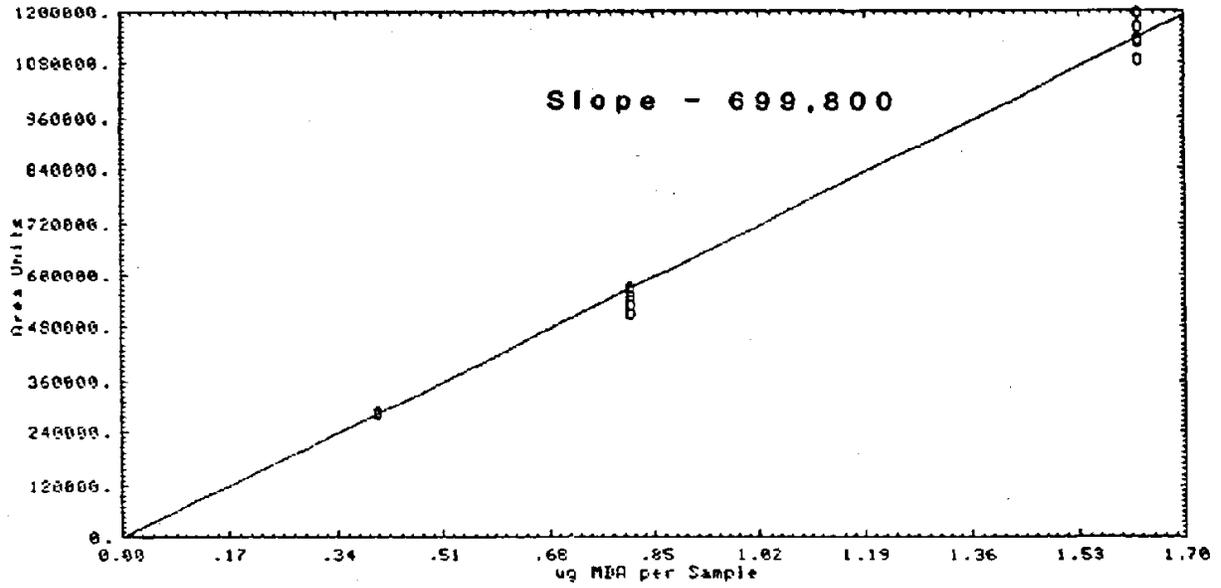


Figure 4.3. Sensitivity.

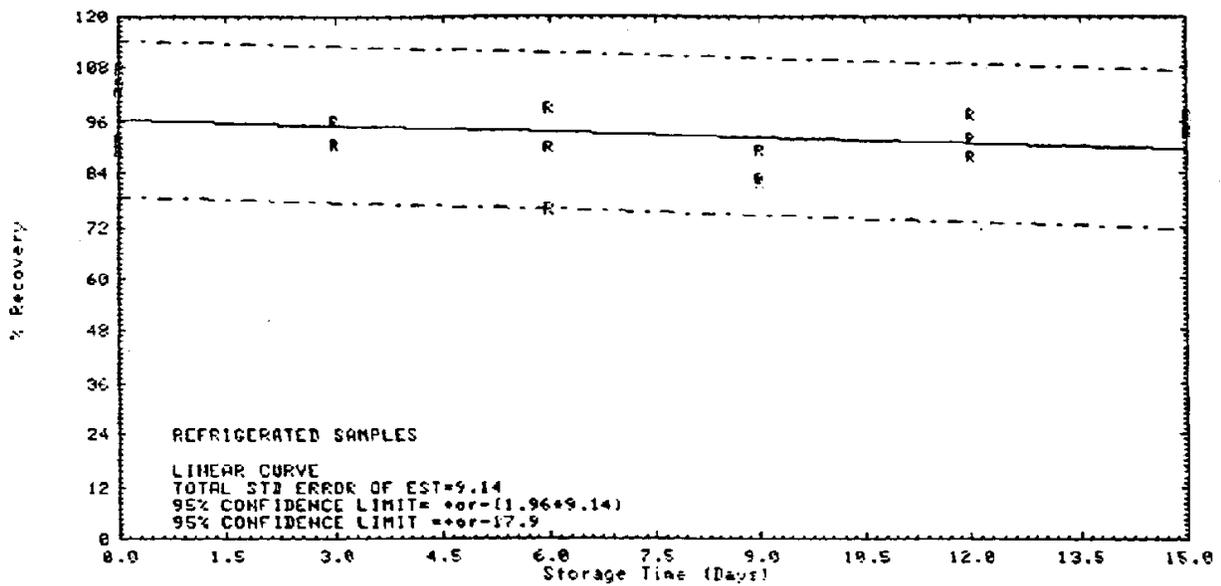


Figure 4.4.1. Refrigerated storage samples.

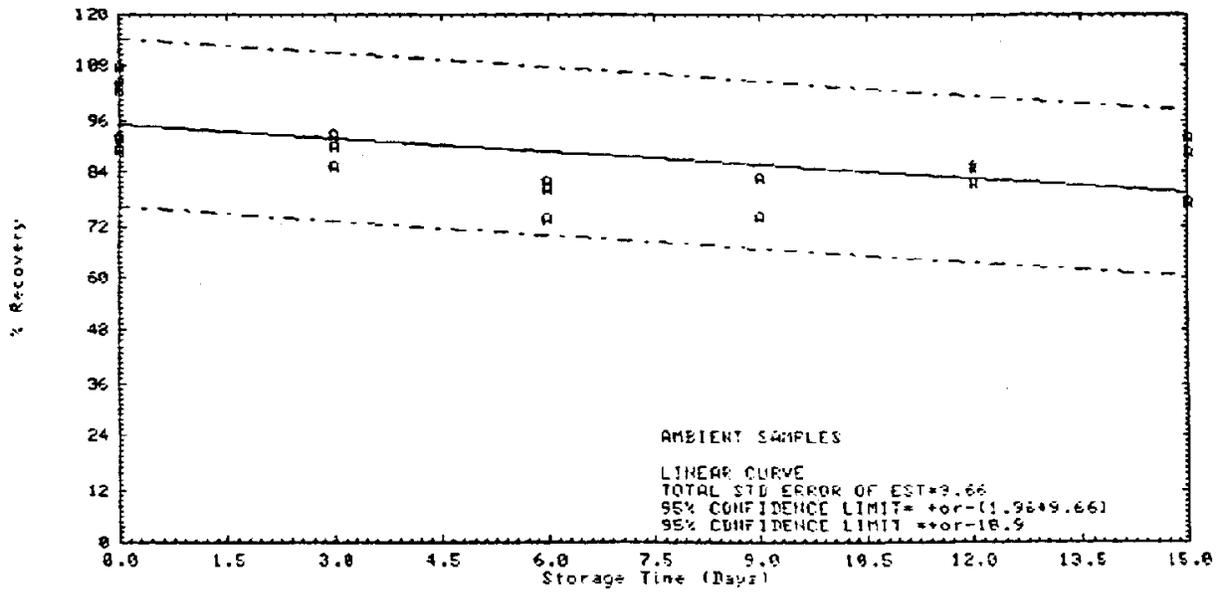


Figure 4.4.2. Ambient storage samples.

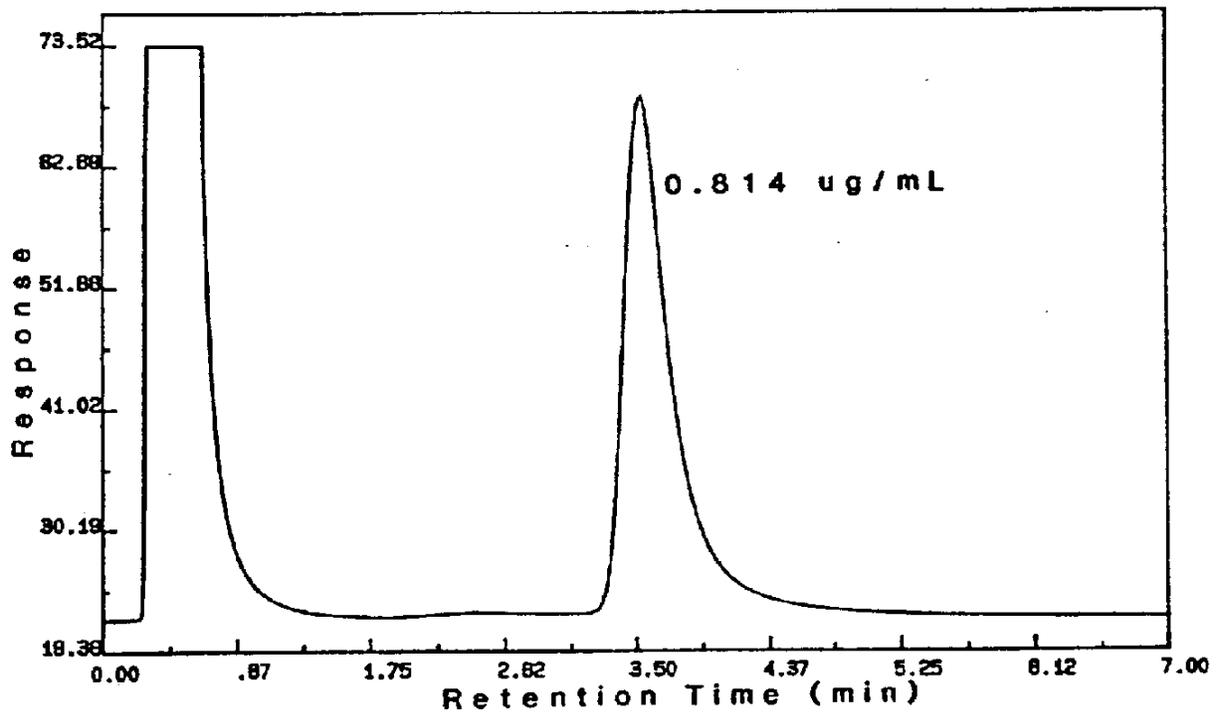


Figure 4.8. Chromatogram of a standard.

5. References

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