Phenothiazine

Method number:	PV2048
Target concentration:	5 mg/m^3 (OSHA TWA PEL)
Procedure:	Samples are collected by drawing a known volume of air through a glass fiber filter. Samples are extracted with methyl tert-butyl ether and analyzed by gas chromatography with a nitrogen-phosphorous detector (GC-NPD). Samples should be protected from sunlight.
Air volume and sampling rate studied:	100 minutes at 1.0 L/min (100 L)
Status of method:	Partially Validated method. This method has been only partially evaluated and is presented for information and trial use.

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1 General Discussion

1.1 Background

1.1.1 History of procedure

The PEL for phenothiazine is 5 mg/m^3. Since phenothiazine is a solid at room temperature, collection on a glass fiber filter was tried and found successful. There was no loss of phenothiazine in the retention studies. The extraction and storage studies were near 100%.

1.1.2 Potential workplace exposure (Ref. 5.1)

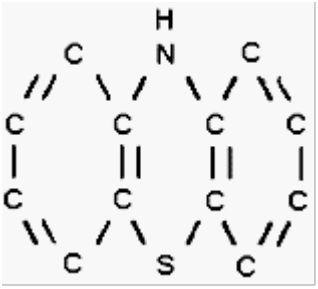
Phenothiazine is used as a pesticide, and is used orally to treat pinworm, threadworm, and roundworm infestations. It is used as a base for the manufacture of pharmaceuticals. It is used as a urinary antiseptic.

1.1.3 Toxic Effects (This section is for information purposes and should not be taken as the basis for OSHA policy.) (Ref. 5.1)

Oral doses of 1 or more grams per day may cause toxic hepatitis, hemolytic anemia, abdominal cramps, tachycardia, gastrointestinal and skin irritation, skin photosensitization, kidney damage, and pruritus. Workers applying phenothiazine in orchards reported skin irritation, including itching, and redness on any exposed surface. The photosensitizing dose is less than 0.75 grams. Workers exposed to between 15 and 48 mg/m^3 during pulverizing and packaging phenothiazine dust developed pinkish-red hair, brown fingernails, and skin irritation.

1.1.4 Physical properties (Ref. 5.2.):

CAS:	92-84-2
IMIS:	2041
RTECS:	57228 (SN5075000)
Synonyms:	dibenzothiazine; Agrazine; thiodiphenylamine; Biverm; Antiverm; Contaverm; Ieeno; ENT 38; Fenoverm; Fentiazine; Helmetina; Lethelmin; Nemazene; Orimon; Padophene; Penthazine; Vermitin; XL-50; Wurm-thional; Souframine
Molecular weight:	199.26
Melting point:	185 °C
Boiling point:	371 °C
Color:	yellow rhombic leaflets or diamond-shaped plates
Molecular formula:	$C_{12}H_9NS$
Compound:	



1.2 Limit defining parameters

1.2.1 The detection limit of the analytical procedure is 1 ng. This is the smallest amount that could be detected under normal operating conditions.

1.2.2 The overall detection limit is 0.03 mg/m^3, based on a 3 mL extraction and a 100-liter air volume. (All mg/m^3 amounts in this study are based on a 100-liter air volume and a 3 mL desorption.)

1.3 Advantages

1.3.1 The sampling procedure is convenient.

1.3.2 The analytical method is reproducible and sensitive.

1.3.3 Reanalysis of samples is possible.

1.3.4 It may be possible to analyze other compounds at the same time.

1.3.5 Interferences may be avoided by proper selection of column and GC parameters.

1.4 Disadvantages

None known

2 Sampling procedure

2.1 Apparatus

2.1.1 A calibrated personal sampling pump, the flow of which can be determined within ±5% at the recommended flow.

2.1.2 A three-piece cassette containing a 37-mm glass fiber filter with a back-up pad.

2.2 Sampling technique

2.2.1 The ends of the filter cassette are opened immediately before sampling.

2.2.2 Connect the filter cassette to the sampling pump with flexible tubing.

2.2.3 Air being sampled should not pass through any hose or tubing before entering the cassette.

2.2.4 Seal the ends of the cassette with plastic caps immediately after sampling. Seal each sample lengthwise with Form OSHA-21 seal.

2.2.5 With each batch of samples, submit at least one blank filter from the same lot used for samples. This filter should be subjected to exactly the same handling as the samples except that no air is drawn through it.

2.2.6 Transport the samples (and corresponding paperwork) to the lab for analysis.

2.2.7 Bulks submitted for analysis must be shipped in a separate mailing container from the samples.

2.3 Extraction efficiency

Six glass fiber filters were liquid spiked at each loading of 16.56 µg (0.4968 mg/m^3), 82.8 µg (2.484 mg/m^3), and 165.6 µg (4.968 mg/m^3) phenothiazine. They were allowed to equilibrate overnight at room temperature. They were opened, placed into a 4-mL vial, extracted with 3-mL of methyl t-butyl ether, for 30 minutes with occasional shaking, and were analyzed by GC-NPD. The overall average was 99.8 % recovered (Table 1).

Table 1
Desorption Efficiency

tube #	% recovered		
	16.56 µg	82.8 µg	165.6 µg
1	99.1	99.9	98.7
2	97.1	101	101
3	103	99.6	lost
4	101	102	101
5	99.0	99.4	101
6	97.9	98.9	99.6
average	100	100	99.5

standard deviation = ±1.51
overall average = 99.8%

2.4 Retention efficiency

Six glass fiber filters were liquid spiked with 165.6 µg (4.968 mg/m^3) phenothiazine. They were placed in a cassette with a second glass fiber filter, and a spacer between the two filters. They were allowed to equilibrate overnight, and then had 100 liters humid air (90% RH) pulled through them. They were opened, extracted, and analyzed by GC-NPD. There was no phenothiazine found on the second glass fiber filter (Table 2). The retention efficiency averaged 99.1 %.

Table 2
Retention Efficiency

sample #	% recovery		total
	'A'	'B'	
1	99.3	0.0	99.3
2	97.8	0.0	97.8
3	101	0.0	101
4	98.6	0.0	98.6
5	100	0.0	100
6	98.0	0.0	98.0

average = 99.1%

2.5 Storage

Glass fiber filters were spiked with 165.6 µg (4.968 mg/m^3) phenothiazine and stored at room temperature on the bench top until opened and analyzed. Half of the storage samples were stored in brown vials, as phenothiazine decomposes in sunlight. The storage samples were exposed to room light. There was little difference between the samples stored in brown and clear glass. The spectrum of room light does not compare to sunlight, so this comparison probably does not mimic sunlight conditions. The recoveries averaged 98.9% for brown glass vials, and 99.6 % for clear glass vials for the 14 days stored (Table 3).

Table 3
Storage Study

days	% recovery	
	brown glass	clear glass
6	102	102
6	99.7	99.0
6	100	101
14	98.3	98.1
14	97.2	98.2
14	96.2	99.5
average	98.9	99.6

overall average = 99.3%

2.6 Precision

The precision was calculated using the area counts from six injections of each standard at concentrations of 16.56, 82.8, 165.6, and 331.2 µg/mL. The pooled coefficient of variation was 0.0152 (Table 4).

Table 4
Precision Study

injection #	16.56 µg/mL	82.8 µg/mL	165.6 µg/mL	331.2 µg/mL
1	17172	89354	200460	364060
2	17032	86143	198930	357320
3	16878	85210	205780	353010
4	17103	85358	204320	355600
5	17013	88439	207290	355490
6	16917	88699	200900	350190
average	17019	87201	202947	355945
standard deviation –	±110	±1838	±3325	±4686
CV -	0.00646	0.0211	0.0164	0.0132

pooled CV = 0.0152

Where:

$$CV\ \left(Coefficient\ of\ Variation\right) = \frac{\left(standard\ deviation\right)}{\left(average\right)}$$

$$Pooled\ CV = \sqrt{\frac{A1\left(CV1\right)^2 + A2\left(CV2\right)^2 + A3\left(CV3\right)^2 + A4\left(CV4\right)^2}{A1 + A2 + A3 + A4}}$$

A1, A2, A3, A4 = number of injections at each level
CV1, CV2, CV3, CV4 = Coefficient of variation at each level

2.7 Air volume and sampling rate studied

2.7.1 The air volume studied is 100 liters.

2.7.2 The sampling rate studied is 1.0 liter per minute.

2.8 Interferences

Suspected interferences should be listed on sample data sheets.

2.9 Safety precautions

2.9.1 Sampling equipment should be placed on an employee in a manner that does not interfere with work performance or safety.

2.9.2 Safety glasses should be worn at all times.

2.9.3 Follow all safety practices that apply to the workplace being sampled.

3 Analytical method

3.1 Apparatus

3.1.1 Gas chromatograph equipped with a nitrogen-phosphorous detector. An HP 5890 gas chromatograph was used for this study. Phenothiazine can also be analyzed by gas chromatography with a flame photometric detector in the sulfur mode, with a detection limit of 0.2 mg/m^3.

3.1.2 GC column capable of separating the analyte from any interference. The column used in this study was a 60-m x 0.32-mm i.d., (1.5-µm d_f RTX-5) capillary column. Other columns that can be used are a 60-m x 0.32-mm i.d., (1.0 µm d_f RTX-1) capillary column or a 30-m x 0.32-mm i.d. (0.5 µm d_f DB-210) capillary column.

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

3.1.4 Two and four milliliter vials with PTFE-lined caps. The samples are extracted in 4-mL vials, and transferred to the 2-mL vials for analysis.

3.1.5 A 1-µL syringe or other convenient size for sample injection.

3.1.6 3-mL pipettes for dispensing the methyl tert-butyl ether.

3.1.7 Volumetric flasks, 10-mL, and other convenient sizes for preparing standards.

3.1.8 Analytical balance capable of weighing milligram amounts.

3.2 Reagents

3.2.1 Purified GC grade nitrogen, hydrogen, and air.

3.2.2 Methyl tert-butyl ether, HPLC grade.

3.2.3 Phenothiazine, Reagent grade

3.3 Sample preparation

3.3.1 Sample cassettes are opened and the filter is placed in a 4-mL vial.

3.3.2 The filter is extracted with 3 mL of methyl t-butyl ether.

3.3.3 The vials are sealed immediately and allowed to extract 30 minutes with occasional shaking.

3.3.4 An aliquot is placed in a 2-mL vial for analysis.

3.4 Standard preparation

3.4.1 Standards are prepared by diluting a known quantity of phenothiazine with methyl tert-butyl ether. Two different stock standards should be prepared, and dilutions of them made.

3.4.2 A series of standards are prepared covering the range from detection limit to the highest sample. At least five different concentrations should be made so that there are enough data points to plot a curve. The range used in this study was 1.656 to 165.6 µg/mL.

3.5 Analysis

3.5.1 Gas chromatograph conditions.

Flow rates	**(mL/min.)**	**Temperature**	**(°C)**
Nitrogen (make-up):	30	Injector:	250
Hydrogen (carrier):	1	Detector:	250
Hydrogen (detector):	2	Column:	250
Air:	30		

Injection size: 1 µL
Chromatogram: (See Figures 1)

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

3.6 Interferences (analytical)

3.6.1 Any compound having the general retention time of the analyte is interference. Possible interferences should be listed on the sample data sheet. GC parameters should be adjusted if necessary so these interferences will pose no problems.

3.6.2 Retention time data on a single column is not considered proof of chemical identity. Samples over the target concentration should be confirmed by GC/Mass Spec or other suitable means.

3.7 Calculations

3.7.1 A curve with area counts versus concentration is calculated from the calibration standards.

3.7.2 The area counts for the samples are plotted with the calibration curve to obtain the concentration of phenothiazine in solution.

3.7.3 To calculate the air concentration of phenothiazine (PT) the following equation is used:

$$mg/m^3 = \frac{(\mu g/mL,\ blank\ corrected)(3\ mL)}{(100\ L)(desorption\ efficiency,\ decimal)}$$

µg/mL = amount of Phenothiazine from calibration curve
3 mL = extraction volume
100 L = air volume of the sample

3.8 Safety precautions

3.8.1 All handling of solvents should be done in a hood.

3.8.2 Avoid skin contact with all solvents.

3.8.3 Wear safety glasses at all times.

4 Recommendations for further study

Collection studies should be performed. Analysis of phenothiazine can also be done by liquid chromatography according to literature.

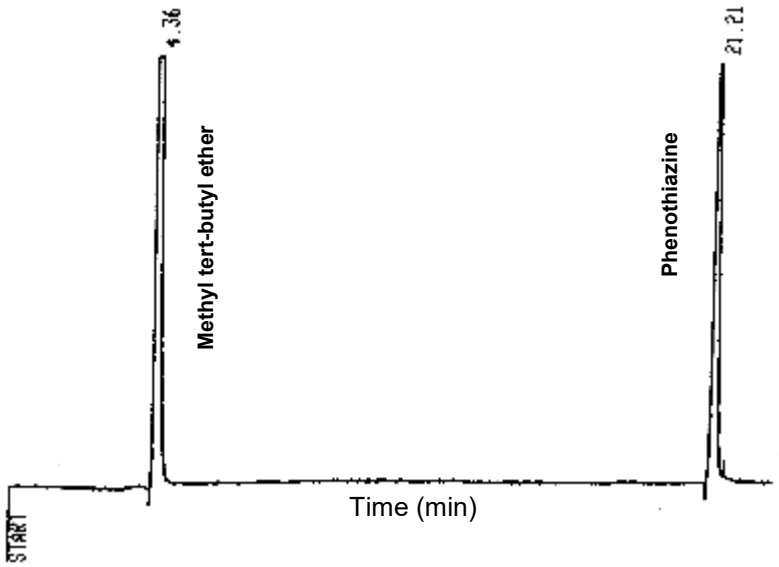


Figure 1. A standard of 165 µg/mL phenothiazine in methyl t-butyl ether.

5 References

5.1 "Documentation of the Threshold Limit Values and Biological Exposure Indices," Fifth Edition, American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH, 1986, p. 472.

5.2 Windholz, M., "The Merck Index," Tenth Edition, Merck & Co., Rahway N.J., 1983, p. 1046.