



Thiophanate-methyl

Method number:	PV2058
Target Concentration:	0.4 mg/m ³ (arbitrary) There is no OSHA permissible exposure level (PEL) or ACGIH threshold limit value (TLV) for thiophanate-methyl.
Procedure:	Samples are collected by drawing known volumes of air through glass fiber filters. Samples are extracted with acetonitrile and analyzed by high performance liquid chromatography (HPLC) using an ultraviolet (UV) detector.
Recommended air volume and sampling rate:	240 minutes at 1.0 L/min (240 L)
Detection limit of the overall procedure	10 µg/m ³ (based on the recommended air volume and the analytical detection limit):
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 OSHA Analytical Laboratory received a set of air samples requesting the analysis of thiophanate-methyl. The samples had been collected on glass fiber filters with air volumes of about 240 liters. This report describes the analytical method developed.

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

The acute oral LD₅₀ in rats has been reported to be 7500 mg/kg and 6640 mg/kg. (Ref. 5.1 and 5.2)

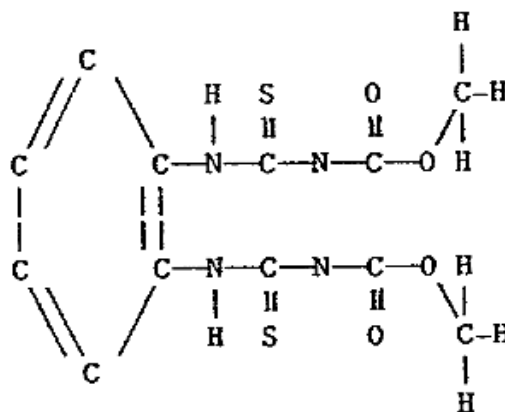
1.1.3 Potential workplace exposure

Thiophanate-methyl has a broad spectrum of plant disease control in vegetables, fruit, turf, soybeans, peanuts, almonds, celery (Ref 5.2). No estimate of worker exposure to thiophanate-methyl could be found.

1.1.4 Physical properties (Ref. 5.1 to 5.3)

Molecular weight: 342.42
Molecular formula: C₁₂H₁₄N₄O₄S₂
CAS #: 23564-05-8
IMIS number: D347
Melting point: 168 °C with decomposition
Solubility: soluble in acetone, methanol, chloroform, and acetonitrile, slightly soluble in other organics, insoluble in water
Chemical name: Dimethyl ((1,2-phenylene) bis-(iminocarbonothioyl)) bis {carbamate}
Synonyms: Cercobin-M, Mildothane, Topsin H, Labilite
Description: colorless crystalline solid
UV scan: Figure 1.

Structure:



1.2 Limit defining parameters

The detection limit of the analytical procedure is 0.5 ng per injection. This is the amount of analyte which will give a peak whose height is approximately five times the baseline noise.

2 Sampling procedure

2.1 Apparatus

- 2.1.1 A personal sampling pump that can be calibrated to within $\pm 5\%$ of the recommended flow rate with the sampling device in line.
- 2.1.2 Glass fiber filters, 37-mm diameter, Gelman Type A, or equivalent.
- 2.1.3 Cassette filter holder for 37-mm filters, Millipore M000037A0, or equivalent.

2.2 Reagents

No sampling reagents are required.

2.3 Sampling technique

- 2.3.1 Immediately before sampling, remove the plastic plugs from the cassette.
- 2.3.2 Attach the cassette to the sampling pump with flexible tubing.
- 2.3.3 Attach the cassette vertically in the employee's breathing zone in such a manner that it does not impede work performance.
- 2.3.4 After sampling for the appropriate time, remove the cassette and seal with plastic plugs.
- 2.3.5 Wrap each cassette end-to-end with a Form OSHA-21 seal.
- 2.3.6 Record the air volume for each sample, and list any possible interference.
- 2.3.7 Submit at least one blank for each set of samples. Handle the blank in the same manner as the samples, except no air is drawn through it.
- 2.3.8 Submit bulk samples for analysis in a separate container.

2.4 Extraction efficiency

Twenty-four glass fiber filters were each liquid spiked with 40 μL of a 2.442 mg/mL thiophanate-methyl standard. After drying, six of the glass fiber filters were each extracted with 5 mL of acetonitrile, shaken for 30 min and then analyzed as in section 3. The results are listed in Table 2.4.

Table 2.4
Extraction Efficiency

sample #	μg spiked	μg found	% recovered
1	97.68	92.46	94.7
2	97.68	91.93	94.1
3	97.68	93.36	95.6
4	97.68	87.78	89.9
5	97.68	85.46	87.5
6	97.68	96.95	99.3

average = 93.5%

2.5 Retention efficiency

The remaining 18 glass fiber filters from above had 240 L of humid air (~80% relative humidity) drawn through them. Six of the filters were then each extracted with 5 mL of acetonitrile, shaken for 30 min and then analyzed as in Section 3. The results are listed in Table 2.5. The rest of the filters were stored, 6 in a drawer at ambient temperature and 6 in a freezer, for storage studies.

Table 2.5
Retention Efficiency

sample #	µg spiked	µg found	% recovered
1	97.68	95.01	97.3
2	97.68	95.93	98.2
3	97.68	99.89	102.3
4	97.68	94.67	96.9
5	97.68	99.18	101.5
6	97.68	103.4	105.9

average = 100.4%

2.6 Sample storage

After 5 days of storage, 6 samples, 3 from ambient storage and 3 from freezer storage, were each extracted with 5 mL of acetonitrile, shaken for 30 min and then analyzed as in section 3. The remaining samples were extracted and analyzed after 8 days of storage. The results are given in Tables 2.6.1 and 2.6.2.

Table 2.6.1
Ambient Storage

sample #	µg spiked	µg found	% recovered
5	97.68	97.63	99.9
5	97.68	96.05	98.3
5	97.68	104.51	107.0
8	97.68	98.16	100.5
8	97.68	96.32	98.6
8	97.68	89.55	91.7

average of 5 days = 101.7%

average of 8 days = 96.9%

Table 2.6.2
Freezer Storage

sample #	µg spiked	µg found	% recovered
5	97.68	96.25	98.5
5	97.68	96.97	99.3
5	97.68	102.3	104.7
8	97.68	97.14	99.4
8	97.68	98.24	100.6
8	97.68	97.52	99.8

average of 5 days = 100.8%

average of 8 days = 99.9%

2.7 Recommended air volume and sampling rate

2.7.1 The recommended air volume is 240 L.

2.7.2 The recommended flow rate is 1.0 L/min.

2.8 Interferences (sampling)

It is not known if any compounds will interfere with the collection and analysis of thiophanate-methyl. Any suspected interference should be reported to the laboratory.

2.9 Safety precautions (sampling)

2.9.1 Attach the sampling equipment in such a manner that it will not interfere with work performance or employee safety.

2.9.2 Follow all safety practices that apply to the work area being sampled.

3 Analytical procedure

3.1 Apparatus

3.1.1 A balance capable of weighing to the nearest tenth of a milligram. A Mettler HL52 balance was used in this evaluation.

3.1.2 A mechanical shaker.

3.1.3 An HPLC with a UV detector. A Hewlett Packard 1090 liquid chromatograph with a diode array detector was used in this evaluation.

3.1.4 An HPLC column capable of separating thiophanate-methyl from any interference. A 5- μ m Hypersil ODS 100-mm x 2.1-mm column was used in this evaluation.

3.1.5 An electronic integrator or some other suitable means for measuring detector response. The Hewlett-Packard (HP) 1090 Chem Station was used in this evaluation.

3.1.6 Volumetric flasks and pipettes various sizes.

3.1.7 Scintillation vials, 20-mL with PTFE caps.

3.1.8 Vials, 2 mL with PTFE caps.

3.2 Reagents

3.2.1 Acetonitrile, HPLC grade was used in this analysis.

3.2.2 Water, HPLC grade was used in this analysis.

3.2.3 Thiophanate-methyl. An EPA standard #6671 with a purity of 99.7% was used in this evaluation.

3.3 Standard preparation

Prepare thiophanate-methyl stock standards by weighing 10 to 14 mg of thiophanate-methyl. Transfer the thiophanate-methyl to separate 10-mL volumetric flasks, and add acetonitrile to the

mark. Make working range standards of 0.5 to 25 µg/mL by pipette dilutions of the stock standards with acetonitrile. Store stock and dilute standards in a freezer.

3.4 Sample preparation

3.4.1 Transfer the glass fiber filter to a 20 mL scintillation vial.

3.4.2 Add 5.0 mL of acetonitrile to each vial and seal with a Teflon-lined cap.

3.4.3 Shake the vials for 30 minutes on a mechanical shaker.

3.4.4 Transfer the sample to a 2-mL vial for use in an HP autosampler

3.5 Analysis

3.5.1 Instrument conditions

Column:	5-µm Hypersil ODS, 100-mm x 2.1-mm
Oven temperature:	40 °C
Mobile phase:	acetonitrile/water (30/70)
Flow:	0.3 mL/min
Wavelengths:	266 nm and 208 nm
Injection volume:	1.0 µL
Retention time:	3.47 min

3.5.2 Chromatogram (Figure 2.)

3.6 Interferences (analytical)

3.6.1 Any collected compound having a similar retention time to that of thiophanate-methyl is interference.

3.6.2 HPLC conditions may be varied to circumvent interferences.

3.6.3 Retention time alone on a single column is not proof of chemical identity. Analyses by an alternate HPLC column, comparison of wavelength responses or confirmation by mass spectrometry are additional means of identification.

3.7 Calculations

3.7.1 Construct a calibration curve (Figure 3.) by plotting detector response versus concentration (µg/mL) of thiophanate-methyl.

3.7.2 Determine the µg/mL of thiophanate-methyl in each sample and blank from the calibration curve.

3.7.3 Blank correct the sample by subtracting the µg/mL found in the blank from the µg/mL found in the sample.

3.7.4 Determine the air concentration by using the following formula.

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

3.8 Safety precautions (analytical)

3.8.1 Avoid skin contact and air exposure to thiophanate-methyl.

3.8.2 Avoid skin contact with all solvents.

3.8.3 Wear safety glasses at all times.

4 Recommendation for further study

This method should be fully validated.

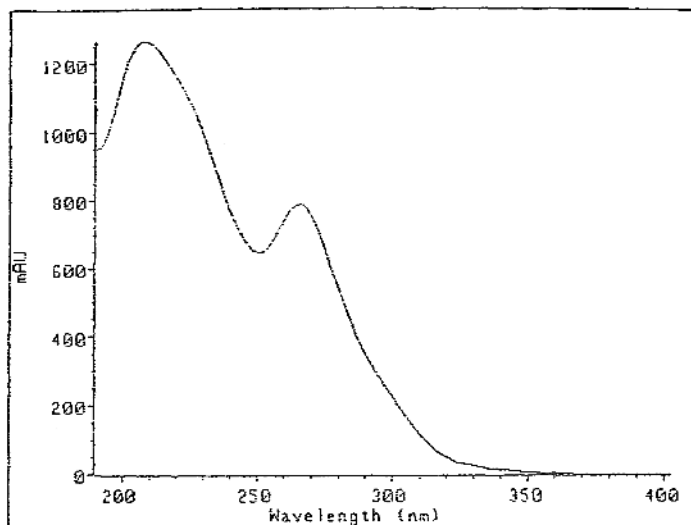


Figure 1.
UV Scan of Thiophanate-methyl

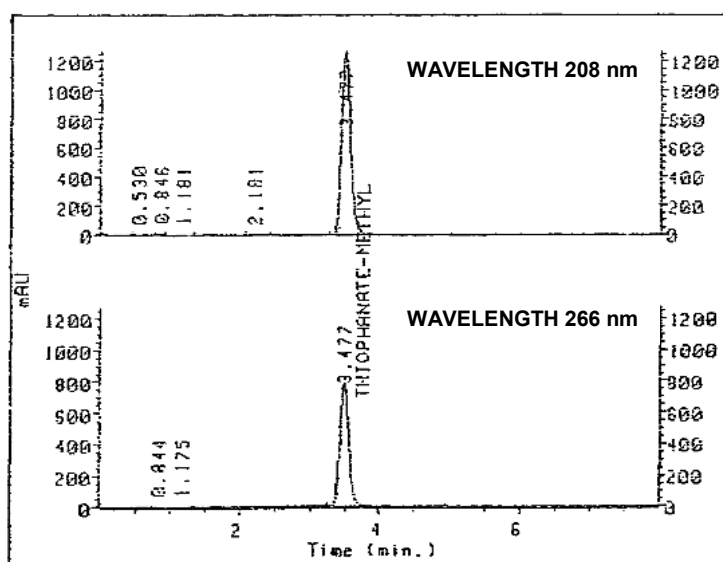


Figure 2.
Chromatogram of Thiophanate-methyl

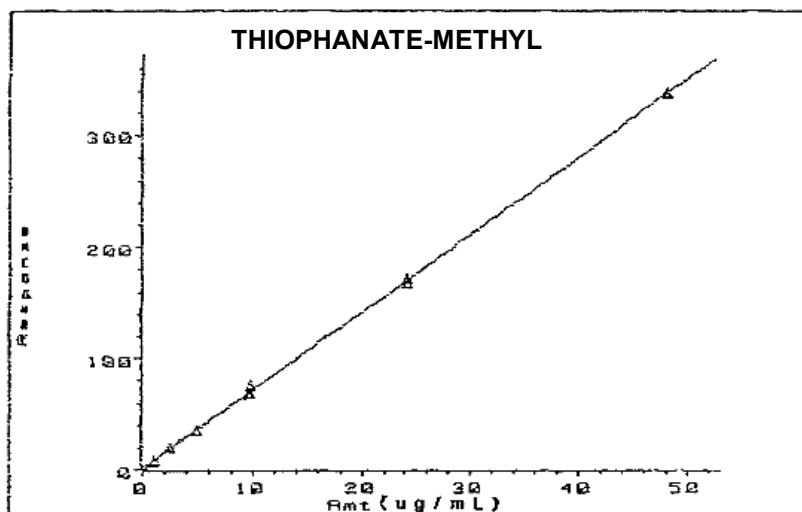


Figure 3.
Calibration Curve

5 References

- 5.1 Registry of Toxic Effects of Chemical Substances 1985-86 Edition; U.S. Department of Health and Human Services: Cincinnati, OH, 1987; DHHS (NIOSH) Publication No. 87-114, p 313.
- 5.2 Farm Chemicals Handbook; Berg, Gordon L. Ed.; Meister: Willoughby, Ohio, 1986; p C231.
- 5.3 Merck Index, 10th ed.; Windholz, Martha Ed.; Merck: Rathway, N.J., 1983; pp 1339-1340.