



Thiourea

Method number:	PV2059
Target Concentration:	60 $\mu\text{g}/\text{m}^3$ (arbitrary). There is no OSHA permissible exposure level (PEL) or ACGIH threshold limit value (TLV) for thiourea.
Procedure:	Samples are collected by drawing known volumes of air through a two-piece sampling cassette containing a glass fiber filter (GFF). The samples are extracted with methanol and analyzed by high performance liquid chromatograph (HPLC) using an ultraviolet (UV) detector.
Recommended air volume and sampling rate:	240 minutes at 2.0 L/min (480 L)
Detection limit of the overall procedure	3.0 $\mu\text{g}/\text{m}^3$ (based on the recommended air volume and the analytical detection limit)
Special precautions:	Samples should be shipped overnight and kept cold until analysis.
Status of method:	Partially validated method. This method is presented for information and trial use only.

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1 General Discussion

1.1 Background

1.1.1 History of procedure

In OSHA method 95, "ETHYLENE THIOUREA" is collected on glass fiber filter (GFF) (Ref. 5.1). Because thiourea and ethylene thiourea are chemically similar, a GFF was evaluated as the sampling media for thiourea.

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

Chronic administration of thiourea in rats has resulted in hepatic tumors, bone marrow depression, and goiters. Thiourea may reasonably be anticipated to be a carcinogen (Ref. 5.2).

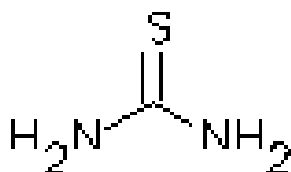
1.1.3 Potential workplace exposure

Thiourea is used both as a photographic fixing agent and to remove stains from negatives. It is also used as an intermediate in the manufacture of fire-retardant resins for lacy fabrics, a vulcanization accelerator, and a reagent for determination of bismuth and selenite ions (Ref. 5.2 and 5.3). There was no information available on the number of workers potentially exposed to thiourea.

1.1.4 Physical properties (Ref. 5.2 and 5.3)

CAS number:	62-56-6
Chemical name:	Thiocarbamide
Common name:	Thiourea
Molecular formula:	CH ₄ N ₂ S
Molecular weight:	76.12
Melting point:	176-178 °C
Solubility:	soluble in alcohol, in 11 parts water, and sparingly soluble in ether.
Appearance:	colorless crystals

Structural formula:



1.2 Limit defining parameters

1.2.1 The detection limit of the analytical procedure.

The detection limit of the analytical procedure is 4.9 ng per injection. This is the amount of analyte which gives a peak whose height is approximately five times the baseline noise.

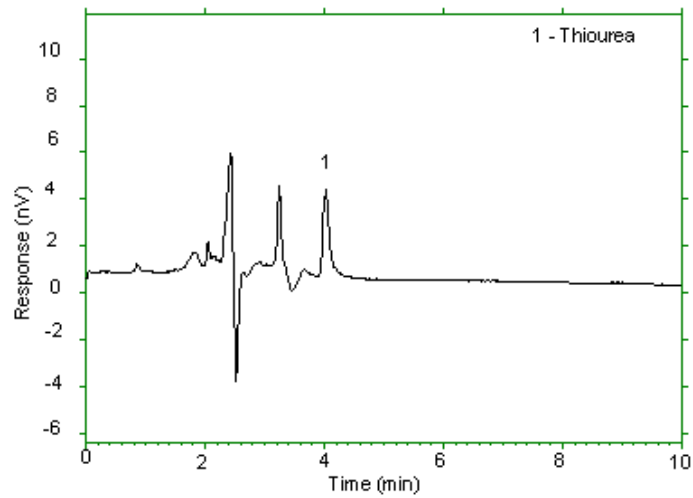


Figure 1.2.1. Chromatogram of the analytical detection limit.

1.2.2 Detection limit of the overall procedure

The detection limit of the overall procedure is 1.47 μg per sample. This is the amount of analyte spiked on a glass fiber filter that, upon analysis, produces a peak similar in size to that of the detection limit of the analytical procedure.

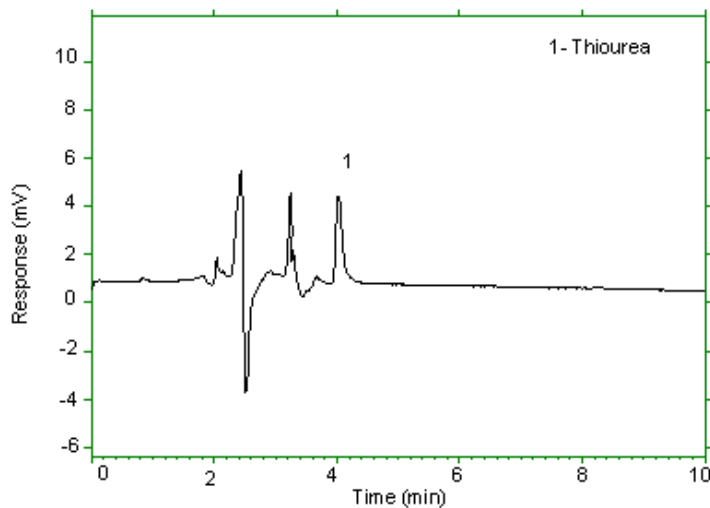


Figure 1.2.2. Chromatogram of the detection limit of the overall procedure.

2 Sampling Procedure

2.1 Apparatus

- 2.1.1 Samples are collected using a personal sampling pump that can be calibrated within $\pm 5\%$ of the recommended flow rate with the sampling device attached.
- 2.1.2 Samples are collected with a two-piece polystyrene cassette containing one glass fiber filter. These cassettes are commercially available from Millipore Corporation.

2.2 Reagents

No sampling reagents are required.

2.3 Sampling technique

2.3.1 Prepare the sampler by removing the top and bottom end plugs from the sampler. Attach the sampler to the sampling pump with a piece of flexible tubing and place it in the worker's breathing zone.

2.3.2 After sampling for the appropriate time, remove the tube and reseal the cassette with the plastic plugs. Wrap each sample end-to-end with a Form OSHA-21 seal.

2.3.3 Record the air volume for each sample and list any possible interference.

2.3.4 Submit at least one blank for each set of samples. The blank is handled in the same manner as the samples except no air is drawn through it.

2.3.5 Submit bulk samples for analysis in a separate container from the air samples.

2.4 Extraction efficiency

Three groups of four GFFs were each liquid spiked with 5 μL , 10 μL , and 20 μL of a 2.94 $\mu\text{g}/\mu\text{L}$ solution of thiourea. These amounts represent 0.5, 1.0, and 2.0 times the target concentration respectively. They were transferred to 4-mL vials, sealed with PTFE-lined caps, and allowed to equilibrate overnight in a drawer at room temperature. The next day the samples were analyzed as per Section 3. The results are listed in Tables 2.4.1, 2.4.2, and 2.4.3. The average extraction efficiencies at 0.5, 1.0, and 2.0 times the target concentration are 0.918, 0.919, and 0.952 respectively.

Table 2.4.1
Extraction Efficiency of Thiourea
at 0.5 \times Target Concentration

sample i.d.	μg spiked	μg recovered	recovery (decimal)
D1	14.70	13.23	0.900
D2	14.70	13.48	0.917
D3	14.70	13.55	0.922
D4	14.70	13.69	0.931

Table 2.4.2
Extraction Efficiency of Thiourea
at 1 \times Target Concentration

sample i.d.	μg spiked	μg recovered	recovery (decimal)
D5	29.40	26.77	0.910
D6	29.40	26.96	0.917
D7	29.40	27.03	0.919
D8	29.40	27.29	0.928

Table 2.4.3
Extraction Efficiency of Thiourea
at 2× Target Concentration

sample i.d.	µg spiked	µg recovered	recovery (decimal)
D9	58.80	56.11	0.954
D10	58.80	55.75	0.948
D11	58.80	56.41	0.959
D12	58.80	55.71	0.947

2.5 Retention efficiency

To test the ability of the sampler to retain the analyte, five samplers were each liquid spiked with 10 µL of a 2.94 µg/µL solution of thiourea. All cassettes were sealed with end-plug and allowed to equilibrate overnight in a drawer at room temperature. The next day 480 L of humid air (80% relative humidity) was drawn through each of the samples at 2.0 L/min. The samples were analyzed as per Section 3. The results are listed in Table 2.5. The average retention efficiency from the five samplers was 0.937.

Table 2.5
Retention Efficiency of Thiourea
at 1× Target Concentration

sample i.d.	µg spiked	µg recovered	recovery (decimal)
RE-1	29.40	28.03	0.953
RE-2	29.40	26.91	0.915
RE-3	29.40	27.58	0.938
RE-4	29.40	27.69	0.942
RE-5	29.40	27.55	0.937

2.6 Sample storage

The storage samples were generated by liquid spiking each of ten GFF with 10 µL of a 2.94 µg/µL solution of thiourea. All cassettes were sealed with end-plugs and allowed to equilibrate overnight in a drawer at room temperature. The next day 480 L of humid air (80% relative humidity) was drawn through each of the sample cassettes at 2.0 L/min. The ten samples were divided into two groups of five cassettes each. The first group was stored in a refrigerator (0 °C); the second group was stored in a drawer at ambient temperature. After eight days, they were extracted and analyzed as in Section 3. The results are listed in Table 2.6.1 and 2.6.2. The average recovery for the refrigerator and ambient temperature storage study were 0.931 and 0.826, respectively.

Table 2.6.1.
Refrigerator Storage

days of storage	µg spiked	µg recovered	recovery (decimal)
8	29.40	28.34	0.964
8	29.40	27.25	0.927
8	29.40	27.06	0.921
8	29.40	27.12	0.922
8	29.40	27.12	0.922

Table 2.6.2.
Ambient Storage

days of storage	µg spiked	µg recovered	recovery (decimal)
8	29.40	22.65	0.770
8	29.40	25.43	0.865
8	29.40	24.42	0.831
8	29.40	24.29	0.826
8	29.40	24.58	0.836

2.7 Recommended air volume and sampling rate

2.7.1 The recommended air volume is 480 L.

2.7.2 The recommended flow rate is 2.0 L/min.

2.8 Interferences (sampling)

It is not known if any compounds will interfere with the collection of thiourea. Any suspected interferences 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 hundredth of a milligram. A Mettler AE240 balance was used in this evaluation to prepare the concentrated standards.

3.1.2 Volumetric flasks, pipettes, and syringes of various, convenient sizes for preparing standards, making dilutions, and making injections.

3.1.3 Glass vials, 4-mL with PTFE-lined caps.

3.1.4 An HPLC equipped with a variable UV detector, and a WISP auto-sampler were used in this evaluation.

3.1.5 An HPLC column capable of separating thiourea from any interference. A 4.6-mm × 250-mm ZORBAX CN column was used in this evaluation.

3.1.6 An electronic integrator or some other suitable means for measuring detector response. The Waters 860 Data System was used in this evaluation.

3.2 Reagents

3.2.1 Methanol, HPLC grade. The solvent used in this evaluation was Optima® grade, obtained from Fisher Scientific, Inc.

3.2.2 Isooctane, HPLC grade. The solvent used in this evaluation was Optima® grade, obtained from Fisher Scientific, Inc.

3.2.3 Isopropanol, HPLC grade. The solvent used in this evaluation was Optima® grade, obtained from Fisher Scientific, Inc.

3.2.4 Thiourea. Thiourea was obtained from Mallinckrodt, INC. with a purity of 100%.

3.3 Standard preparation

3.3.1 Prepare stock standards by weighing 10-20 mg of thiourea in 10-mL volumetric flasks and diluting to volume with methanol.

3.3.2 Prepare analytical standards by diluting the stock standards with methanol. A 9.6 µg/mL standard solution corresponds to the target concentration.

3.3.3 Prepare a sufficient number of analytical standards to generate a calibration curve. Analytical standard concentrations must bracket sample concentrations.

3.4 Sample preparation

3.4.1 Transfer the GFF to a 4-mL vial.

3.4.2 Add 3.0 mL of methanol to each vial.

3.4.3 Cap the vials and shake them on a mechanical shaker for 30 min.

3.5 Analysis

3.5.1 Instrument conditions

column:	4.6-mm × 250-mm ZORBAX CN
eluent:	isooctane/isopropanol/methanol, 45:10:45 (v/v/v)
flow rate:	1.0 mL/min
injection volume:	10 µL
retention time:	4.0 min
UV detector:	234-nm
Chromatogram:	

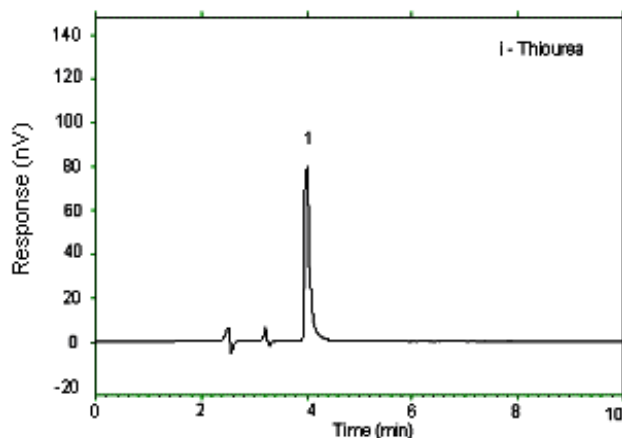


Figure 3.5.1. Chromatogram at the target concentration.

3.6 Interferences (analytical)

3.6.1 Any compound that absorbs at 234-nm and has a similar retention time as the analyte is a potential interference. Generally, chromatographic conditions can be altered to separate interference from the analyte.

3.6.2 Retention time on a single column is not considered proof of chemical identity. Additional means of identification include using an alternate HPLC column, detection at another wavelength (peak ratioing). Other possible means of identification might include gas chromatography/flame ionization detector or gas chromatography/mass spectrometry.

3.7 Calculations

3.7.1 Construct a calibration curve by plotting detector response versus concentration ($\mu\text{g/mL}$) of thiourea.

3.7.2 Determine the $\mu\text{g/mL}$ of thiourea in samples and blank from the calibration curve.

3.7.3 Blank correct each sample by subtracting the $\mu\text{g/mL}$ found in the blank from the $\mu\text{g/mL}$ found in samples.

3.7.4 Determine the air concentration by using the following formulae.

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

$$\text{ppm} = \frac{(\text{mg} / \text{m}^3)(24.46)}{(76.12)}$$

Where:

24.46 = molar volume (Liters/mole) at 101.3 kPa (760 mmHg) and 25 °C

76.12 = molecular weight (g/mole) of thiourea

3.8 Safety precautions (analytical)

3.8.1 Avoid skin contact and air exposure to thiourea.

3.8.2 Avoid skin contact and air exposure with all solvents.

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

4 Recommendation for Further Study

This method needs to be fully validated.

5 References

5.1 Chan, Y.; Method #95, "ETHYLENE THIOUREA"; OSHA Analytical Laboratory, unpublished, 1992

5.2 Budavari, S., O'Neill M.J., Smith, A., and Heckelman, P.E., The Merck Index, 11th ed., Merck & Co., Inc., Rahway, N.J., 1989; p 1476.

5.3 Bern, H.A., Boyland, E., and Brown, T.B. etc., IRAC Monographs: Evaluation of Carcinogenic Risk, 1974; Vol. 7, pp. 95-105.