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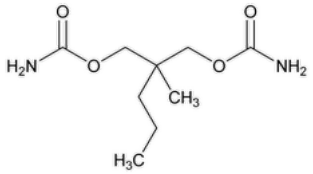
Meprobamate



$C_9H_{18}N_2O_4$ 218.25

1,3-Propanediol, 2-methyl-2-propyl-, dicarbamate;

2-Methyl-2-propyl-1,3-propanediol dicarbamate CAS RN®: 57-53-4; UNII: 9I7LNY769Q.

DEFINITION

Meprobamate contains NLT 97.0% and NMT 101.0% of meprobamate ($C_9H_{18}N_2O_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Sample: 1 mg in 200 mg

Acceptance criteria: The IR absorption spectrum of a potassium bromide dispersion of the *Sample*, previously dried, exhibits maxima only at the same wavelengths as that of a similar preparation of USP Meprobamate RS. If a difference appears, dissolve portions of both the *Sample* and the Reference Standard in acetone at a concentration of 8 mg/mL. Dilute 0.1-mL portions of the acetone solutions with 1 mL of *n*-heptane, and remove the solvents by evaporation under nitrogen at a temperature of 30°. Dry the residues under vacuum at room temperature for 30 min, and repeat the test on the residues.

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Mobile phase: Acetonitrile and water (30:70)

Standard solution: 5 mg/mL of USP Meprobamate RS prepared as follows. Dissolve the Standard first in acetonitrile using 30% of final volume. Sonicate if necessary to dissolve, and cool to room temperature. Dilute with water to volume.

Sample solution: 5 mg/mL of Meprobamate prepared as follows. Dissolve the sample first in acetonitrile using 30% of final volume. Sonicate if necessary to dissolve, and cool to room temperature. Dilute with water to volume.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 200 nm

Column: 4.6-mm × 25-cm; 4-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: 2 times the retention time of meprobamate

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of meprobamate ($C_9H_{18}N_2O_4$) in the portion of Meprobamate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Meprobamate RS in the *Standard solution* (mg/mL)

C_U = concentration of Meprobamate in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–101.0% on the dried basis

IMPURITIES

• **Organic Impurities: Procedure 1**

Standard solutions: Dissolve USP Meprobamate RS in alcohol, and mix to obtain *Standard solution A* with a known concentration of 1.0 mg/mL. Dilute quantitatively with alcohol to the obtain the *Standard solutions* with the compositions given in *Table 1*.

Table 1

Standard Solution	Dilution	Concentration (mg RS/mL)	Percentage (%, for Comparison with Sample)
A	(Undiluted)	1.0	1.0
B	(4 in 5)	0.8	0.8
C	(3 in 5)	0.6	0.6
D	(2 in 5)	0.4	0.4
E	(1 in 5)	0.2	0.2

Sample solution: 100 mg/mL of Meprobamate in alcohol

Chromatographic system

(See *Chromatography ⟨621⟩, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: Thin-layer chromatographic plate coated with a 0.25-mm layer of chromatographic silica gel

Application volume: 2 µL

Developing solvent system: Hexane, acetone, and pyridine (70:30:10)

Spray reagent: 5 mg/mL of vanillin in a cooled mixture of sulfuric acid and alcohol (80:20)

Analysis

Samples: *Standard solutions* and *Sample solution*

Position the plate in a chromatographic chamber, and develop the chromatograms in the *Developing solvent system* until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and air-dry the plate for 15 min. Heat the plate at 100° for 15 min, cool, and spray with *Spray reagent*. Heat the plate at 110° for 15–20 min, cool, and allow the plate to develop blue-purple spots at room temperature. [Note—Color development requires about 30–60 min.] Examine the plate, and compare the intensities of any secondary spots of the *Sample solution* with those of the principal spots of the *Standard solutions*.

Acceptance criteria: No secondary spot of the *Sample solution* is larger or more intense than the principal spot of *Standard solution A* (1.0%), and the sum of the intensities of all secondary spots of the *Sample solution* corresponds to NMT 2.0%.

• **Organic Impurities, Procedure 2: Limit of Methyl Carbamate**

Standard solution: 1.0 mg/mL of methyl carbamate

Sample solution: Transfer 1.0 g of finely powdered Meprobamate to a beaker, add 5.0 mL of water, and stir to wet the powder completely. Filter the slurry through a small plug of glass wool in the stem of a glass funnel. Use the clear filtrate.

Mobile phase: Water

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 200 nm

Column: 3.9–4.6-mm × 25–30-cm; packing L1

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The peak response of the *Sample solution* is not greater than that of the *Standard solution*, corresponding to NMT 0.5% of methyl carbamate.

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩**

  Analysis: Dry a sample under vacuum at 60° for 3 h.

  Acceptance criteria: NMT 0.5%

- **Melting Range or Temperature ⟨741⟩:** 103°–107°, but the range between the beginning and end of melting is NMT 2°.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards ⟨11⟩**

  USP Meprobamate RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MEPROBAMATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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