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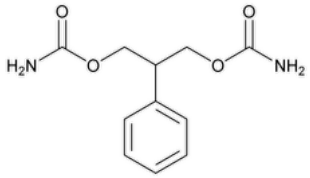
Felbamate



$C_{11}H_{14}N_2O_4$ 238.24

1,3-Propanediol, 2-phenyl-, dicarbamate;

2-Phenyl-1,3-propanediol dicarbamate CAS RN®: 25451-15-4; UNII: X72RBB02N8.

DEFINITION

Felbamate contains NLT 98.0% and NMT 102.0% of felbamate ($C_{11}H_{14}N_2O_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

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

• **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, methanol, and water (126:84:790)

Diluent: Acetonitrile, methanol, and water (222:148:630)

System suitability solution: 0.05 mg/mL of USP Felbamate Related Compound A RS and 0.2 mg/mL of USP Felbamate RS in *Mobile phase*

Standard stock solution: 1.0 mg/mL of USP Felbamate RS prepared as follows. Dissolve a suitable quantity of USP Felbamate RS in 10% of the volumetric flask volume of methanol. Sonicate and shake to completely dissolve, and dilute with *Diluent*.

Standard solution: 0.2 mg/mL of USP Felbamate RS from *Standard stock solution* in *Mobile phase*

Sample stock solution: 1.0 mg/mL of Felbamate prepared as follows. Dissolve a suitable quantity of Felbamate in 10% of the volumetric flask volume of methanol. Sonicate and shake to completely dissolve, and dilute with *Diluent*.

Sample solution: 0.2 mg/mL of Felbamate from *Sample stock solution* in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.8 mL/min

Injection volume: 20 µL

Run time: 3 times the retention time of felbamate

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between felbamate related compound A and felbamate, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of felbamate ($C_{11}H_{14}N_2O_4$) in the portion of Felbamate taken:

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

r_U = peak response of felbamate from the *Sample solution*

r_S = peak response of felbamate from the *Standard solution*

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Limit of Methylcarbamate**

Mobile phase: Water

Standard solution: 0.1 mg/mL of methylcarbamate in water

Sample solution: Suspend 1 g of Felbamate in 5 mL of water, and mix on a vortex mixer for 1 min followed by sonication for 5 min. Filter the slurry, and use as the *Sample solution*.

Chromatographic system

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

Mode: LC

Detector: UV 200 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 10%

Analysis

Samples: *Standard solution* and *Sample solution*

Acceptance criteria: The peak response for methylcarbamate in the *Sample solution* does not exceed the peak response for methylcarbamate in the *Standard solution* (0.05%).

- **Early Eluting Organic Impurities**

Mobile phase, Diluent, Standard stock solution, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution: 1 µg/mL of USP Felbamate RS in *Mobile phase* from *Standard stock solution*

Sample solution: 1.0 mg/mL of Felbamate prepared as follows. Dissolve a suitable quantity of Felbamate in 10% of the volumetric flask volume of methanol. Sonicate and shake to completely dissolve, and dilute with *Diluent*.

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between felbamate related compound A and felbamate, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 10%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Identify the impurities using the relative retention times shown in *Table 1*.

Calculate the percentage of each impurity in the portion of Felbamate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of felbamate from the *Standard solution*

C_S = concentration of USP Felbamate RS in the *Standard solution* (µg/mL)

C_U = concentration of Felbamate in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Phenylpropanediol[a]	0.43	1.7	0.15
Felbamate related compound A	0.65	1.3	0.15
Felbamate	1.0	—	—
N-Aminocarbonyl felbamate[b]	1.43	0.89	0.15
Felbamate related compound B[c]	2.23	—	—
Individual unspecified impurity[d]	—	1.0	0.1

[a] 2-Phenylpropane-1,3-diol.

[b] 3-Carbamoyloxy-2-phenylpropyl allophanate.

[c] This impurity is quantified using the test for *Late Eluting Organic Impurities*.

[d] Quantify individual unspecified impurities eluting before felbamate related compound B.

• **Late Eluting Organic Impurities**

Mobile phase: Acetonitrile, methanol, and water (222:148:630)

System suitability solution: 1 µg/mL each of USP Felbamate RS and USP Felbamate Related Compound B RS in *Mobile phase*

Standard solution: 1 µg/mL of USP Felbamate RS in *Mobile phase*

Sample solution: 1.0 mg/mL of Felbamate prepared as follows. Dissolve a suitable quantity of Felbamate in 10% of the volumetric flask volume of methanol. Sonicate and shake to completely dissolve, and dilute with *Mobile phase*.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.8 mL/min

Injection volume: 20 µL

Run time: 10 times the retention time of felbamate

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 3 between felbamate and felbamate related compound B, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 10%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Identify the impurities using the relative retention times shown in *Table 2*.

Calculate the percentage of each impurity in the portion of Felbamate taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of felbamate from the *Standard solution*

C_S = concentration of USP Felbamate RS in the *Standard solution* (µg/mL)

C_U = concentration of Felbamate in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Felbamate	1.0	—	—
Felbamate related compound B	1.9	1.29	0.15
Felbamate dimer[a]	9.1	1.0	0.15
Individual unspecified impurity[b]	—	1.0	0.1
Total impurities[c]	—	—	0.75

[a] 3,3'-Carbonylbis(oxy)bis(2-phenylpropane-3,1-diyl) dicarbamate.

[b] Quantify individual unspecified impurities eluting after felbamate related compound B.

[c] Sum of all impurities from *Table 1* and *Table 2*.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers, and store at room temperature.

• **USP Reference Standards** ⟨11⟩

USP Felbamate RS

USP Felbamate Related Compound A RS

3-Hydroxy-2-phenylpropyl carbamate.

$C_{10}H_{13}NO_3$ 195.22

USP Felbamate Related Compound B RS

Phenethyl carbamate.

$C_9H_{11}NO_2$ 165.19

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

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

Chromatographic Database Information: Chromatographic Database

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