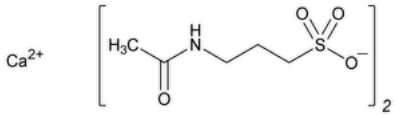
Status: Currently Official on 13-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-5C47B2B1-667F-4E17-A178-A490D9E231FF_6_en-US
DOI: https://doi.org/10.31003/USPNF_M1153_06_01
DOI Ref: 6z0f2

Acamprosate Calcium



$C_{10}H_{20}CaN_2O_8S_2$ 400.48

1-Propanesulfonic acid, 3-(acetylamino)-, calcium salt (2:1);

Calcium 3-(acetylamino)propane-1-sulfonate CAS RN®: 77337-73-6.

DEFINITION

Acamprosate Calcium contains NLT 98.0% and NMT 102.0% of acamprosate calcium ($C_{10}H_{20}CaN_2O_8S_2$), 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*.

• **C.** **Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Calcium*:** Meets the requirements

ASSAY

• **Procedure**

Mobile phase: Add 5.0 mL of triethylamine per 1 L of water and adjust with phosphoric acid to a pH of 4.0.

System suitability solution: 10 mg/mL of USP Acamprosate Calcium RS and 0.005 mg/mL each of USP Acamprosate Related Compound B RS and glacial acetic acid in water. Sonication may be used to aid in dissolution.

Standard solution: 0.3 mg/mL of USP Acamprosate Calcium RS in water. Sonication may be used to aid in dissolution.

Sample solution: 0.3 mg/mL of Acamprosate Calcium in water. Sonication may be used to aid in dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Flow rate: 0.7 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of the acamprosate peak

System suitability

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

[Note—See *Table 1* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between acetic acid and acamprosate related compound B; NLT 1.3 between acamprosate related compound B and acamprosate, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acamprosate calcium ($C_{10}H_{20}CaN_2O_8S_2$) in the portion of Acamprosate Calcium 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 Acamprosate Calcium RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

Change to read:

• **Limit of Acamprosate Related Compound A**

Solution A: 5 g/L of fluorescamine in acetonitrile. Use within 24 h of preparation.

Buffer: 13.8 g/L of monobasic sodium phosphate prepared as follows. Transfer a suitable amount of monobasic sodium phosphate to a volumetric flask. Dissolve in 90% of the final flask volume of water. Adjust with 10 N sodium hydroxide TS or phosphoric acid to a pH of 6.5. Dilute with water to volume.

Mobile phase: Acetonitrile, methanol, and *Buffer* (10:10:80)

Diluent: 24.6 g/L of boric acid prepared as follows. Transfer a suitable amount of boric acid to an appropriate volumetric flask. Dissolve in 90% of the final flask volume of water. Adjust with 10 N sodium hydroxide TS to a pH of 10.4. Dilute with water to volume.

Standard stock solution A: 250 µg/mL of USP Acamprosate Related Compound A RS in water

Standard stock solution B: 1 µg/mL of USP Acamprosate Related Compound A RS from *Standard stock solution A* in *Diluent*

Standard solution: Transfer 3.0 mL of *Standard stock solution B* to an appropriate container. Add 0.15 mL of *Solution A* and shake vigorously for 30 s. Heat in a water bath at 50° for 30 min. Cool under a stream of cold water, centrifuge, and pass the supernatant through a suitable membrane filter.

Sample stock solution A: 20 mg/mL of Acamprosate Calcium in water

Sample stock solution B: 2000 µg/mL of Acamprosate Calcium from *Sample stock solution A* in *Diluent*

Sample solution: Transfer 3.0 mL of *Sample stock solution B* to an appropriate container. Add 0.15 mL of *Solution A* and shake for 30 s. Heat in a water bath at 50° for 30 min. Cool under a stream of cold water, centrifuge, and pass the supernatant through a suitable membrane filter.

Chromatographic system

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

Mode: LC

Detector: UV 261 nm

Column: 4.6-mm × 15-cm; 3- or 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Run time: NLT 2 times the retention time of acamprosate related compound A

System suitability

Sample: *Standard solution*

[Note—The relative retention times for fluorescamine and acamprosate related compound A are about 0.5 and 1.0, respectively. Acamprosate calcium is not detected by this chromatographic system.]

Suitability requirements

Resolution: NLT 2.0 between fluorescamine and acamprosate related compound A

Relative standard deviation: NMT 5.0% for acamprosate related compound A

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acamprosate related compound A in the portion of Acamprosate Calcium 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 Acamprosate Related Compound A RS▲ (ERR 1-Dec-2018) in the *Standard solution* (µg/mL)

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

Acceptance criteria: NMT 0.05%

• **Organic Impurities**

Mobile phase: Add 5.0 mL of triethylamine per 1 L of water and adjust with phosphoric acid to a pH of 4.0.

System suitability solution: 10 mg/mL of USP Acamprosate Calcium RS and 0.005 mg/mL each of USP Acamprosate Related Compound B RS and glacial acetic acid in water. Sonication may be used to aid in dissolution.

Standard solution: 0.005 mg/mL of USP Acamprosate Calcium RS in water. Sonication may be used to aid in dissolution.

Sample solution: 10 mg/mL of Acamprosate Calcium in water. Sonication may be used to aid in dissolution.

Chromatographic system

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

Mode: LC

Detector: UV 210 nm

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

Flow rate: 0.7 mL/min

Injection volume: 20 µL

Run time: NLT 6 times the retention time of the acamprosate peak

System suitability

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

[NOTE—The relative retention time for acetic acid is 0.7; see *Table 1* for the other relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between acetic acid and acamprosate related compound B; NLT 1.3 between acamprosate related compound B and acamprosate, *System suitability solution*

Tailing factor: NMT 1.5 for acamprosate, *Standard solution*

Relative standard deviation: NMT 15.0% for acetic acid, *System suitability solution*; NMT 5% for acamprosate, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Acamprosate Calcium taken:

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

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

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

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

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

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Calcium[a]	0.4	—
Acamprosate related compound B	0.8	0.05
Acamprosate	1.0	—
N-Methyl acamprosate[b]	1.9	0.05
Any individual unspecified impurity	—	0.05
Total impurities[c]	—	0.5

[a] Included for identification only. This peak is due to the calcium counterion and hence is not an impurity.

[b] 3-(*N*-Methylacetamido)propane-1-sulfonate.

[c] The sum of acamprosate related compound A from the *Limit of Acamprosate Related Compound A* test and all impurities from the test for *Organic Impurities*.

SPECIFIC TESTS

• **pH** ⟨791⟩

Sample solution: 0.05 g/mL of Acamprosate Calcium in carbon dioxide-free water

Acceptance criteria: 5.5–7.0

• **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 3 h.

Acceptance criteria: NMT 0.4%

ADDITIONAL REQUIREMENTS

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

USP Acamprosate Calcium RS

USP Acamprosate Related Compound A RS

3-Aminopropane-1-sulfonic acid.

$C_3H_9NO_3S$ 139.17

USP Acamprosate Related Compound B RS

Calcium 3-formamidopropane-1-sulfonate.

$C_8H_{16}CaN_2O_8S_2$ 372.42

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

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

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(2)

Current DocID: GUID-5C47B2B1-667F-4E17-A178-A490D9E231FF_6_en-US

DOI: https://doi.org/10.31003/USPNF_M1153_06_01

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