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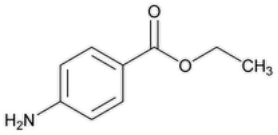
Benzocaine



$C_9H_{11}NO_2$ 165.19

Benzoic acid, 4-amino-, ethyl ester;

Ethyl *p*-aminobenzoate CAS RN®: 94-09-7; UNII: U3RSY48JW5.

DEFINITION

Benzocaine, dried over phosphorus pentoxide for 3 h, contains NLT 98.0% and NMT 102.0% of benzocaine ($C_9H_{11}NO_2$).

IDENTIFICATION

Change to read:

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

Sample: Previously dried over phosphorus pentoxide for 3 h

Acceptance criteria: Meets the requirements

• **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**

Solution A: Acetic acid, triethylamine, and water (20:1:980). The pH should be between 2.95 and 3.0 (adjust as needed).

Mobile phase: Methanol and *Solution A* (40:60)

Standard solution: 0.024 mg/mL of USP Benzocaine RS in *Mobile phase*

Sample solution: 0.024 mg/mL of Benzocaine in *Mobile phase*

Chromatographic system

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

Mode: LC

Detector: UV 285 nm

Column: 2.0-mm × 15-cm; 5-µm packing L11

Flow rate: 0.2 mL/min

Injection volume: 10 µL

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 benzocaine ($C_9H_{11}NO_2$) in the portion of Benzocaine 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 Benzocaine RS in the *Standard solution* (mg/mL)

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

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

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Chloride**

Analysis: To a solution of 200 mg in 5 mL of alcohol, previously acidified with a few drops of diluted nitric acid, add a few drops of silver nitrate TS.

Acceptance criteria: No turbidity is produced immediately.

- **Organic Impurities**

Solution A: Add 1.0 mL of trifluoroacetic acid in 1 L of water.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
34	50	50
35	90	10
38	90	10

Diluent: *Solution A* and *Solution B* (1:1)

Standard stock solution: 0.1 mg/mL each of USP Benzocaine RS, USP Aminobenzoic Acid RS, and USP Ethyl 4-nitrobenzoate RS in *Diluent*. Sonicate for 2–5 min to dissolve before diluting to final volume.

Standard solution: 1 µg/mL each of USP Benzocaine RS, USP Aminobenzoic Acid RS, and USP Ethyl 4-nitrobenzoate RS in *Diluent* from the *Standard stock solution*

Sample solution: 1 mg/mL of Benzocaine in *Diluent*. Sonicate for 2–5 min to assist in dissolution as needed before diluting to final volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 10 from any two peaks

Relative standard deviation: NMT 2.0% for each peak corresponding to benzocaine, aminobenzoic acid, and ethyl 4-nitrobenzoate

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of aminobenzoic acid and ethyl 4-nitrobenzoate in the portion of Benzocaine taken:

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

r_U = peak response of aminobenzoic acid or ethyl 4-nitrobenzoate from the *Sample solution*

r_S = peak response of corresponding reference standard from the *Standard solution*

C_S = concentration of USP Aminobenzoic Acid RS or USP Ethyl 4-nitrobenzoate RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any other individual unspecified impurity in the portion of Benzocaine taken:

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

r_U = peak response of any other individual impurity from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*. Disregard peaks less than 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Aminobenzoic acid	0.29	0.10
Benzocaine	1.0	—
Ethyl 4-nitrobenzoate	2.1	0.10
Any other unspecified impurity	—	0.10
Total impurities	—	1.0

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry over phosphorus pentoxide for 3 h.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers.

• **USP Reference Standards** ⟨11⟩

USP Aminobenzoic Acid RS

Benzoic acid, 4-amino.

$C_7H_7NO_2$ 137.14

USP Benzocaine RS

USP Ethyl 4-nitrobenzoate RS

Benzoic acid, 4-nitro-, ethyl ester.

$C_9H_9NO_4$ 195.17

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

Topic/Question	Contact	Expert Committee
BENZOCAINE	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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