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Benzocaine Ointment

DEFINITION
Benzocaine Ointment contains NLT 90.0% and NMT 110.0% of the labeled amount of benzocaine ($C_9H_{11}NO_2$) in a suitable ointment base.

IDENTIFICATION
- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **Procedure**

Solution A: 0.1% Trifluoroacetic acid, prepared by adding 1.0 mL of trifluoroacetic acid to 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 solution: 0.1 mg/mL of USP Benzocaine RS in *Diluent*. Sonication may be needed to aid in the dissolution.

Sample solution: Nominally 0.1 mg/mL of benzocaine in *Diluent* prepared as follows

Ointments having water-soluble bases: Transfer a portion of Ointment, equivalent to 10 mg of benzocaine, into a volumetric flask, and dissolve in *Diluent*.

Ointments having water-insoluble bases: Transfer a portion of Ointment, equivalent to 10 mg of benzocaine, into a volumetric flask, and dissolve in tetrahydrofuran, using about 2% of the final volume, then dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of the filtrate.

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

Mode: LC

Detector: UV 280 nm. For *Identification* test *B*, use a diode array detector in the range of 200–400 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

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benzocaine ($C_9H_{11}NO_2$) in the portion of Ointment taken:

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

r_U = peak response of benzocaine 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 = nominal concentration of benzocaine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

Solution A: 0.1% Trifluoroacetic acid, prepared by adding 1.0 mL of trifluoroacetic acid to 1 L of water

Solution B: Acetonitrile

Mobile phase: See *Table 1* in the *Assay*.

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

System suitability solution: 0.2 mg/mL of USP Benzocaine RS and 0.01 mg/mL each of USP Aminobenzoic Acid RS and USP Ethyl 4-Nitrobenzoate RS in *Diluent*

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

Sample solution: Nominally 1 mg/mL of benzocaine in *Diluent* prepared as follows

Ointments having water-soluble bases: Transfer a portion of Ointment, equivalent to 50 mg of benzocaine, into a volumetric flask, and dissolve in *Diluent*.

Ointments having water-insoluble bases: Transfer a portion of Ointment, equivalent to 50 mg of benzocaine, into a volumetric flask, and dissolve in about 10% of final volume of tetrahydrofuran, then dilute with *Diluent* to volume. Pass through a suitable filter of 0.45-µm pore size, discarding the first 2–3 mL of the filtrate.

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

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

Suitability requirements

Resolution: NLT 10 between aminobenzoic acid and benzocaine, and between benzocaine and ethyl 4-nitrobenzoate, *System suitability solution*

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

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of aminobenzoic acid and ethyl 4-nitrobenzoate in the portion of Ointment 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 the 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 = nominal concentration of benzocaine in the *Sample solution* (mg/mL)

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

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

r_U = peak response for any other individual unspecified 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 = nominal 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 individual unspecified impurity	—	0.10
Total impurities	—	1.0

PERFORMANCE TESTS

• **Minimum Fill ⟨755⟩:** Meets the requirements

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, protected from light, and store at room temperature at 15°–25°.

• **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 OINTMENT	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

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