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Benzocaine, Butamben, and Tetracaine Hydrochloride Gel

DEFINITION

Benzocaine, Butamben, and Tetracaine Hydrochloride Gel is Benzocaine, Butamben, and Tetracaine Hydrochloride in a suitable gel base. It contains NLT 90.0% and NMT 110.0% of the labeled amount of benzocaine ($C_9H_{11}NO_2$), butamben ($C_{11}H_{15}NO_2$), and tetracaine hydrochloride ($C_{15}H_{24}N_2O_2 \cdot HCl$).

IDENTIFICATION

- **A.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.
- **B.** The UV spectrum of the major peaks of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Solution A: 0.1% formic acid in water

Solution B: 0.1% formic acid in acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	91	9
2.5	50	50
3.9	50	50
4	91	9
5	91	9

Diluent: Acetonitrile and water (20:80)

Standard solution: 175 µg/mL of USP Benzocaine RS and 25 µg/mL each of USP Butamben RS and USP Tetracaine Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Benzocaine RS, USP Butamben RS, and USP Tetracaine Hydrochloride RS to a suitable volumetric flask and dissolve in 20% of the total volume of acetonitrile. Dilute with water to volume.

Sample solution: Nominally 175 µg/mL of benzocaine and 25 µg/mL each of butamben and tetracaine hydrochloride, prepared as follows. Transfer a suitable quantity of Gel into a suitable volumetric flask and dissolve in 20% of the total volume of acetonitrile. [Note—Sonication for about 1 min may be necessary.] Dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: UV 300 nm. For *Identification B*, use a diode array detector in the range of 200–400 nm.

Column: 2.1-mm × 5-cm; 1.7-µm packing L1

Flow rate: 0.6 mL/min

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 2 between benzocaine and tetracaine

Relative standard deviation: NMT 2.0% for each of the three analyte peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benzocaine ($C_9H_{11}NO_2$), butamben ($C_{11}H_{15}NO_2$), and tetracaine hydrochloride ($C_{15}H_{24}N_2O_2 \cdot HCl$) in the portion of Gel taken:

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

r_U = peak response of the corresponding analyte from the *Sample solution*

r_S = peak response of the corresponding analyte from the *Standard solution*

C_S = concentration of the corresponding Reference Standard in the *Standard solution* (µg/mL)

C_U = nominal concentration of the corresponding analyte in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

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

IMPURITIES

• **Organic Impurities**

Mobile phase, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 10 µg/mL each of USP Benzocaine RS, USP Tetracaine Hydrochloride RS, USP Butamben RS, and USP Ethyl 4-Nitrobenzoate RS prepared as follows. Transfer a suitable amount of USP Benzocaine RS, USP Tetracaine Hydrochloride RS, USP Butamben RS, and USP Ethyl 4-Nitrobenzoate RS to a suitable volumetric flask and dissolve in 20% of the total volume of acetonitrile. Dilute with water to volume.

Standard solution: 3.4 µg/mL each of USP Benzocaine RS and USP Ethyl 4-Nitrobenzoate RS and 1 µg/mL of USP Tetracaine Hydrochloride RS prepared as follows. Transfer a suitable amount of USP Benzocaine RS, USP Tetracaine Hydrochloride RS, and USP Ethyl 4-Nitrobenzoate RS to a suitable volumetric flask and dissolve in 20% of the total volume of acetonitrile. Dilute with water to volume.

Sample solution: Nominally 1.68 mg/mL of benzocaine, 0.24 mg/mL of butamben, and 0.24 mg/mL of tetracaine prepared as follows. Transfer a suitable quantity of Gel into a suitable volumetric flask and dissolve in 20% of the total volume of acetonitrile. Dilute with water to volume. [Note—Sonication for about 1 min may be necessary.]

System suitability

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

[Note—See *Table 2* for relative retention times.]

Suitability requirements

Resolution: NLT 2 between butamben and ethyl 4-nitrobenzoate; NLT 2 between benzocaine and tetracaine, *System suitability solution*

Relative standard deviation: NMT 5.0% for each of the analyte peaks, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of 4-aminobenzoic acid in the portion of Gel taken:

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

r_U = peak response of 4-aminobenzoic acid 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* (µg/mL)

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

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

Calculate the percentage of ethyl 4-nitrobenzoate in the portion of Gel taken:

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

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

r_S = peak response of ethyl 4-nitrobenzoate from the *Standard solution*

C_S = concentration of USP Ethyl 4-Nitrobenzoate RS in the *Standard solution* (µg/mL)

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

Calculate the percentage of tetracaine related compound B and any individual unspecified degradation product in the portion of Gel taken:

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

r_U = peak response of tetracaine related compound B or any individual unspecified degradation product from the *Sample solution*

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

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

C_U = nominal concentration of tetracaine hydrochloride in the *Sample solution* (µg/mL)

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

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

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
4-Aminobenzoic acid	0.23	1.3	0.3
Benzocaine	1.0	—	—
Tetracaine	1.07	—	—
Tetracaine related compound B[a]	1.34	0.6	0.4
Butamben	1.45	—	—
Ethyl 4-nitrobenzoate	1.50	—	0.2
Any individual unspecified degradation product	—	1.0	0.4
Total degradation products	—	—	2.0

[a] 4-(Butylamino)benzoic acid.

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count is NMT 10^2 cfu/g. The total combined molds and yeasts count is NMT 10^1 cfu/g. It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers in a cool dry place and avoid freezing.

• **USP Reference Standards ⟨11⟩**

USP Benzocaine RS

USP Butamben RS

USP Ethyl 4-Nitrobenzoate RS

Ethyl *p*-nitrobenzoate.

$C_9H_9NO_4$ 195.17

USP Tetracaine Hydrochloride RS

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

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

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