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Benzethonium Chloride Topical Solution

DEFINITION
Benzethonium Chloride Topical Solution contains NLT 95.0% and NMT 105.0% of the labeled amount of benzethonium chloride ($C_{27}H_{42}ClNO_2$).

IDENTIFICATION

Change to read:

• **A.** ▲The UV absorption spectra of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

ASSAY

Change to read:

• **Procedure**

▲**Buffer:** 20 mL/L of triethylamine in water. Adjust with phosphoric acid to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (42:58)

Diluent: Acetonitrile and water (40:60)

Standard solution: 0.2 mg/mL of USP Benzethonium Chloride RS in *Diluent*. Sonication may be necessary for complete dissolution.

Sample solution: Nominally equivalent to 0.2 mg/mL of benzethonium chloride in *Diluent* prepared as follows. Weigh an amount of Topical Solution equivalent to 2 mg of benzethonium chloride into a 50-mL round-bottom flask. Evaporate on a rotavap under vacuum and heat at 35° to dryness. Pipette 10 mL of *Diluent* and sonicate for about 10 min and mix. Pass the solution through a suitable filter of 0.2-µm pore size discarding the first 1–2 mL.

Chromatographic system

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

Mode: LC

Detector: UV 225 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15 cm; 5-µm packing L7

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of benzethonium chloride ($C_{27}H_{42}ClNO_2$) in the portion of Topical Solution taken:

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

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

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

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

C_U = nominal concentration of benzethonium chloride in the *Sample solution* (mg/mL)▲ (USP 1-May-2022)

Acceptance criteria: 95.0%–105.0%

IMPURITIES

Add the following:

▲• **Organic Impurities**

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

System suitability solution: 0.15 mg/mL each of USP Benzethonium Chloride RS and USP Methylbenzethonium Chloride RS in *Diluent*. Sonication may be necessary for complete dissolution.

Standard solution: 0.002 mg/mL of USP Benzethonium Chloride RS in *Diluent*. Sonication may be necessary for complete dissolution.

Sensitivity solution: 0.001 mg/mL of USP Benzethonium Chloride RS in *Diluent* from *Standard solution*

Sample solution: Nominally equivalent to 1 mg/mL of benzethonium chloride in *Diluent* prepared as follows. Weigh an amount of Topical Solution equivalent to 10 mg of benzethonium chloride into a 10-mL volumetric flask. Evaporate on rotavap under vacuum and heat at 35° to dryness. Add about 8 mL of *Diluent*, sonicate for about 10 min, and dilute with *Diluent* to volume. Pass the solution through a suitable filter of 0.2-µm pore size discarding the first 1–2 mL.

System suitability

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

[Note—The relative retention times for benzethonium and methylbenzethonium are 1.0 and 1.47, respectively.]

Suitability requirements

Resolution: NLT 7.0 between benzethonium and methylbenzethonium peaks, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10.0%, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of the sample 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 benzethonium from the *Standard solution*

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

C_U = nominal concentration of benzethonium chloride in the *Sample solution* (mg/mL)

Acceptance criteria

Total impurities: NMT 1.0%▲ (USP 1-May-2022)

Change to read:

• ▲▲ (USP 1-May-2022) **Limit of Nitrites**

▲**Naphthylamine solution:** Boil 30 mg of 1-naphthylamine in 70 mL of water. Decant the colorless solution from the blue-violet residue, and mix with 30 mL of glacial acetic acid.▲ (USP 1-May-2022)

Sample: One drop of Topical Solution on a spot plate

Analysis: To the *Sample* add one drop each of glacial acetic acid, sulfanilic acid in acetic acid (1 in 100), and ▲*Naphthylamine solution*.▲ (USP 1-May-2022)

Acceptance criteria: No red color develops in the resulting solution within 10 min.

SPECIFIC TESTS

Delete the following:

▲• **Oxidizing Substances**

Sample: 5 mL

Analysis: To the *Sample* add 0.5 mL of potassium iodide TS and a few drops of 3 N hydrochloric acid.

Acceptance criteria: The solution does not acquire a yellow color.▲ (USP 1-May-2022)

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

Add the following:

▲• **USP Reference Standards** ⟨11⟩

USP Benzethonium Chloride RS

USP Methylbenzethonium Chloride RS▲ (USP 1-May-2022)

Topic/Question	Contact	Expert Committee
BENZETHONIUM CHLORIDE TOPICAL SOLUTION	Documentary Standards Support	SM12020 Small Molecules 1

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