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Benzalkonium Chloride Solution

DEFINITION

Benzalkonium Chloride Solution contains NLT 95.0% and NMT 105.0% of the labeled amount of benzalkonium chloride in a solution having a concentration of 1.0% or more; and NLT 93.0% and NMT 107.0% of the labeled amount of benzalkonium chloride in a solution having a concentration of less than 1.0%. It may contain a suitable coloring agent and may contain NMT 10% of alcohol.

[CAUTION—Mixing Benzalkonium Chloride Solution with ordinary soaps and anionic detergents may decrease or destroy the bacteriostatic activity of the Solution.**]**

IDENTIFICATION

• A.

Analysis: To 2 mL of a solution having an equivalent of 10 mg/mL of benzalkonium chloride add 1 mL of 2 N nitric acid.

Acceptance criteria: A white precipitate is formed and is dissolved after adding 5 mL of [alcohol](#).

• B. [IDENTIFICATION TESTS—GENERAL \(191\)](#), [Chloride](#):

A solution of it in a mixture of equal volumes of water and [alcohol](#) meets the requirements.

• C.

Analysis: Dissolve the residue, obtained by evaporating on a steam bath a volume of Solution equivalent to 200 mg of benzalkonium chloride, in 1 mL of [sulfuric acid](#). Add 100 mg of [sodium nitrate](#), and heat on a steam bath for 5 min. Cool, dilute with water to 10 mL, add 500 mg of zinc dust, and warm for 5 min on a steam bath. To 2 mL of the clear supernatant add 1 mL of sodium nitrite solution (1 in 20), cool in ice water, then add 3 mL of a solution of 500 mg of [2-naphthol](#) in 10 mL of [6 N ammonium hydroxide](#).

Acceptance criteria: An orange-red color is produced.

• D. CHROMATOGRAPHIC IDENTITY

Analysis: Proceed as directed in the test for *Ratio of Alkyl Components*.

Acceptance criteria: The retention times of the major peaks for benzalkonium chloride of the *Sample solution* correspond to those of the *Standard solution*.

ASSAY

• RATIO OF ALKYL COMPONENTS

Solution A: Adjust a 0.1 M solution of [sodium acetate](#) with [glacial acetic acid](#) to a pH of 5.0.

Mobile phase: Acetonitrile and *Solution A* (9:11). Acetonitrile and *Solution A* may be adjusted from (2:3) to (3:2) to meet system suitability requirements.

Standard solution: 4 mg/mL of benzalkonium chloride prepared from [USP Benzalkonium Chloride RS](#) and water

Sample solution: Transfer a volume of Solution, equivalent to 400 mg of benzalkonium chloride, to a 100-mL volumetric flask, and dilute with water to volume.

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; packing [L10](#) or 4.6-mm × 25-cm; 10-μm packing [L10](#)

Flow rate: 2 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

[NOTE—See [Table 1](#). Relative retention times are provided for information only, and the Standard should be used to ensure appropriate peak identification.]

Table 1

Name	Relative Retention Time
C ₁₀ homolog	0.9
C ₁₂ homolog	1.0
C ₁₄ homolog	1.3
C ₁₆ homolog	1.7

Suitability requirements

Resolution: NLT 1.5 between the C₁₂ and C₁₄ homologs

Relative standard deviation: NMT 2.0% for the C₁₂ homolog

Analysis

Samples: *Standard solution* and *Sample solution*

Identify the homolog peaks by comparison of the retention times from the *Sample solution* with those of the *Standard solution*.

Calculate the percentage of each quaternary ammonium homolog in the portion of Solution taken:

$$\text{Result} = \frac{r_U \times M_r}{\sum_i (r_U \times M_r)} \times 100$$

r_U = peak area of each homolog from the *Sample solution*

M_r = molecular weight of each homolog. The molecular weights of the C₁₀, C₁₂, C₁₄, and C₁₆ homologs are 312, 340, 368, and 396, respectively.

Acceptance criteria: On the solid basis, the content of the *n*-C₁₂H₂₅ homolog is NLT 40.0%, and the content of the *n*-C₁₄H₂₉ homolog is NLT 20.0% of the total alkylbenzyltrimethylammonium chloride content. The amount of the *n*-C₁₂H₂₅ and *n*-C₁₄H₂₉ homolog components together is NLT 70.0% of the total alkylbenzyltrimethylammonium chloride content.

• **TOTAL ALKYL BENZYL DIMETHYLAMMONIUM CHLORIDES**

Sample solution: Evaporate or dilute with water to 30 mL a volume of Solution equivalent to 500 mg of benzalkonium chloride.

Analysis: Transfer the *Sample solution*, with the aid of a minimum quantity of water, to a glass-stoppered, 250-mL conical separator. Transfer 25 mL of [methylene chloride](#). Add 10 mL of 0.1 N sodium hydroxide, and 10.0 mL of freshly prepared potassium iodide solution (1 in 20), insert the stopper in the separator, shake, allow the layers to separate, and discard the methylene chloride layer. Wash the aqueous layer with three 10-mL portions of [methylene chloride](#), and discard the washings. Transfer the aqueous layer to a glass-stoppered, 250-mL conical flask, and rinse the separator with three 5-mL portions of water, adding the washings to the flask. Add 40 mL of cold [hydrochloric acid](#) to the flask, mix, and titrate with 0.05 M potassium iodate VS until the solution becomes light brown in color. Add 5 mL of [methylene chloride](#), insert the stopper into the flask, and shake vigorously. Continue the titration, dropwise, with shaking after each addition, until the methylene chloride layer no longer changes color and the aqueous layer is clear yellow. Record the titrant volume, V_T , in mL. Perform a blank determination, using 20 mL of water as the sample, and record the titrant volume, V_B , in mL. [NOTE— $V_B > V_T$.] The difference between the two titrations represents the amount of potassium iodate equivalent to the weight of benzalkonium chloride in the sample. Each mL of 0.05 M potassium iodate is equivalent to $x/10$ mg of benzalkonium chloride, where x represents the average molecular weight of the sample, derived by summing, for all homologs, the products:

$$\text{Result } (x) = \sum_i [(r_U/r_T) \times M_r]$$

r_U = peak area of each homolog from the test for *Ratio of Alkyl Components*

r_T = sum of all the peak areas of the homologs from the test for *Ratio of Alkyl Components*

M_r = molecular weight of each homolog. The molecular weights of the C₁₀, C₁₂, C₁₄, and C₁₆ homologs are 312, 340, 368, and 396, respectively.

Acceptance criteria

For labeled concentrations of NLT 1.0%: 95.0%–105.0%

For labeled concentrations less than 1.0%: 93.0%–107.0%