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Sodium Cetostearyl Sulfate

DEFINITION

Sodium Cetostearyl Sulfate is a mixture of sodium cetyl sulfate and sodium stearyl sulfate. It contains NLT 40.0% of sodium cetyl sulfate ($C_{16}H_{33}NaSO_4$), and the sum of the sodium cetyl sulfate content and sodium stearyl sulfate ($C_{18}H_{37}NaSO_4$) content is NLT 90.0% (both contents calculated on the anhydrous basis). It may contain a suitable buffer.

IDENTIFICATION

• **A.** The retention times of the two major peaks of *Sample solution C* correspond to those of the *System suitability solution*, as obtained in the *Assay*.

• **B.** Sodium Cetostearyl Sulfate imparts an intense yellow color to a nonluminous flame.

• **C.**

Sample solution: 1.0 mg/mL in alcohol

Analysis: Heat 10 mL of the *Sample solution* to boiling on a water bath, shaking frequently. Filter immediately, and evaporate to dryness. Dissolve the residue in 7 mL of water, add 3 mL of diluted hydrochloric acid, and evaporate the solution to half its volume. Allow to cool, and filter. To the filtrate add 1 mL of barium chloride solution (60 mg/mL).

Acceptance criteria: A white crystalline precipitate is formed.

ASSAY

• **Procedure**

System suitability solution: 5 mg/mL each of USP Cetyl Alcohol RS and USP Stearyl Alcohol RS in alcohol

Internal standard solution: 4 mg/mL of 1-heptadecanol in alcohol

Sample solution A: Dissolve 300 mg of Sodium Cetostearyl Sulfate in 50 mL of alcohol, and add 2 mL of the *Internal standard solution* and 48 mL of water. Extract the solution with four 25-mL portions of pentane, adding 10–15 mL of saturated sodium chloride solution, if necessary, to facilitate the separation of the layers. Combine the organic layers, and reserve the hydroalcoholic layers for the preparation of *Sample solution C* and *Sample solution D*. Wash the organic layer with two 30-mL portions of water, dry over anhydrous sodium sulfate, and filter.

Sample solution B: Dissolve 300 mg of Sodium Cetostearyl Sulfate in 50 mL of alcohol, and add 50 mL of water. Extract the solution with four 25-mL portions of pentane, adding 10–15 mL of saturated sodium chloride solution, if necessary, to facilitate the separation of the layers. Combine the organic layers, wash with two 30-mL portions of water, dry over anhydrous sodium sulfate, and filter.

Sample solution C: Transfer 25 mL of the hydroalcoholic solution obtained in the preparation of *Sample solution A* to a 200-mL flask that can be fitted with a reflux condenser. Add 20 mL of hydrochloric acid and 10 mL of the *Internal standard solution*, and boil under reflux for 2 h. Allow to cool. Extract with four 20-mL portions of pentane. Wash the combined organic layer with two 20-mL portions of water, dry over anhydrous sodium sulfate, and filter.

Sample solution D: Transfer 25 mL of the hydroalcoholic solution obtained in the preparation of *Sample solution A* to a 200-mL flask that can be fitted with a reflux condenser. Add 20 mL of hydrochloric acid and 10 mL of alcohol, and boil under reflux for 2 h. Allow to cool. Extract with four 20-mL portions of pentane. Wash the combined organic layer with two 20-mL portions of water, dry over anhydrous sodium sulfate, and filter.

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.25-mm × 25-m fused silica capillary; phase G2

Temperatures

Injection port: 250°

Detector: 250°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
150	5	250	Duration of analysis

Carrier gas: Nitrogen

Flow rate: 1 mL/min

Injection volume: 1 µL

Injection type: Split ratio 100:1

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 4.0 between cetyl alcohol and stearyl alcohol

Relative standard deviation: NMT 1.5%

Analysis

Correction for interference: Inject *Sample solution A* and *Sample solution B* into the chromatograph, record the chromatograms, and measure the areas for the major peaks.

If *Sample solution B* shows a peak at the same retention time as the internal standard peak of *Sample solution A*, calculate the ratio, *R*:

$$R = S_{CB}/S_I$$

S_{CB} = peak response of cetyl alcohol from *Sample solution B*

S_I = peak response with the same retention time as the internal standard of *Sample solution B*

If *R* is less than 300, calculate the corrected area, $S_{A(corr)}$, of the peak corresponding to the internal standard of *Sample solution A*:

$$S_{A(corr)} = S_{HA} - (S_I \times S_{CA}/S_{CB})$$

S_{HA} = peak response of the internal standard from *Sample solution A*

S_I = peak response with the same retention time as the internal standard of *Sample solution B*

S_{CA} = peak response of cetyl alcohol from *Sample solution A*

S_{CB} = peak response of cetyl alcohol from *Sample solution B*

Inject *Sample solution C* and *Sample solution D* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Carry out the *Correction for interference* in the same manner as for *Sample solution A*, and calculate the corrected area of the peak corresponding to the internal standard of *Sample solution C*, $S_{C(corr)}$.

Samples: *System suitability solution*, *Sample solution C*, and *Sample solution D*

[NOTE—The substances are eluted in the following order: cetyl alcohol, 1-heptadecanol (internal standard), and stearyl alcohol. Identify the cetyl alcohol and stearyl alcohol peaks in the chromatograms of the *Sample solutions* by comparison with the *System suitability solution*.]

Calculate the percentage of sodium cetyl sulfate ($C_{16}H_{33}NaSO_4$) in the portion of Sodium Cetostearyl Sulfate taken:

$$\text{Result} = (r_C \times W_{CH})/(S_{C(corr)} \times W_C) \times F \times 100$$

r_C = peak response of cetyl alcohol from *Sample solution C*

W_{CH} = weight of the internal standard added in the preparation of *Sample solution C* (mg)

$S_{C(corr)}$ = corrected area of the peak corresponding to the internal standard of *Sample solution C*

W_C = weight of Sodium Cetostearyl Sulfate taken to prepare *Sample solution C*, calculated on the anhydrous basis (mg)

F = correction factor, 1.421

Calculate the percentage of sodium stearyl sulfate ($C_{18}H_{37}NaSO_4$) in the portion of Sodium Cetostearyl Sulfate taken:

$$\text{Result} = (B_C \times W_{CH})/(S_{C(corr)} \times W_C) \times F \times 100$$

B_C = peak response of stearyl alcohol from *Sample solution C*

W_{CH} = weight of the internal standard added in the preparation of *Sample solution C* (mg)

$S_{C(corr)}$ = corrected area of the peak corresponding to the internal standard of *Sample solution C*

W_C = weight of Sodium Cetostearyl Sulfate taken to prepare *Sample solution C*, calculated on the anhydrous basis (mg)

F = correction factor, 1.377

Acceptance criteria

Sodium cetyl sulfate: NLT 40.0% on the anhydrous basis

Sum of sodium cetyl sulfate and sodium stearyl sulfate: NLT 90.0% on the anhydrous basis

IMPURITIES

• **Limit of Sodium Chloride and Sodium Sulfate**

Sodium chloride

Sample: 5 g

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N silver nitrate VS

Endpoint detection: Potentiometric

Analysis: Dissolve the *Sample* in 50 mL of water, and add diluted nitric acid dropwise until the solution is neutral to blue litmus paper. To the resulting solution add 1 mL of potassium chromate TS and titrate with *Titrant*.

Calculate the percentage of sodium chloride (NaCl) in the portion of Sodium Cetostearyl Sulfate taken:

$$\text{Result} = (V \times N)/W \times F$$

V = volume of the *Titrant* (mL)

N = actual normality of the *Titrant*

W = weight of Sodium Cetostearyl Sulfate (g)

F = equivalence factor for sodium chloride, 5.844

Sodium sulfate

Dichloroacetic acid solution: Dilute 67 mL of dichloroacetic acid with water to 300 mL, and neutralize to blue litmus paper using ammonia TS. Cool, add 33 mL of dichloroacetic acid, and dilute with water to 600 mL.

Sample: 0.5 g

Titrimetric system

Mode: Direct titration

Titrant: 0.01 M lead nitrate VS

Endpoint detection: Visual

Analysis: Dissolve the *Sample* in 20 mL of water, warming gently if necessary, and add 1 mL of a solution containing 0.5 g/L of dithizone in acetone. If the solution is red, add 1 N nitric acid dropwise until a bluish-green color is obtained. To the resulting solution add 2.0 mL of *Dichloroacetic acid solution* and 80 mL of acetone, and titrate with *Titrant* until a persistent orange-red color is obtained.

Calculate the percentage of sodium sulfate (Na_2SO_4) in the portion of Sodium Cetostearyl Sulfate taken:

$$\text{Result} = (V \times M)/W \times F$$

V = volume of *Titrant* (mL)

M = actual molarity of *Titrant*

W = weight of Sodium Cetostearyl Sulfate (g)

F = equivalence factor for sodium sulfate, 14.20

Acceptance criteria: The sum of the percentages of sodium chloride and sodium sulfate is NMT 8.0%.

• **Limit of Free Cetostearyl Alcohol**

Analysis: Examine the chromatogram of *Sample solution A*, obtained as directed in the *Assay*.

Calculate the percentage of free cetostearyl alcohol in the portion of Sodium Cetostearyl Sulfate taken:

$$\text{Result} = 100(r_A + r_B) \times W_{IS}/(S_{A(corr)} \times W)$$

r_A = peak response of the cetyl alcohol peak from *Sample solution A*

r_B = peak response of stearyl alcohol from *Sample solution A*

W_{IS} = weight of the internal standard added in the preparation of *Sample solution A* (mg)

$S_{A(corr)}$ = corrected peak area corresponding to the internal standard of *Sample solution A* (see *Assay*)

W = weight of Sodium Cetostearyl Sulfate taken to prepare *Sample solution A* (mg)

Acceptance criteria: NMT 4.0%

SPECIFIC TESTS

• **Acidity or Alkalinity**

Sample: 500 mg

Analysis: Dissolve the *Sample* by heating in a mixture of 10 mL of water and 15 mL of 90% alcohol. Add 0.1 mL of phenolphthalein TS.

Acceptance criteria: The resulting solution is colorless. Add 0.1 mL of 0.1 N sodium hydroxide, and the resulting solution becomes red.

• **Water Determination ⟨921⟩, *Method I*:** NMT 1.5%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in well-closed containers. No storage requirements specified.

• **Labeling:** Label it to indicate the name and concentration of any added buffer.

• **USP Reference Standards ⟨11⟩**

USP Cetyl Alcohol RS

USP Stearyl Alcohol RS

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

Topic/Question	Contact	Expert Committee
SODIUM CETOSTEARYL SULFATE	Documentary Standards Support	CE2020 Complex Excipients
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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