SODIUM LAURILSULFATE

(NATRII LAURILSULFAS)

Draft proposal for inclusion for The International Pharmacopoeia

(August 2020)

DRAFT FOR COMMENTS

Please send any comments you may have on this draft working document to Dr Herbert Schmidt, Technical Officer, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (email: schmidt@who.int) by 31 October 2020.

Working documents are sent out electronically and they will also be placed on the WHO Medicines website (http://www.who.int/medicines/areas/quality_safety/quality_assurance/guidelines/en/) for comments under the “Current projects” link. If you wish to receive our draft guidelines, please send your e-mail address to jonessi@who.int and your name will be added to our electronic mailing list.

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SCHEDULE FOR THE ADOPTION PROCESS OF DOCUMENT QAS/20.857:

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[Note from the Secretariat. It is proposed to include the monograph on Sodium laurilsulfate in the The International Pharmacopoeia.]

The monograph is based on the corresponding, internationally-harmonized text developed by the Pharmacopoeial Discussion Group (PDG). Editorial modifications have been made in order to be in line with the style used in The International Pharmacopoeia.]
SODIUM LAURILSULFATE
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This monograph is based on the corresponding, internationally-harmonized text developed by the Pharmacopoeial Discussion Group (PDG). Editorial modifications have been made in order to be in line with the style used in The International Pharmacopoeia.

Chemical name. Sodium dodecyl sulfate. \( \text{C}_{12}\text{H}_{25}\text{NaO}_{4}\text{S} \). CAS Reg. No. 151-21-3.

Description. White or pale yellow, powder or crystals.

Solubility. Freely soluble in water giving an opalescent solution, partly soluble in ethanol (~750 g/L) TS.

Category. Anionic surfactant.

Storage. Sodium laurilsulfate should be kept in a well-closed container.

Requirements

Definition. Sodium laurilsulfate is a mixture of sodium alkyl sulfates consisting mainly of sodium dodecyl sulfate (\( \text{C}_{12}\text{H}_{25}\text{NaO}_{4}\text{S} \)). It contains not less than 85.0% of sodium alkyl sulfates, calculated as \( \text{C}_{12}\text{H}_{25}\text{NaO}_{4}\text{S} \).

Identity tests

A. Carry out the test as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from sodium laurilsulfate RS or with the reference spectrum of sodium laurilsulfate.
B. Place 2.5 g in a silica or platinum crucible and add 2 mL of sulfuric acid (~500 g/L) TS. Heat on a water-bath, then cautiously raise the temperature progressively over an open flame. Ignite, preferably in a muffle furnace, at 575 °C to 625 °C. Continue heating until all black particles have disappeared. Cool, add a few drops of a sulfuric acid (~100 g/L) TS, and heat and ignite as above. Add a few drops of ammonium carbonate (158 g/L) TS, evaporate to dryness, and ignite as above. Cool, dissolve the residue in 50 mL of water R and mix. The solution yields reaction B, described under 2.1 General identification tests as a characteristic of sodium.

C. Prepare a 100 g/L solution. After acidification with hydrochloric acid (~420 g/L) TS and boiling for 20 minutes, no precipitate is formed. Add barium chloride (120 g/L) TS; a white precipitate is produced.

Alkalinity. Dissolve 1.0 g in 100 mL of carbon dioxide-free water R and add 0.1 mL of phenol red/ethanol TS1; not more than 0.5 mL of hydrochloric acid (0.1 mol/L) VS is required to change the colour of the indicator.

Non-esterified alcohols. Dissolve 10.0 g in 100 mL of water R, add 100 mL of ethanol (~750 g/L) TS and shake the solution with 3 quantities, each of 50 mL, of light petroleum R2, adding sodium chloride R, if necessary, to promote separation of the 2 layers. Wash the combined organic layers with 3 quantities, each of 50 mL, of water R, dry over anhydrous sodium sulfate R, filter and evaporate on a water-bath until the solvent has evaporated. Heat the residue at 105 °C for 30 minutes and cool; the residue weighs a maximum of 0.4 g (4.0%).

Sodium chloride and sodium sulphate

Sodium chloride. Dissolve 5.00 g in 50 mL of water R, add nitric acid (~130 g/L) TS dropwise, if necessary, until the solution is neutral, and add 5.0 mL of sodium chloride (5.84 g/L) TS. Titrate with silver nitrate (0.1 mol/L) VS, while stirring vigorously to
disperse the silver chloride, using 0.1 mL of fluorescein sodium (2g/L) TS as indicator, to the first appearance of turbidity with solution colour change from yellowish-green to orange through yellow. Perform a blank determination. Each mL of silver nitrate (0.1 mol/L) VS is equivalent to 5.844 mg of NaCl.

_Sodium sulphate._ Dissolve 1.00 g in 10 mL of water R, add 100 mL of ethanol (~750 g/L) TS and heat at a temperature just below the boiling point for 2 hours. Filter while hot through a glass filter with a porosity of 4 µm to 10 µm and wash with 100 mL of boiling ethanol (~750 g/L) TS. Dissolve the precipitate by washing with 150 mL of water R, collecting the washings in a beaker. Add 10 mL of dilute hydrochloric acid R, heat to boiling, add 25 mL of barium chloride (120 g/L) TS and allow to stand overnight. Collect the precipitate by filtration (maximum pore size 16 µm) and wash with water R until the last washing shows no opalescence with silver nitrate (0.1 mol/L) VS. Dry the precipitate, ignite to constant mass at 500 °C to 600 °C by raising the temperature gradually, and weigh as barium sulfate. Each mg of barium sulfate is equivalent to 0.609 mg of Na$_2$SO$_4$.

The sum of the percentage contents of NaCl and Na$_2$SO$_4$ is not greater than 8.0%

_Assay._ Dissolve 1.15 g in water R, warming if necessary, and dilute to 1000.0 mL with the same solvent. To 20.0 mL of the solution, add 15 mL of dichloromethane R and 10 mL of dimidium bromide/sulfan blue TS and mix. Titrate with benzethonium chloride (0.004 mol/L) VS, shaking vigorously and allowing the layers to separate before each addition, until the pink colour of the dichloromethane layer is completely discharged and a greyish-blue colour is obtained. Each mL of benzethonium chloride (0.004 mol/L) VS is equivalent to 1.154 mg of sodium alkyl sulfates, expressed as C$_{12}$H$_{25}$NaO$_4$S.
New reagents

Sulfuric acid (~500 g/L) TS

Procedure. Cool separately 10 mL of water R and 5 mL of sulfuric acid (~1760 g/L) TS to about -5 °C. Carefully add the acid to the water keeping the solution as cool as possible and mix gently (approximately 5 mol/L); d~1.29.

Ammonium carbonate (158 g/L) TS

A 158 g/L solution of ammonium carbonate R1.

Ammonium carbonate R1

A mixture of varying proportions of ammonium hydrogen carbonate (NH₄HCO₃) and ammonium carbamate (NH₂COONH₄). It liberates not less than 30 per cent m/m of NH₃.

Description. White or almost white translucent mass.

Solubility. Slowly soluble in about 4 parts of water. It is decomposed by boiling water.

Assay. Dissolve 2.00 g in 25 mL of water R. Slowly add 50.0 mL of hydrochloric acid (1 mol/L) VS, titrate with sodium hydroxide (1 mol/L) VS, using 0.1 mL of methyl orange ethanol TS1 as indicator. Each mL of hydrochloric acid (1 mol/L) VS is equivalent to 17.03 mg of NH₃.

Storage. Store at a temperature below 20 °C.

Methyl orange ethanol TS1

Procedure. Dissolve 0.1 g of methyl orange R in 80 mL of water R and dilute to 100 mL with ethanol (~750 g/L) TS.
Test for sensitivity. A mixture of 0.1 mL of methyl orange ethanol TS1 and 100 mL of carbon-dioxide-free water R is yellow. Not more than 0.1 mL of hydrochloric acid (1 mol/L) VS is required to change the colour to red.

Colour change. pH 3.0 (red) to pH 4.4 (yellow).

Barium chloride (120 g/L) TS

A solution of barium chloride R containing about 120 g of barium chloride per litre.

Phenol red/ethanol TS1

Procedure. Dissolve 0.1 g of phenol red R in a mixture of 2.82 mL of sodium hydroxide (1 mol/L) VS and 20 mL of ethanol (~750 g/L) TS and dilute to 100 mL with water R.

Test for sensitivity. Add 0.1 mL of the phenol red solution to 100 mL of carbon dioxide-free water R; the solution is yellow. Not more than 0.1 mL of sodium hydroxide (0.02 mol/L) VS is required to change the colour to reddish-violet.

Colour change. pH 6.8 (yellow) to pH 8.4 (reddish-violet).

Light petroleum R2

Description. Clear, colourless, flammable liquid without fluorescence.

Solubility. Practically insoluble in water, miscible with ethanol (~750 g/L) TS.

Boiling range. (1.2.4). 50–70 °C.

Mass density. \( \rho_{20} = 0.661 \) to 0.664 kg/L.

Sodium chloride (5.84 g/L) TS

A 5.84 g/L solution of sodium chloride R1 in water R.
Sodium chloride R1

Use sodium chloride as described in the monograph for Sodium chloride.

Fluorescein sodium TS

A 2 g/L solution of fluorescein sodium R in water R.

Fluorescein sodium R

Use fluorescein sodium as described in the monograph for Fluorescein sodium.

Dimidium bromide/sulfan blue TS

Procedure. Dissolve separately 0.5 g of dimidium bromide R and 0.25 g of sulfan blue R in 30 mL of a hot mixture of 1 volume of anhydrous ethanol R and 9 volumes of water R, stir, mix the two solutions, and dilute to 250 mL with the same mixture of solvents. Mix 20 mL of this solution with 20 mL of a 14.0 per cent V/V solution of sulfuric acid R previously diluted with about 250 mL of water R and dilute to 500 mL with water R.

Storage. Store protected from light.

Dimidium bromide R

C_{20}H_{18}BrN_{3}. 3,8-Diamino-5-methyl-6-phenylphenanthridinium bromide. CAS Reg. No. 518-67-2.

Description. Dark-red crystals.

Solubility. Slightly soluble in water at 20 °C, sparingly soluble in water at 60 °C and in ethanol (~750 g/L) TS.

Storage. Store protected from light.
Sulfan blue R

Sodium \[((4\text{-diethylamino})\text{phenyl})(2,4\text{-disulfonatophenyl})\text{methylene}]\text{cyclohexa}-2,5\text{-dien-1-ylidene}]\text{diethylammonium}. \(\text{C}_{27}\text{H}_{31}\text{N}_{2}\text{NaO}_{6}\text{S}_{2}\). CAS Reg. No. 129-17-9.

*Appearance.* Violet powder.

*Solubility.* Soluble in water.

*Colour of solution.* Dilute solutions are blue and turn yellow on the addition of concentrated hydrochloric acid.

Benzethonium chloride (0.004 mol/L) VS

*Procedure.* Dissolve 1.792 g of benzethonium chloride R, previously dried to constant mass at 100 °C to 105 °C, in water R and dilute to 1000.0 mL with the same solvent.

*Method of standardization.* Dissolve 0.350 g of the dried substance in 35 mL of a mixture of 30 volumes of anhydrous acetic acid R and 70 volumes of acetic anhydride R. Titrate with perchloric acid (0.1 mol/L) VS, using 0.05 mL of crystal violet /acetic acid TS1 as indicator. Carry out a blank titration. Each mL of perchloric acid (0.1 mol/L) VS is equivalent to 44.81 mg of \(\text{C}_{27}\text{H}_{42}\text{ClNO}_{2}\).

Benzethonium chloride R

Benzyldimethyl[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethyl]ammonium chloride. \(\text{C}_{27}\text{H}_{42}\text{ClNO}_{2}\). CAS Reg. No. 121-54-0.

*Description.* Fine, white or almost white powder or colourless crystals.

*Solubility.* Soluble in water and in ethanol (~750 g/L) TS.

*Melting point.* About 163 °C.

*Storage.* Store protected from light.
Crystal violet/acetic acid TS1

A solution of crystal violet R dissolved in anhydrous acetic acid R containing about 5 g/L

Test for sensitivity. To 50 mL of anhydrous acetic acid R, add 0.1 mL of the crystal violet solution. On addition of 0.1 mL of perchloric acid (0.1 mol/L) VS, the bluish-purple solution turns bluish-green.

New reference substance

Sodium laurilsulfate RS

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