Mobile phase: A mixture of water and methanol (1:1).

Flow rate: Adjust the flow rate so that the retention time of santonin is about 7 minutes.

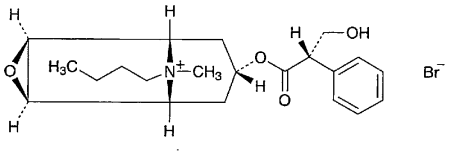
Selection of column: Proceed with 1 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of santonin and the internal standard in this order with the resolution between these peaks being not less than 2.5.

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Scopolamine Butylbromide

臭化ブチルスコポラミン



$C_{21}H_{30}BrNO_4$: 440.37

(1*S*,2*S*,4*R*,5*R*,7*s*)-9-Butyl-7-[(2*S*)-3-hydroxy-2-phenylpropanoyloxy]-9-methyl-3-oxa-9-azoniatricyclo[3.3.1.$0^{2,4}$]nonane bromide

[*149-64-4*]

Scopolamine Butylbromide, when dried, contains not less than 98.5% of $C_{21}H_{30}BrNO_4$.

Description Scopolamine Butylbromide occurs as white crystals or crystalline powder.

It is very soluble in water, freely soluble in acetic acid (100), soluble in ethanol (95), sparingly soluble in methanol, slightly soluble in acetic anhydride, and practically insoluble in diethyl ether.

Melting point: about 140°C (with decomposition).

Identification **(1)** To 1 mg of Scopolamine Butylbromide add 3 to 4 drops of fuming nitric acid, and evaporate on a water bath to dryness. After cooling, dissolve the residue in 1 mL of *N,N*-dimethylformamide, and add 6 drops of tetraethylammonium hydroxide TS: a red-purple color develops.

(2) Determine the absorption spectrum of a solution of Scopolamine Butylbromide (1 in 1000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Determine the infrared absorption spectrum of Scopolamine Butylbromide, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) A solution of Scopolamine Butylbromide (1 in 20) responds to the Qualitative Tests for bromide.

Optical rotation $[\alpha]_D^{20}$: −18.0 – −20.0° (after drying, 1 g, water, 10 mL, 100 mm).

pH Dissolve 1.0 g of Scopolamine Butylbromide in 10 mL of water: the pH of this solution is between 5.5 and 6.5.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Scopolamine Butylbromide in 10 mL of water: the solution is clear, and has no more color than the following control solution.

Control solution: To 0.5 mL of Matching Fluid F add diluted hydrochloric acid (1 in 40) to make 20 mL.

(2) Heavy metals—Proceed with 2.0 g of Scopolamine Butylbromide according to Method 1, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Related substances—Dissolve 0.10 g of Scopolamine Butylbromide in the mobile phase to make exactly 10 mL, and use this solution as the sample solution. Separately, dissolve 0.010 g of scopolamine hydrobromide in the mobile phase to make exactly 100 mL. Pipet 10 mL of this solution, add the mobile phase to make exactly 50 mL, and use this solution as the standard solution (1). Pipet 5 mL of the standard solution (1), add the mobile phase to make exactly 10 mL, and use this solution as the standard solution (2). Perform the test with 20 μL each of the sample solution and the standard solutions (1) and (2) as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of these solutions by the automatic integration method: the peak area of scopolamine from the sample solution is not larger than that from the standard solution (2), and each area of the peaks other than the peak appearing in the first elution and the peak of scopolamine and butylscopolamine from the sample solution are not larger than the peak area from the standard solution (1).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 210 nm).

Column: A stainless steel column about 4 mm in inside diameter and 15 to 25 cm in length, packed with octylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

Column temperature: A constant temperature of about 30°C.

Mobile phase: Dissolve 2 g of sodium lauryl sulfate in 370 mL of water and 680 mL of methanol, and adjust the pH to 3.6 with diluted phosphoric acid (1 in 10).

Flow rate: Adjust the flow rate so that the retention time of butylscopolamine is about 7 minutes.

Selection of column: Dissolve 5 mg each of Scopolamine Butylbromide and scopolamine hydrobromide in 50 mL of the mobile phase. Proceed with 20 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of scopolamine and butylscopolamine in this order with the resolution between these peaks being not less than 5.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of scopolamine obtained from 20 μL of the standard solution (2) is between 5 and 10 mm.

Time span of measurement: About twice as long as the retention time of butylscopolamine.

Loss on drying Not more than 1.0% (1 g, 105°C, 4 hours).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.8 g of Scopolamine Butylbromide, previously dried, dissolve in 40 mL of acetic acid

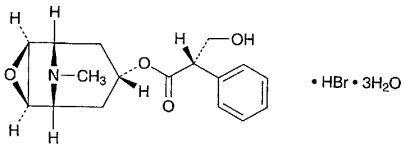
(100) and 30 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 44.04 mg of $C_{21}H_{30}BrNO_4$

Containers and storage Containers—Tight containers.

Scopolamine Hydrobromide

臭化水素酸スコポラミン



$C_{17}H_{21}NO_4.HBr.3H_2O$: 438.31
(1*S*,2*S*,4*R*,5*R*,7*s*)-9-Methyl-3-oxa-9-azatricyclo-[3.3.1.$0^{2,4}$]non-7-yl (2*S*)-3-hydroxy-2-phenylpropanoate monohydrobromide trihydrate [*6533-68-2*]

Scopolamine Hydrobromide, when dried, contains not less than 98.5% of $C_{17}H_{21}NO_4.HBr$ (mol. wt.: 384.26).

Description Scopolamine Hydrobromide occurs as colorless or white crystals, or white granules or powder. It is odorless.

It is freely soluble in water, sparingly soluble in ethanol (95) and in acetic acid (100), and practically insoluble in diethyl ether.

Identification (1) To 1 mg of Scopolamine Hydrobromide add 3 to 4 drops of fuming nitric acid, evaporate on a water bath to dryness, and cool. Dissolve the residue in 1 mL of *N,N*-dimethylformamide, and add 6 drops of tetraethylammonium hydroxide TS: a red-purple color is produced.

(2) A solution of Scopolamine Hydrobromide (1 in 20) responds to the Qualitative Tests for bromide.

Optical rotation $[\alpha]_D^{20}$: −24.0 – −26.0° (after drying, 0.5 g, water, 10 mL, 100 mm).

Melting point 195 – 199°C (after drying; previously heat the bath to 180°C).

Purity (1) Clarity and color of solution—Dissolve 0.5 g of Scopolamine Hydrobromide in 10 mL of water: the solution is clear and colorless.

(2) Acid—Dissolve 0.50 g of Scopolamine Hydrobromide in 15 mL of water, and add 0.50 mL of 0.02 mol/L sodium hydroxide and 1 drop of methyl red-methylene blue TS: a green color develops.

(3) Apoatropine—Dissolve 0.20 g of Scopolamine Hydrobromide in 20 mL of water, add 0.60 mL of 0.002 mol/L potassium permanganate VS, and allow to stand for 5 minutes: the red color in the solution does not disappear.

(4) Other alkaloids—Dissolve 0.15 g of Scopolamine Hydrobromide in 3 mL of water, and use this solution as the sample solution.

(i) To 1 mL of the sample solution add 2 to 3 drops of ammonia TS: no turbidity is produced.

(ii) To 1 mL of the sample solution add 2 to 3 drops of potassium hydroxide TS: a transient white turbidity might be produced, and disappears clearly in a little while.

Loss on drying Not more than 13.0% [1.5 g; first dry in a desiccator (silica gel) for 24 hours, then dry at 105°C for 3 hours].

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.5 g of Scopolamine Hydrobromide, previously dried in 10 mL of acetic acid (100) by warming. After cooling, add 40 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 38.427 mg of $C_{17}H_{21}NO_4.HBr$

Containers and storage Containers—Tight containers. Storage—Light-resistant.

Secretin

セクレチン

His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Glu-Leu-Ser-Arg-Leu-Arg-Asp-Ser-Ala-Arg-Leu-Gln-Arg-Leu-Leu-Gln-Gly-Leu-Val-NH_2

$C_{130}H_{220}N_{44}O_{41}$: 3055.41
[*1393-25-5*]

Secretin is a peptide obtained from the upper part of hog small intestine (duodenum mucous membrane), having a pancreatic juice secretion-stimulating activity. It contains not less than 16,000 secretin Units and not more than 21,500 secretin Units per 1 mg, calculated on the de-acetic acid basis.

Description Secretin occurs as a white to pale yellow-white powder.

Identification Dissolve an amount of Secretin in bovine serum albumin TS for secretin so that each mL of the solution contains 20 secretin Units, and use this solution as the sample solution. Separately, dissolve an amount of Secretin Reference Standard in bovine serum albumin TS for Secretin Reference Standard so that each mL of the solution contains 20 secretin Units, and use this solution as the standard solution. Anesthetize a male Wistar rat, weighing 300 to 400 g, starved in advance for 24 hours, by injecting 1.2 g per kg body mass of ethyl carbamate into the abdominal cavity. Fix the animal on the back, cut and open the skin to reveal the femoral vein, insert a cannula filled with isotonic sodium chloride solution into the vein, and sew up the incision. Through the cannula inject 0.2 mL of the standard solution. Shave off the fur of the abdominal region, cut and open the region 3 to 4 cm below the central xiphoid process, and tie up the common bile duct at the duodenal ostial and the stomach at the pylorus, then insert a cannula into an upper