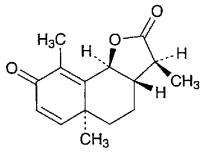
and titrate with 0.1 mol/L sodium hydroxide VS (indicator: 3 drops of phenolphthalein TS).

Each mL of 0.1 mol/L sodium hydroxide VS
= 13.812 mg of $C_7H_6O_3$

Containers and storage Containers—Well-closed containers.

Santonin

サントニン



$C_{15}H_{18}O_3$: 246.30
(3*S*,3a*S*,5a*S*,9b*S*)-3a,5,5a,9b-Tetrahydro-3,5a,9-trimethylnaphtho[1,2-*b*]furan-2,8(3*H*,4*H*)-dione
[*481-06-1*]

Santonin contains not less than 98.5% of $C_{15}H_{18}O_3$.

Description Santonin occurs as colorless crystals, or a white, crystalline powder. It is odorless, and tasteless at first, but afterward develops a slightly bitter taste.

It is freely soluble in boiling ethanol (95) and in chloroform, sparingly soluble in ethanol (95), slightly soluble in hot water and in diethyl ether, and practically insoluble in water.

It becomes yellow by light.

Identification (1) Dissolve 0.2 g of Santonin in 2 mL of potassium hydrox-ide-ethanol TS: a red color develops.

(2) Shake 0.01 g of powdered Santonin with 1 mL of diluted sulfuric acid (1 in 2), boil, and cool. Add 1 drop of dilute iron (III) chloride TS: a purple color develops.

Optical rotation $[\alpha]_D^{20}$: −170 – −175° (0.2 g, chloroform, 10 mL, 100 mm).

Melting point 172 – 175°C

Purity (1) Alkaloids—Boil 0.5 g of Santonin with 20 mL of diluted sulfuric acid (1 in 100), cool, and filter. Dilute 10 mL of the filtrate with water to 30 mL, add 3 drops of iodine TS, and allow to stand for 3 hours: no turbidity is produced.

(2) Artemisin—Dissolve 1.0 g of powdered Santonin in 2 mL of chloroform by slight warming: the solution is clear and colorless, or any yellow color produced is not darker than Matching Fluid A.

(3) Phenols—Boil 0.20 g of Santonin with 10 mL of water, cool, and filter. To the filtrate add bromine TS until the color of the solution becomes yellow: no turbidity is produced.

(4) Acid-coloring substances—Moisten 0.01 g of Santonin with nitric acid: no color develops immediately. Moisten Santonin with sulfuric acid, previously cooled to 0°C: no color is produced immediately.

Residue on ignition Not more than 0.25% (1 g).

Assay Weigh accurately about 0.25 g of Santonin, dissolve in 10 mL of ethanol (95) by warming, add exactly 20 mL of 0.1 mol/L sodium hydroxide VS, and heat on a water bath under a reflux condenser for 5 minutes. Cool quickly, and titrate the excess sodium hydroxide with 0.05 mol/L hydrochloric acid VS (indicator: 3 drops of phenolphthalein TS). Perform a blank determination.

Each mL of 0.1 mol/L sodium hydroxide VS
= 24.631 mg of $C_{15}H_{18}O_3$

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

Santonin Tablets

サントニン錠

Santonin Tablets contain not less than 92% and not more than 108% of the labeled amount of santonin ($C_{15}H_{18}O_3$: 246.30).

Method of preparation Prepare as directed under Tablets, with Santonin.

Identification To a portion of powdered Santonin Tablets, equivalent to 0.5 g of Santonin according to the labeled amount, add 50 mL of chloroform, shake, filter, and evaporate the filtrate to dryness. Proceed with this as directed in the Identification under Santonin.

Assay Weigh accurately, and powder not less than 20 Santonin Tablets. Weigh accurately a portion of the powder, equivalent to about 0.05 g of santonin ($C_{15}H_{18}O_3$), add 40 mL of methanol, shake for 10 minutes, and add methanol to make 50 mL. Centrifuge this solution, pipet 5 mL of the supernatant liquid, add exactly 3 mL of the internal solution, add methanol to make 10 mL, and use this solution as the sample solution. Separately, dissolve about 0.05 g of santonin for assay, accurately weighed, in methanol to make exactly 50 mL. Pipet 5 mL of this solution, add exactly 3 mL of the internal solution, add methanol to make 10 mL, and use this solution as the standard solution. Perform the test with 1 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of santonin to that of the internal standard.

Amount (mg) of santonin ($C_{15}H_{18}O_8$)
= amount (mg) of Santonin Reference Standard
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of ethyl paraoxybenzoate in ethanol (95) (1 in 1000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 254 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

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.

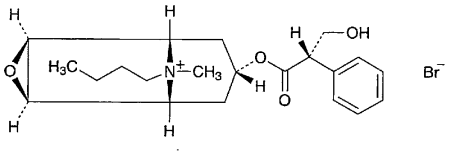
Selection of column: Proceed with 1 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of santonin and the internal standard in this order with the resolution between these peaks being not less than 2.5.

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