Assay Weigh accurately about 0.05 g each of Tocopherol Calcium Succinate and Tocopherol Succinate Reference Standard, previously dried, dissolve in a mixture of ethanol (99.5) and diluted acetic acid (100) (1 in 5) (9:1) to make exactly 50 mL, and use these solutions as the sample solution and the standard solution. Pipet 20 μL each of the sample solution and the standard solution, and perform the test as directed under the Liquid Chromatography according to the following operating conditions. Determine the peak heights, H_T and H_S, of tocopherol succinate in these solutions, respectively.

$$\text{Amount (mg) } C_{66}H_{106}CaO_{10} = \text{amount (mg) of Tocopherol Succinate Reference Standard} \times \frac{H_T}{H_S} \times \frac{1099.6}{1061.6}$$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 284 nm).

Column: A stainless steel column about 4 mm in inside diameter and 15 to 30 cm in length, packed with octadecylsilanized silica gel (5 to 10 μL in particle diameter).

Column temperature: Room temperature.

Mobile phase: A mixture of methanol, water and acetic acid (100) (97:2:1).

Flow rate: Adjust the flow rate so that the retention time of tocopherol succinate is about 8 minutes.

Selection of column: Dissolve 0.05 g each of tocopherol succinate and tocopherol in 50 mL of a mixture of ethanol (99.5) and diluted acetic acid (100) (1 in 5) (9:1). Proceed with 20 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of tocopherol succinate and tocopherol in this order with the resolution between these peaks being not less than 2.0.

System repeatability: Repeat the test five times with the standard solution under the above operating conditions: the relative standard deviation of the peak height of tocopherol succinate is not more than 0.8%.

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Tocopherol Nicotinate

Vitamin E Nicotinate

dl-α-Tocopherol Nicotinate

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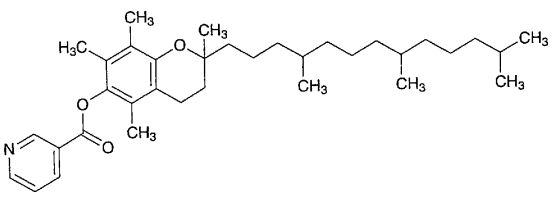


$C_{35}H_{53}NO_3$: 535.80

2,5,7,8-Tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl nicotinate [*51898-34-1*]

Tocopherol Nicotinate contains not less than 96.0% of nicotinic acid *dl*-α-tocopherol ($C_{35}H_{53}NO_3$).

Description Tocopherol Nicotinate occurs as a yellow to orange-yellow liquid or solid.

It is freely soluble in ethanol (99.5), and practically insoluble in water.

A solution of Tocopherol Nicotinate in ethanol (99.5) (1 in 10) shows no optical rotation.

It is affected by light.

Identification **(1)** Determine the absorption spectrum of a solution of Tocopherol Nicotinate in ethanol (99.5) (1 in 20,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Tocopherol Nicotinate Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared spectrum of Tocopherol Nicotinate, if necessary melt by warming, as directed in the liquid film method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Tocopherol Nicotinate Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

Purity **(1)** Heavy metals—Proceed with 1.0 g of Tocopherol Nicotinate according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(2) Arsenic—Prepare the test solution with 1.0 g of Tocopherol Nicotinate according to Method 4, and perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—Dissolve 0.05 g of Tocopherol Nicotinate in 50 mL of ethanol (99.5), and use this solution as the sample solution. Pipet 7 mL of this solution, add ethanol (99.5) to make exactly 200 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of both solutions by the automatic integration method: the total area of the peaks other than tocopherol nicotinate from the sample solution is not larger than the peak area of tocopherol nicotinate from the standard solution, and the area of a peak which has a retention time 0.8 to 0.9 times that of tocopherol nicotinate from the sample solution is not larger than 4/7 of the peak area of tocopherol nicotinate from the standard solution.

Operating conditions—

Detector, column, and column temperature: Proceed as directed in the operating conditions in the Assay.

Mobile phase: A mixture of methanol and water (19:1).

Flow rate: Adjust the flow rate so that the retention time of tocopherol nicotinate is about 20 minutes.

Time span of measurement: About 1.5 times as long as the retention time of tocopherol nicotinate after the solvent peak.

System suitability—

Test for required detection: To exactly 1 mL of the sample solution add ethanol (99.5) to make exactly 100 mL, and use this solution as the test solution for system suitability. Pipet 1 mL of the test solution for system suitability, add ethanol (99.5) to make exactly 10 mL. Confirm that the peak

area of tocopherol nicotinate obtained from 10 μL of this solution is equivalent to 7 to 13% of that of tocopherol nicotinate obtained from 10 μL of the test solution for system suitability.

System performance: Dissolve 0.05 g of Tocopherol Nicotinate and 0.25 g of tocopherol in 100 mL of ethanol (99.5). When the procedure is run with 10 μL of this solution under the above operating conditions, tocopherol and tocopherol nicotinate are eluted in this order with the resolution between these peaks being not less than 8.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of tocopherol nicotinate is not more than 2.0%.

Assay Weigh accurately about 0.05 g each of Tocopherol Nicotinate and Tocopherol Nicotinate Reference Standard, dissolve each in ethanol (99.5) to make exactly 50 mL, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with exactly 5 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and determine peak areas, A_T and A_S, of tocopherol nicotinate of these solutions.

$$\text{Amount (mg) of } C_{35}H_{53}NO_3 = \text{amount (mg) of Tocopherol Nicotinate Reference Standard} \times \frac{A_T}{A_S}$$

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 264 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 35°C.

Mobile phase: Methanol

Flow rate: Adjust the flow rate so that the retention time of tocopherol nicotinate is about 10 minutes.

System suitability—

System performance: Dissolve 0.05 g of Tocopherol Nicotinate and 0.25 g of tocopherol in 100 mL of ethanol (99.5). When the procedure is run with 5 μL of this solution under the above operating conditions, tocopherol and tocopherol nicotinate are eluted in this order with the resolution between these peaks being not less than 3.

System repeatability: When the test is repeated 6 times with 5 μL of the standard solution under the above operating conditions: the relative standard deviation of the peak areas of tocopherol nicotinate is not more than 0.8%

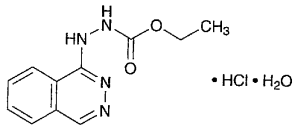
Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Todralazine Hydrochloride

Ecarazine Hydrochloride

塩酸トドララジン



$C_{11}H_{12}N_4O_2.HCl.H_2O$: 286.71

Ethyl 2-(phthalazin-1-yl)hydrazinecarboxylate monohydrochloride monohydrate

[*3778-76-5*, anhydride]

Todralazine Hydrochloride contains not less than 98.5% of $C_{11}H_{12}N_4O_2.HCl$ (mol. wt.: 268.70), calculated on the anhydrous basis.

Description Todralazine Hydrochloride occurs as white crystals or crystalline powder. It has a slight, characteristic odor, and has a bitter taste.

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

The pH of a solution of Todralazine Hydrochloride (1 in 200) is between 3.0 and 4.0.

Identification (1) To 2 mL of a solution of Todralazine Hydrochloride (1 in 200) add 5 mL of silver nitrate-ammonia TS: the solution becomes turbid, and a black precipitate is formed.

(2) Determine the absorption spectrum of a solution of Todralazine Hydrochloride in 0.1 mol/L hydrochloric acid TS (3 in 100,000) 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 Todralazine Hydrochloride as directed in the potassium chloride 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 Todralazine Hydrochloride (1 in 50) responds to the Qualitative Tests (1) for chloride.

Purity (1) Clarity and color of solution—Dissolve 0.30 g of Todralazine Hydrochloride in 10 mL of water: the solution is clear and colorless to pale yellow.

(2) Sulfate—Proceed the test with 2.0 g of Todralazine Hydrochloride. Prepare the control solution with 0.50 mL of 0.005 mol/L sulfuric acid VS (not more than 0.012%).

(3) Heavy metals—Proceed with 1.0 g of Todralazine Hydrochloride according to Method 2, and perform the test.

Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(4) Arsenic—Prepare the test solution with 1.0 g of Todralazine Hydrochloride according to Method 1, and perform the test using Apparatus B (not more than 2 ppm).

(5) Related substances—Dissolve 0.050 g of Todralazine