tained from the sample solution show, respectively, the same color and the same *R*f value as the corresponding spot from the standard solution.

(4) A solution of Protirelin Tartrate (1 in 40) responds to the Qualitative Tests for tartrate.

Optical rotation $[\alpha]_D^{20}$: −50.0 – −53.0° (0.5 g calculated on the anhydrous basis, water, 25 mL, 100 mm).

pH Dissolve 1.0 g of Protirelin Tartrate in 100 mL of water: the pH of this solution is between 3.0 and 4.0.

Purity **(1)** Clarity and color of solution—Dissolve 0.10 g of Protirelin Tartrate in 10 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 1.0 g of Protirelin Tartrate 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).

(3) Arsenic—Take 1.0 g of Protirelin Tartrate in a porcelain crucible. Add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 10), ignite the ethanol, and heat gradually to incinerate. If a carbonized material still remains in this method, moisten with a small quantity of nitric acid, and ignite to incinerate. After cooling, add 10 mL of dilute hydrochloric acid, heat on a water bath to dissolve the residue, use this solution as the test solution, and perform the test using Apparatus B (not more than 2 ppm).

(4) Other peptides and free amino acids—Dissolve 0.60 g of Protirelin Tartrate in 10 mL of water, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add water to make exactly 200 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate (1) of silica gel for thin-layer chromatography. Spot 5 μL of the sample solution on a plate (2) of silica gel for thin-layer chromatography. Develop the plates with a mixture of chloroform, methanol and ammonia solution (28) (6:4:1) to a distance of about 10 cm, and dry at 100°C for 30 minutes. Spray evenly a mixture of a solution of sulfanilic acid in 1 mol/L hydrochloric acid TS (1 in 200) and a solution of sodium nitrite (1 in 20) (1:1) on the plate (1), and air-dry the plate. Then, spray evenly a solution of sodium carbonate decahydrate (1 in 10) on the plate: the spots other than the principal spot from the sample solution are not more intense than those from the standard solution in color. On the other hand, spray evenly a solution of ninhydrin in acetone (1 in 50) on the plate (2), and dry at 80°C for 5 minutes: no colored spot is obtained.

Water Not more than 4.5% (0.2 g, direct titration).

Residue on ignition Not more than 0.20% (0.5 g).

Assay Weigh accurately about 0.5 g of Protirelin Tartrate, dissolve in 80 mL of acetic acid (100) by warming, cool, 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
= 51.25 mg of $C_{16}H_{22}N_6O_4.C_4H_6O_6$

Containers and storage Containers—Well-closed containers.

Pyrantel Pamoate

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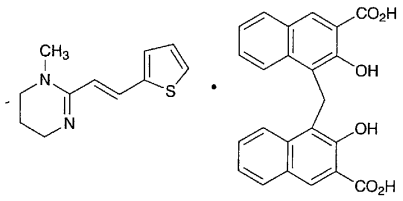


$C_{11}H_{14}N_2S.C_{23}H_{16}O_6$: 594.68
(*E*)-1,4,5,6-Tetrahydro-1-methyl-2-[(*E*)-2-(thien-2-yl)vinyl]pyrimidine mono[4,4′-methylenebis(3-hydroxy-2-naphthoate)] (1/1) [*22204-24-6*]

Pyrantel Pamoate, when dried, contains not less than 98.0% of $C_{11}H_{14}N_2S.C_{23}H_{16}O_6$.

Description Pyrantel Pamoate occurs as a light yellow to yellow, crystalline powder. It is odorless and tasteless.

It is sparingly soluble in *N,N*-dimethylformamide, very slightly soluble in methanol and in ethanol (95), and practically insoluble in water, in ethyl acetate and in diethyl ether.

Melting point: 256 – 264°C (with decomposition).

Identification **(1)** To 0.05 g of Pyrantel Pamoate add 10 mL of methanol and 1 mL of a mixture of hydrochloric acid and methanol (1:1), and shake vigorously: a yellow precipitate is produced. Filter the solution, and use the filtrate as the sample solution. Use the precipitate for the test (2). To 0.5 mL of the sample solution add 1 mL of a solution of 2,3-indolinedione in sulfuric acid (1 in 1000): a red color develops.

(2) Collect the precipitate obtained in the test (1), wash with methanol, and dry at 105°C for 1 hour. To 0.01 g of the dried precipitate add 10 mL of methanol, shake well, and filter. To 5 mL of the filtrate add 1 drop of iron (III) chloride TS: a green color develops.

(3) Dissolve 0.1 g of Pyrantel Pamoate in 50 mL of N,N-dimethylformamide, and add methanol to make 200 mL. To 2 mL of the solution add a solution of hydrochloric acid in methanol (9 in 1000) to make 100 mL. Determine the absorption spectrum of the solution 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.

(4) Determine the infrared absorption spectrum of Pyrantel Pamoate, 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.

Purity **(1)** Chloride—To 1.0 g of Pyrantel Pamoate add 10 mL of dilute nitric acid and 40 mL of water, and heat on a water bath with shaking for 5 minutes. After cooling, add water to make 50 mL, and filter. To 20 mL of the filtrate add 2 mL of dilute nitric acid and water to make 50 mL. Proceed the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.036%).

(2) Sulfate—To 0.75 g of Pyrantel Pamoate add 5 mL of dilute hydrochloric acid and water to make 100 mL, and

heat on a water bath for 5 minutes with shaking. After cooling, add water to make 100 mL, and filter. To 20 mL of the filtrate add water to make 50 mL. Proceed the test using this solution as the test solution. Prepare the control solution with 0.45 mL of 0.005 mol/L sulfuric acid VS (not more than 0.144%).

(3) Heavy metals—Proceed with 1.0 g of Pyrantel Pamoate according to Method 2, and perform the test. Prepare the control solution with 3.0 mL of Standard Lead Solution (not more than 30 ppm).

(4) Arsenic—Prepare the test solution with 1.0 g of Pyrantel Pamoate according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(5) Related substances—The procedure should be performed under protection from direct sunlight in light-resistant vessels. Dissolve 0.10 g of Pyrantel Pamoate in 10 mL of *N,N*-dimethylformamide, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add *N,N*-dimethylformamide to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate, water and acetic acid (100) (3:1:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the spot of pyrantel and the spot of pamoic acid from the sample solution are not more intense than the spot of pyrantel (*Rf* value: about 0.3) from the standard solution.

Loss on drying Not more than 1.0% (1 g, 105°C, 2 hours).

Residue on ignition Not more than 0.30% (1 g).

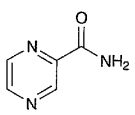
Assay Weigh accurately about 0.5 g of Pyrantel Pamoate, previously dried, add 25 mL of chloroform and 25 mL of sodium hydroxide TS, shake for 15 minutes, and extract. Extract further with two 25-mL portions of chloroform. Filter each extract through 5 g of anhydrous sodium sulfate on a pledget of absorbent cotton. Combine the chloroform extracts, add 30 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (indicator: 2 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 59.47 mg of $C_{11}H_{14}N_2S.C_{23}H_{16}O_6$

Containers and storage Containers—Tight containers.

Pyrazinamide

ピラジナミド



$C_5H_5N_3O$: 123.11
Pyrazine-2-carboxamide [*98-96-4*]

Pyrazinamide, when dried, contains not less than 99.0% of $C_5H_5N_3O$.

Description Pyrazinamide occurs as white crystals or crystalline powder. It is odorless, and has a slightly bitter taste.

It is sparingly soluble in water, slightly soluble in ethanol (95), and very slightly soluble in diethyl ether.

The pH of a solution of Pyrazinamide (1 in 100) is between 5.0 and 7.0.

Identification (1) Dissolve 0.1 g of Pyrazinamide in 10 mL of water, and add 1 mL of iron (II) sulfate TS: an orange-red color develops, and it changes to blue on the addition of 1 mL of sodium hydroxide TS.

(2) Boil gently 0.5 g of Pyrazinamide with 5 mL of sodium hydroxide TS: the gas evolved changes moistened red litmus paper to blue.

(3) Determine the absorption spectrum of a solution of Pyrazinamide in 0.1 mol/L hydrochloric acid TS (1 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.

Melting point 188 - 193°C

Purity (1) Sulfate—Perform the test with 0.6 g of Pyrazinamide. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.032%).

(2) Heavy metals—Proceed with 1.0 g of Pyrazinamide 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).

(3) Arsenic—Prepare the test solution with 1.0 g of Pyrazinamide according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Readily carbonizable substances—Perform the test with 0.20 g of Pyrazinamide: the solution has no more color than Matching Fluid A.

(5) Monocarboxylic acid and dicarboxylic acid—Dissolve 0.10 g of Pyrazinamide in 10 mL of water by warming, and add 0.5 mL of 0.05 mol/L potassium iodate VS and 0.5 g of potassium iodide. Then add 1 mL of chloroform, and shake vigorously: the chloroform layer has no more color than the following control solution.

Control solution: Proceed as directed above, but without Pyrazinamide.

Loss on drying Not more than 0.5% (1 g, in vacuum, silica gel, 4 hours).

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

Assay Weigh accurately about 0.3 g of Pyrazinamide, previously dried, in a 500 mL Kjeldahl flask, add 200 mL of water and 50 mL of a solution of sodium hydroxide (2 in 5), and connect the flask to a distillation apparatus having a spray trap. Dip the lower end of the condenser into 40 mL of a solution of boric acid (1 in 25) contained in an absorption flask. Boil gently for 20 minutes, then boil strongly, and continue the distillation until the distillate measures 200 mL. Cool the Kjeldahl flask, add 75 mL of water, repeat the distillation, and receive 70 mL of the distillate into the same absorption flask. Rinse the lower end of the condenser with a small quantity of water, combine the rinsings with the distillate, and titrate with 0.05 mol/L sulfuric acid VS until the color of the solution changes from green through pale grayish blue to light red-purple (indicator: 3 drops of bromocresol green-methyl red TS). Perform a blank determi-