

Internal standard solution—A solution of ethylefrin hydrochloride (3 in 10,000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column about 4 mm in inside diameter and 15 to 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (about 5 μ m in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 1.0 g of sodium lauryl sulfate in 500 mL of diluted phosphoric acid (1 in 1000), and adjust the pH to 3.0 with sodium hydroxide TS. To 240 mL of this solution add 70 mL of tetrahydrofuran.

Flow rate: Adjust the flow rate so that the retention time of dihydrocodeine is about 9 minutes.

Selection of column: Proceed with 20 μ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of dihydrocodeine and the internal standard in this order with the resolution between these peaks being not less than 4.

Containers and storage Containers—Tight containers.

10% Dihydrocodeine Phosphate Powder

リン酸ジヒドロコデイン散 10%

10% Dihydrocodeine Phosphate Powder contains not less than 9.3% and not more than 10.7% of dihydrocodeine phosphate ($C_{18}H_{23}NO_3 \cdot H_3PO_4$; 399.38).

Method of preparation

Dihydrocodeine Phosphate	100 g
Lactose	a sufficient quantity
To make 1000 g	

Prepare as directed under Powders, with the above ingredients.

Identification Determine the absorption spectrum of a solution of 10% Dihydrocodeine Phosphate Powder (1 in 1000) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 281 nm and 285 nm.

Assay Weigh accurately about 2.5 g of 10% Dihydrocodeine Phosphate Powder, dissolve in water to make exactly 100 mL, then pipet 2 mL of this solution, add exactly 10 mL of the internal standard solution and water to make 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of dihydrocodeine phosphate for assay, separately determined its loss on drying (105°C, 4 hours), dissolve in water to make exactly 100 mL, then pipet 10 mL of this solution, add exactly 10 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 20 μ L 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 dihydrocodeine to that of the internal standard.

Amount (mg) of dihydrocodeine phosphate ($C_{18}H_{23}NO_3 \cdot H_3PO_4$)

= dihydrocodeine phosphate for assay, calculated on the dried basis

$$\times \frac{Q_T}{Q_S} \times 5$$

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Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 1.0 g of sodium lauryl sulfate in 500 mL of diluted phosphoric acid (1 in 1000), and adjust the pH to 3.0 with sodium hydroxide TS. To 240 mL of this solution add 70 mL of tetrahydrofuran.

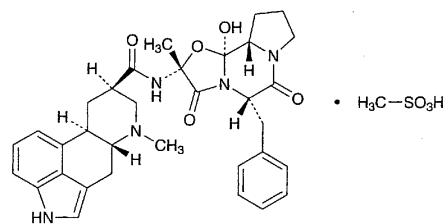
Flow rate: Adjust the flow rate so that the retention time of dihydrocodeine is about 9 minutes.

Selection of column: Proceed with 20 μ L of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of dihydrocodeine and the internal standard in this order with the resolution between these peaks being not less than 4.

Containers and storage Containers—Tight containers.

Dihydroergotamine Mesilate

メシル酸ジヒドロエルゴタミン



$C_{33}H_{37}N_5O_5 \cdot CH_4O_3S$; 679.78

(5'S, 10R)-5'-Benzyl-9,10-dihydro-12'-hydroxy-2'-methylergotaman-3',6',18-trione monomethanesulfonate [6190-39-2]

Dihydroergotamine Mesilate contains not less than 97.0% of $C_{33}H_{37}N_5O_5 \cdot CH_4O_3S$, calculated on the dried basis.

Description Dihydroergotamine Mesilate occurs as a white to yellowish white or grayish white to reddish white powder.

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

It is gradually colored by light.

Melting point: about 214°C (with decomposition).

Identification (1) Dissolve 1 mg of Dihydroergotamine Mesilate in 5 mL of a solution of L-tartaric acid (1 in 100). To 1 mL of this solution add 2 mL of 4-dimethylaminobenzaldehyde-ferric chloride TS, and shake: a blue color develops.

(2) To 0.1 g of Dihydroergotamine Mesilate add 0.4 g of sodium hydroxide, stir well, and incinerate by gradual ignition. After cooling, add 10 mL of water to the residue, heat to boiling, cool, and filter. To the filtrate add 0.5 mL of hydrochloric acid: the solution responds to the Qualitative Tests for sulfate. Separately, to 0.1 g of Dihydroergotamine Mesilate add 5 mL of dilute hydrochloric acid, shake for 5 minutes, filter, and to the filtrate add 1 mL of barium chloride TS: the solution is clear.

(3) Determine the absorption spectrum of a solution of Dihydroergotamine Mesilate in methanol (1 in 20,000) 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.

(4) Determine the infrared absorption spectrum of Dihydroergotamine Mesilate, 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.

Optical rotation $[\alpha]_D^{20}$: $-16.7 - -22.7^\circ$ [0.5 g, calculated on the dried basis, a mixture of ethanol (99.5), chloroform and ammonia solution (28) (10:10:1), 20 mL, 100 mm].

pH Dissolve 0.05 g of Dihydroergotamine Mesilate in 50 mL of water: the pH of this solution is between 4.4 and 5.4.

Purity (1) Clarity and color of solution—Dissolve 0.10 g of Dihydroergotamine Mesilate in 0.1 mL of a solution of methanesulfonic acid (7 in 100) and 50 mL of water: the solution is clear, and has no more color than the following control solutions [1] or [2].

Control solution [1]: Pipet 0.6 mL of Ferric Chloride Stock CS and 0.15 mL of Cobaltous Chloride Stock CS, mix, and add diluted hydrochloric acid (1 in 40) to make exactly 100 mL.

Control solution [2]: Pipet 0.6 mL of Ferric Chloride Stock CS, 0.25 mL of Cobaltous Chloride Stock CS and 0.1 mL of copper (II) sulfate CS, mix, and add diluted hydrochloric acid (1 in 40) to make exactly 100 mL.

(2) Related substances—Conduct this procedure without exposure to daylight, using light-resistant vessels. Dissolve 0.10 g of Dihydroergotamine Mesilate in 5 mL of a mixture of chloroform and methanol (9:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of chloroform and methanol (9:1) to make exactly 200 mL, and use this solution as the standard solution (1). Pipet 10 mL of the standard solution (1), add a mixture of chloroform and methanol (9:1) to make exactly 25 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 5 μ L each of the sample solution and the standard solutions (1) and (2) on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of dichloromethane, ethyl acetate, methanol and ammonia solution (28) (50:50:6:1) to a distance of about 15 cm, and dry the plate with cold wind within 1 minute. Develop the plate again immediately with a freshly

prepared mixture of dichloromethane, ethyl acetate, methanol and ammonia solution (28) (50:50:6:1) to a distance of about 15 cm, and air-dry the plate. Spray evenly 4-dimethylaminobenzaldehyde TS for spraying on the plate, and dry the plate with warm wind: the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution (1), and the spots, which are more intense than the spot from the standard solution (2), are not more than two.

Loss on drying Not more than 4.0% (0.5 g, in vacuum at a pressure not exceeding 0.67 kPa, 100°C, 6 hours).

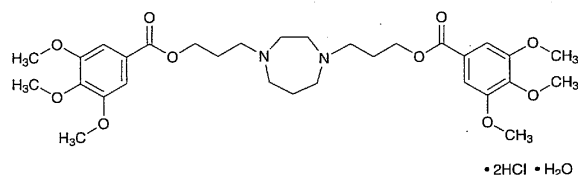
Assay Weigh accurately about 0.2 g of Dihydroergotamine Mesilate, dissolve in 170 mL of a mixture of acetic anhydride and acetic acid (100) (10:1), and titrate with 0.02 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.02 mol/L perchloric acid VS
= 13.596 mg of $C_{33}H_{37}N_5O_5 \cdot CH_4O_3$

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

Dilazep Hydrochloride

塩酸ジラゼプ



$C_{31}H_{44}N_2O_{10} \cdot 2HCl \cdot H_2O$: 695.63
3,3'-(1,4-Diazepane-1,4-diyl)dipropyl bis(3,4,5-trimethoxybenzoate) dihydrochloride monohydrate [20153-98-4, anhydride]

Dilazep Hydrochloride contains not less than 98.0% of $C_{31}H_{44}N_2O_{10} \cdot 2HCl$ (mol. wt.: 677.62), calculated on the dried basis.

Description Dilazep Hydrochloride occurs as a white, crystalline powder. It is odorless.

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

Melting point: 200 – 204°C Immerse the sample in a bath of 110°C, and raise the temperature at the rate of about 3°C per minute from 140°C to 150°C, about 10°C per minute from 160°C to 195°C and about 1°C per minute from 195°C.

Identification (1) To 1 mL of a solution of Dilazep Hydrochloride (1 in 100) add 0.1 mL of a solution of hydroxylammonium chloride (1 in 10) and 0.1 mL of 8 mol/L potassium hydroxide TS, and warm in a water bath of 70°C for 10 minutes. After cooling, add 0.5 mL of dilute hydrochloric acid and 0.1 mL of iron (III) chloride TS: a purple color develops.