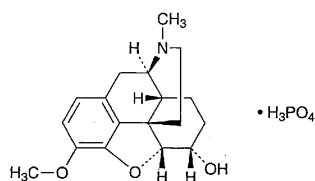


Dihydrocodeine Phosphate

リン酸ジヒドロコデイン



$C_{18}H_{23}NO_3 \cdot H_3PO_4$: 399.38

(5*R*,6*S*)-4,5-Epoxy-3-methoxy-17-methylmorphinan-6-ol monophosphate [24204-13-5]

Dihydrocodeine Phosphate contains not less than 98.0% of $C_{18}H_{23}NO_3 \cdot H_3PO_4$, calculated on the dried basis.

Description Dihydrocodeine Phosphate occurs as a white to yellowish white, crystalline powder.

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

The pH of a solution of Dihydrocodeine Phosphate (1 in 10) is between 3.0 and 5.0.

It is affected by light.

Identification (1) Determine the absorption spectrum of a solution of Dihydrocodeine Phosphate (1 in 10,000) 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.

(2) Determine the infrared spectrum of Dihydrocodeine Phosphate, 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.

(3) A solution of Dihydrocodeine Phosphate (1 in 20) responds to the Qualitative Test (1) for phosphate.

Purity (1) Chloride—Perform the test with 0.5 g of Dihydrocodeine Phosphate. Prepare the control solution with 0.30 mL of 0.01 mol/L hydrochloric acid (not more than 0.021%).

(2) **Sulfate**—Perform the test with 0.20 g of Dihydrocodeine Phosphate. Prepare the control solution with 1.0 mL of 0.005 mol/L sulfuric acid (not more than 0.240%).

(3) **Related substances**—Dissolve 0.20 g of Dihydrocodeine Phosphate in 10 mL of diluted ethanol (95) (1 in 2), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add diluted ethanol (95) (1 in 2) to make exactly 50 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μ L of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-chromatography. Develop the plate with a mixture of ethanol (99.5), toluene, acetone and ammonia solution (28) (14:14:7:1) to a distance of about 15 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the

principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying Not more than 1.0% (0.5 g, 105°C, 4 hours).

Assay Weigh accurately about 0.5 g of Dihydrocodeine Phosphate, dissolve in 70 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from purple through blue to greenish blue (indicator: 3 drops of crystal violet TS). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 39.938 mg of $C_{18}H_{23}NO_3 \cdot H_3PO_4$

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

1% Dihydrocodeine Phosphate Powder

リン酸ジヒドロコデイン散 1%

1% Dihydrocodeine Phosphate Powder contains not less than 0.90% and not more than 1.10% 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 1% Dihydrocodeine Phosphate Powder (1 in 100) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 281 nm and 285 nm.

Assay Weigh accurately about 5 g of 1% Dihydrocodeine Phosphate Powder, 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 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.

$$\begin{aligned} & \text{Amount (mg) of dihydrocodeine phosphate} \\ & (C_{18}H_{23}NO_3 \cdot H_3PO_4) \\ & = \text{amount (mg) of dihydrocodeine phosphate} \\ & \text{for assay, calculated on the dried basis} \\ & \times \frac{Q_T}{Q_S} \end{aligned}$$