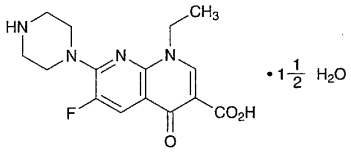
Enoxacin

エノキサシン



$C_{15}H_{17}FN_4O_3.1½H_2O$: 347.34
1-Ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(piperazin-1-yl)-1,8-naphthyridine-3-carboxylic acid sesquihydrate
[*84294-96-2*]

Enoxacin, when dried, contains not less than 98.5% of $C_{15}H_{17}FN_4O_3$ (mol. wt.: 320.32).

Description Enoxacin occurs as white to pale yellow-brown crystals or crystalline powder.

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

It dissolves in dilute sodium hydroxide TS.

It is gradually colored by light.

Identification (1) Place 0.02 g of Enoxacin and 0.05 g of sodium in a test tube, and heat gradually to ignition with precaution. After cooling, add 0.5 mL of methanol and then 5 mL of water, and heat to boiling. To this solution add 2 mL of dilute acetic acid, and filter: the filtrate responds to the Qualitative Tests (2) for fluoride.

(2) Dissolve 0.05 g of Enoxacin in dilute sodium hydroxide TS to make 100 mL. To 1 mL of the solution add water 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.

(3) Determine the infrared absorption spectrum of Enoxacin 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.

Melting point 225 - 229°C (after drying).

Purity (1) Sulfate—Dissolve 1.0 g of Enoxacin in 50 mL of dilute sodium hydroxide TS, shake with 10 mL of dilute hydrochloric acid, and centrifuge. Filter the supernatant liquid, and to 30 mL of the filtrate add water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.50 mL of 0.005 mol/L sulfuric acid VS add 25 mL of dilute sodium hydroxide TS, 5 mL of dilute hydrochloric acid TS and water to make 50 mL (not more than 0.048%).

(2) Heavy metals—Proceed with 1.0 g of Enoxacin 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 Enoxacin according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.050 g of Enoxacin in 25 mL of a mixture of chloroform and methanol (7:3), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of chloroform and methanol (7:3) 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 of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of 1-butanol, 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 principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying 7.0 - 9.0% (1 g, 105°C, 3 hours).

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

Assay Weigh accurately about 0.3 g of Enoxacin, previously dried, dissolve in 30 mL of acetic acid (100), 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
= 32.032 mg of $C_{15}H_{17}FN_4O_3$

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

Ephedrine Hydrochloride

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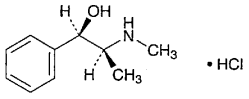

$C_{10}H_{15}NO.HCl$: 201.69
(1*R*,2*S*)-2-Methylamino-1-phenylpropan-1-ol monohydrochloride [*50-98-6*]

Ephedrine Hydrochloride, when dried, contains not less than 99.0% of $C_{10}H_{15}NO.HCl$.

Description Ephedrine Hydrochloride occurs as white crystals or crystalline powder.

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

Identification (1) Determine the absorption spectrum of a solution of Ephedrine Hydrochloride (1 in 2000) 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 absorption spectrum of Ephedrine Hydrochloride, previously dried, 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.

(3) A solution of Ephedrine Hydrochloride (1 in 15) responds to the Qualitative Tests for chloride.

Optical rotation $[\alpha]_D^{20}$: −33.0 - −36.0° (after drying, 1 g, water, 20 mL, 100 mm).

pH Dissolve 1.0 g of Ephedrine Hydrochloride in 20 mL of water: the pH of this solution is between 4.5 and 6.5.

Melting point 218 - 222°C

Purity (1) Clarity and color of solution—Dissolve 0.5 g of Ephedrine Hydrochloride in 10 mL of water: the solution is clear and colorless.

(2) Sulfate—Dissolve 0.05 g of Ephedrine Hydrochloride in 40 mL of water, add 1 mL of dilute hydrochloric acid and 1 mL of barium chloride TS, and allow to stand for 10 minutes: no turbidity is produced.

(3) Heavy metals—Proceed with 1.0 g of Ephedrine Hydrochloride according to Method 2, and perform the test. Prepare the control solution with 1.0 mL of Standard Lead Solution (not more than 10 ppm).

(4) Related substances—Dissolve 0.05 g of Ephedrine Hydrochloride in 50 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 100 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, and calculate the areas of each peak by the automatic integration method: the total area of the peaks other than ephedrine from the sample solution is not larger than the peak area of ephedrine from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 210 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 45°C.

Mobile phase: A mixture of a solution of sodium lauryl sulfate (1 in 128), acetonitrile and phosphoric acid (640:360:1).

Flow rate: Adjust the flow rate so that the retention time of ephedrine is about 14 minutes.

Time span of measurement: About 3 times as long as the retention time of ephedrine after the solvent peak.

System suitability—

Test for required detectability: To exactly 1 mL of the standard solution add the mobile phase to make exactly 20 mL. Confirm that the peak area of ephedrine obtained from 10 μL of this solution is equivalent to 4 to 6% of that from the standard solution.

System performance: Dissolve 1 mg of ephedrine hydrochloride for assay and 4 mg of atropine sulfate in 100 mL of diluted methanol (1 in 2). When the procedure is run with 10 μL of this solution under the above operating conditions, ephedrine and atropine are eluted in this order with the resolution between these peaks being not less than 1.5.

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 ephedrine is not more than 2.0%.

Loss on drying Not more than 0.5% (1 g, 105°C, 3 hours).

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

Assay Weigh accurately about 0.4 g of Ephedrine Hydrochloride, previously dried, and dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3) 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
= 20.170 mg of $C_{10}H_{15}NO.HCl$

Containers and storage Containers—Well-closed containers.

Ephedrine Hydrochloride Injection

塩酸エフェドリン注射液

Ephedrine Hydrochloride Injection is aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of ephedrine hydrochloride ($C_{10}H_{15}NO.HCl$: 201.69).

Method of preparation Prepare as directed under Injections, with Ephedrine Hydrochloride.

Description Ephedrine Hydrochloride Injection is a clear, colorless liquid.

pH: 4.5 - 6.5

Identification To a volume of Ephedrine Hydrochloride Injection, equivalent to 0.05 g of Ephedrine Hydrochloride according to the labeled amount, add water to make 100 mL, and determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 249 nm and 253 nm, between 255 nm and 259 nm, and between 261 nm and 265 nm.

Bacterial endotoxins Less than 7.5 EU/mg.

Assay To an exact volume of Ephedrine Hydrochloride Injection, equivalent to about 0.04 g of ephedrine hydrochloride ($C_{10}H_{15}NO.HCl$) according to the labeled amount, add exactly 10 mL of the internal standard solution and water to make 200 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.04 g of ephedrine hydrochloride for assay, previously dried at 105°C for 3 hours, add exactly 10 mL of the internal standard solution to dissolve, add water to make 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, and calculate the ratios, Q_T and Q_S, of the peak area of ephedrine to that of the internal standard of each solution.

Amount (mg) of ephedrine hydrochloride ($C_{10}H_{15}NO.HCl$)
= amount (mg) of ephedrine hydrochloride for assay
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of etilefrine hydrochloride (1 in 500).