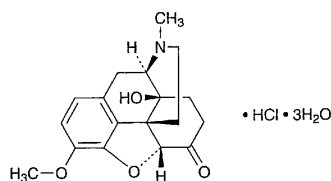


Oxycodone Hydrochloride

塩酸オキシコドン



$C_{18}H_{21}NO_4 \cdot HCl \cdot 3H_2O$: 405.87
(5*R*)-4,5-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one monohydrochloride trihydrate
[124-90-3, anhydride]

Oxycodone Hydrochloride contains not less than 98.0% of $C_{18}H_{21}NO_4 \cdot HCl$ (mol. wt.: 351.83), calculated on the anhydrous basis.

Description Oxycodone Hydrochloride occurs as a white, crystalline powder.

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

The pH of a solution dissolved 1.0 g of Oxycodone Hydrochloride in 10 mL of water is between 3.8 and 5.8.

It is affected by light.

Identification (1) Determine the absorption spectrum of a solution of Oxycodone Hydrochloride (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 absorption spectrum of Oxycodone Hydrochloride 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 Oxycodone Hydrochloride (1 in 50) responds to the Qualitative Tests (2) for chloride.

Optical rotation $[\alpha]_D^{20}$: $-140 - -149^\circ$ (0.5 g, calculated on the anhydrous basis, water, 25 mL, 100 mm).

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

(2) Morphine—Dissolve 0.010 g of Oxycodone Hydrochloride in 1 mL of water, add 5 mL of 1-nitroso-2-naphthole TS and 2 mL of a solution of potassium nitrate (1 in 10), and warm at 40°C for 2 minutes. To this solution add 1 mL of a solution of sodium nitrite (1 in 5000), and warm at 40°C for 5 minutes. After cooling, add 10 mL of chloroform, shake, centrifuge, and separate the water layer: the color of the solution is not more intense than a pale red.

(3) Codeine—Dissolve 0.010 g of Oxycodone Hydrochloride in 5 mL of sulfuric acid, add 1 drop of iron (III) chloride TS, and warm: no blue color is produced. Add 1 drop of nitric acid: no red color develops.

(4) Thebaine—Dissolve 0.10 g of Oxycodone Hydrochloride

in 2 mL of diluted hydrochloric acid (1 in 10), and heat the solution in a water bath for 25 minutes. After cooling, add 0.5 mL of 4-aminoantipyrine hydrochloride TS and 0.5 mL of a solution of potassium hexacyanoferrate (III) (1 in 100), and shake. Then shake the solution with 2 mL of ammonia TS and 3 mL of chloroform: no red color develops in the chloroform layer.

Water 12 – 15% (0.2 g, direct titration).

Residue on ignition Not more than 0.1% (0.5 g).

Assay Weigh accurately about 0.5 g of Oxycodone Hydrochloride, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), 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
= 35.183 mg of $C_{18}H_{21}NO_4 \cdot HCl$

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

Oxydol

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Oxydol contains not less than 2.5 w/v% and not more than 3.5 w/v% of hydrogen peroxide (H_2O_2 : 34.01). It contains suitable stabilizers.

Description Oxydol occurs as a clear, colorless liquid. It is odorless or has an odor resembling that of ozone.

It gradually decomposes upon standing or upon vigorous agitation.

It rapidly decomposes when in contact with oxidizing substances as well as reducing substances.

It, when alkalinized, decomposes with effervescence.

It is affected by light.

pH: 3.0 – 5.0

Specific gravity d_{20}^{20} : about 1.01

Identification 1 mL of Oxydol responds to the Qualitative Tests for peroxide.

Purity (1) Acid—To 25.0 mL of Oxydol add 2 drops of phenolphthalein TS and 2.5 mL of 0.1 mol/L sodium hydroxide VS: a red color develops.

(2) Heavy metals—To 5.0 mL of Oxydol add 20 mL of water and 2 mL of ammonia TS, evaporate on a water bath to dryness, dissolve the residue in 2 mL of dilute acetic acid by heating, add water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 2 mL of dilute acetic acid, 2.5 mL of Standard Lead Solution and water to make 50 mL (not more than 5 ppm).

(3) Arsenic—To 1.0 mL of Oxydol add 1 mL of ammonia TS, evaporate on a water bath to dryness, take the residue, prepare the test solution according to Method 1, and perform the test using Apparatus B (not more than 2 ppm).

(4) Organic stabilizer—Extract 100 mL of Oxydol with 50-mL, 25-mL and 25-mL portions of a mixture of chlo-

roform and diethyl ether (3:2) successively, combine the extracts in a tared vessel, and evaporate the combined extract on a water bath. Dry the residue over silica gel to constant mass: the mass of the residue is not more than 0.050 g.

(5) Nonvolatile residue—Evaporate 20.0 mL of Oxydol on a water bath to dryness, and dry the residue at 105°C for 1 hour: the mass of the residue is not more than 0.020 g.

Assay Pipet 1.0 mL of Oxydol, transfer it to a flask containing 10 mL of water and 10 mL of dilute sulfuric acid, and titrate with 0.02 mol/L potassium permanganate VS.

Each mL of 0.02 mol/L potassium permanganate VS = 1.7007 mg of H₂O₂

Containers and storage Containers—Tight containers.

Storage—Light-resistant, and not exceeding 30°C.

Oxygen

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O₂: 32.00

Oxygen contains not less than 99.5 v/v% of O₂.

Description Oxygen is a colorless gas, and is odorless.

1 mL of Oxygen dissolves in 32 mL of water, and in 7 mL of ethanol (95) at 20°C and at a pressure of 101.3 kPa.

1000 mL of Oxygen at 0°C and at a pressure of 101.3 kPa weighs about 1.429 g.

Identification (1) Put a glowing splinter of wood into Oxygen: it bursts into flame immediately.

(2) Transfer 1 mL each of Oxygen and oxygen directly from metal cylinders with a pressure-reducing valve to gas-measuring tubes or syringes for gas chromatography, using a polyvinyl chloride induction tube. Perform the test with these gases as directed under the Gas Chromatography according to the conditions of Purity (2): the retention time of principal peak from Oxygen coincides with that of oxygen.

Purity Keep the containers of Oxygen between 18°C and 22°C for not less than 6 hours before carrying out the following tests, and calculate the volume to be used with reference to the gas at 20°C and at 101.3 kPa.

(1) Acid or alkali—To 400 mL of freshly boiled and cooled water add 0.3 mL of methyl red TS and 0.3 mL of bromothymol blue TS, and boil for 5 minutes. Transfer 50 mL of this solution to each of three Nessler tubes marked A, B and C. Add 0.10 mL of 0.01 mol/L hydrochloric acid VS to tube A, 0.20 mL of 0.01 mol/L hydrochloric acid VS to tube B, stopper each of the tubes, and cool. Pass 1000 mL of Oxygen through the solution in tube A for 15 minutes, employing delivery tube with an orifice approximately 1 mm in diameter and extending to within 2 mm of the bottom of the Nessler tube: the color of the solution in tube A is not deeper orange-red than that of the solution in tube B and not deeper yellow-green than that of the solution in tube C.

(2) Carbon dioxide—Pass 1000 mL of Oxygen through 50 mL of barium hydroxide TS in a Nessler tube, in the same manner as directed in (1): any turbidity produced does not exceed that of the following control solution.

Control solution: To 50 mL of barium hydroxide TS in a

Nessler tube add 1 mL of a solution of 0.1 g of sodium hydrogen carbonate in 100 mL of freshly boiled and cooled water.

(3) Oxidizing substances—Transfer 15 mL of potassium iodide-starch TS to each of two Nessler tubes marked A and B, add 1 drop of acetic acid (100) to each of the tubes, mix, and use these as solution A and solution B, respectively. Pass 2000 mL of Oxygen through solution A for 30 minutes in the same manner as directed in (1): the color of solution A is the same as that of the stoppered, untreated solution B.

(4) Chloride—Pour 50 mL of water into each of two Nessler tubes marked A and B, add 0.5 mL of silver nitrate TS to each of the tubes, mix, and use these as solution A and solution B, respectively. Pass 1000 mL of Oxygen through solution A in the same manner as directed in (1): the turbidity of solution A is the same as that of solution B.

(5) Nitrogen—Introduce 1.0 mL of Oxygen into a gas-measuring tube or syringe for gas chromatography from a metal hermetic container under pressure through a pressure-reducing valve and a directly connected polyvinyl tube. Perform the test as directed under the Gas Chromatography according to the following conditions, and determine the peak area A_T of nitrogen. Introduce 0.50 mL of nitrogen into the gas mixer, draw carrier gas into the mixer to make exactly 100 mL, and allow to mix thoroughly. Perform the test in the same manner with 1.0 mL of this mixture as directed above, and determine the peak area A_S of nitrogen: A_T is not larger than A_S .

Operating conditions—

Detector: A thermal-conductivity detector.

Column: A column about 3 mm in inside diameter and about 3 m in length, packed with 250- to 355- μ m zeolite for gas chromatography (0.5 mm).

Column temperature: A constant temperature of about 50°C.

Carrier gas: Hydrogen or helium.

Flow rate: Adjust the flow rate so that the retention time of nitrogen is about 5 minutes.

Selection of column: Introduce 0.5 mL of nitrogen into a gas mixer, add Oxygen to make 100 mL, and mix well. Proceed with 1.0 mL of the mixture under the above operating conditions. Use a column giving well-resolved peaks of Oxygen and nitrogen in this order.

Assay (1) Apparatus—The apparatus is shown diagrammatically in the accompanying figure. A is a 100-mL gas buret having a two-way stopcock a, b - c, d - e and e - f are graduated in 0.1 mL, and c - d is graduated in 2 mL. A is properly connected with a leveling tube B by a thick rubber tube. Fill ammonium chloride-ammonia TS up to the middle of A and B. Place in the absorption ball g of the gas pipette C a coil of copper wire, not more than 2 mm in diameter, which extends to the uppermost portion of the bulb, add 125 mL of ammonium chloride-ammonia TS, and stopper with a rubber stopper i. Connect C with A using the thick rubber tube.

(2) Procedure—Open a, set B downward and draw the liquid in g to the stopcock opening a. Then close a. Open a to the intake tube h, and fill A and h with ammonium chloride-ammonia TS by lifting B. Close a, connect h with a container of Oxygen, open a, set B downward and measure accurately 100 mL of Oxygen. Open a toward C, and transfer the Oxygen to g by lifting B. Close a, and rock C gently for 5 minutes. Open a, draw the residual gas back into A by set-