

(3) Place 2 g of Cloxazolam in a 200-mL flask, add 50 mL of ethanol (95) and 25 mL of sodium hydroxide TS, and boil under a reflux condenser for 4 hours. After cooling, neutralize with dilute hydrochloric acid, and extract with 30 mL of dichloromethane. Dehydrate with 3 g of anhydrous sodium sulfate, filter, and evaporate the dichloromethane of the filtrate. Dissolve the residue in 5 mL of methanol by heating on a water bath, and cool immediately in an ice bath. Collect the crystals, and dry the crystals in vacuum at 60°C for 1 hour: it melts between 87°C and 91°C.

(4) Determine the absorption spectrum of a solution of Cloxazolam in ethanol (99.5) (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.

(5) Proceed with Cloxazolam as directed under the Flame Coloration Test (2), and perform the test: a green color appears.

Absorbance $E_{1\text{cm}}^{1\%}$ (244 nm): 390 – 410 (after drying, 1 mg, ethanol (99.5), 100 mL).

Purity (1) Chloride—To 1.0 g of Cloxazolam add 50 mL of water, allow to stand for 1 hour with occasional shaking, and filter. To 25 mL of this filtrate add 6 mL of dilute nitric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.20 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.014%).

(2) Heavy metals—Proceed with 1.0 g of Cloxazolam 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—Place 1.0 g of Cloxazolam in a Kjeldahl flask, add 5 mL of sulfuric acid and 5 mL of nitric acid, and heat gently. Repeat the addition of 2 to 3 mL of nitric acid at times, and continue heating until a colorless to light yellow solution is obtained. After cooling, add 15 mL of saturated ammonium oxalate solution, and heat the solution until dense white fumes are evolved, and evaporate to a volume of 2 to 3 mL. After cooling, dilute with water to 10 mL, and perform the test with this solution as the test solution using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.05 g of Cloxazolam in 10 mL of dichloromethane, and use this solution as the sample solution. Pipet 1 mL of this solution, add dichloromethane 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 10 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Immediately after air-drying, develop the plate with a mixture of toluene and acetone (5:1) 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 that from the standard solution.

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 0.5 g of Cloxazolam, previously dried, and dissolve in 50 mL of acetic acid (100). Titrate with 0.1 mol/L perchloric acid VS until the color of

the solution changes from purple through blue to blue-green (indicator: 2 drops of crystal violet TS). Perform a blank determination.

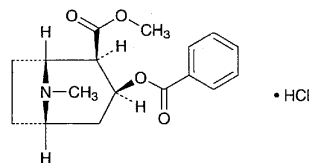
Each mL of 0.1 mol/L perchloric acid VS
= 34.922 mg of $\text{C}_{17}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}_2$

Containers and storage Containers—Tight containers.

Storage—Light-resistant.

Cocaine Hydrochloride

塩酸コカイン



$\text{C}_{17}\text{H}_{21}\text{NO}_4 \cdot \text{HCl}$: 339.81
(1*R*,2*R*,3*S*,5*S*)-2-Methoxycarbonyl-8-methyl-8-azabicyclo[3.2.1]oct-3-yl benzoate monohydrochloride [53-21-4]

Cocaine Hydrochloride, when dried, contains not less than 98.0% of $\text{C}_{17}\text{H}_{21}\text{NO}_4 \cdot \text{HCl}$.

Description Cocaine Hydrochloride occurs as colorless crystals or a white crystalline powder.

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

Identification (1) Determine the absorption spectrum of a solution of Cocaine Hydrochloride in 0.01 mol/L hydrochloric acid TS (1 in 10,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 1: both spectra exhibit similar intensities of absorption at the same wavelengths. Separately, determine the absorption spectrum of a solution of Cocaine Hydrochloride in 0.01 mol/L hydrochloric acid TS (1 in 50,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum 2: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Cocaine Hydrochloride, 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 Cocaine Hydrochloride (1 in 50) responds to the Qualitative Tests (2) for chloride.

Optical rotation $[\alpha]_D^{20}$: -70 – -73° (after drying, 0.5 g, water, 20 mL, 100 mm).

Purity (1) Acid—Dissolve 0.5 g of Cocaine Hydrochloride in 10 mL of water, add 1 drop of methyl red TS, and neutralize with 0.01 mol/L sodium hydroxide VS: the consumed volume is not more than 1.0 mL.

(2) Cinnamyl cocaine—Dissolve 0.10 g of Cocaine Hydrochloride in 5 mL of water, and add 0.3 mL of diluted sulfuric acid (1 in 20) and 0.10 mL of 0.02 mol/L potassium permanganate VS: the red color does not disappear within 30 minutes.

(3) Isoatropyl cocaine—Dissolve 0.10 g of Cocaine Hydrochloride in 30 mL of water in a beaker. Transfer 5 mL of this solution to a test tube, add 1 drop of ammonia TS, and mix. After the precipitate is coagulated, add 10 mL of water, and transfer the mixture to the former beaker, to which 30 mL of water has been added previously. Wash the test tube with 10 mL of water, combine the washings with the mixture in the beaker, add 3 drops of ammonia TS to the combined mixture, and mix gently: a crystalline precipitate is produced. Allow to stand for 1 hour: the supernatant liquid is clear. Loss on drying Not more than 1.0% (1 g, 105°C, 4 hours). Residue on ignition Not more than 0.1% (0.5 g).

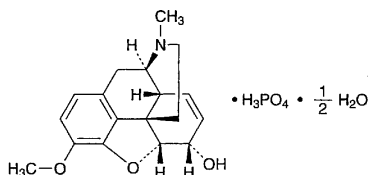
Assay Weigh accurately about 0.5 g of Cocaine Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 33.982 mg of $C_{17}H_{21}NO_4 \cdot HCl$

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

Codeine Phosphate

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$C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot 1/2 H_2O$: 406.37
(5R,6S)-7,8-Didehydro-4,5-epoxy-3-methoxy-17-methylmorphinan-6-ol monophosphate hemihydrate
[41444-62-6]

Codeine Phosphate contains not less than 98.0% of codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4$: 397.36), calculated on the anhydrous basis.

Description Codeine Phosphate occurs as white to yellowish white crystals or crystalline powder.

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

The pH of a solution of Codeine 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 Codeine Phosphate (1 in 10,000) as directed un-

der 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 Codeine Phosphate, previously dried at 105°C for 4 hours, 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 Codeine Phosphate (1 in 20) responds to the Qualitative Tests (1) for phosphate.

Optical rotation $[\alpha]_D^{20}$: $-98 - -102^\circ$ (0.4 g calculated on the anhydrous basis, water, 20 mL, 100 mm).

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

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

(3) Related substances—Dissolve 0.20 g of Codeine Phosphate in 10 mL of a mixture of 0.01 mol/L hydrochloric acid TS and ethanol (99.5) (4:1), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add a mixture of 0.01 mol/L hydrochloric acid TS and ethanol (99.5) (4:1) 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 10 μ L 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 ethanol (99.5), toluene, acetone and ammonia solution (28) (14:14:7:1) 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.

Water 1.5 – 3.0% (0.5 g, direct titration).

Assay Dissolve about 0.5 g of Codeine Phosphate, accurately weighed, 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
= 39.736 mg of $C_{18}H_{21}NO_3 \cdot H_3PO_4$

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

1% Codeine Phosphate Powder

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10% Codeine Phosphate Powder contains not less than 0.90% and not more than 1.10% of codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot 1/2 H_2O$: 406.37).