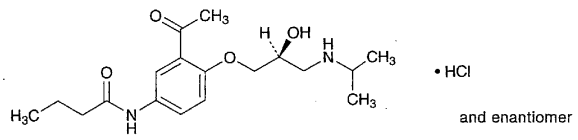
Official Monographs For Part I, JPXIV

Acebutolol Hydrochloride

塩酸アセブトロール



$C_{18}H_{28}N_2O_4.HCl$: 372.89
N-{3-Acetyl-4-[(*RS*)-2-hydroxy-3-(isopropylamino)propyloxy]phenyl}butanamide monohydrochloride [*34381-68-5*]

Acebutolol Hydrochloride, when dried, contains not less than 98.0% and not more than 102.0% of $C_{18}H_{28}N_2O_4.HCl$.

Description Acebutolol Hydrochloride occurs as white to pale yellowish white crystals or crystalline powder.

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

A solution of Acebutolol Hydrochloride (1 in 20) shows no optical rotation.

Identification (1) Determine the absorption spectrum of a solution of Acebutolol Hydrochloride in 0.01 mol/L hydrochloric acid TS (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.

(2) Determine the infrared absorption spectrum of Acebutolol 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 Acebutolol Hydrochloride (1 in 100) responds to the Qualitative Tests for chloride.

Melting point 141 – 145°C

Purity (1) Heavy metals—Proceed with 1.0 g of Acebutolol 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).

(2) Arsenic—Prepare the test solution with 1.0 g of Acebutolol Hydrochloride according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—Dissolve 0.040 g of Acebutolol Hydrochloride in 2 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 25 mL, and pipet 1 mL of this solution, add methanol to make exactly 20 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 for thin-layer chromatography. Develop the plate with the upper layer of a mixture of water, 1-butanol and acetic acid (100) (5:4:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 365 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, 3 hours).

Residue on ignition Not more than 0.20% (1 g).

Assay Weigh accurately about 0.25 g of Acebutolol Hydrochloride, previously dried, dissolve in 20 mL of acetic acid (100), add 80 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

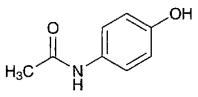
Each mL of 0.1 mol/L perchloric acid VS
= 37.289 mg of $C_{18}H_{28}N_2O_4.HCl$

Containers and storage Containers—Well-closed containers.

Acetaminophen

Paracetamol

アセトアミノフェン



$C_8H_9NO_2$: 151.16
N-(4-Hydroxyphenyl)acetamide [*103-90-2*]

Acetaminophen, when dried, contains not less than 98.0% of $C_8H_9NO_2$.

Description Acetaminophen occurs as white crystals or crystalline powder.

It is freely soluble in methanol and in ethanol (95), sparingly soluble in water, and very slightly,soluble in diethyl ether.

It dissolves in sodium hydroxide TS.

Identification Determine the infrared absorption spectra of Acetaminophen, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of dried Acetaminophen Reference Standard: both spectra exhibit similar intensities of absorption at the same wave numbers.

Melting point 169 - 172°C

Purity **(1)** Chloride—Dissolve 4.0 g of Acetaminophen in 100 mL of water by heating, cool with shaking in ice water, allow to stand until ordinary temperature is attained, add water to make 100 mL, and filter. To 25 mL of the 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 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.014%).

(2) Sulfate—To 25 mL of the filtrate obtained in (1) add 1 mL of dilute hydrochloric acid and water to make 50 mL, and perform the test using this solution as the test solution. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.019%).

(3) Heavy metals—Proceed with 2.0 g of Acetaminophen according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(4) Arsenic—Prepare the test solution with 1.0 g of Acetaminophen according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(5) Related substances—Dissolve 0.050 g of Acetaminophen in 1 mL of methanol, add the mobile phase to make 50 mL, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 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. Determine each peak area of both solutions by the automatic integration method: the total area of all peaks other than the peak area of acetaminophen from the sample solution is not larger than the peak area of acetaminophen from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 225 nm).

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

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

Mobile phase: A mixture of 0.05 mol/L potassium dihydrogenphosphate, pH 4.7 and methanol (4:1)

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

Selection of column: Dissolve 0.01 g each of Acetaminophen and *p*-aminophenol in 1 mL of methanol, add the mobile phase to make 50 mL, to 1 mL of this solution add the mobile phase to make 10 mL. Proceed with 10 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of *p*-aminophenol and acetaminophen in this order with the resolution between these peaks being not less than 7.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of acetaminophen obtained from 10 μL of the standard solution is about 15% of the full scale.

Time span of measurement: About 6 times as long as the retention time of acetaminophen after the solvent peak.

Loss on drying Not more than 0.3% (0.5 g, 105°C, 2 hours).

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

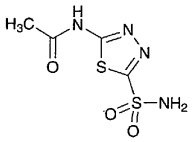
Assay Weigh accurately about 0.02 g each of Acetaminophen and Acetaminophen Reference Standard, previously dried, dissolve in 2 mL of methanol, and add water to make exactly 100 mL. Pipet 3 mL each of these solutions, add water to make exactly 100 mL, and use these solutions as the sample solution and the standard solution, respectively. Determine the absorbances, A_T and A_S, of the sample solution and the standard solution at the wavelength of maximum absorption at about 244 nm as directed under the Ultraviolet-visible Spectrophotometry, using water as the blank.

Amount (mg) of $C_8H_9NO_2$
= amount (mg) of Acetaminophen Reference Standard
$\times \frac{A_T}{A_S}$

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

Acetazolamide

アセタゾラミド



$C_4H_6N_4O_3S_2$: 222.25
N-(5-Sulfamoyl-1,3,4-thiadiazol-2-yl)acetamide [*59-66-5*]

Acetazolamide contains not less than 98.0% and not more than 102.0% of $C_4H_6N_4O_3S_2$, calculated on the dried basis.

Description Acetazolamide occurs as a white to pale yellowish white, crystalline powder. It is odorless, and has a slight bitter taste.

It is slightly soluble in ethanol (95), very slightly soluble in water, and practically insoluble in diethyl ether.

Melting point: about 255°C (with decomposition).

Identification **(1)** To 0.1 g of Acetazolamide add 5 mL of sodium hydroxide TS, then add 5 mL of a solution of 0.1 g of hydroxylammonium chloride and 0.05 g of copper (II) sulfate pentahydrate in 10 mL of water: a light yellow color develops. Then heat this solution for 5 minutes: a deep yel-