Identification (1) Shake 0.5 mL of a solution of Methylbenactyzium Bromide (1 in 100) with 5 mL of phosphate buffer solution, pH 7.0, 2 to 3 drops of bromothymol blue TS and 5 mL of chloroform: a yellow color develops in the chloroform layer.

(2) To about 1 g of Methylbenactyzium Bromide add 5 mL of water and 10 mL of sodium hydroxide TS, allow to stand for 5 minutes, add 5 mL of dilute hydrochloric acid, collect the precipitate, wash well with water, recrystallize from a mixture of water and ethanol (95) (10:3), and dry at 105°C for 1 hour: the crystals melt between 145°C and 150°C. Continue the heating up to about 200°C: a red color develops.

(3) Add 2 mL of dilute nitric acid to 5 mL of a solution of Methylbenactyzium Bromide (1 in 10): the solution responds to the Qualitative Tests (1) for bromide.

Melting point 168 - 172°C

Purity (1) Clarity and color of solution—Dissolve 1.0 g of Methylbenactyzium Bromide in 10 mL of water: the solution is clear and colorless.

(2) Sulfate—Perform the test with 0.5 g of Methylbenactyzium Bromide. Prepare the control solution with 0.40 mL of 0.005 mol/L sulfuric acid VS (not more than 0.038%).

(3) Heavy metals—Proceed with 2.0 g of Methylbenactyzium Bromide according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

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

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

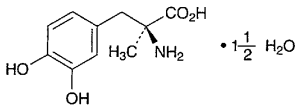
Assay Weigh accurately about 0.5 g of Methylbenactyzium Bromide, previously dried, and dissolve in 80 mL of a mixture of acetic anhydride and acetic acid (100) (4:1). Titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 42.24 mg of $C_{21}H_{28}BrNO_3$

Containers and storage Containers—Tight containers.

Methyldopa

メチルドパ



$C_{10}H_{13}NO_4.1½H_2O$: 238.24
(2*S*)-2-Amino-3-(3,4-dihydroxyphenyl)-2-methylpropanoic acid sesquihydrate [*41372-08-1*]

Methyldopa contains not less than 98.0% of $C_{10}H_{13}NO_4$ (mol.wt.: 211.21), calculated on the anhydrous basis.

Description Methyldopa occurs as a white to pale grayish white, crystalline powder.

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

It dissolves in dilute hydrochloric acid.

Identification (1) To 0.01 g of Methyldopa add 3 drops of ninhydrin TS, and heat in a water bath for 3 minutes: a purple color develops.

(2) Determine the absorption spectrum of a solution of Methyldopa in 0.1 mol/L hydrochloric acid TS (1 in 25,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Methyldopa Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

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

Optical rotation $[\alpha]_D^{20}$: −25 - −28° (calculated on the anhydrous basis, 1 g, aluminum (III) chloride TS, 20 mL, 100 mm).

Purity (1) Acid—Shake 1.0 g of Methyldopa with 100 mL of freshly boiled and cooled water, and add 0.20 mL of 0.1 mol/L sodium hydroxide VS and 2 drops of methyl red TS: a yellow color develops.

(2) Chloride—Perform the test with 0.5 g of Methyldopa. Prepare the control solution with 0.40 mL of 0.01 mol/L hydrochloric acid VS (not more than 0.028%).

(3) Heavy metals—Proceed with 2.0 g of Methyldopa according to Method 2, 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 Methyldopa in 5 mL of dilute hydrochloric acid, and perform the test using Apparatus B (not more than 2 ppm).

(5) 3-*O*-Methylmethyldopa—Dissolve 0.10 g of Methyldopa in methanol to make exactly 10 mL, and use this solution as the sample solution. Separately, dissolve 5 mg of 3-*O*-methylmethyldopa for thin-layer chromatography in methanol 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 20 μL each of the sample solution and the standard solution on a plate of cellulose for thin-layer chromatography. Develop the plate with a mixture of 1-butanol, water and acetic acid (100) (13:5:3) to a distance of about 10 cm, and air-dry the plate. Spray evenly 4-nitroaniline-sodium nitrite TS on the plate, and air-dry the plate, then spray evenly a solution of sodium carbonate decahydrate (1 in 4) on the plate: the spot from the sample solution corresponding to that from the standard solution is not more intense than the spot from the standard solution.

Water 10.0 - 13.0% (0.2 g, direct titration).

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

Assay Weigh accurately about 0.3 g of Methyldopa, dissolve in 80 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 blue-green (indicator: 2 to 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
= 21.122 mg of $C_{10}H_{13}NO_4$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Methyldopa Tablets

メチルドパ錠

Methyldopa Tablets contain not less than 90% and not more than 110% of the labeled amount of methyldopa ($C_{10}H_{13}NO_4$: 211.21).

Method of preparation Prepare as directed under Tablets, with Methyldopa.

Identification **(1)** To a quantity of powdered Methyldopa Tablets, equivalent to 0.1 g of Methyldopa according to the labeled amount, add 10 mL of water, and heat in a water bath for 5 minutes with occasional shaking. After cooling, centrifuge for 5 minutes at 2000 rotations per minute, apply 1 drop of the supernatant solution to a filter paper, and dry with warm air. Place 1 drop of ninhydrin TS over the spot, and heat for 5 minutes at 100°C: a purple color develops.

(2) To 0.5 mL of the supernatant liquid obtained in the Identification (1) add 2 mL of 0.05 mol/L sulfuric acid TS, 2 mL of iron (II) tartrate TS and 4 drops of ammonia TS, and shake well: a deep purple color develops.

(3) To 0.7 mL of the supernatant liquid obtained in the Identification (1) add 0.1 mol/L hydrochloric acid TS to make 20 mL. To 10 mL of this solution add 0.1 mol/L hydrochloric acid TS to make 100 mL, and determine the absorption spectrum of the solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 277 nm and 283 nm.

Dissolution test Perform the test with 1 tablet of Methyldopa Tablets at 50 revolutions per minute according to Method 2 under the Dissolution Test, using 900 mL of water as the test solution. Take 30 mL or more of the dissolved solution 60 minutes after start of the test, and filter through a membrane filter with pore size of not more than 0.8 μm. Discard the first 10 mL of the filtrate, pipet the subsequent V mL, add water to make exactly V' mL so that each mL contains about 25 μg of methyldopa ($C_{10}H_{13}NO_4$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 0.056 g of methyldopa for assay (its loss on drying is determined, separately, at 125°C for 2 hours), and dissolve in water to make exactly 200 mL. Pipet 10 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Determine the absorbances, A_T and A_S, of the sample solution and the standard solution at 280 nm as directed under the Ultraviolet-visible Spectrophotometry.

The dissolution rate of Methyldopa Tablets in 60 minutes is not less than 75%.

Dissolution rate (%) with respect to the labeled amount of methyldopa ($C_{10}H_{13}NO_4$)

$$= W_S \times \frac{A'}{A_S} \times \frac{V'}{V} \times \frac{1}{C} \times 45$$

W_S: Amount (mg) of methyldopa for assay, calculated on the dried basis.

C: Labeled amount (mg) of methyldopa ($C_{10}H_{13}NO_4$) in 1 tablet.

Assay Weigh accurately and powder not less than 20 Methyldopa Tablets. Weigh accurately a portion of the powder, equivalent to about 0.1 g of methyldopa ($C_{10}H_{13}NO_4$), add 50 mL of 0.05 mol/L sulfuric acid TS, shake thoroughly for 15 minutes, add 0.05 mol/L sulfuric acid TS to make exactly 100 mL, and filter through a dry filter paper. Discard the first 20 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.11 g of Methyldopa Reference Standard (previously dry at 125°C for 2 hours, and determine the loss on drying), dissolve in 0.05 mol/L sulfuric acid TS to make exactly 100 mL, and use this solution as the standard solution. Pipet 5 mL each of the sample solution and the standard solution, add exactly 5 mL of iron (II) tartrate TS, and add ammonia-ammonium acetate buffer solution, pH 8.5, to make exactly 100 mL. Perform the test with these solutions as directed under the Ultraviolet-visible Spectrophotometry, using a solution prepared with 5 mL of 0.05 mol/L sulfuric acid TS in the same manner, as the blank. Determine the absorbances, A_T and A_S, of the subsequent solutions of the sample solution and the standard solution at 520 nm, respectively.

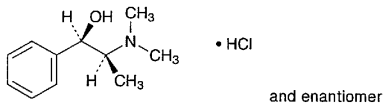
Amount (mg) of methyldopa ($C_{10}H_{13}NO_4$)
= amount (mg) of Methyldopa Reference Standard, calculated on the dried basis

$$\times \frac{A_T}{A_S}$$

Containers and storage Containers—Well-closed containers.

dl-Methylephedrine Hydrochloride

dl-塩酸メチルエフェドリン



and enantiomer

$C_{11}H_{17}NO.HCl$: 215.72
(1*RS*,2*SR*)-2-Dimethylamino-1-phenylpropan-1-ol monohydrochloride [*18760-80-0*]

dl-Methylephedrine Hydrochloride, when dried, contains not less than 99.0% of $C_{11}H_{17}NO.HCl$.

Description *dl*-Methylephedrine Hydrochloride occurs as colorless crystals or a white, crystalline powder. It is odorless, and has a bitter taste.

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