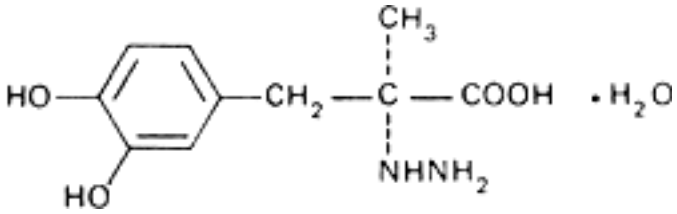
Carbidopa (Carbidopum)

Molecular formula. $C_{10}H_{14}N_2O_4,H_2O$

Relative molecular mass. 244.2

Graphic formula.



Chemical name. (-)-L-α-Hydrazino-3,4-dihydroxy-α-methylhydrocinnamic acid monohydrate; (*S*)-α-hydrazino-3,4-dihydroxy-α-methylbenzenepropanoic acid monohydrate; CAS Reg. No. 38821-49-7 (monohydrate).

Description. A white to creamy white powder; odourless or almost odourless.

Solubility. Slightly soluble in water; very slightly soluble in ethanol (~750 g/l) TS; practically insoluble in ether R.

Category. Antiparkinsonism drug.

Storage. Carbidopa should be kept in a well-closed container, protected from light.

Requirements

Definition. Carbidopa contains not less than 99.0% and not more than 101.0% of $C_{10}H_{14}N_2O_4$, calculated with reference to the anhydrous substance.

Identity tests

A. Carry out the examination as described under 1.7 Spectrophotometry in the infrared region. The infrared absorption spectrum is concordant with the spectrum obtained from carbidopa RS or with the *reference spectrum* of carbidopa.

B. To 5 mg add 1 mL of water, 1 mL of pyridine R, and 5 mg of 4-nitrobenzoyl chloride R, mix and allow to stand for 3 minutes; the solution remains colourless, but after boiling changes to a pale yellow colour. While shaking, add 0.1 mL of sodium carbonate (200 g/l) TS; an orange colour is produced.

Specific optical rotation. Use a 10 mg/mL solution in aluminium chloride TS and calculate with reference to the anhydrous substance; $[\alpha]_D^{20\,°C}$ = -22.5° to -26.5°.

Heavy metals. Use 1.0 g for the preparation of the test solution as described under 2.2.3 Limit test for heavy metals, Procedure 3; determine the heavy metals content according to Method A; not more than 20 µg/g.

Sulfated ash. Not more than 1.0 mg/g.

Water. Determine as described under 2.8 Determination of water by the Karl Fischer method, Method A, using about 0.5 g of the substance; the water content is not less than 69 mg/g and not more than 79 mg/g.

Methyldopa and 3-*O*-Methylcarbidopa. Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography, using a stainless steel column 20 cm long and 4 mm in internal diameter packed with particles of silica gel, 10 µm in diameter, the surface of which has been modified with chemically bonded octylsilyl groups. As the mobile phase, use a mixture of 98 volumes of potassium dihydrogen phosphate (13.6 g/l) TS and 2 volumes of methanol R at a flow rate of 1.5 mL per minute. As detector use an ultraviolet spectrophotometer at a wavelength of about 282 nm, fitted with a low-volume flow cell (10 µl is suitable).

Prepare the following solutions in hydrochloric acid (0.1 mol/l) VS containing (A) 0.050 mg of methyldopa RS, 0.050 mg of (-)-3-(4-hydroxy-3-methoxyphenyl)-2-hydrazino-2-methylalanine RS and 0.10 mg of (-)-3-(4-hydroxy-3-methoxyphenyl)-2-methylalanine RS per mL, the last serving as an internal standard, (B) 10 mg of the test substance per mL, and (C) 10 mg of the test substance and 0.10 mg of the internal standard per mL.

In the chromatogram obtained with solution A the peaks, excluding the solvent peak, are due to (*a*) methyldopa, (*b*) (-)-3-(4-hydroxy-3-methoxyphenyl)-2-methylalanine and (*c*) (-)-3-(4-hydroxy-3-methoxyphenyl)-2-hydrazino-2-methylalanine in order of their emergence. The ratios of the areas of the peaks (*a*) and (*c*) to the area of the peak due to the internal standard are greater than the corresponding ratios in the chromatogram obtained with solution C.

Assay. Dissolve about 0.3 g, accurately weighed, in 25.0 mL of perchloric acid (0.1 mol/l) VS with the aid of a minimum of heat. Titrate the excess perchloric acid with sodium acetate/glacial acetic acid (0.1 mol/l) VS, determining the end-point potentiometrically as described under 2.6 Non-aqueous titration, Method A. Each mL of perchloric acid (0.1 mol/l) VS is equivalent to 22.62 mg of $C_{10}H_{14}N_2O_4$.