

**System repeatability:** When the test is repeated 5 times with 20  $\mu\text{L}$  of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of 1,1'-[3,3'-dithiobis(2-methyl-1-oxopropyl)]-L-dipropylene is not more than 2.0%.

**Loss on drying** Not more than 1.0% (1 g, in vacuum, 80°C, 3 hours).

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

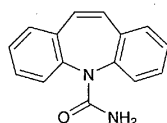
**Assay** Weigh accurately about 0.3 g of Carbamazepine, dissolve in 100 mL of water, add 20 mL of dilute sulfuric acid and 1 g of potassium iodide, and shake. Titrate with 1/60 mol/L potassium iodate VS (indicator: 2 mL of starch TS). Perform a blank determination in the same manner, and make any necessary correction.

Each mL of 1/60 mol/L potassium iodate VS  
= 21.729 mg of  $\text{C}_9\text{H}_{15}\text{NO}_3\text{S}$

**Containers and storage** Containers—Tight containers.

## Carbamazepine

カルバマゼピン



$\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}$ : 236.27  
5*H*-Dibenz[*b,f*]azepine-5-carboxamide [298-46-4]

Carbamazepine, when dried, contains not less than 97.0% and not more than 103.0% of  $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}$ .

**Description** Carbamazepine occurs as a white to slightly yellowish white powder. It is odorless and tasteless at first, and leaves a slightly bitter aftertaste.

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

**Identification (1)** To 0.1 g of Carbamazepine add 2 mL of nitric acid, and heat on a water bath for 3 minutes: an orange-red color is produced.

(2) To 0.1 g of Carbamazepine add 2 mL of sulfuric acid, and heat on a water bath for 3 minutes: a yellow color is produced with a green fluorescence.

(3) Examine Carbamazepine under ultraviolet light: the solution shows an intense blue fluorescence.

(4) Determine the absorption spectrum of the solution obtained in the Assay 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.

**Melting point** 189 – 193°C

**Purity (1)** Clarity and color of solution—Dissolve 1.0 g of Carbamazepine in 10 mL of chloroform: the solution is clear and colorless to pale yellow.

(2) Acid—To 2.0 g of Carbamazepine add exactly 40

mL of water, stir well for 15 minutes, and filter through a glass filter (G3). To 10 mL of this filtrate add 1 drop of phenolphthalein TS and 0.50 mL of 0.01 mol/L sodium hydroxide VS: a red color is produced.

(3) Alkali—To 10 mL of the filtrate obtained in (2) add 1 drop of methyl red TS and 0.50 mL of 0.01 mol/L hydrochloric acid VS: a red color is produced.

(4) Chloride—Dissolve 0.25 g of Carbamazepine in 30 mL of acetone, 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 as follows: to 0.20 mL of 0.01 mol/L hydrochloric acid VS add 30 mL of acetone, 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.028%).

(5) Heavy metals—Proceed with 2.0 g of Carbamazepine 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).

(6) Related substances—Dissolve 0.25 g of Carbamazepine in 10 mL of chloroform, and use this solution as the sample solution. Separately, dissolve 5.0 mg of iminodibenzyl in chloroform 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  $\mu\text{L}$  each of the sample solution and the standard solution on a plate of silica gel for thin-layer chromatography. Develop the plate with a mixture of toluene and methanol (19:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly potassium dichromate-sulfuric acid TS on the plate: the spots other than the principal spot obtained from the sample solution is not more intense than the spot from the standard solution.

**Loss on drying** Not more than 0.5% (1 g, 105°C, 2 hours).

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

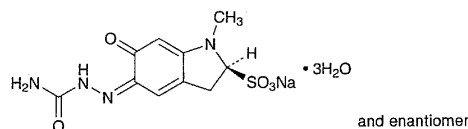
**Assay** Dissolve about 0.05 g of Carbamazepine, previously dried and accurately weighed, in ethanol (95) to make exactly 250 mL. Dilute 5 mL of this solution with ethanol (95) to exactly 100 mL. Perform the test as directed under the Ultraviolet-visible Spectrophotometry, and determine the absorbance  $A$  of this solution at the wavelength of maximum absorption at about 285 nm.

$$\text{Amount (mg) of } \text{C}_{15}\text{H}_{12}\text{N}_2\text{O} = \frac{A}{490} \times 50,000$$

**Containers and storage** Containers—Tight containers.

## Carbazochrome Sodium Sulfonate

カルバゾクロムスルホン酸ナトリウム



$\text{C}_{10}\text{H}_{11}\text{N}_4\text{NaO}_5\text{S} \cdot 3\text{H}_2\text{O}$ : 376.32  
Monosodium (*RS*)-2,3,5,6-tetrahydro-1-methyl-6-oxo-5-semicarbazonoindole-2-sulfonate trihydrate  
[51460-26-5, anhydride]

Carbazochrome Sodium Sulfonate contains not less than 98.0% and not more than 102.0% of  $C_{10}H_{11}N_4NaO_5S$  (mol. wt.: 322.27), calculated on the anhydrous basis.

**Description** Carbazochrome Sodium Sulfonate occurs as orange-yellow, crystals or crystalline powder.

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

A solution of Carbazochrome Sodium Sulfonate (1 in 100) shows no optical rotation.

Melting point: about 210°C (with decomposition).

**Identification (1)** Determine the absorption spectrum of a solution of Carbazochrome Sodium Sulfonate (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 Carbazochrome Sodium Sulfonate 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 Carbazochrome Sodium Sulfonate (1 in 100) responds to the Qualitative Tests (1) for sodium salt.

**pH** Dissolve 0.8 g of Carbazochrome Sodium Sulfonate in 50 mL of water by warming, and cool: the pH of this solution is between 5.0 and 6.0.

**Purity (1)** Clarity of solution—Dissolve 1.0 g of Carbazochrome Sodium Sulfonate in 50 mL of water by warming, and allow to cool: the solution is clear. Perform the test with this solution as directed under the Ultraviolet-visible Spectrophotometry: the absorbance at 590 nm is not more than 0.070.

(2) Heavy metals—Proceed with 1.0 g of Carbazochrome Sodium Sulfonate 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) Related substances—Dissolve 0.050 g of Carbazochrome Sodium Sulfonate in 100 mL of water, and use this solution as the sample solution. Pipet 2 mL of the sample solution, add water to make exactly 200 mL, and use this solution as the standard solution. Perform the test with 10  $\mu$ L 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 these solutions by the automatic integration method: the total area of the peaks other than the peak of carbazochrome sulfonate from the sample solution is not larger than the peak area of carbazochrome sulfonate from the standard solution.

**Operating conditions—**

**Detector:** An ultraviolet absorption photometer (wavelength: 360 nm).

**Column:** A stainless steel column about 4 mm in inside diameter and about 25 cm in length, packed with octadecylsilylanized silica gel for liquid chromatography (5 to 10  $\mu$ m in particle diameter).

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

**Mobile phase:** Dissolve 1.2 g of ammonium dihydrogenphosphate in 1000 mL of water, and filter through a membrane filter if necessary. To 925 mL of this solution add 75 mL of ethanol (95), shake, and adjust with phosphoric acid to a pH of 3.

**Flow rate:** Adjust the flow rate so that the retention time of carbazochrome sulfonate is between 6 and 8 minutes.

**Selection of column:** Dissolve 0.010 g each of Carbazochrome Sodium Sulfonate and carbazochrome in 100 mL of water by warming. Proceed with 10  $\mu$ L of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of carbazochrome sulfonate and carbazochrome in this order with the resolution between these peaks being not less than 3.

**Detection sensitivity:** Adjust the detection sensitivity so that the peak height of carbazochrome sulfonate obtained from 10  $\mu$ L of the standard solution composes about 5% of the full scale.

**Time span of measurement:** About 3 times as long as the retention time of carbazochrome sulfonate after the solvent peak.

**Water** 13.0 – 16.0% (0.3 g, direct titration).

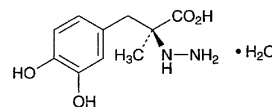
**Assay** Weigh accurately about 0.25 g of Carbazochrome Sodium Sulfonate, dissolve in 50 mL of water, apply to a chromatographic column, 10 mm in diameter, previously prepared with 20 mL of strongly acidic ion exchange resin for column chromatography (type H), and allow to flow at a rate of 4 mL per minute. Wash the column with 150 mL of water, combine the washing and the former effluent solution, and titrate with 0.05 mol/L sodium hydroxide VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.05 mol/L sodium hydroxide VS  
= 16.114 mg of  $C_{10}H_{11}N_4NaO_5S$

**Containers and storage** Containers—Well-closed containers.

## Carbidopa

カルビドパ



$C_{10}H_{14}N_2O_4 \cdot H_2O$ : 244.24

(2S)-2-(3,4-Dihydroxybenzyl)-2-hydrazinopropanoic acid monohydrate [38821-49-7]

Carbidopa contains not less than 98.0% of  $C_{10}H_{14}N_2O_4 \cdot H_2O$ .

**Description** Carbidopa occurs as a white to yellowish white powder.

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

Melting point: about 197°C (with decomposition).