

(ii) Procedure: Weigh accurately about 5.5 g of Calcium Polystyrene Sulfonate, previously dried, add 300 mL of water of 25°C, and mix for 5 minutes. Transfer this turbid solution to the sedimentation tube J, keeping a temperature at 25°C, add water of 25°C to 2 mm below the mark F of 20 cm of the sedimentation tube J, and then insert the pipet. Open the two-way stopcock C, exhaust air, add exactly water from the vent-hole D to the mark F of 20 cm, and close the two-way stopcock C. Shake the apparatus well vertically and horizontally, disperse Calcium Polystyrene Sulfonate in water, and then open the two-way stopcock, and allow to stand at $25 \pm 1^\circ\text{C}$ for 5 hours and 15 minutes.

Then, draw exactly the meniscus of the turbid solution in sedimentation tube J up to the mark of pipet bulb A by suction, open the two-way stopcock C to the outlet of pipet H, and transfer exactly measured 20 mL of the turbid solution to a weighing bottle. Repeat the procedure, and combine exactly measured 20 mL of the turbid solution. Evaporate 20 mL of this turbid solution on a water bath to dryness, dry to constant mass at 105°C, and weigh the residue as W_S (g). Pipet 20 mL of used water, and weigh the residue in the same manner as W_B (g). Calculate the difference mi (g) between W_S and W_B , and calculate the amount of microparticles (S) by the following equation: the amount of microparticles is not more than 0.1%.

$$S (\%) = \frac{mi (\text{g}) \times V (\text{mL})}{20 (\text{mL}) \times \left(\begin{array}{l} \text{amount (g) of Calcium} \\ \text{Polystyrene Sulfonate} \end{array} \right)}$$

V : Actual volume (mL) to the mark of 20 cm at which the suction part of pipet is inserted.

Assay (1) Calcium—Weigh accurately about 1.0 g of Calcium Polystyrene Sulfonate, previously dried, and disperse in 5 mL of 3 mol/L hydrochloric acid TS. Transfer this mixture, and wash out completely with the aid of a small quantity of 3 mol/L hydrochloric acid TS to a column 12 mm in inside diameter and 70 mm in length, packed with a pledget of fine glass wool in the bottom of it, placing a 50-mL volumetric flask as a receiver under the column. Then collect about 45 mL of eluate, adding 3 mol/L hydrochloric acid TS to the column, and add water to make exactly 50 mL. Pipet 20 mL of this solution, adjust with ammonia TS to a pH of exactly 10. Titrate immediately with 0.05 mol/L disodium dihydrogen ethylenediamine tetraacetate VS until the red-purple color of the solution disappears, and a blue color develops (indicator: 0.04 g eriochrome black T-sodium chloride indicator). Perform a blank determination, and make any necessary correction.

Each mL of 0.05 mol/L disodium dihydrogen ethylenediamine tetraacetate VS
= 2.0039 mg of Ca

(2) Potassium exchange capacity—Pipet 50 mL of Standard Potassium Stock Solution into a glass-stoppered flask containing about 1.0 g of dried Calcium Polystyrene Sulfonate, accurately weighed, stir for 120 minutes, filter, and discard the first 20 mL of the filtrate. Pipet 5 mL of the subsequent filtrate, and add 0.02 mol/L hydrochloric acid TS to make exactly 100 mL. Pipet 10 mL of this solution, add 0.02 mol/L hydrochloric acid TS to make exactly 1000 mL, and use this solution as the sample solution. Separately, measure exactly a suitable volume of Standard Potassium

Stock Solution, dilute with 0.02 mol/L hydrochloric acid TS to make solutions containing 0.5 to 2.5 μg of potassium (K: 39.10) per mL, and use these solutions as the standard solutions. Perform the test with the sample solution and the standard solutions according to the Atomic Absorption Spectrophotometry under the following conditions, and determine the amount, Y (mg), of potassium in 1000 mL of the sample solution, using the calibration curve obtained from the standard solutions. The exchange quantity for potassium per g of dried Calcium Polystyrene Sulfonate is 0.053 to 0.071 g, calculating by the following equation.

$$\begin{aligned} &\text{Exchange quantity (mg) for potassium (K) per g of} \\ &\text{dried Calcium Polystyrene Sulfonate} \\ &= \frac{X - 100 Y}{W} \end{aligned}$$

X : The amount (mg) of potassium in 50 mL of Standard Potassium Stock Solution before exchange.

W : The amount (g) of dried Calcium Polystyrene Sulfonate taken.

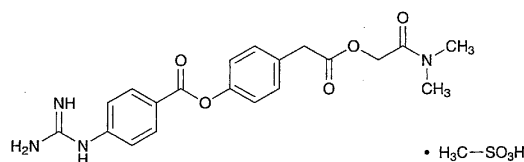
Gas: Combustible gas—Acetylene
Supporting gas—Air

Lamp: A potassium hollow-cathode lamp
Wavelength: 766.5 nm

Containers and storage Containers—Tight containers.

Camostat Mesilate

メシル酸カモスタット



$\text{C}_{20}\text{H}_{22}\text{N}_4\text{O}_5 \cdot \text{CH}_4\text{O}_3\text{S}$: 494.52
N,N-Dimethylcarbamoylmethyl 4-(4-guanidinobenzoyloxy)phenylacetate monomethanesulfonate [59721-29-8]

Camostat Mesilate, when dried, contains not less than 98.5% of $\text{C}_{20}\text{H}_{22}\text{N}_4\text{O}_5 \cdot \text{CH}_4\text{O}_3\text{S}$.

Description Camostat Mesilate occurs as white crystals or crystalline powder.

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

Identification (1) To 4 mL of a solution of Camostat Mesilate (1 in 2000) add 2 mL of 1-naphthol TS and 1 mL of diacetyl TS, and allow to stand for 10 minutes: a red color develops.

(2) Determine the absorption spectrum of a solution of Camostat Mesilate (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of a solution of Camostat Mesilate Reference Standard prepared in the same manner as the sample solution: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) To 0.1 g of Camostat Mesilate add 0.2 g of sodium hydroxide, fuse by gentle heating, and continue to heat for 20 to 30 seconds. After cooling, add 0.5 mL of water and 3 mL of dilute hydrochloric acid, and heat: the gas evolved changes moistened potassium iodate-starch paper to blue.

Melting point 194 – 198°C

Purity (1) Heavy metals—Dissolve 1.0 g of Camostat Mesilate in 40 mL of water by warming, and add 2 mL of dilute acetic acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution with 2.0 mL of Standard Lead Solution and 2 mL of dilute acetic acid (not more than 20 ppm).

(2) Arsenic—Dissolve 2.0 g of Camostat Mesilate in 20 mL of 2 mol/L hydrochloric acid TS by heating in a water bath, and continue to heat for 20 minutes. After cooling, centrifuge, take 10 mL of the supernatant liquid, and use this solution as the test solution. Perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—Dissolve 0.030 g of Camostat Mesilate in 10 mL of ethanol (95), and use this solution as the sample solution. Pipet 1 mL of the sample solution, add ethanol (95) 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 μ 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 ethyl acetate, water and acetic acid (100) (3:1:1) to a distance of about 10 cm, and air-dry the plate. Allow the plate to stand overnight in iodine vapor: 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% (1 g, silica gel, 105°C, 3 hours).

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

Assay Weigh accurately about 0.05 g each of Camostat Mesilate and Camostat Mesilate Reference Standard, previously dried, and dissolve each in water to make exactly 50 mL. Pipet 5 mL each of these solutions, add exactly 5 mL of the internal standard solution, and use these solutions as the sample solution and the standard solution, respectively. Perform the test with 2 μ L each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S , of the peak area of camostat to that of the internal standard.

$$\begin{aligned} & \text{Amount (mg) of } C_{20}H_{22}N_4O_5 \cdot CH_4O_3S \\ & = \text{amount (mg) of Camostat Mesilate} \\ & \quad \text{Reference Standard} \\ & \quad \times \frac{Q_T}{Q_S} \end{aligned}$$

Internal standard solution—A solution of butyl parahydroxybenzoate in ethanol (95) (1 in 1500).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 265 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilylated silica gel for liquid chromatography (5 μ m in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: A mixture of methanol, a solution of sodium 1-heptane sulfonate (1 in 500), a solution of sodium lauryl sulfate (1 in 1000) and acetic acid (100) (200:100:50:1).

Flow rate: Adjust the flow rate so that the retention time of camostat is about 10 minutes.

System suitability—

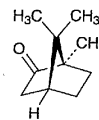
System performance: When the procedure is run with 2 μ L of the standard solution under the above operating conditions, camostat and the internal standard are eluted in this order with the resolution between these peaks being not less than 5.

System repeatability: When the test is repeated 6 times with 2 μ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of camostat to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

d-Camphor

d-カンフル



$C_{10}H_{16}O$: 152.23
(1*R*,4*R*)-Bornan-2-one [464-49-3]

d-Camphor contains not less than 96.0% of $C_{10}H_{16}O$.

Description *d*-Camphor occurs as colorless or white, translucent crystals, crystalline powder or masses. It has a characteristic, agreeable odor, and a slightly bitter taste, followed by a pleasant, cooling sensation.

It is freely soluble in ethanol (95), in diethyl ether and in carbon disulfide, and slightly soluble in water.

It slowly volatilizes at room temperature.

Identification Dissolve 0.1 g of *d*-Camphor in 2 mL of methanol, add 1 mL of 2,4-dinitrophenylhydrazine TS, and heat for 5 minutes on a water bath: an orange-red precipitate is formed.

Optical rotation $[\alpha]_D^{20}$: +41.0 – +43.0° (5 g, ethanol (95), 50 mL, 100 mm).

Melting point 177 – 182°C

Purity (1) Water—Shake 1.0 g of *d*-Camphor with 10 mL of carbon disulfide: the solution is clear.

(2) Chlorinated compounds—Mix 0.20 g of finely powdered *d*-Camphor with 0.4 g of sodium peroxide in a dry, hard glass test tube. Suspend the tube at an angle of 45° by means of a clamp placed at the upper end, and heat the tube gently, starting near the upper end, and gradually bringing the heat toward the lower part of the tube until incineration is complete. Dissolve the residue in 20 mL of warm water,