Camostat Mesilate Tablets

カモスタットメシル酸塩錠

Camostat Mesilate Tablets contain not less than 95.0% and not more than 105.0% of the labeled amount of camostat mesilate ($C_{20}H_{22}N_4O_5.CH_4O_3S$: 494.52).

Method of preparation Prepare as directed under Tablets, with Camostat Mesilate.

Identification To a quantity of powdered Camostat Mesilate Tablets, equivalent to 0.15 g of Camostat Mesilate, add 150 mL of ethanol (95), and warm in a water bath at 50℃ for 15 minutes while shaking. After cooling to room temperature, centrifuge. Evaporate 1 mL of the supernatant liquid to dryness in a water bath. Dissolve the residue in 100 mL of water, and determine the absorption spectrum of this solution as directed under Ultraviolet-visible Spectrophotometry *<2.24>*: it exhibits a maximum between 264 nm and 268 nm.

Uniformity of dosage units *<6.02>* Perform the Mass variation test, or the Content uniformity test according to the following method: it meets the requirement.

To 1 tablet of Camostat Mesilate Tablets add 10 mL of a mixture of acetonitrile, dimethylsulfoxide and methanesulfonic acid (500:500:1), and shake thoroughly while warming in a water bath at 60℃ until the tablet is completely disintegrated. After cooling, add a mixture of acetonitrile, dimethylsulfoxide and methanesulfonic acid (500:500:1) to make exactly V mL so that each mL contains about 5 mg of camostat mesilate ($C_{20}H_{22}N_4O_5.CH_4O_3S$), and centrifuge. Pipet 2 mL of the supernatant liquid, add exactly 2 mL of the internal standard solution, and use this solution as the sample solution. Then, proceed as directed in the Assay.

Amount (mg) of camostat mesilate ($C_{20}H_{22}N_4O_5.CH_4O_3S$)
$= M_S \times Q_T / Q_S \times V / 20$

M_S: Amount (mg) of Camostat Mesilate RS taken

Internal standard solution — A solution of propyl parahydroxybenzoate in a mixture of acetonitrile, dimethylsulfoxide and methanesulfonic acid (500:500:1) (1 in 700).

Dissolution *<6.10>* When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium, the dissolution rate in 30 minutes of Camostat Mesilate Tablets is not less than 80%.

Start the test with 1 tablet of Camostat Mesilate Tablets, withdraw not less than 20 mL of the medium at the specified minute after starting the test, and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard not less than 10 mL of the first filtrate, pipet V mL of the subsequent filtrate, add water to make exactly V' mL so that each mL contains about 10 μg of camostat mesilate ($C_{20}H_{22}N_4O_5.CH_4O_3S$), and use this solution as the sample solution. Separately, weigh accurately about 50 mg of Camostat Mesilate RS, previously dried at 105℃ (silica gel) for 3 hours, and dissolve in water to make exactly 100 mL. Pipet 2 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 standard solution at 266 nm as directed under Ultraviolet-visible Spectrophotometry *<2.24>*.

Dissolution rate (%) with respect to the labeled amount of camostat mesilate ($C_{20}H_{22}N_4O_5.CH_4O_3S$)
$= M_S \times A_T / A_S \times V' / V \times 1 / C \times 18$

M_S: Amount (mg) of Camostat Mesilate RS taken
C: Labeled amount (mg) of camostat mesilate ($C_{20}H_{22}N_4O_5.CH_4O_3S$) in 1 tablet

Assay To 20 tablets of Camostat Mesilate Tablets add 60 mL of a mixture of acetonitrile, dimethylsulfoxide and methanesulfonic acid (500:500:1), and shake while warming in a water bath at 60℃ until the tablets are disintegrated. After cooling, add a mixture of acetonitrile, dimethylsulfoxide and methanesulfonic acid (500:500:1) to make exactly 100 mL, and centrifuge. Pipet V mL of the supernatant liquid, equivalent to about 0.5 g of camostat mesilate ($C_{20}H_{22}N_4O_5.CH_4O_3S$), add a mixture of acetonitrile, dimethylsulfoxide and methanesulfonic acid (500:500:1) to make exactly 100 mL. Pipet 2 mL of this solution, add exactly 2 mL of the internal standard solution, and use this solution as the sample solution. Separately, weigh accurately about 0.1 g of Camostat Mesilate RS, previously dried at 105℃ (silica gel) for 3 hours, and dissolve in a mixture of acetonitrile, dimethylsulfoxide and methanesulfonic acid (500:500:1) to make exactly 20 mL. Pipet 2 mL of this solution, add exactly 2 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 1 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* 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.

Amount (mg) of camostat mesilate ($C_{20}H_{22}N_4O_5.CH_4O_3S$) in 1 tablet
$= M_S \times Q_T / Q_S \times 25 / V$

M_S: Amount (mg) of Camostat Mesilate RS taken

Internal standard solution — A solution of propyl parahydroxybenzoate in a mixture of acetonitrile, dimethysulfoxide and methanesulfonic acid (500:500:1) (1 in 700).

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 octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

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

Mobile phase: A mixture of methanol, water, [a solution of sodium lauryl sulfate in a mixture of water and methanol (1:1) (1 in 20)], [a solution of sodium 1-heptane sulfonate in a mixture of water and methanol (1:1) (1 in 20)] and acetic acid (100) (400:250:6:1:1)

Flow rate: Adjust so that the retention time of camostat is about 13 minutes.

System suitability—

System performance: When the procedure is run with 1 μL of the standard solution under the above operating conditions, the internal standard and camostat 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 1 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratio of the peak area of camostat to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.