Ergotamine Tartrate, Anhydrous Caffeine and Isopropylantipyrine Tablets

Dissolution <6.10> Perform the test with 1 tablet of Ergotamine Tartrate, Anhydrous Caffeine and Isopropylentipyrine Tablets at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium. 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 the first 10 mL of the filtrate, pipet *V* mL of the subsequent filtrate, add the mobile phase to make exactly *V*′ mL so that each mL contains about 0.5 μg of ergotamine tartrate ($(C_{33}H_{35}N_5O_5)_2.C_4H_6O_6$), about 25 μg of anhydrous caffeine ($C_8H_{10}N_4O_2$) and about 150 μg of isopropylantipyrine ($C_{14}H_{18}N_2O$) according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about 50 mg of Ergotamine Tartrate RS, previously dried at 60ºC in vacuum for 4 hours, and dissolve in the mobile phase to make exactly 50 mL. Pipet 2 mL of this solution, add the mobile phase to make exactly 20 mL, and use this solution as the standard stock solution (1). Separately, weigh accurately about 50 mg of Anhydrous Caffeine RS, previously dried at 80ºC for 4 hours, dissolve in the mobile phase to make exactly 50 mL, and use this solution as the standard stock solution (2). Further, weigh accurately about 60 mg of Isopropylantipyrine RS, previously dried in vacuum with silica gel for 5 hours, dissolve in the mobile phase, add exactly 2 mL of the standard stock solution (1) and exactly 10 mL of the standard stock solution (2), and add the mobile phase to make exactly 100 mL. Pipet 5 mL of this solution, add the mobile phase to make exactly 20 mL, and use this solution as the standard solution. Perform the test with exactly 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography <2.01> according to the following conditions, and determine the peak areas, A_{Ta} and A_{Sa}, of ergotamine tartrate, the peak areas, A_{Tb} and A_{Sb}, of caffeine, and the peak areas, A_{Tc} and A_{Sc}, of isopropylantipyrine.

The requirements are met if Ergotamine Tartrate, Anhydrous Caffeine and Isopropylentipyrine Tablets conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of ergotamine tartrate ($(C_{33}H_{35}N_5O_5)_2.C_4H_6O_6$)

$= M_{Sa} \times A_{Ta}/A_{Sa} \times V'/V \times 1/C_a \times 9/10$

Dissolution rate (%) with respect to the labeled amount of anhydrous caffeine ($C_8H_{10}N_4O_2$)

$= M_{Sb} \times A_{Tb}/A_{Sb} \times V'/V \times 1/C_b \times 45$

Dissolution rate (%) with respect to the labeled amount of isopropylantipyrine ($C_{14}H_{18}N_2O$)

$= M_{Sc} \times A_{Tc}/A_{Tc} \times V'/V \times 1/C_c \times 225$

M_{Sa}: Amount (mg) of Ergotamine Tartrate RS

M_{Sb}: Amount (mg) of Anhydrous Caffeine RS

M_{Sc}: Amount (mg) of Isopropylantipyrine RS

C_a: Labeled amount (mg) of ergotamine tartrate ($(C_{33}H_{35}N_5O_5)_2.C_4H_6O_6$) in 1 tablet

C_b: Labeled amount (mg) of anhydrous caffeine ($C_8H_{10}N_4O_2$) in 1 tablet

C_c: Labeled amount (mg) of isopropylantipyrine ($C_{14}H_{18}N_2O$) in 1 tablet

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 290 nm).

A fluorophotometer (excitation wavelength: 320 nm, fluorescence wavelength: 388 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 40°C

Mobile phase: To 1.36 mL of phosphoric acid add water to make 2000 mL. To 1500 mL of this solution add 500 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of caffeine is about 2.7 minutes.

System suitability —

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, in fluorescence detection, the number of theoretical plates and the symmetry factor of the peak of ergotamine tartrate are not less than 2000 and not more than 2.5, respectively. In ultraviolet absorption detection, caffeine and isopropylantipyrine are eluted in this order with the resolution between these peaks being not less than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviations of the peak areas of ergotamine tartrate, caffeine and isopropylantipyrine are not more than 3.0%, respectively.

Dissolution Requirements

	Labeled amount	Specified minute	Dissolution rate
Ergotamine tartrate	0.5 mg		Not less than 70%
Anhydrous caffeine	25 mg	45 minutes	Not less than 80%
Isopropylantipyrine	150 mg		Not less than 80%

	Labeled amount	Specified minute	Dissolution rate
Ergotamine tartrate	1 mg	30 minutes	Not less than 70%
Anhydrous caffeine	50 mg		Not less than 80%
Isopropylantipyrine	300 mg		Not less than 80%

Ergotamine Tartrate RS Ergotamine Tartrate (JP).

Anhydrous Caffeine RS Anhydrous Caffeine (JP). When dried, it contains not less than 99.0% of caffeine ($C_8H_{10}N_4O_2$).

Isopropylantipyrine RS Isopropylantipyrine (JP). When dried, it contains not less than 99.0% of isopropylantipyrine ($C_{14}H_{18}N_2O$).