Chlorpheniramine Maleate 0.5 mg/g, Salicylamide 45 mg/g, Acetaminophen 25 mg/g and Anhydrous Caffeine 5 mg/g Granules

Dissolution *<6.10>* Weigh accurately about 2 g of Chlorpheniramine Maleate 0.5 mg/g, Salicylamide 45 mg/g, Acetaminophen 25 mg/g and Anhydrous Caffeine 5 mg/g Granules, and perform the test at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium. Drop the sample so that it disperses in the medium. Withdraw exactly 30 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, and use the subsequent filtrate as the sample solution (1). Pipet 15 mL of the sample solution (1), add exactly 1 mL of 1 mol/L hydrochloric acid TS, and use this solution as the sample solution (2).

The requirements are met if Chlorpheniramine Maleate 0.5 mg/g, Salicylamide 45 mg/g, Acetaminophen 25 mg/g and Anhydrous Caffeine 5 mg/g Granules conform to the dissolution requirements.

Chlorpheniramine Maleate

Separately, weigh accurately about 17 mg of Chlorpheniramine Maleate RS, previously dried at 105ºC for 3 hours, and dissolve in water to make exactly 100 mL. To exactly 2 mL of this solution add water to make exactly 300 mL. Pipet 15 mL of this solution, add exactly 1 mL of 1 mol/L hydrochloric acid TS, and use this solution as the standard solution. Perform the test with exactly 150 μL each of the sample solution (2) and standard solution as directed Liquid Chromatography *<2.01>* according to the following conditions, and determine the peak areas, A_T and A_S, of chlorpheniramine.

Dissolution rate (%) with respect to the labeled amount of chlorpheniramine maleate ($C_{16}H_{19}ClN.C_4H_4O_4$)

$= M_S/M_T \times A_T/A_S \times 1/C \times 6$

M_S: Amount (mg) of Chlorpheniramine Maleate RS

M_T: Amount (g) of sample

C: Labeled amount (mg) of chlorpheniramine maleate ($C_{16}H_{19}ClN_2.C_4H_4O_4$) in 1 g

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 225 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 40ºC.

Mobile phase: A mixture of a solution of sodium 1-octanesulfonate in diluted phosphoric acid (1 in

1000) (1 in 500) and acetonitrile (7:3).

Flow rate: Adjust the flow rate so that the retention time of chlorpheniramine is about 8 minutes.

System suitability —

System performance: When the procedure is run with 150 µL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of chlorpheniramine are not less than 3000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 150 µL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of chlorpheniramine is not more than 1.5%.

Salicylamide, Acetaminophen and Anhydrous Caffeine

Separately, weigh accurately about 17 mg of Anhydrous Caffeine RS, previously dried at 80ºC for 4 hours, dissolve in water to make exactly 100 mL, and use this solution as the standard stock solution. Then, weigh accurately about 30 mg of Salicylamide RS, previously dried in silica gel for 4 hours, and about 17 mg of Acetaminophen RS, previously dried at 105ºC for 2 hours, dissolve in about 50 mL of water, add exactly 20 mL of the standard stock solution, then add water to make exactly 300 mL, and use this solution as the standard solution. Perform the test with exactly 30 µL each of the sample solution (1) and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and determine the peak area, A_{Ta} and A_{Sa}, of salicylamide, A_{Tb} and A_{Sb}, of acetaminophen, and A_{Tc} and A_{Sc}, of caffeine.

Dissolution rate (%) with respect to the labeled amount of salicylamide ($C_7H_7NO_2$)

$= M_{Sa}/M_T \times A_{Ta}/A_{Sa} \times 1/C_a \times 300$

Dissolution rate (%) with respect to the labeled amount of acetaminophen ($C_8H_9NO_2$)

$= M_{Sb}/M_T \times A_{Tb}/A_{Sb} \times 1/C_b \times 300$

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

$= M_{Sc}/M_T \times A_{Tc}/A_{Sc} \times 1/C_c \times 60$

M_{Sa}: Amount (mg) of Salicylamide RS

M_{Sb}: Amount (mg) of Acetaminophen RS

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

M_T: Amount (g) of sample

C_a: Labeled amount (mg) of salicylamide ($C_7H_7NO_2$) in 1 g

C_b: Labeled amount (mg) of acetaminophen ($C_8H_9NO_2$) in 1 g

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

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 270 nm).

Column: A stainless steel column 3.9 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (10 μm in particle diameter).

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

Mobile phase: A mixture of water, methanol and acetic acid (100) (88:11:1).

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

System suitability —

System performance: When the procedure is run with 30 μL of the standard solution under the above operating conditions, acetaminophen, salicylamide and caffeine are eluted in this order, and the resolutions between the peaks of acetaminophen and salicylamide and between the peaks of salicylamide and caffeine are not less than 3, respectively, and the numbers of theoretical plates and the symmetry factors of their peaks are not less than 3000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 30 μL of the standard solution under the above operating conditions, the relative standard deviations of the peak areas of acetaminophen, salicylamide and caffeine are not more than 1.5%, respectively.

Dissolution Requirements

	Labeled amount	Specified minute	Dissolution rate
Chlorpheniramine Maleate	0.5 mg/g	15 minutes	Not less than 85%
Salicylamide	45 mg/g		Not less than 80%
Acetaminophen	25 mg/g		Not less than 80%
Anhydrous Caffeine	5 mg/g		Not less than 85%

Chlorpheniramine Maleate RS Chlorpheniramine Maleate (JP). When dried, it contains not less than 99.0% of chlorpheniramine maleate ($C_{16}H_{19}ClN_2.C_4H_4O_4$).

Salicylamide RS Salicylamide. When dried, it contains not less than 99.0% of salicylamide ($C_7H_7NO_2$).

Acetaminophen RS Acetaminophen (JP). When dried, it contains not less than 99.0% of acetaminophen ($C_8H_9NO_2$).

Anhydrous Caffeine RS Anhydrous Caffeine (JP). When dried, it contains not less than 99.0% of

caffeine ($C_8H_{10}N_4O_2$).