Diprophylline 25 mg, Methoxyphenamine Hydrochloride 25 mg, Noscapine 5 mg and Chlorpheniramine Maleate 2 mg Capsules

Dissolution *<6.01>*

[pH 1.2] Perform the test with 1 capsule of Diprophylline 25 mg, Methoxyphenamine Hydrochloride 25 mg, Noscapine 5 mg and Chlorpheniramine Maleate 2 mg Capsules at 50 revolutions per minute according to the Paddle method, using 900 mL of 1st fluid for dissolution test 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, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 28 mg of Noscapine RS, previously dried at 105ºC for 4 hours, and dissolve in acetonitrile to make exactly 100 mL. Pipet 2 mL of this solution, add 1st fluid for dissolution test to make exactly 100 mL, and use this solution as the standard solution (1). Perform the test with exactly 50 μL each of the sample solution and standard solution (1) as directed under Liquid Chromatography *<2.01>* according to the following conditions, and determine the peak areas, A_T and A_S, of noscapine in each solution.

The requirements are met if Diprophylline 25 mg, Methoxyphenamine Hydrochloride 25 mg, Noscapine 5 mg and Chlorpheniramine Maleate 2 mg Capsules conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of noscapine ($C_{22}H_{23}NO_7$)

$= M_S \times A_T/A_S \times 1/C \times 18$

M_S: Amount (mg) of Noscapine RS

C: Labeled amount (mg) of noscapine ($C_{22}H_{23}NO_7$) in 1 capsule

[Water] Perform the test with 1 capsule of Diprophylline 25 mg, Methoxyphenamine Hydrochloride 25 mg, Noscapine 5 mg and Chlorpheniramine Maleate 2 mg Capsules 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, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 28 mg of Diprophylline RS, previously dried at 105ºC for 4 hours, dissolve in water to make exactly 50 mL, and use this solution as the standard stock solution (1). Then, weigh accurately about 28 mg of Methoxyphenamine Hydrochloride RS, previously dried in vacuum over phosphorus (V) oxide for 24 hours, dissolve in water to make exactly 50 mL, and use this solution as the standard stock solution (2). Furthermore, weigh accurately about 22 mg of Chlorpheniramine Maleate RS, previously dried at 105ºC for 3 hours, and dissolve in water to make exactly 50 mL. Pipet 5 mL of this solution, add water to make exactly 50

mL, and use this solution as the standard stock solution (3). Pipet 5 mL each of the standard stock solution (1), standard stock solution (2) and standard stock solution (3), then add water to make exactly 100 mL, and use this solution as the standard solution (2). Perform the test with exactly 50 μL each of the sample solution and standard solution (2) as directed under Liquid Chromatography <2.01> according to the following conditions, and determine the peak areas, A_{Ta} and A_{Sa}, of diprophylline, the peak areas, A_{Tb} and A_{Sb}, of methoxyphenamine, and the peak areas, A_{Tc} and A_{Sc}, of chlorpheniramine.

The requirement are met if Diprophylline 25 mg, Methoxyphenamine Hydrochloride 25 mg, Noscapine 5 mg and Chlorpheniramine Maleate 2 mg Capsules conform to the dissolution requirements.

Dissolution rate (%) with respect to the labeled amount of diprophylline ($C_{10}H_{14}N_4O_4$)

$= M_{Sa} \times A_{Ta}/A_{Sa} \times 1/C_a \times 90$

Dissolution rate (%) with respect to the labeled amount of methoxyphenamine hydrochloride ($C_{11}H_{17}NO.HCl$)

$= M_{Sb} \times A_{Tb}/A_{Sb} \times 1/C_b \times 90$

Dissolution rate (%) with respect to the labeled amount of chlorpheniramine maleate ($C_{16}H_{19}ClN_2.C_4H_4O_4$)

$= M_{Sc} \times A_{Tc}/A_{Sc} \times 1/C_c \times 9$

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

M_{Sb}: Amount (mg) of Methoxyphenamine Hydrochloride RS

M_{Sc}: Amount (mg) of Chlorpheniramine Maleate RS

C_a: Labeled amount (mg) of diprophylline ($C_{10}H_{14}N_4O_4$) in 1 capsule

C_b: Labeled amount (mg) of methoxyphenamine hydrochloride ($C_{11}H_{17}NO.HCl$) in 1 capsule

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

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 262 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 7.5 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (3 μm in particle diameter).

Column temperature: A constant temperature of about 40ºC.

Mobile phase A: Dissolve 7.8 g of sodium dihydrogen phosphate dihydrate in water to make 1000 mL, add diluted phosphoric acid (1 in 10), and adjust to pH3.5. To 900 mL of this solution add 100 mL of acetonitrile.

Mobile phase B: Dissolve 7.8 g of sodium dihydrogen phosphate dihydrate in water to make 1000

mL, and adjust to pH 3.5 with diluted phosphoric acid (1 in 10). To 100 mL of this solution add 400 mL of acetonitrile.

Flowing of the mobile phase: Control the gradient by mixing the mobile phases A and B as directed in the following table.

Time after injection of sample (min)	Mobile phase A (vol%)	Mobile phase B (vol%)
0 - 0.1	100 → 80	0 → 20
0.1 - 10	80	20
10 - 10.1	80 → 100	20 → 0
10.1 - 19	100	0

Flow rate: 1.0 mL per minute.

System suitability —

System performance: When the procedure is run with 50 μL of the standard solution (1) under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of noscapine are not less than 10,000 and not more than 2.0, respectively. And when the procedure is run with 50 μL of the standard solution (2) under the above operating conditions, diprophylline, methoxyphenamine and chlorpheniramine are eluted in this order with the resolutions between adjacent peaks being not less than 5, respectively.

System repeatability: When the test is repeated 6 times with 50 μL each of the standard solutions (1) and (2) according to the above operating conditions, the relative standard deviations of the peak areas of diprophylline, methoxyphenamine, noscapine and chlorpheniramine are not more than 2.0%, respectively.

Dissolution Requirements

	Labeled amount	pH	Specified minute	Dissolution rate
Noscapine	5 mg	1.2	15 minutes	Not less than 80%
Diprophylline	25 mg			Not less than 80%
Methoxyphenamine Hydrochloride	25 mg	Water	15 minutes	Not less than 80%
Chlorpheniramine Maleate	2 mg			Not less than 80%

Diprophylline RS Diprophylline. When dried, it contains not less than 99.0% of diprophylline ($C_{10}H_{14}N_4O_4$).

Methoxyphenamine Hydrochloride RS Methoxyphenamine Hydrochloride. When dried, it contains not less than 99.0% of methoxyphenamine hydrochloride ($C_{11}H_{17}NO.HCl$).

Noscapine RS Noscapine (JP). When dried, it contains not less than 99.0% of noscapine ($C_{22}H_{23}NO_7$).