Calcium Pantothenate 100 mg/g, Riboflavin 3 mg/g, Pyridoxine Hydrochloride 30 mg/g and Nicotinamide 15 mg/g Granules

Dissolution *<6.10>* Conduct this procedure without exposure to light. Weigh accurately about 1 g of Calcium Pantothenate 100 mg/g, Riboflavin 3 mg/g, Pyridoxine Hydrochloride 30 mg/g and Nicotinamide 15 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. Start the test, 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, use the subsequent filtrate as the sample solution (1). Pipet 5 mL of the subsequent filtrate, add 0.1 mol/L hydrochloric acid TS to make exactly 10 mL, and use this solution as the sample solution (2).

The requirements are met if Calcium Pantothenate 100 mg/g, Riboflavin 3 mg/g, Pyridoxine Hydrochloride 30 mg/g and Nicotinamide 15 mg/g Granules conform to the dissolution requirements.

Calcium Pantothenate

Separately, weigh accurately about 22 mg of Calcium Pantothenate RS, previously dried at 105ºC for 4 hours, dissolve in water to make exactly 200 mL, and use this solution as the standard solution. Perform the test with exactly 10 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_T and A_S, of pantothenic acid of both solutions.

Dissolution rate (%) with respect to the labeled amount of calcium pantothenate ($C_{18}H_{32}CaN_2O_{10}$)
$= M_S/M_T \times A_T/A_S \times 1/C \times 450$

M_S: Amount (mg) of Calcium Pantothenate RS
M_T: Amount (g) of sample
C: Labeled amount (mg) of calcium pantothenate ($C_{18}H_{32}CaN_2O_{10}$) in 1 g

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 210 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 35ºC.

Mobile phase: Dissolve 1.36 g of potassium dihydrogen phosphate in water to make 1000 mL, and adjust the pH to 3.5 with diluted phosphoric acid (1 in 100). To 900 mL of this solution add 100 mL of methanol.

Flow rate: Adjust the flow rate so that the retention time of pantothenic acid is about 9 minutes.

System suitability

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of pantothenic acid are not less than 5000 and not more than 1.5, 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 deviation of the peak area of pantothenic acid is not more than 1.0%.

Riboflavin, Pyridoxine Hydrochloride, Nicotinamide

Separately, weigh accurately about 17 mg of Riboflavin RS, previously dried for 2 hours at 105ºC, dissolve in water by warming, add water to make exactly 100 mL after cooling, and use this solution as the standard stock solution (1). Separately, weigh accurately about 17 mg of Pyridoxine Hydrochloride RS, previously dried under reduced pressure for 4 hours using silica gel as a desiccant, dissolve in water to make exactly 50 mL, and use this solution as the standard stock solution (2). Separately, weigh accurately about 17 mg of Nicotinamide RS, previously dried under reduced pressure for 4 hours using silica gel as a desiccant, dissolve in water to make exactly 100 mL, and use this solution as the standard stock solution (3). Pipet 2 mL of the standard stock solution (1), 10 mL of the standard stock solution (2) and 10 mL of the standard stock solution (3), and add water to make exactly 100 mL. Pipet 10 mL of this solution, add 0.1 mol/L hydrochloric acid TS to make exactly 20 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution (2) and standard solution as directed under Liquid chromatography *<2.01>*, and calculate the peak areas, A_{Ta} and A_{Sa}, of riboflavin, A_{Tb} and A_{Sb}, of pyridoxine and A_{Tc} and A_{Sc}, of nicotinamide of these solutions.

Dissolution rate (%) with respect to the labeled amount of riboflavin ($C_{17}H_{20}N_4O_6$)

$= M_{Sa}/M_T \times A_{Ta}/A_{Sa} \times 1/C_a \times 18$

Dissolution rate (%) with respect to the labeled amount of pyridoxine hydrochloride ($C_8H_{11}NO_3 \cdot HCl$)

$= M_{Sb}/M_T \times A_{Tb}/A_{Sb} \times 1/C_b \times 180$

Dissolution rate (%) with respect to the labeled amount of nicotinamide ($C_6H_6N_2O$)

$= M_{Sc}/M_T \times A_{Tc}/A_{Sc} \times 1/C_c \times 90$

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

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

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

M_T: Amount (g) of sample

C_a Labeled amount (mg) of riboflavin ($C_{17}H_{20}N_4O_6$) in 1 g

C_b: Labeled amount (mg) of pyridoxine hydrochloride ($C_8H_{11}NO_3$·HCl) in 1 g

C_c: Labeled amount (mg) of nicotinamide ($C_6H_6N_2O$) in 1 g

Operating conditions

Detector: An ultraviolet absorption photometer (wavelength: 268 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 30ºC.

Mobile phase: Dissolve 1.08 g of sodium 1-octanesulfonate in a mixture of water, methanol and acetic acid (100) (74:25:1) to make 1000 mL.

Flow rate: Adjust the flow rate so that the retention time of nicotinamide is about 4 minutes.

System suitability

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, nicotinamide, riboflavin and pyridoxine are eluted in this order with the resolution between the neighboring peaks being not less than 1.5.

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 nicotinamide, riboflavin and pyridoxine are not more than 2.0%, respectively.

Dissolution Requirements

	Labeled amount	Specified minute	Dissolution rate
Calcium Pantothenate	100 mg/g	15 minutes	Not less than 85%
Riboflavin	3 mg/g		Not less than 70%
Pyridoxine Hydrochloride	30 mg/g		Not less than 80%
Nicotinamide	15 mg/g		Not less than 80%

Calcium Pantothenate RS Calcium Pantothenate (JP). When dried, it contains from 5.83 to 5.94% of Nitrogen (N: 14.0).

Riboflavin RS Riboflavin (JP). When dried, it contains not less than 99.0% of riboflavin ($C_{17}H_{20}N_4O_6$).

Pyridoxine Hydrochloride RS Pyridoxine Hydrochloride (JP). When dried, it contains not less than 99.0% of pyridoxine hydrochloride ($C_8H_{11}NO_3 \cdot HCl$).

Nicotinamide RS Nicotinamide (JP). When dried, it contains not less than 99.0% of nicotinamide ($C_6H_6N_2O$).