Thiamine Disulfide 10 mg, Pyridoxine Hydrochloride 50 mg and Cyanocobalamin 0.25 mg Tablets

Dissolution <*6.10*> Conduct this procedure without exposure to light. Perform the test with 1 tablet of Thiamine Disulfide 10 mg, Pyridoxine Hydrochloride 50 mg and Cyanocobalamin 0.25 mg 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 time 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 2 mL of the sample solution (1), add exactly 2 mL of 0.1 mol/L hydrochloric acid TS, and use this solution as the sample solution (2).

The requirements are met if Thiamine Disulfide 10 mg, Pyridoxine Hydrochloride 50 mg and Cyanocobalamin 0.25 mg Tablets conform to the dissolution requirements.

Thiamine Disulfide and Pyridoxine Hydrochloride

Separately, weigh accurately about 15 mg of Thiamine Disulfide RS (previously determine the water <*2.48*> with 0.2 g by direct titration in volumetric titration), dissolve in 0.1 mol/L hydrochloric acid TS to make exactly 50 mL, and use this solution as the standard stock solution (1). Then, weigh accurately about 25 mg of Pyridoxine Hydrochloride RS, previously dried in vacuum with silica gel for 4 hours, dissolve in 0.1 mol/L hydrochloric acid TS to make exactly 50 mL, and use this solution as the standard stock solution (2). To 2 mL of the standard stock solution (1) add exactly 6 mL of the standard stock solution (2), then add 0.1 mol/L hydrochloric acid TS to make exactly 50 mL. Pipet 2 mL of this solution, add exactly 2 mL of water, and use this solution as the standard solution. Perform the test with exactly 20 μL each of the sample solution (2) and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine the peak area, A_{Ta} and A_{Sb}, of thiamine disulfide, and A_{Ta} and A_{Sb}, of pyridoxine.

Dissolution rate (%) with respect to the labeled amount of thiamine disulfide ($C_{24}H_{34}N_8O_4S_2$)

$= M_{Sa} \times A_{Ta}/A_{Sa} \times 1/C_a \times 72$

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

$= M_{Sb} \times A_{Tb}/A_{Sb} \times 1/C_b \times 216$

M_{Sa}: Amount (mg) of Thiamine Disulfide RS, calculated on the anhydrous basis

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

C_a: Labeled amount (mg) of thiamine disulfide ($C_{24}H_{34}N_8O_4S_2$) in 1 tablet

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

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 250 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: Dissolve 6.80 g of potassium dihydrogenphosphate and 0.26 g of sodium 1-octanesulfonate in water to make 1000 mL, and adjust to pH 2.1 with phosphoric acid. To 870 mL of this solution add 130 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of pyridoxine is about 3 minutes.

System suitability —

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, pyridoxine and thiamine disulfide are eluted in this order with the resolution between these peaks being not less than 5, and the numbers of theoretical plates and the symmetry factors of their peaks are not less than 1500 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviations of the peak areas of pyridoxine and thiamine disulfide are not more than 2.0%, respectively.

Cyanocobalamin

Separately, weigh accurately about 20 mg of Cyanocobalamin RS (previously determine the loss on drying *<2.41>*, previously dried in vacuum over phosphorus (V) oxide at 100ºC for 4 hours (not more than 0.67 kPa)), and dissolve in water to make exactly 200 mL. To exactly 5 mL of this solution add water to make exactly 100 mL. Pipet 5 mL of this solution, add water to make exactly 100 mL, and use this solution as the standard solution. Perform the test with exactly 100 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 areas, A_{Tc} and A_{Sc}, of cyanocobalamin.

Dissolution rate (%) with respect to the labeled amount of cyanocobalamin ($C_{63}H_{88}CoN_{14}O_{14}P$)
$= M_{Sc} \times A_{Tc}/A_{Sc} \times 1/C_c \times 9/8$

M_{Sc}: Amount (mg) of Cyanocobalamin RS, calculated on the anhydrous basis

C_c: Labeled amount (mg) of cyanocobalamin ($C_{63}H_{88}CoN_{14}O_{14}P$) in 1 tablet

Operating conditions —

Detector: An ultraviolet absorption photometer (wavelength: 361 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: Dissolve 3.85 g of ammonium acetate in about 900 mL of water, adjust to pH 4.0 with acetic acid (100), and add water to make 1000 mL. To 890 mL of this solution add 110 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of cyanocobalamin is about 7 minutes.

System suitability —

System performance: When the procedure is run with 100 μL of the standard solution under the above operating conditions, the number of theoretical plates and symmetry factor of the peak of cyanocobalamin are not less than 1500 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 100 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of cyanocobalamin is not more than 3.0%.

Dissolution Requirements

	Labeled amount	Specified time	Dissolution rate
Thiamine Disulfide	10 mg	3 hours	Not less than 80%
Pyridoxine Hydrochloride	50 mg	3 hours	Not less than 80%
Cyanocobalamin	0.25 mg	3 hours	Not less than 85%