Sodium Valproate Extended-release Tablets A

バルプロ酸ナトリウム徐放錠 A

Sodium Valproate Extended-release Tablets A contain not less than 95.0% and not more than 105.0% of the labeled amount of sodium valproate ($C_8H_{15}NaO_2$: 166.19).

Method of preparation Prepare as directed under Tablets, with Sodium Valproate.

Identification To a quantity of powdered Sodium Valproate Extended-release Tablets A, equivalent to 0.2 g of Sodium Valproate, add 20 mL of water, shake thoroughly, and centrifuge. To 2 mL of the supernatant liquid add 1 mL of a solution of cobalt (II) nitrate hexahydrate (1 in 20), and heat on a water bath: a purple precipitate is formed.

Uniformity of dosage units <*6.02*> Perform the test according to the following method: it meets the requirement of the Content uniformity test.

Crush 1 tablet of Sodium Valproate Extended-release Tablets A, add exactly *V*/40 mL of the internal standard solution, add 4*V*/5 mL of a mixture of methanol and water (3:2), shake vigorously, add a mixture of methanol and water (3:2) to make *V* mL so that each mL contains about 1 mg of sodium valproate ($C_8H_{15}NaO_2$), and filter through a membrane filter with a pore size not exceeding 0.45 μm. Discard the first 5 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.1 g of sodium valproate for assay, previously dried at 105℃ for 3 hours, add exactly 2.5 mL of the internal standard solution, add a mixture of methanol and water (3:2) to make 100 mL, and use this solution as the standard solution. Then, proceed as directed in the Assay.

Amount (mg) of sodium valproate ($C_8H_{15}NaO_2$)
$= M_S \times Q_T / Q_S \times V / 100$

M_S: Amount (mg) of sodium valproate for assay taken

Internal standard solution —A solution of ethyl parahydroxybenzoate in a mixture of methanol and water (3:2) (1 in 5000).

Dissolution <*6.10*> When the test is performed at 50 revolutions per minute according to the Paddle method, using 900 mL of water as the dissolution medium, the dissolution rates of a 100-mg tablet in 4 hours, in 6 hours and in 12 hours are 15 to 45%, 40 to 70%, and not less than 75%, respectively, and those of a 200-mg tablet in 4 hours, in 6 hours and in 12 hours are 15 to 45%, 35 to 65%, and not less than 75%, respectively.

Start the test with 1 tablet of Sodium Valproate Extended-release Tablets A, withdraw exactly 20 mL of the medium at the specified minutes after starting the test and supply exactly 20 mL of water warmed to 37±0.5℃ immediately after withdrawing of the medium every time. Filter the media 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 water to make exactly *V′* mL so that each mL contains about 0.11 mg of sodium valproate ($C_8H_{15}NaO_2$), and use these solutions as the sample solutions. Separately, weigh accurately about 56 mg of sodium valproate for assay, previously dried at 105℃ 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 solution. Perform the test with exactly 50 μL each of the sample solutions and standard solution as directed under Liquid Chromatography <*2.01*> according to the following conditions, and determine the peak areas, $A_{T(n)}$ and A_S, of valproic acid in each solution.

Dissolution rate (%) with respect to the labeled amount of sodium valproate ($C_8H_{15}NaO_2$) on the *n*th medium withdrawing (n = 1, 2, 3)

$$= M_S \times \left\{ \frac{A_{T(n)}}{A_S} + \sum_{i=1}^{n-1} \left(\frac{A_{T(i)}}{A_S} \times \frac{1}{45} \right) \right\} \times \frac{V'}{V} \times \frac{1}{C} \times 180$$

M_S: Amount (mg) of sodium valproate for assay taken
C: Labeled amount (mg) of sodium valproate ($C_8H_{15}NaO_2$) in 1 tablet

Operating conditions—

Perform as directed in the operating conditions in the Assay.

System suitability—

System performance: When the procedure is run with 50 μL of the standard solution under the above operating conditions, the number of theoretical plates and the symmetry factor of the peak of valproic acid are not less than 3000 and not more than 2.0, respectively.

System repeatability: When the test is repeated 6 times with 50 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak area of valproic acid is not more than 1.5%.

Assay Weigh accurately the mass of not less than 20 Sodium Valproate Extended-release Tablets A, and powder. Weigh accurately a portion of the powder, equivalent to about 0.1 g of sodium valproate ($C_8H_{15}NaO_2$), add about 80 mL of the mobile phase, shake thoroughly, add the mobile phase to make exactly 100 mL, and centrifuge. Pipet 20 mL of the supernatant liquid, add exactly 5 mL of the internal

standard solution, and use this solution as the sample solution. Separately, weigh accurately about 0.1 g of sodium valproate for assay, previously dried at 105℃ for 3 hours, dissolve in the mobile phase to make exactly 100 mL. Pipet 20 mL of this solution, add exactly 5 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and standard solution as directed under Liquid Chromatography *<2.01>* according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of valproic acid to that of the internal standard.

Amount (mg) of sodium valproate ($C_8H_{15}NaO_2$)
$= M_S \times Q_T / Q_S$

M_S: Amount (mg) of sodium valproate for assay taken

Internal standard solution — A solution of ethyl parahydroxybenzoate in the mobile phase (1 in 50,000).

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 25℃.

Mobile phase: A mixture of 0.05 mol/L sodium dihydrogen phosphate TS (pH 3.0) and acetonitrile for liquid chromatography (1:1).

Flow rate: Adjust so that the retention time of valproic acid is about 6 minutes.

System suitability —

System performance: When the procedure is run with 10 μL of the standard solution under the above operating conditions, the internal standard and valproic acid are eluted in this order with the resolution between these peaks being not less than 7.

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 ratio of the peak area of valproic acid to that of the internal standard is not more than 1.0%.

Containers and storage Containers — Tight containers.