DEPARTMENT OF DRUG ADMINISTRATION

National Medicines Laboratory

ANALYTICAL METHOD VALIDATION COMMITTEE

Sodium Valproate and Valproic Acid Sustained ReleaseTablets

Analytical Profile No.: SVT 074/075/ AP 031

Sodium Valproate and Valproic Acid Sustained Release Tablets contain not less than 90 % and not more than 110 % of the stated amount of Sodium Valproate.

1. Identification: In the assay, the principle peak in the chromatogram obtained with the test solution should correspond to the peak in the chromatogram obtained with the reference solution of Sodium Valproate.

Tests:

2. Dissolution:

2.1 Dissolution parameters:

Apparatus: Paddle

Medium: 1000 ml Water

Speed and time: 50 rpm, 1 hour, 4 hour, 8 hour, 12 hour and 20 hour

Withdraw a suitable volume of medium at the determined time interval and filter. Replace the withdrawn volume with same medium.

2.2 Test Solution: Filter the resulting solution through 0.2 micron membrane filter.

2.3 Reference Solution: Weigh accurately about 25 mg of Sodium Valproate reference standard in 50 ml volumetric flask and add about 30 ml diluents and sonicate for about 10 min and make volume with diluents. Dilute 5 ml of the filtrate to 50 ml with same solvent. Filter the resulting solution through 0.2 micron membrane filter. (500 ppm)

2.4 Chromatographic Condition: Proceed as directed under the Assay.

2.5 Procedure: Inject 25 µl of reference solution five times as per above mentioned chromatographic conditions. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0 and the relative standard deviation for replicate injections in not more than 2.0%. Inject 25 µl test solution, record the chromatograms. Calculate the % release per tablet.

2.6 Limit:

15 to 35 % in 1st hour

35 to 55 % in 4th hour

55 to 70 % in 8th hour

70 to 85 % in 12th hour

NLT 75 % of the stated amount in 20th hour

3. Assay

3.1 Test Solution: Weigh and powder 20 tablets. Weigh powder eq. to 250 mg of Sodium Valproate in 100 ml volumetric flask. Add about 70 ml of diluent and sonicate for 15 minutes, make up the volume to 100 ml with diluent. Filter and dilute 5 ml of the filtrate to 25 ml with diluent. Filter the resulting solution through 0.2 micron membrane filter. (500 ppm)

3.2 Reference Solution: Weigh accurately about 12.5 mg of Sodium Valproate reference standard in 25 ml volumetric flask and add 15 ml diluent in it. Sonicate for about 10 min and make volume with diluent. Filter the resulting solution through 0.2 micron membrane filter. (500 ppm)

3.3 Chromatographic System:

Column: C18, (250*4.6 mm), 5 µm

Flow rate: 1.0 ml/min

Injection volume: 25 µl

Wavelength: 220 nm

Detector: UV

Column temperature: 35 °C

Buffer: 0.32 % Potassium dihydrogen phosphate, adjust pH 3.0 ± 0.05 with Orthophosphoric acid

Mobile phase: Buffer: Acetonitrile (45:55)

Diluent: Water: Acetonitrile (1:1)

3.4 Procedure: Inject 25 µl of reference solution five times. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0 and the relative standard deviation for replicate injections in not more than 2.0%. Inject 25 µl of each of the sample solution separately. Calculate the content of Sodium Valproate in each tablet.

4. Other Tests: As per pharmacopoieal requirement.