ANALYTICAL METHOD VALIDATION COMMITTEE FOR NON PHARMACOPOEIAL PRODUCT

DEPARTMENT OF DRUG ADMINISTRATION

Sodium Valproate Tablet (Sustained Release)

Sodium Valproate Tablet 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 sample solution should correspond to the peak in the chromatogram obtained with the reference standard solution of Sodium Valproate.

2. Assay:

2.1 Reagents Required:

1. Acetonitrile (HPLC Grade)
2. Orthophosphoric acid (HPLC Grade)
3. Potassium dihydrogen phosphate
4. HPLC Grade water

2.2 Preparation of reagent solution:

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

2.2.2 Mobile phase: Buffer: Acetonitrile (45:55)

Mix buffer and Acetonitrile, cool to room temperature and filter the solution through 0.2 micron filter paper using vacuum pump.

2.2.3 Diluent: Water: Acetonitrile (1:1)

2.3 Chromatographic system

2.3.1 Column: Octyldecylsilane (C18), (250*4.6 mm), 5 µm

2.3.2 Flow rate: 1.0 ml/min

2.3.3 Detector: UV Detector

2.3.4 Wavelength: 220 nm

2.3.5 Injection volume: 25 µl

2.3.6 Oven temperature: 35 °C

2.4 Standard Solution: Weigh accurately about 12.5 mg of Sodium Valproate RS 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 0.22 micron nylon membrane filter. (500 ppm)

2.5 Sample Preparation: Weigh and powder 20 tablets. Weigh powder eq. to 250 mg of Sodium Valproate in 100ml volumetric flask. Add about 70ml 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 0.22 micron nylon membrane filter. (500 ppm)

2.6 Procedure

Inject 25 µl of standard preparation five/six times. The test is not valid unless the column efficiency is not less than 2000 theoretical plates. The tailing factor is not more than 2.0 and the relative standard deviation for replicate injections in not more than 2.0%. After the completion of the system suitability test parameter, inject 25 µl of each of the sample solution separately. Calculate the content of Sodium Valproate in each tablet by using following formula:

2.7 Calculations:

Content of Sodium Valproate per Tablet:

$$\frac{\textbf{Spl Peak Area}}{\textbf{Std Peak Area}} \textbf{ X } \frac{\textbf{Std wt}}{\textbf{Std Dil.}} \textbf{ X } \frac{\textbf{Spl Dil.}}{\textbf{Spl wt}} \textbf{ X Average wt X Std Potency } (\%) \textbf{X} \frac{(\textbf{100} - \textbf{Std LOD})}{\textbf{100}}$$

3.0 Dissolution:

3.1 Dissolution Medium: Water

3.2 Dissolution test condition

3.2.1 Volume : 1000 ml

3.2.2 Apparatus: 1 (Paddle)

3.2.3 RPM : 50

3.2.4 Time : 1st hour, 4th hour, 8th hour, 12th hour and 20th hour

3.3 Standard Solution:

Weigh accurately about 25 mg of Sodium Valproate RS 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. (500 ppm) Filter the resulting solution through 0.22 micron nylon membrane filter.

3.4 Sample Solution:

Transfer one tablet into each vessel and run the apparatus for 20 hours. Withdraw a suitable volume of sample at the determined time interval, filter, and replace the withdrawn volume with same medium. Filter the resulting solution through 0.22 micron nylon membrane filter.

Separately inject 25 µl of standard and sample solution under test into chromatograph, record the chromatograms. Calculate the % release by comparison with the standard solution using following formula.

3.8 Calculation:

$$\%\,\boldsymbol{release} = \frac{\boldsymbol{Spl\ Area}}{\boldsymbol{Std\ Area}}\ \boldsymbol{X}\ \frac{\boldsymbol{Std\ wt}}{\boldsymbol{Std\ Dil}}\ \boldsymbol{X}\ \frac{\mathbf{1000}}{\boldsymbol{Label\ Claim}}\ \boldsymbol{X\ Std.Potency}\ (\%)\boldsymbol{X}\ \frac{\mathbf{100} - \boldsymbol{LOD}}{\mathbf{100}}\ \boldsymbol{X}\ \mathbf{100}\ \%$$

3.9 Tolerence Limit: In 1st hour - 15 to 35%

In 4th hour - 35 to 55%

In 8th hour - 55 to 70%

In 12th hour - 70 to 85%

In 20th hour - NLT 75% of the stated amount