Government of Nepal
Ministry of Health and Population
Department of Drug Administration
National Medicines Laboratory
Quality and Method Validation Section

Analytical profile of Clomipramine Hydrochloride Tablets

Analytical Profile No.: Clomi 078/079/AP 100

Clomipramine Hydrochloride Tablets contains not less than 90.0% and not more than 110.0% of the stated amount of Clomipramine Hydrochloride.

Usual Strength: 10 mg, 25 mg, 50 mg

1. Identification:

In the Assay, the principle peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests:

2. Dissolution: *Deteremine by UV-Vis spectrophotometer*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 500ml of 0.1N HCl

Speed and Time: 50 rpm and 30 minutes

Withdraw a suitable volume of the medium and filter.

2.2 Test Solution: Use the filtrate

2.3 Reference Solution: Weigh accurately about 23 mg of Clomipramine Hydrochloride WS in 100 ml volumetric flask. Add about 70 ml of dissolution media, sonicate to dissolve, cool to room temperature and make up the volume with same solvent. Further dilute 10 ml of this solution to 100 ml with same solvent.

2.4 Procedure: Measure the absorbance of the reference and test solutions at the wavelength of maxima at 252 nm using dissolution medium as blank.

Calculate the percent release of Clomipramine Hydrochloride.

2.5 Limit: Not less than 80 percent (D) of the stated amount of Clomipramine Hydrochloride.

3. Uniformity of Content

Determine by liquid chromatography, as described in the Assay, using the following solution as the test solution.

Test Solution: Place a tablet in a 100ml volumetric flask, add 70ml of methanol, sonicate to disperse whole tablet with intermittent shaking. Cool, make up the volume to 100 ml with same solvent and filter.

4. Assay: *Determine by liquid chromatography*

4.1 Test Solution: Weigh and powder 20 tablets. Weigh a quantity of powder equivalent to 25mg of Clomipramine Hydrochloride into 250 ml volumetric flask, add about 150 ml of methanol, sonicate with intermittent shaking, cool and make volume to 250 ml with same solvent.

4.2 Reference Solution: Weigh accurately about 25 mg of Clomipramine Hydrochloride WS in 250 ml volumetric flask. Add about 150 ml of methanol, sonicate to dissolve, cool and make volume to 250 ml with same solvent.

4.3 Chromatographic system:

- **Column:** C18, (250 x 4.6 mm), 5 µ particle size
- **Flow rate:** 1.0 ml/min
- **Wavelength:** 254 nm
- **Column Oven Temperature:** 35 ºC
- **Injection volume:** 10 µl
- **Detector:** UV
- **Mobile Phase:** Transfer 20 ml of solution A and 2 ml of triethylamine to 500ml volumetric flask and dilute to 500 ml with water. Transfer this solution to 1000 ml volumetric flask, adjust pH to 3.2 with phosphoric acid, dilute to 1000 ml with acetonitrile, filter and degas.

  Solution A: Transfer 2.75 g of sodium 1-heptanesulfonate to 50 ml volumetric flask. Dissolve in 25 ml of water and dilute to 50 ml with glacial acetic acid.

4.4 Procedure: Inject the reference solution five times and sample solutions. 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 is not more than 2.0%. Measure the peak responses. Calculate the content of Clomipramine Hydrochloride in the tablets.

5. Other tests: As per pharmacopoeial requirements.