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

Analytical profile of Paracetamol, Phenylephrine Hydrochloride, Chlorpheniramine Maleate Tablets

Analytical Profile No.: Para Phe Chlor 080/81/AP 144

Paracetamol, Phenylephrine hydrochloride and Chlorpheniramine Maleate tablets contains not less than 90.0% and not more than 110.0% of the stated amount of Paracetamol, Phenylephrine hydrochloride and Chlorpheniramine Maleate.

Usual Strength: Each uncoated tablets contains

Paracetamol 500 mg

Phenylephrine Hydrochloride 10 mg

Chlorpheniramine Maleate 2 mg/4 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 certified reference solution.

2. Dissolution: *Determine by liquid chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900 ml Phosphate Buffer (Dissolve 54.44 gm. Of Potassium dihydrogen phosphate in 6000 ml of water pH 6.5 adjust with 0.2N NaOH).

RPM and Time: 50 RPM and 30 minutes.

Withdraw a suitable volume of the medium and filter.

2.3 Test Solution: Use the filtrate.

2.4 Reference Solution 1: Weigh accurately about 111 mg of Phenylephrine Hydrochloride WS and 22.2 mg of Chlorpheniramine Maleate WS and carefully transfer it to 100 ml of volumetric flask, add Approx. 70 ml of mobile phase and sonicate for 5 minutes to dissolve completely. Cool to room temperature. Make up the volume up to mark with mobile phase.

Reference Solution 2: Weigh accurately about 55 mg of Paracetamol WS and carefully transfer it to 100 ml volumetric flask, add approx. 70 ml of mobile phase and sonicate for 5 minutes to dissolve completely. Cool to room temperature and add **1 ml of reference solution (1).** Make up the volume up to mark with mobile phase. Shake well to dissolve and filter.

2.5 Procedure: Use the chromatographic system as described in the Assay using 20 µl as injection volume. Inject the reference solution and the test solution.
Calculate the percent release of Paracetamol, Phenylephrine Hydrochloride, and Chlorpheniramine Maleate.

2.6 Limit: Not less than 75 percent (D) of the stated amount of Paracetamol, Phenylephrine Hydrochloride, Chlorpheniramine Maleate.

3. Uniformity of Content

Determine by liquid chromatography

3.1 Test Solution: Take 1 tablet and carefully transfer it to 50 ml volumetric flask, add approx. 15 ml of diluents and sonicate for approximately 5 minutes until the tablet disintegrate completely. Cool to room temperature. Make up the volume up to the mark with diluents. Shake well and filter.

3.2 Reference Solution 1: Weigh accurately about 40 mg of Chlorpheniramine Maleate WS and carefully transfer it to 100 ml of volumetric flask, add approx. 70 ml of diluents and sonicate for 5 minutes to dissolve completely. Cool to room temperature. Make up the volume up to mark with diluents. Shake well to dissolve.

3.3 Reference Solution 2: Weigh accurately about 20 mg of Phenylephrine WS and carefully transfer it to 100 ml volumetric flask, add approx. 70 ml of diluents and sonicate for 5 minutes to dissolve completely. Cool to room temperature and add **10 ml of reference solution (1).** Make up the volume up to mark with diluents. Shake well to dissolve and filter.

3.4 Procedure: Use the chromatographic system as described in the Assay using 20 µl as injection volume. Inject the reference solution and the test solution.

3.5 Limit: NLT 85.0% and NMT 11530% of the obtained average content of Phenylephrine HCl and Chlorpheniramine Maleate.

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4. Assay: *Determine by liquid chromatography*

4.1 Test solution 1(For Phenylephrine Hydrochloride and Chlorpheniramine Maleate): weigh and powder 20 tablets. Disperse a quantity of powder equivalent to two times the average weight of tablet and carefully transfer it to the 100 ml volumetric flask, add approx. 70 ml of diluents and sonicate for 5 minutes to dissolve completely. Cool to room temperature. Make up the volume up to the mark with diluents, stir for 15 minutes and filter.

[Note: For tablet with Chlorpheniramine Maleate of strength 4 mg further dilute to make final concentration of 40 mcg/ml and use this solution for determination of chlorpheniramine.]

4.2 Test solution 2 (For Paracetamol): Take 1 ml of test solution (1) to 50 ml volumetric flask and make up the volume up to mark with diluents. Shake well to dissolve and filter.

4.3 Reference solution 1: Weigh accurately about 40 mg of Chlorpheniramine Maleate WS and carefully transfer it to 100 ml of volumetric flask, add approx. 70 ml of diluents and sonicate for five minutes to dissolve completely. Cool to room temperature. Make up the volume up to mark with diluents.

4.4 Reference Solution 2: Weigh accurately about 20 mg of Paracetamol WS and 20 mg of Phenylephrine Hydrochloride WS and carefully transfer it to 100 ml volumetric flask, add approx. 70 ml of diluents and sonicate for 5 minutes to dissolve completely. Cool to room temperature and add **10 ml of reference solution (1).** Make up the volume up to mark with diluents. Shake well to dissolve and filter.

4.5 Chromatographic system:

Column: C18 (4.6mmX 250-mm, 5µ)

Flow rate: 1.0 ml/min

Wavelength: 280 nm

Injection volume: 20µl

Column Temperature: 30ºC

Diluents: A mixture of methanol and water in the ratio of 58:42 and pH adjusted to 3.0 with phosphoric acid

Mobile Phase: Dissolve about 1.1 gm. of 1-octanesulphonate in 1000 ml of diluents and filter and sonicate.

4.6 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 Paracetamol, Phenylephrine Hydrochloride, and Chlorpheniramine Maleate.

5. Other tests: As per pharmacopoeial requirements.