DEPARTMENT OF DRUG ADMINISTRATION

National Medicines Laboratory

ANALYTICAL METHOD VALIDATION COMMITTEE

Paracetamol & Chlorzoxazone Tablets

Analytical Profile No.: Chl Para 075/076/AP 025

Paracetamol and Chlorzoxazone Tablets contain not less than 90 per cent and not more than 110 per cent of the stated amount of Paracetamol and Chlorzoxazone.

1. Identification:

1.1 Paracetamol: 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 Paracetamol.

1.2 Chlorzoxazone: 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 Chlorzoxazone.

Tests:

2. Dissolution: (Paracetamol & Chlorzoxazone)

2.1 Dissolution Parameter:

Apparatus: Paddle

Medium: 900 ml Phosphate buffer pH 6.8

Speed and time: 75 rpm and 60 minutes

Temperature : 37˚C ± 0.5˚C

Withdraw the suitable volume of the medium and filter.

Determine by Liquid Chromatography

2.2 Test Solution: Use the filtrate, filter the final solution through 0.2 µm membrane filter.

2.3 Reference Solution:

2.3.1 Paracetamol Reference Solution: Weigh accurately about 100 mg of Paracetamol reference standard in 100 ml volumetric flask, add 70 ml of methanol, sonicate for 5 minutes and make up the volume with same solvent.

2.3.2 Chlorzoxazone Reference Solution: Weigh accurately about 100 mg of Chlorzoxazone reference standard in 100 ml volumetric flask, add 70 ml of methanol, sonicate for 5 minutes and make up the volume with same solvent.

2.3.3 Combined Reference Solution: Pipette 2 ml of Paracetamol & Chlorzoxazone reference solution in 100 ml volumetric flask and make up the volume with dissolution medium. Filter the combined reference solution through 0.2 µm membrane filter.

2.4 Chromatographic System and Procedure: Proceed as directed under Assay.

2.5 Limit: NLT 70 % (D) of the stated amount.

3. Assay: *Determine by Liquid Chromatography*

3.1 Test Solution: Weigh individually 20 tablets & crush them into fine powder. Weigh accurately a quantity of powder equivalent to 100 mg of Chlorzoxazone, add 70 ml of methanol, sonicate for 15 minutes and dilute to 100 ml with same solvent, filter. Dilute 2 ml of resulting solution to 100 ml with mobile phase.

3.2 Reference Solution:

3.2.1 Paracetamol Reference Solution: Weigh accurately about 100 mg of Paracetamol reference standard in 100 ml volumetric flask, add 70 ml of methanol, sonicate for 5 minutes and make up the volume with same solvent.

3.2.2 Chlorzoxazone Reference Solution: Weigh accurately about 100 mg of Chlorzoxazone reference standard in 100 ml volumetric flask, add 70 ml of methanol, sonicate for 5 minutes and make up the volume with same solvent.

3.2.3 Combined Reference Solution: Pipette 2 ml of Paracetamol & Chlorzoxazone reference solution in 100 ml volumetric flask and make up the volume with mobile phase. Filter the combined reference solution through 0.2 µm membrane filter.

3.3 Chromatographic System:

Column: a stainless steel column 25 cm x 4.6 mm, packed with octadecyl silane bonded to porous silica (5 µm),

Flow rate: 1.5 ml per minute,

Wavelength: 271 nm,

Injection volume: 20 µl,

Column temperature: ambient

Detector: UV

Phosphate buffer pH 3.0: 0.05 M disodium hydrogen phosphate, adjust the pH to 3.0 with dilute phosphoric acid.

Mobile phase: a mixture of 65 volumes of acetonitrile and 35 volumes of 0.05 M phosphate buffer pH 3.0

3.4 Procedure: Inject 20 µl of reference solution five times as per above mentioned chromatographic condition and obtain respective chromatograms. In the chromatogram obtained from the standard preparation, the column efficiency determined from the major peak should not be less than 2000 theoretical plates, the tailing factor should be not more than 2.0 and the relative standard deviation of five replicate injections should not more be than 2.0 %. Resolution between two peaks should be not less than 2. Inject 20 µl of the sample preparation and chromatograph as per above mentioned chromatographic condition. Calculate the content of Paracetamol and Chlorzoxazone in each tablet.

4. Other tests: As per pharmacopoeial requirements.