Department of Drug Administration
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE FOR NON PHARMACOPOEIAL PRODUCT

Paracetamol and Ibuprofen Suspension

Analytical Profile No.: Ibu ParS 073/074/ AP 011

Paracetamol and Ibuprofen Suspension contains not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of Paracetamol and Ibuprofen.

1. Identification:

1.1 Ibuprofen: Extract a quantity of the suspension containing 0.5 g of Ibuprofen with 20 ml of acetone, filter and evaporate the filtrate to dryness in the current of air without heating. The residue obtained in the test after recrystallization from light petroleum (40 °C to 60 °C) melts at about 75 °C.

or

Determine by IR spectrophotometer. Compare the spectrum obtained with Ibuprofen reference standard.

1.2 Paracetamol: 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 of Paracetamol.

Tests:

2. pH: 4 to 7

3. wt/ml: As per manufacturer's specification.

4. Assay

4.1 Ibuprofen

Weigh accurately a quantity of the suspension containing about 100 mg of Ibuprofen, extract with 60 ml of chloroform for 15 minutes and filter through a sintered - glass crucible of porosity 3. Wash the residue with three quantities, each of 10 ml, of chloroform and gently evaporate the filtrate just to dryness on water bath. Dissolve the residue in 100 ml of ethanol (95 per cent), previously neutralized to phenolpthalein solution, and titrate with 0.1 M sodium hydroxide using phenolpthalein solution as indicator.

1 ml of 0.1 M *Sodium Hydroxide* is equivalent to 0.02063 g of C13H18O2

Standardise the prepared sodium hydroxide solution with potassium hydrogen phthalate.

Calculation:

Content of Ibuprofen=

$$Volume\ consumed\ by\ Test \times\ Actual\ Normality \times \frac{20.63}{0.1\ \times Wt\ of\ \ Sample} \times 5 \times Wt\ per\ ml$$

4.2 Paracetamol: Determine by liquid chromatography

4.2.1 Solvent Mixture: A mixture of 0.4 volumes of formic acid, 15 volumes of methanol and 85 volumes of water.

4.2.2 Test solution:

Transfer a quantity of the suspension containing about 62.5 mg of paracetamol in a 100 ml volumetric flask and add about 60 ml of the solvent mixture. Dissolve by sonicating for about 10 minutes, cool to room temperature and dilute to 100 ml with the solvent mixture. Centrifuge the resulting solution. Dilute 2 ml of this solution to 50 ml with the solvent mixture. Filter the resulting solution through 0.2 µm membrane filter.

4.2.3 Reference Solution:

Weigh accurately about 31.25 mg of Paracetamol WS and transfer into 50 ml volumetric flask. Add about 40 ml of the solvent mixture, dissolve by sonicating for about 10 minutes, cool to room temperature and make up the volume using same solvent. Dilute 2 ml of this solution to 50 ml with the solvent mixture. Filter through 0.2 micron membrane filter.

4.2.4 Chromatographic system

Column: C18, 25 cm x 4.6 mm, 5 µm

Injection volume: 20 µl

Flow rate: 1.0 ml per minute

Wavelength: 243 nm

Column temperature: Ambient

Detector: Spectrophotometer

Mobile phase: Dissolve 1.60 g butane sulphonate in 1000 ml of solvent mixture.

4.2.5 Procedure:

Inject reference solution and the test solution five/six times. The test is not valid unless the column efficiency determined from the major peak is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation of replicate injections is not more than 2.0 %. Inject 20 µl of standard and sample solution separately and obtain the respective chromatogram. Measure the peak responses.

Calculate the content of paracetamol per tablet.