ANALYTICAL METHOD VALIDATION COMMITTEE FOR NON PHARMACOPOEIAL PRODUCT

DEPARTMENT OF DRUG ADMINISTRATION

Paracetamol & Ibuprofen Suspension

Paracetamol & Ibuprofen Suspension contain not less than 95% and not more than 105% of the stated amount of Paracetamol & Ibuprofen.

1. Identification:

1.1. Ibuprofen: Extract a quantity of the powdered tablet containing 0.5 g of Ibuprofen with 20 ml of acetone, filter and evaporate the filtrate to drynedd in the current of air with out heating. The residue obtained in the test after recrystallization from light petroleum (40 °C to 60 °C) melts at about 75 °C.

1.2. Paracetamol

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 Paracetamol.

2. pH

Operate the pH meter accordind to the manufacturer's instruction. Calibrate the pH meter using the standard buffer solution. Determine the pH of the syrup by using the calibrated pH meter.

Tolerence Limit: 4 to 7

3. wt/ml

First dry the pycnometer in the hot air oven and cool it in dessicator for 5 to 10 minutes. Take the weight of the empty pycnometer together with its stopper (W_1). Fill the pycnometer with water, put the stopper, wipe it dry outside with the help of tissue paper. Now take the weight of pycnometer and water (W_2). Throw water, dry the pycnometer and fill the pycnometer with the syrup, put the stopper, wipe it dry outside with the help of tissue paper. Take the weight of pycnometer and suspension (W_3). The calculate wt/ml

wt/ml (g/ml) = $\frac{W3-W1}{W2-W1}$ **x volume of 1 g of water at various temperature**

4. Assay

4.1 Assay of Ibuprofen

4.1.1 Reagents:

4.1.1.1 0.1 M NaOH: Dissolve 4.2 g of sodium hydroxide in sufficient water to produce 1000 ml water. Standardise the solution in the following manner.

Weigh accuraetly about 500 mg of potassium hydrogen phthalate, previously powdered and dried at 120 ° C for 2 hours, and dissolve in 75 ml of carbondioxide free water. Add 0.1 ml of

phenolphthalein solution and titrate with the sodium hydroxide solution until pink color is obtained.

1 ml of 0.1 M Sodium hydroxide is equivalent to 20.42 mg of Ibuprofen

4.1.1.2 Phenolphthalein solution: 1 % solution of phenolphthalein in ethanol (95 %)

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%), previously neutralized to phenolpthalein solution as indicator.

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

Calculation:

Amount in % =

$$Volume\ consumed\ by\ Test \times Actual\ Normality \times \frac{20.63}{0.1 \times Wt\ of\ Sample} \times 5 \times \frac{Wt}{ml} \times True\ Value/Claim$$

4.2 Assay of Paracetamol

4.2.1 Reagents:

4.2.1.1 Solvent Mixture: 0.4 volume of formic acid, 15 volumes of methanol and 85 volumes of water.

4.2.1.2 Mobile phase: 1.60 g butanesulphonate in 1000 ml of solvent mixture. Cool to room temperature and filter the solution through 0.2 micron filter paper using vacuum pump.

4.2.2 Standard Solution:

Weigh accurately about 31.25 mg of Paracetamol 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 dilute to 50 ml with the solvent mixture. Dilute 2 ml of this solution to 50 ml with the solvent mixture. Filter through 0.2 micron filter paper.

4.2.3 Test Solution:

Shake a quantity of the suspension containing about 62.5 mg of Paracetamol in 60 ml of the solvent mixture. Add about 40 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 through 0.2 micron filter paper.

4.2.4 Chromatographic condition

Column : 4.6 mm × 25 cm, 5 µm packing (Shim-Pack Gist, C18)

Flow rate : 1 ml/min

Injection volume: 20 µl

4.2.5 Procedure: Inject the reference solution five/six times and sample solutions. 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%. Calculate the content of paracetamol in the suspension by using the following formula.

Calculation:

Amount in % =

$$\frac{Area\ of\ spl}{Area\ of\ Std} \times \frac{Conc.\ of\ std}{Conc.of\ spl} \times \frac{Potency\ of\ std}{100} \times \frac{100 - LOD}{100} \times 5\ x\ wt/ml$$