DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE

Iron Polymaltose and Folic acid Capsules

Analytical Profile No.: IPFC 076/077/AP 062

Iron Polymaltose and Folic acid Capsules contains not less than 90 % and not more than 110 % of the stated amount of elemental iron and folic acid.

1. Identification:

1.1 Ferric iron: Dissolve a quantity of the substance under examination containing about 10 mg of iron in 1 ml of water or use 1 ml of the prescribed solution. Add 1 ml of potassium ferrocyanide solution; an intense blue precipitate, insoluble in dilute hydrochloric acid is produced.

1.2 Polymaltose: Add 2-3 drops of solution of maltose (1 in 50) to 5 ml of hot alkaline cupric tartrate, a red precipitate is produced.

1.3. Folic acid: 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. Uniformity of Content (for Folic acid): *Determine by liquid chromatography*

Proceed as described in the Assay, using 100 µl as injection volume and the following test solution and reference solution.

2.1 Test solution: Disperse 1 capsule in the solvent mixture and dilute to obtain a solution containing 0.0004 per cent w/v of folic acid in the solvent mixture and filter through 0.2 µm membrane filter.

2.2 Reference solution: A 0.0004 per cent w/v of folic acid RS in the solvent mixture and filter through 0.2 µm membrane filter.

2.3 Limit: 85 % - 115 % of the stated amount

3. Assay:

3.1 Elemental Iron: Weigh accurately about 0.3 g equivalent of Iron polymaltose (300 mg Polymaltose equivalent to 100 mg of elemental iron) add 50 ml of water and 3 ml of hydrochloric

acid. Dissolve completely by heating to boiling. Cool rapidly by adding 100 ml of water, add 4 g potassium iodide, close the flask, allow to stand in dark for 30 minutes and titrate the liberated iodine with 0.1 M sodium thiosulphate using starch solution, added towards the end of titration, as indicator. Repeat the operation without the substance under examination. The difference between the titration volumes indicates the amount of iodine liberated by the ferric ion.

1 ml of 0.1 M sodium thiosulphate is equivalent to 0.005585 g of ferric ion.

% content of elemental Iron =

$$\frac{\text{Volume of thiosulphate} * 0.005585 * \text{Factor of sod thiosulphate} * \text{average fill weight of capsule}}{\text{Wt of sample taken}}$$

3.2 Folic acid: Determine by Liquid Chromatography

3.2.1 Solvent mixture: A mixture of 800 volumes of 0.57 % w/v solution of dipotassium hydrogen phosphate and 135 volumes of methanol.

3.2.2 Test solution: Weigh accurately a quantity of the mixed contents of 20 capsules containing about 1 mg equivalent of folic acid in a 100 ml volumetric flask, dissolve by sonicating in solvent mixture for 10 minutes, cool to room temperature and dilute to 100 ml with solvent mixture. Centrifuge and filter the resulting solution through 0.2 µm membrane filter.

3.2.3 Reference Solution: A solution containing 0.001 per cent w/v solution of Folic acid RS in solvent mixture. Filter the solution through 0.2 µm membrane filter.

3.2.4 Chromatographic system

Column: C18, 250 cm x 4.6 mm, 5 µm

Flow rate: 1.0 ml per minute

Wavelength: 277 nm

Injection volume: 10 µl

Column Temperature: 30 ^{O}C

Detector: UV

Mobile Phase: A mixture of 135 volumes of methanol and 800 volumes of a solution containing 0.938 per cent w/v sodium perchlorate and 0.075 per cent w/v of potassium

dihydrogen orthophosphate adjusted to pH 7.2 with 0.1 M potassium hydroxide and diluted to 1000 ml with water.

3.2.5 Procedure: Inject reference solution five times and test solution. 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 per cent. Inject test solution, measure peak responses and calculate the content of folic acid in each capsule.

4. Other tests: As per pharmacopoeial requirement.