DEPARTMENT OF DRUG ADMINISTRATION
National Medicines Laboratory
ANALYTICAL METHOD VALIDATION COMMITTEE

Amlodipine & Ramipril Tablets

Analytical Profile No.: Amlo Rami 076/077/AP063

Amlodipine & Ramipril Tablets contain not less than 95 % and not more than 105 % of the stated amount of Amlodipine & Ramipril.

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 reference solution.

Tests:

2. Dissolution: *Determine by liquid chromatography*

2.1 Dissolution Parameter

Apparatus: Paddle

Medium: 900 ml of 0.1 N HCl

Speed and Time: 75 rpm & 45 minutes

Temperature: 37± 0.5℃

2.2 Test Solution:

Withdraw a suitable volume of the medium and filter through 0.2 µm membrane filter. Use the filtrate.

2.3 Reference Solution:

2.3.1 Ramipril Reference Solution:

Accurately weigh and transfer about 28 mg of Ramipril RS into 100 ml volumetric flask, add about 70 ml of solvent mixture, sonicate to dissolve and dilute to volume with solvent mixture and mix well.

2.3.2 Amlodipine Reference Solution:

Accurately weigh and transfer about 31 mg of Amlodipine Besylate RS into 100 ml volumetric flask, add about 70 ml of solvent mixture, sonicate to dissolve and dilute to volume with solvent mixture and mix well.

2.3.3 Combined Reference Solution:

Pipette out 2 ml of Ramipril Reference Solution and 5 ml of Amlodipine Reference Solution into a 200 ml volumetric flask and dilute to volume with solvent mixture and mix well. Filter the resulting solution through 0.2 µm membrane filter.

2.4 Chromatographic System: Proceed as directed under the Assay

2.5 Procedure:

Inject the reference solution five times and obtain respective chromatogram using above mentioned chromatographic conditions. 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, the relative standard deviation for replicate injections in not more than 2.0% and the resolution between Ramipril and Amlodipine is not less than 2. After injecting reference solution inject test solution and blank solution. Calculate the per cent release of Amlodipine and Ramipril**.**

2.6 Limit:

Not less than 75% (D) of the stated amount

3. Uniformity of Content: *Determine by liquid chromatography*

3.1 Test solution:

Weigh 10 tablets individually and transfer each into 50 ml volumetric flask. Add about 35 ml of solvent mixture shake to disperse, sonicate for about 20 minutes; cool and make up the volume to the mark with solvent mixture. Centrifuge the solution at 3000 rpm for 10 minutes.

3.2 Reference Solution:

Proceed as directed under the Assay.

3.3 Chromatographic System and Procedure*:*

Proceed as described in the Assay. Calculate the content of Ramipril and Amlodipine in the tablets.

3.4 Limit*:*

85 % - 115 % of the stated amount

4. Assay: *Determine by Liquid Chromatography*

4.1 Solvent Mixture: 0.1 N HCl : Methanol (20:80)

4.2 Test Solution:

Determine the average weight of 20 tablets. Transfer 10 tablets into 250 ml volumetric flask, add about 170 ml of solvent mixture, shake gently to disperse, sonicate for about 20 minutes with intermittent shaking, cool and make up the volume to the mark with solvent mixture. Centrifuge the solution at 3000 rpm for 10 minutes. Filter the clear supernatant through 0.2 µm membrane filter.

4.3 Reference Solution

4.3.1 Ramipril Reference Solution:

Accurately weigh and transfer about 25 mg of *Ramipril RS* into 50 ml volumetric flask, add about 35 ml of solvent mixture, sonicate to dissolve and dilute to volume with solvent mixture and mix well.

4.3.2 Amlodipine Reference Solution:

Accurately weigh and transfer about 70 mg of *Amlodipine Besylate RS* into 50 ml volumetric flask, add about 35 ml of solvent mixture, sonicate to dissolve and dilute to volume with solvent mixture and mix well.

4.3.3 Combined Reference Solution:

Pipette out 10 ml of Ramipril Reference Solution and 10 ml of Amlodipine Reference Solution into a 50 ml volumetric flask and dilute to volume with solvent mixture and mix well. Filter the resulting solution through µm membrane filter.

4.4 Chromatographic system:

Column:	C18, (250 x 4.6 mm), 5 µm
Flow rate:	1.5 ml/min
Wavelength:	210 nm
Injection volume:	5 µl
Column Temperature:	50ºC

Mobile phase: A mixture of 60 volumes of buffer solution and 40 volumes of Acetonitrile.
Buffer solution: Prepared by dissolving 5.0 g of Sodium perchlorate monohydrate in 1000 ml of HPLC water, and adjusting pH to 2.5 with orthophosphoric acid.

4.5 Procedure:

Inject the combined reference solution five times as per above mentioned chromatographic conditions. 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, the relative standard deviation for replicate injections in not more than 2.0% and the resolution between Ramipril and Amlodipine is not less than 2. After injecting the reference solution, separately inject test solution and obtain the respective chromatograms. Calculate the content of Ramipril and Amlodipine in the tablets.

5. Other tests: As per pharmacopoeial requirement.