

Amlodipine and Atenolol Tablets

Amlodipine Besylate and Atenolol Tablets; Amlodipine Besilate and Atenolol Tablets.

Amlodipine and Atenolol Tablets contain amlodipine besylate equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of amlodipine, $C_{20}H_{25}ClN_2O_5$ and atenolol, $C_{14}H_{22}N_2O_3$.

Usual strengths. Amlodipine, 2.5 mg and Atenolol, 25 mg; Amlodipine, 2.5 mg and Atenolol, 50 mg; Amlodipine, 5 mg and Atenolol, 50 mg.

Identification

In the Assay, the principal peaks in the chromatogram obtained with the test solution correspond to the peaks in the chromatogram obtained with the reference solution.

Tests

Dissolution. (2.5.2)

Apparatus No. 1,

Medium: 900 ml of 0.01 M hydrochloric acid.

Speed and time. 75 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Solvent mixture. 50 volumes of the mobile phase A and 50 volumes of acetonitrile.

Test solution. Use the filtrate, dilute if necessary with the dissolution medium.

Reference solution (a). A 0.112 per cent w/v solution of atenolol RS in the solvent mixture.

Reference solution (b). A 0.075 per cent w/v solution of amlodipine besylate RS in the solvent mixture.

Reference solution (c). Dilute a suitable volume of reference solution (a) and reference solution (b) with dissolution medium to obtain a solution having similar concentration to the test solution.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with phenyl group (5 μ m) (Such as Zorbax SB-Phenyl),
- sampler temperature: 20 $^{\circ}$,
- mobile phase: A. a buffer solution prepared by dissolving 1.36 g of potassium dihydrogen orthophosphate in 1000 ml of water, adjusted to pH 5.5 with dilute sodium hydroxide,
B. acetonitrile.
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 225 nm,
- injection volume: 50 μ l.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	75	25
15	20	80
16	75	25
20	75	25

Inject reference solution (c). 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 is not more than 2.0 per cent for amlodipine and atenolol peak.

Inject reference solution (c) and the test solution.

Calculate the contents of $C_{20}H_{25}ClN_2O_5$ and $C_{14}H_{22}N_2O_3$ in the medium.

D. Not less than 70 per cent of the stated amount of $C_{20}H_{25}ClN_2O_5$ and $C_{14}H_{22}N_2O_3$.

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of powdered tablets containing 100 mg of atenolol in 30 ml of mobile phase A, with the aid of ultrasound with intermittent shaking for 15 minutes, and dilute to 50.0 ml with the same solvent, centrifuge the solution at 4000 rpm for 10 minutes and use the supernatant liquid.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 μ m) (Such as Kromasil 100^o-5-C-18),
- mobile phase: A. a mixture of 80 volumes of a buffer solution prepared by dissolving 3.4 g of *potassium dihydrogen phosphate*, 0.8 g of *sodium octane-1 sulphonic acid* and 0.4 g of *tetrabutylammonium hydrogen sulphate* in 1000 ml of *water*, 18 volumes of *methanol* and 2 volumes of *tetrahydrofuran*, mix and adjusted to pH 3.0 with *orthophosphoric acid*,
B. *methanol*.
- a gradient programme using the conditions given below,
- spectrophotometer set at 238 nm (for amlodipine) and 273 nm (for atenolol),
- injection volume: 20 μ l.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)	Flow rate (ml per minute)
0	90	10	1.0
25	90	10	1.0
32	50	50	1.5
50	50	50	1.5
60	90	10	1.0
70	90	10	1.0

The relative retention time with respect to amlodipine peak for amlodipine impurity D is about 0.81.

Inject the test solution and record the chromatogram at 238 nm and 273 nm.

For Atenolol-

Atenolol related impurities elutes up to 30 minutes at 273 nm, the area of any secondary peak is not more than 0.5 per cent and the sum of areas of all the secondary peaks is not more than 2.0 per cent, calculated by area normalisation. Ignore any peak corresponding to amlodipine and benzene sulphonate (relative retention time at about 0.28 with respect to atenolol peak).

For Amlodipine-

Amlodipine related impurities elutes after 30 minutes at 238 nm, the area of any peak corresponding to amlodipine impurity D is not more than 0.5 per cent, any other secondary peak is not more than 0.5 per cent and the sum of areas of all the secondary peaks, other than amlodipine impurity D is not more than 2.0 per cent, calculated by area normalisation. Ignore any peak corresponding to atenolol and benzene sulphonate (relative retention time at about 0.05 with respect to amlodipine peak).

Uniformity of content. Complies with the test stated under Tablets.

For Amlodipine — Determine by liquid chromatography (2.4.14), as described under Assay with the following modifications.

Test solution. Disperse one intact tablet in 30 ml of the solvent mixture with the aid of ultrasound for 15 minutes with intermittent shaking, and dilute to 50.0 ml with the solvent mixture, centrifuge at 3000 rpm for 5 minutes. Dilute 5.0 ml of the supernatant liquid to 100.0 ml with 0.01 M *hydrochloric acid*.

Inject the reference solution and the test solution.

Calculate the content of $C_{27}H_{44}O$ in the tablet.

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. 50 volumes of the mobile phase A and 50 volumes of *acetonitrile*.

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing about 50 mg of atenolol in the solvent mixture with the aid of ultrasound for 15 minutes with intermittent shaking, and dilute to 100.0 ml with the solvent mixture, centrifuge at 3000 rpm for 5 minutes. Dilute 5.0 ml of the supernatant liquid to 50.0 ml with 0.01 M hydrochloric acid.

Reference solution. A solution containing 0.05 per cent w/v of *atenolol RS* and 0.007 per cent w/v of *amlodipine besylate RS* in the solvent mixture. Dilute a suitable volume of the solution with 0.01 M hydrochloric acid to obtain a solution having similar concentration to the test solution.

Use chromatographic system as described under Dissolution.

Inject the reference solution. 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 is not more than 2.0 per cent for amlodipine and atenolol peak.

Inject the reference solution and the test solution

Calculate the content of the $C_{20}H_{25}ClN_2O_5$ and $C_{14}H_{22}N_2O_3$ in the tablets.

Storage. Store protected from moisture.

Labelling. The label states the strength in terms of the equivalent amount of amlodipine and atenolol.

Draft for Comments