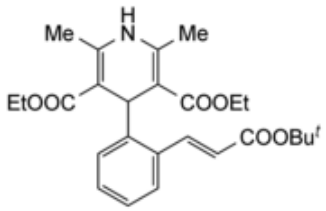
Edition: BP 2025 (Ph. Eur. 11.6 update)

Lacidipine

General Notices



$C_{26}H_{33}NO_6$ 455.6 *103890-78-4*

Action and use

Calcium channel blocker.

Preparation

Lacidipine Tablets

DEFINITION

Lacidipine is diethyl (*E*)-4-{2-[(*tert*-butoxycarbonyl)vinyl]phenyl}-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate. It contains not less than 97.5% and not more than 102.0% of $C_{26}H_{33}NO_6$, calculated with reference to the anhydrous, propan-2-ol–free substance.

CHARACTERISTICS

A white to pale yellow crystalline powder. It melts at about 178°.

Practically insoluble in *water*; freely soluble in *acetone*; sparingly soluble in *absolute ethanol*.

Carry out all of the following procedures protected from light and prepare solutions immediately before use.

IDENTIFICATION

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of Lacidipine (*RS 407*).

B. In the Assay, the principal peak in the chromatogram obtained with solution (1) has the same retention time as the principal peak in the chromatogram obtained with solution (2).

TESTS

Propan-2-ol

Carry out the method for *gas chromatography*, Appendix III B. Prepare a 0.002% v/v solution of *1,4-dioxan* (internal standard) in *dimethylacetamide* (solution A).

(1) 0.002% v/v solution of *propan-2-ol* in solution A.
(2) 2% w/v of the substance being examined in solution A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a glass column (60 m × 0.32 mm) bonded with a film (5 µm) of *polymethylsiloxane* (CP-Sil 5CB is suitable).
(b) Use *helium* as the carrier gas at 1.7 mL per minute.
(c) Use a temperature gradient as described below.
(d) Use an injection temperature of 170°.
(e) Use a detector temperature of 250°.
(f) Inject 1 µL of each solution.

Time (Minutes)	Temperature	Comment
0 - 1	60°	isothermal
1 - 18	60°→110°	linear increase 3°/minute
18 – 20	110°→200°	linear increase 50°/minute
20 – 27	200°	isothermal

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (1) shows two clearly separated peaks. The retention time for propan-2-ol is about 6.2 minutes and that for dioxan is about 15 minutes.

LIMITS

In the chromatogram obtained with solution (2):

the percentage content of propan-2-ol is not more than 0.5% w/w.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute 1 volume of a 0.1% w/v solution of the substance being examined in *absolute ethanol* to 5 volumes with the mobile phase.
(2) Dilute 1 volume of solution (1) to 500 volumes with the mobile phase.

(3) Dilute 1 volume of a 0.1% w/v solution of *lacidipine impurity standard BPCRS* in *absolute ethanol* to 5 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm x 4.6 mm) packed with *cyanosilyl silica gel for chromatography* (5 µm) (Spherisorb CN is suitable).
(b) Use isocratic elution using the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 240 nm.
(f) Inject 20 µL of each solution.
(g) If necessary adjust the composition of the mobile phase so that, in the chromatogram obtained with solution (3), the retention time of the peak due to lacidipine is about 10 minutes.
(h) For solution (1), allow the chromatography to proceed for 2 times the retention time of the principal peak.

MOBILE PHASE

3 volumes of *absolute ethanol* and 97 volumes of n-*hexane*.

SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) closely resembles the chromatogram supplied with *lacidipine impurity standard BPCRS*.

LIMITS

In the chromatogram obtained with solution (1):

the area of any peak due to lacidipine impurity B is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.2%, taking into account the correction factor of 0.5);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the total nominal content of impurities is not greater than 0.5%.

Water

Not more than 0.2% w/w, Appendix IX C. Use 0.5 g.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute 5 volumes of a 0.1% w/v solution of the substance being examined in *absolute ethanol* to 100 volumes with the mobile phase.
(2) Dilute 5 volumes of a 0.1% w/v solution of *lacidipine BPCRS* in *absolute ethanol* to 100 volumes with the mobile phase.
(3) Dilute 1 volume of a 0.1% w/v solution of *lacidipine impurity standard BPCRS* in *absolute ethanol* to 5 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure described under Related substances may be used.

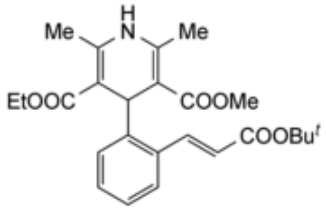
SYSTEM SUITABILITY

The test is not valid unless the chromatogram obtained with solution (3) closely resembles the corresponding chromatogram supplied with *lacidipine impurity standard BPCRS*.

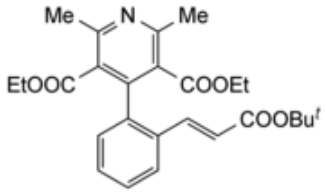
DETERMINATION OF CONTENT

Calculate the content of $C_{26}H_{33}NO_6$ from the chromatograms obtained and using the declared content of $C_{26}H_{33}NO_6$ in *lacidipine BPCRS*.

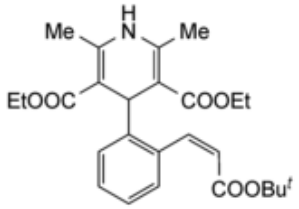
IMPURITIES



A. Ethyl methyl (*E*)-4-{2-[2-(*tert*-butoxycarbonyl)vinyl]phenyl}-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate,



B. Diethyl (*E*)-4-{2-[2-(*tert*-butoxycarbonyl)vinyl]phenyl}-2,6-dimethylpyridine-3,5-dicarboxylate,



C. Diethyl (*Z*)-4-{2-[2-(*tert*-butoxycarbonyl)vinyl]phenyl}-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate.