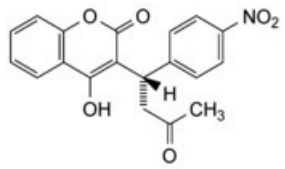
Edition: BP 2025 (Ph. Eur. 11.6 update)

Acenocoumarol

General Notices



and enantiomer

C19H15NO6 353.3 *152-72-7*

Action and use

Vitamin K epoxide reductase inhibitor; oral anticoagulant.
Preparation

Acenocoumarol Tablets

DEFINITION

Acenocoumarol is (*RS*)-4-hydroxy-3-(1-*p*-nitrophenyl-3-oxobutyl)coumarin. It contains not less than 98.5% and not more than 100.5% of C19H15NO6, calculated with reference to the dried substance.

CHARACTERISTICS

An almost white to buff powder.

Practically insoluble in *water* and in *ether*; slightly soluble in *ethanol (96%)*. It dissolves in aqueous solutions of the alkali hydroxides. It exhibits polymorphism.

IDENTIFICATION

The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of acenocoumarol *(RS 001)*. If the spectra are not concordant, dissolve 0.1 g of the substance being examined in 10 mL of *acetone* and add *water* drop wise until the solution becomes turbid. Heat on a water bath until the solution is clear and allow to stand. Filter, wash the crystals with a mixture of equal volumes of *acetone* and *water* and dry at 100° at a pressure of 2 kPa for 30 minutes. Prepare a new spectrum of the residue.

TESTS

Clarity and colour of solution

A. A2.0% w/v solution in *acetone* is *clear*, Appendix IV A.
B. The *absorbance* of a 4-cm layer of a 2.0% w/v solution in *acetone* at 460 nm is not more than 0.12, Appendix II B.
C. A2.0% w/v solution in 0.1M *sodium hydroxide* is *clear*, Appendix IV A, and yellow.

Light absorption

Absorbance of a 0.001% w/v solution in a mixture of 1 volume of 1M *hydrochloric acid* and 9 volumes of *methanol* at the maximum at 306 nm, 0.50 to 0.54, calculated with reference to the dried substance, Appendix II B.

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solutions in *acetone*.

(1) 2.0% w/v of the substance being examined.
(2) 0.0020% w/v of the substance being examined.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel GF254*.
(b) Use the mobile phase as described below.
(c) Apply 20 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, allow it to dry in air and immediately examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

20 volumes of *glacial acetic acid*, 50 volumes of *cyclohexane* and 50 volumes of *dichloromethane*.

LIMITS

Any *secondary spot* in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (2) (0.1%).

Loss on drying

When dried to constant weight at 105°, loses not more than 0.5% of its weight. Use 1 g.

Sulfated ash

Not more than 0.1%, Appendix IX A.

ASSAY

Dissolve 0.6 g in 50 mL of *acetone* and titrate with *0.1M sodium hydroxide VS* using *bromothymol blue solution R3* as indicator. Repeat the operation without the substance being examined. The difference between the titrations represents the amount of sodium hydroxide required. Each mL of *0.1M sodium hydroxide VS* is equivalent to 35.33 mg of C19H15NO6.