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

Acenocoumarol Tablets

General Notices

Action and use

Vitamin K epoxide reductase inhibitor; oral anticoagulant.

DEFINITION

Acenocoumarol Tablets contain Acenocoumarol.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of acenocoumarol, $C_{19}H_{15}NO_6$

92.5 to 107.5% of the stated amount.

IDENTIFICATION

A. Heat a quantity of the powdered tablets containing 50 mg of Acenocoumarol with 30 mL of *acetone* under a reflux condenser for 5 minutes, filter and wash the residue with two 10 mL quantities of *acetone*. Evaporate the combined filtrate and washings to 5 mL, 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. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of acenocoumarol *(RS 001)*.
B. The *light absorption*, Appendix II B, of the final solution obtained in the Assay exhibits maxima at 283 nm and 306 nm.
C. Heat 25 mg of the residue obtained in test A with 2.5 mL of *glacial acetic acid*, 0.5 mL of *hydrochloric acid* and 0.2 g of *zinc powder* on a water bath for 5 minutes, cool and filter. To the filtrate add 0.05 mL of *sodium nitrite solution* and add the mixture to 10 mL of a 1% w/v solution of *2-naphthol* containing 3 mL of 5M *sodium hydroxide*. A bright red precipitate is produced.

TESTS

Related substances

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

(1) Shake a quantity of the powdered tablets containing 20 mg of Acenocoumarol with 5 mL of *acetone*, centrifuge and use the supernatant liquid.
(2) Dilute 1 volume of solution (1) to 200 volumes with *acetone*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel GF_{254}*.
(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, dry in air and immediately examine under *ultraviolet light (254 nm)*.

MOBILE PHASE

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

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) (0.5%).

Uniformity of content

Tablets containing less than 2 mg and/or less than 2% w/w of Acenocoumarol comply with the requirements stated under Tablets using the following method of analysis. Finely crush one tablet, add 30 mL of *methanol*, stir the mixture for 30 minutes and filter through sintered glass, washing the residue with three 15 mL quantities of *methanol*. To the combined filtrate and washings add 10 mL of 1M *hydrochloric acid* and sufficient *methanol* to produce 100 mL. If necessary dilute further with a solvent prepared by diluting 1 volume of 1M *hydrochloric acid* to 10 volumes with *methanol* to produce a solution containing about 0.001% w/v of Acenocoumarol. Measure the *absorbance* of the resulting solution at the maximum at 306 nm, Appendix II B. Calculate the content of $C_{19}H_{15}NO_6$ taking 521 as the value of A (1%, 1 cm) at the maximum at 306 nm.

ASSAY

Weigh and powder 20 tablets. To a quantity of the powder containing 1 mg of Acenocoumarol add 30 mL of *methanol*, stir the mixture for 30 minutes and filter through sintered glass, washing the residue with three 15 mL quantities of *methanol*. To the combined filtrate and washings add 10 mL of 1M *hydrochloric acid* and sufficient *methanol* to produce 100 mL and measure the *absorbance* of the resulting solution at the maximum at 306 nm, Appendix II B. Calculate the content of $C_{19}H_{15}NO_6$ taking 521 as the value of A (1%, 1 cm) at the maximum at 306 nm.