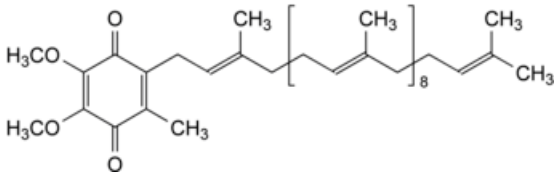
Edition: BP 2025 (Ph. Eur. 11.6 update)

Ubidecarenone

General Notices

(Ph. Eur. monograph 1578)



$C_{59}H_{90}O_4$ 863 *303-98-0*

Action and use

Co-enzyme in mitochondrial electron transport.

Ph Eur

DEFINITION

2-[(*all-E*)-3,7,11,15,19,23,27,31,35,39-Decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl]-5,6-dimethoxy-3-methylbenzene-1,4-dione.

Content

98.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

Yellow or orange, hygroscopic, crystalline powder.

Solubility

Practically insoluble in water, soluble in acetone, very slightly soluble in anhydrous ethanol.

It gradually decomposes and darkens on exposure to light.

mp

About 48 °C.

Carry out all operations protected from light.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison ubidecarenone CRS.

B. Examine the chromatograms obtained in the assay.

Results The principal peak in the chromatogram obtained with the test solution is similar in retention time and size to the principal peak in the chromatogram obtained with reference solution (a).

TESTS

Related substances

Liquid chromatography (2.2.29). *Carry out the test protected from light.*

Test solution Dissolve 25.0 mg of the substance to be examined in 25.0 mL of anhydrous ethanol R by heating at about 50 °C for 2 min. Allow to cool.

Reference solution (a) Dissolve 25.0 mg of ubidecarenone CRS in 25.0 mL of anhydrous ethanol R by heating at about 50 °C for 2 min. Allow to cool.

Reference solution (b) Dissolve 2 mg of ubidecarenone impurity D CRS in 2.0 mL of the test solution by heating at about 50 °C for 2 min. Allow to cool. Dilute 1.0 mL of this solution to 50.0 mL with anhydrous ethanol R.

Reference solution (c) Dilute 1.0 mL of the test solution to 100.0 mL with anhydrous ethanol R. Dilute 5.0 mL of this solution to 10.0 mL with anhydrous ethanol R.

Column:

— *size*: *l* = 0.2 m, Ø = 4.6 mm;

— *stationary phase*: end-capped octadecylsilyl silica gel for chromatography R (5 µm);

— *temperature*: 30 °C.

Mobile phase anhydrous ethanol R, methanol R2 (20:80 *V/V*).

Flow rate 1.7 mL/min.

Detection Spectrophotometer at 275 nm.

Injection 10 µL of the test solution and reference solutions (b) and (c).

Run time Twice the retention time of ubidecarenone.

Identification of impurities Use the chromatogram obtained with reference solution (b) to identify the peak due to impurity D.

Relative retention With reference to ubidecarenone (retention time = about 14 min): impurity D = about 0.7.

System suitability Reference solution (b):

— resolution: minimum 6.5 between the peaks due to impurity D and ubidecarenone.

Calculation of percentage contents:

— for each impurity, use the concentration of ubidecarenone in reference solution (c).

Limits:

— *impurity D*: maximum 0.3 per cent;

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.6 per cent,

— *reporting threshold*: 0.05 per cent.

Impurity F

Liquid chromatography (2.2.29). *Carry out the test protected from light.*

Test solution Dissolve 25.0 mg of the substance to be examined in 25.0 mL of *hexane R*.

Reference solution (a) Dissolve the contents of a vial of *ubidecarenone for system suitability CRS* (containing impurity F) in 1.0 mL of *hexane R*.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with *hexane R*.

Column:

— *size*: *l* = 0.25 m, *Ø* = 4.0 mm;

— *stationary phase*: *silica gel for chromatography R* (7 µm).

Mobile phase *ethyl acetate R*, *hexane R* (3:97 *V/V*).

Flow rate 2 mL/min.

Detection Spectrophotometer at 275 nm.

Injection 20 µL.

Run time 1.2 times the retention time of ubidecarenone.

Identification of impurities Use the chromatogram supplied with *ubidecarenone for system suitability CRS* and the chromatogram obtained with reference solution (a) to identify the peak due to impurity F.

Relative retention With reference to ubidecarenone (retention time = about 10 min): impurity F = about 0.85.

System suitability Reference solution (a):

— *resolution*: minimum 1.5 between the peaks due to impurity F and ubidecarenone.

Limit:

— *impurity F*: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent).

Water (2.5.12)

Maximum 0.2 per cent, determined on 3.00 g.

Sulfated ash (2.4.14)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Liquid chromatography (2.2.29) as described in the test for related substances with the following modification.

Injection Test solution and reference solution (a).

Calculate the percentage content of $C_{59}H_{90}O_4$ taking into account the assigned content of *ubidecarenone CRS*.

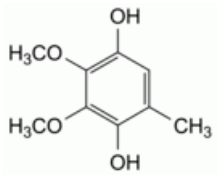
STORAGE

In an airtight container, protected from light.

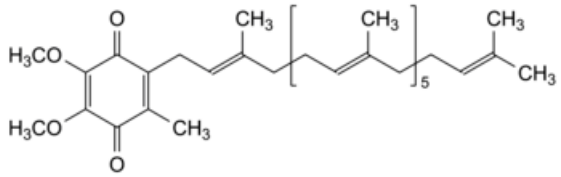
IMPURITIES

Specified impurities D, F.

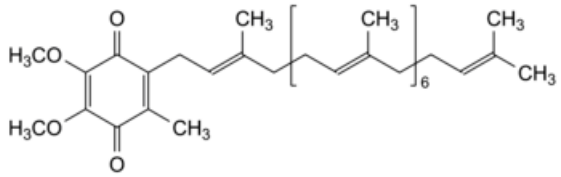
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A, B, C, E, G.



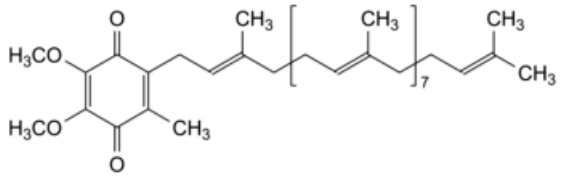
A. 2,3-dimethoxy-5-methylbenzene-1,4-diol,



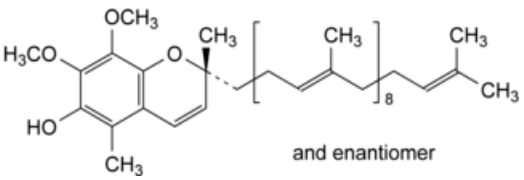
B. 2-[(*all-E*)-3,7,11,15,19,23,27-heptamethyloctadocosa-2,6,10,14,18,22,26-heptaenyl]-5,6-dimethoxy-3-methylbenzene-1,4-dione (ubiquinone-7),



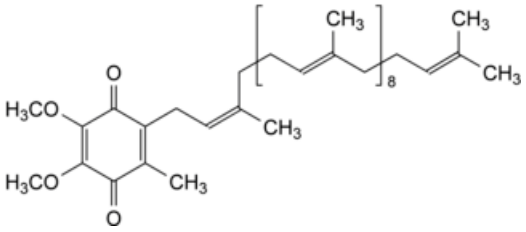
C. 5,6-dimethoxy-3-methyl-2-[(*all-E*)-3,7,11,15,19,23,27,31-octamethyldotriaconta-2,6,10,14,18,22,26,30-octaenyl]benzene-1,4-dione (ubiquinone-8),



D. 5,6-dimethoxy-3-methyl-2-[(*all-E*)-3,7,11,15,19,23,27,31,35-nonamethylhexatriaconta-2,6,10,14,18,22,26,30,34-nonaenyl]benzene-1,4-dione (ubiquinone-9),



E. (2*RS*)-7,8-dimethoxy-2,5-dimethyl-2-[(*all-E*)-4,8,12,16,20,24,28,32,36-nonamethylheptatriaconta-3,7,11,15,19,23,27,31,35-nonaenyl]-2*H*-1-benzopyran-6-ol (ubicromenol),



F. 2-[(2*Z*,6*E*,10*E*,14*E*,18*E*,22*E*,26*E*,30*E*,34*E*)-3,7,11,15,19,23,27,31,35,39-decamethyltetraconta-2,6,10,14,18,22,26,30,34,38-decaenyl]-5,6-dimethoxy-3-methylbenzene-1,4-dione (ubidecarenone (*Z*)-isomer),

G. unknown structure.

Ph Eur