System suitability:

- the chromatogram obtained with reference solution (c) is similar to the chromatogram provided with *carteolol for system suitability CRS*; the peaks due to impurity H and carteolol show base-line separation;
- *signal-to-noise ratio*: minimum 10 for the principal peak in the chromatogram obtained with reference solution (d);
- *number of theoretical plates*: minimum 6000, calculated for the principal peak in the chromatogram obtained with reference solution (a).

Limits:

- *impurity H*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);
- *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);
- *total*: not more than half the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);
- *disregard limit*: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.02 per cent).

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 60 mL of *ethanol (96 per cent) R*. Add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 mL of *0.1 M sodium hydroxide* is equivalent to 32.88 mg of $C_{16}H_{25}N_2O_3Cl$.

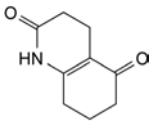
STORAGE

In an airtight container.

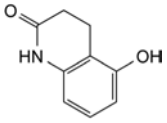
IMPURITIES

Specified impurities: H.

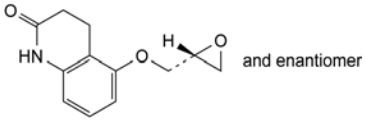
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical 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, D, E, F, G, I.*



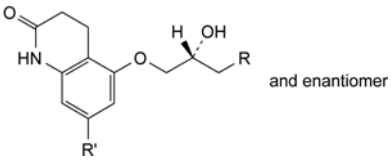
A. 4,6,7,8-tetrahydroquinoline-2,5(1*H*,3*H*)-dione,



B. 5-hydroxy-3,4-dihydroquinolin-2(1*H*)-one,



C. 5-[[(2*RS*)-oxiran-2-yl]methoxy]-3,4-dihydroquinolin-2(1*H*)-one,

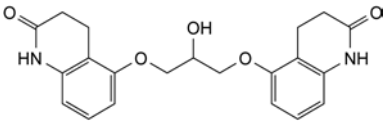


D. R = Cl, R′ = H: 5-[(2*RS*)-3-chloro-2-hydroxypropoxy]-3,4-dihydroquinolin-2(1*H*)-one,

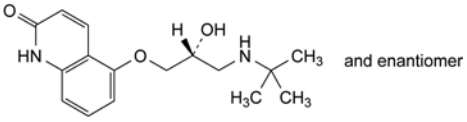
F. R = OCH_3, R′ = H: 5-[(2*RS*)-2-hydroxy-3-methoxypropoxy]-3,4-dihydroquinolin-2(1*H*)-one,

G. R = OH, R′ = H: 5-[(2*RS*)-2,3-dihydroxypropoxy]-3,4-dihydroquinolin-2(1*H*)-one,

I. R = NH-C(CH_3)$_3$, R′ = Br: 7-bromo-5-[(2*RS*)-3-[(1,1-(dimethylethyl)amino]-2-hydroxypropoxy]-3,4-dihydroquinolin-2(1*H*)-one,



E. 5,5′-[(2-hydroxypropan-1,3-diyl)bis(oxy)]bis(3,4-dihydroquinolin-2(1*H*)-one),



H. 5-[(2*RS*)-3-[(1,1-dimethylethyl)amino]-2-hydroxypropoxy]-quinolin-2(1*H*)-one.

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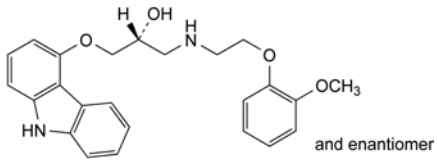
corrected 6.0

CARVEDILOL

Carvedilolum



$C_{24}H_{26}N_2O_4$ M_r 406.5
[72956-09-3]

DEFINITION

(2*RS*)-1-(9*H*-Carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)-ethyl]amino]propan-2-ol.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: practically insoluble in water, slightly soluble in alcohol, practically insoluble in dilute acids.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *Ph. Eur. reference spectrum of carvedilol.*

If the spectrum obtained shows differences, dissolve the substance to be examined in *2-propanol R*, evaporate to dryness and record a new spectrum using the residue.

TESTS

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 25.0 mg of the substance to be examined in the mobile phase and dilute to 25.0 mL with the mobile phase.

Reference solution (a). Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b). Dissolve 5.0 mg of *carvedilol impurity C CRS* in 5.0 mL of the test solution and dilute to 100.0 mL with the mobile phase.

Reference solution (c). Dilute 1.0 mL of reference solution (b) to 100.0 mL with the mobile phase. Dilute 2.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

– *size*: *l* = 0.125 m, Ø = 4.6 mm,

– *stationary phase*: *octylsilyl silica gel for chromatography R* (5 µm),

– *temperature*: 55 °C.

Mobile phase: dissolve 1.77 g of *potassium dihydrogen phosphate R* in *water R* and dilute to 650 mL with the same solvent; adjust to pH 2.0 with *phosphoric acid R* and add 350 mL of *acetonitrile R*.

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 240 nm.

Injection: 20 µL.

Run time: 8 times the retention time of carvedilol.

Relative retention with reference to carvedilol (retention time = about 4 min): impurity A = about 0.6; impurity C = about 3.5; impurity B = about 6.7.

System suitability: reference solution (b):

– *resolution*: minimum 17 between the peaks due to carvedilol and to impurity C.

Limits:

– *correction factor*: for the calculation of content, multiply the peak area of impurity A by 2,

– *impurity A*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent),

– *impurity C*: not more than twice the area of the corresponding peak in the chromatogram obtained with reference solution (c) (0.02 per cent),

– *any other impurity*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),

– *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent),

– *disregard limit*: the area of the principal peak in the chromatogram obtained with reference solution (c) (0.01 per cent).

Heavy metals (*2.4.8*): maximum 10 ppm.

2.0 g complies with limit test C. Prepare the standard using 2.0 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

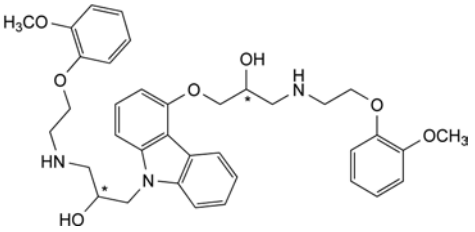
Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

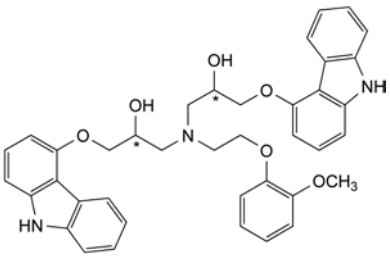
Dissolve 0.350 g in 60 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 40.65 mg of $C_{24}H_{26}N_2O_4$.

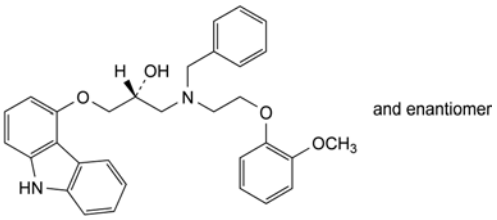
IMPURITIES



A. 1-[[9-[2-hydroxy-3-[[2-(2-methoxyphenoxy)ethyl]amino]-propyl]-9*H*-carbazol-4-yl]oxy]-3-[[2-(2-methoxyphenoxy)ethyl]-amino]propan-2-ol,



B. 1,1′-[[2-(2-methoxyphenoxy)ethyl]nitrilo]bis[3-(9*H*-carbazol-4-yloxy)propan-2-ol],



C. (2*RS*)-1-[benzyl[2-(2-methoxyphenoxy)ethyl]amino]-3-(9*H*-carbazol-4-yloxy)propan-2-ol.

01/2008:1497

CASTOR OIL, HYDROGENATED

Ricini oleum hydrogenatum

DEFINITION

Fatty oil obtained by hydrogenation of *Virgin Castor oil (0051)*. It consists mainly of the triglyceride of 12-hydroxystearic (12-hydroxyoctadecanoic) acid.

CHARACTERS

Appearance: fine, almost white or pale yellow powder or almost white or pale yellow masses or flakes.

Solubility: practically insoluble in water, slightly soluble in methylene chloride, very slightly soluble in anhydrous ethanol, practically insoluble in light petroleum.

IDENTIFICATION

A. Melting point (*2.2.14*): 83 °C to 88 °C.

B. Hydroxyl value (see Tests).

C. Composition of fatty acids (see Tests).

TESTS

Acid value (*2.5.1*): maximum 4.0, determined on 10.0 g dissolved in 75 mL of hot *ethanol (96) per cent R*.

Hydroxyl value (*2.5.3, Method A*): 145 to 165, determined on a warm solution.

Iodine value (*2.5.4, Method A*): maximum 5.0.

Alkaline impurities. Dissolve 1.0 g by gentle heating in a mixture of 1.5 mL of *ethanol (96) per cent R* and 3 mL of *toluene R*. Add 0.05 mL of a 0.4 g/L solution of *bromophenol*