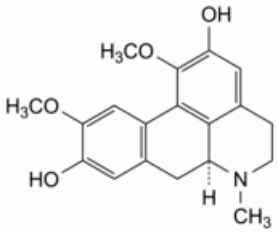
Edition: BP 2025 (Ph. Eur. 11.6 update)

Boldine

General Notices

(Ph. Eur. monograph 2971)



$C_{19}H_{21}NO_4$ 327.4 *476-70-0*

Action and use

Antioxidant.

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DEFINITION

(6a*S*)-1,10-Dimethoxy-6-methyl-5,6,6a,7-tetrahydro-4*H*-dibenzo[*de*,*g*]quinoline-2,9-diol, of vegetable origin.

Content

98.5 per cent to 100.5 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white or yellowish, crystalline powder.

Solubility

Very slightly soluble in water, soluble in ethanol (96 per cent) and in methylene chloride. It dissolves in dilute acid solutions.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison *boldine CRS*.

TESTS

Specific optical rotation (*2.2.7*)

+ 121.0 to + 127.0 (anhydrous substance).

Dissolve 0.500 g in *ethanol (96 per cent) R* and dilute to 50.0 mL with the same solvent.

Related substances

Liquid chromatography (*2.2.29*).

Test solution Dissolve 12.0 mg of the substance to be examined in 8 mL of *methanol R* using sonication and dilute to 10.0 mL with *methanol R*.

Reference solution (a) Dilute 1.0 mL of the test solution to 10.0 mL with *methanol R*. Dilute 1.0 mL of this solution to 10.0 mL with *methanol R*.

Reference solution (b) Dissolve 12 mg of *boldine for system suitability CRS* (containing impurities C and E) in 8 mL of *methanol R* using sonication and dilute to 10 mL with *methanol R*.

Reference solution (c) In order to prepare impurity A *in situ*, add 0.5 mL of *strong hydrogen peroxide solution R* to 5 mL of reference solution (b) and stir for 1 h.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: *end-capped extra-dense bonded octylsilyl silica gel for chromatography R* (5 µm);

— *temperature*: 30 °C.

Mobile phase:

— *mobile phase A*: dissolve 1.54 g of *ammonium acetate R* in 950 mL of *water for chromatography R*, adjust to pH 8.50 ± 0.05 with *diethylamine R* and dilute to 1000 mL with *water for chromatography R*;

— *mobile phase B*: *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	85	15
2 - 38	85 → 64	15 → 36
38 - 50	64 → 20	36 → 80
50 - 53	20	80

Flow rate 1.2 mL/min.

Detection Spectrophotometer at 302 nm.

Injection 10 µL.

Identification of impurities Use the chromatogram supplied with *boldine for system suitability CRS* and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities A, C and E.

Relative retention With reference to boldine (retention time = about 23 min): impurity A = about 0.25; impurity C = about 0.6; impurity E = about 1.6.

System suitability Reference solution (b):

— *resolution*: minimum 10.0 between the peaks due to impurity C and boldine.

Calculation of percentage contents:

— for each impurity, use the concentration of boldine in reference solution (a).

Limits:

— *impurity C*: maximum 1.5 per cent;

— *impurity A*: maximum 0.3 per cent;

— *impurity E*: maximum 0.15 per cent;

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

— *total*: maximum 1.5 per cent;

— *reporting threshold*: 0.05 per cent.

2-Propanol (*2.4.24*)

Maximum 1.0 per cent.

Water (*2.5.32*)

Maximum 0.5 per cent, determined on 0.100 g using the evaporation technique at 120 °C.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

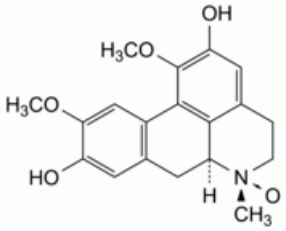
Dissolve 0.200 g in 50 mL of *glacial acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 32.74 mg of $C_{19}H_{21}NO_4$.

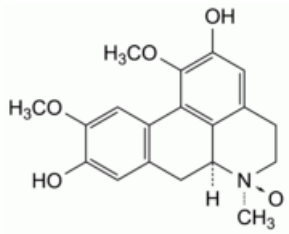
IMPURITIES

Specified impurities *A, C, E.*

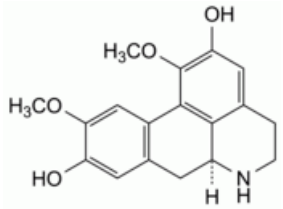
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical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



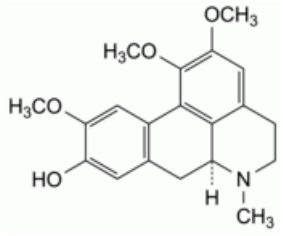
A. (6*S*,6a*S*)-2,9-dihydroxy-1,10-dimethoxy-6-methyl-5,6,6a,7-tetrahydro-4*H*-dibenzo[*de,g*]quinoline *N*-oxide,



B. (6*R*,6a*S*)-2,9-dihydroxy-1,10-dimethoxy-6-methyl-5,6,6a,7-tetrahydro-4*H*-dibenzo[*de*,*g*]quinoline *N*-oxide,



C. (6a*S*)-1,10-dimethoxy-5,6,6a,7-tetrahydro-4*H*-dibenzo[*de*,*g*]quinoline-2,9-diol,



D. (6a*S*)-1,2,10-trimethoxy-6-methyl-5,6,6a,7-tetrahydro-4*H*-dibenzo[*de*,*g*]quinolin-9-ol,

E. unknown structure.

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