– *impurities C, D at 350 nm*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) at 350 nm (0.05 per cent);
– *unspecified impurities*: for each impurity, at the wavelength giving the higher value for the impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) at the same wavelength (0.10 per cent);
– *total*: not more than 0.3 per cent;
– *disregard limit*: 0.3 times the area of the principal peak in the chromatogram obtained with reference solution (a) at the same wavelength (0.03 per cent).

Heavy metals (*2.4.8*): maximum 20 ppm.

1.0 g complies with test F. Prepare the reference solution using 2 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 for 4 h.

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

ASSAY

In order to avoid overheating during the titration, mix thoroughly throughout and stop the titration immediately after the end-point has been reached.

Dissolve 0.250 g in a mixture of 5 mL of *anhydrous formic acid R* and 50 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 35.14 mg of $C_{14}H_{13}N_3O_4S_2$.

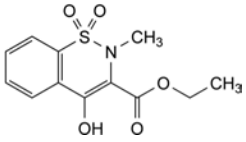
STORAGE

Protected from light.

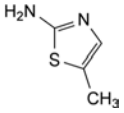
IMPURITIES

Specified impurities: A, B, C, D.

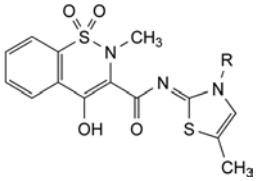
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



A. ethyl 4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate 1,1-dioxide,

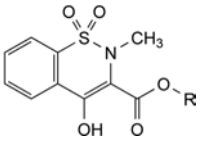


B. 5-methylthiazol-2-amine,



C. R = CH_3: *N*-[(2*Z*)-3,5-dimethylthiazol-2(3*H*)-ylidene]-4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide,

D. R = C_2H_5: *N*-[(2*Z*)-3-ethyl-5-methylthiazol-2(3*H*)-ylidene]-4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide,



E. R = CH_3: methyl 4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate 1,1-dioxide,

F. R = $CH(CH_3)_2$: isopropyl 4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate 1,1-dioxide.

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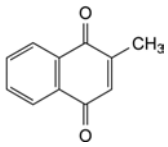
MENADIONE

Menadionum



$C_{11}H_8O_2$ M_r 172.2
[58-27-5]

DEFINITION

Menadione contains not less than 98.5 per cent and not more than the equivalent of 101.0 per cent of 2-methylnaphthalene-1,4-dione, calculated with reference to the dried substance.

CHARACTERS

A pale-yellow, crystalline powder, practically insoluble in water, freely soluble in toluene, sparingly soluble in alcohol and in methanol. It is unstable in light.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 105 °C to 108 °C.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *menadione CRS*.

C. Dissolve about 1 mg in 5 mL of *alcohol R*, add 2 mL of *ammonia R* and 0.2 mL of *ethyl cyanoacetate R*. An intense bluish-violet colour develops. Add 2 mL of *hydrochloric acid R*. The colour disappears.

D. Dissolve about 10 mg in 1 mL of *alcohol R*, add 1 mL of *hydrochloric acid R* and heat in a water-bath. A red colour develops.

TESTS

Related substances. *Carry out the test protected from bright light.* Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution. Dissolve 0.2 g of the substance to be examined in *acetone R* and dilute to 10 mL with the same solvent.

Reference solution. Dilute 0.5 mL of the test solution to 100 mL with *acetone R*.

Apply separately to the plate 5 µL of each solution. Develop over a path of 15 cm using a mixture of 1 volume of *nitromethane R*, 2 volumes of *acetone R*, 5 volumes of *ethylene chloride R* and 90 volumes of *cyclohexane R*. Dry the plate in a current of hot air. Repeat the development and drying a further two times. Examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with the test solution, apart from

the principal spot, is not more intense than the spot in the chromatogram obtained with the reference solution (0.5 per cent).

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying over *diphosphorus pentoxide R* at a pressure of 2 kPa to 3 kPa for 4 h.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.150 g in 15 mL of *glacial acetic acid R* in a flask with a stopper fitted with a valve. Add 15 mL of *dilute hydrochloric acid R* and 1 g of *zinc powder R*. Close the flask. Allow the mixture to stand for 60 min, protected from light, with occasional shaking. Filter the solution over a cotton wad, wash with three quantities, each of 10 mL, of *carbon dioxide-free water R*. Add 0.1 mL of *ferroin R* and immediately titrate the combined filtrate and washings with *0.1 M ammonium and cerium nitrate*.

1 mL of *0.1 M ammonium and cerium nitrate* is equivalent to 8.61 mg of $C_{11}H_8O_2$.

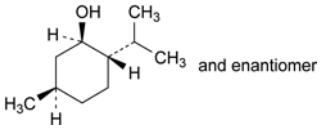
STORAGE

Store protected from light.

01/2008:0623
corrected 7.0

MENTHOL, RACEMIC

Mentholum racemicum



$C_{10}H_{20}O$ M_r 156.3
[89-78-1]

DEFINITION

Mixture of equal parts of (1*RS*,2*SR*,5*RS*)-5-methyl-2-(1-methylethyl)cyclohexanol.

CHARACTERS

Appearance: free-flowing or agglomerated, crystalline powder or prismatic or acicular, colourless, shiny crystals.

Solubility: practically insoluble in water, very soluble in ethanol (96 per cent) and in light petroleum, freely soluble in fatty oils and in liquid paraffin, very slightly soluble in glycerol.

mp: about 34 °C.

IDENTIFICATION

First identification: A, C.

Second identification: B, D.

A. Optical rotation (see Tests).

B. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 25 mg of the substance to be examined in *methanol R* and dilute to 5 mL with the same solvent.

Reference solution. Dissolve 25 mg of *menthol CRS* in *methanol R* and dilute to 5 mL with the same solvent.

Plate: *TLC silica gel G plate R*.

Mobile phase: *ethyl acetate R, toluene R* (5:95 *V/V*).

Application: 2 µL.

Development: over a path of 15 cm.

Drying: in air, until the solvents have evaporated.

Detection: spray with *anisaldehyde solution R* and heat at 100-105 °C for 5-10 min.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

C. Examine the chromatograms obtained in the test for related substances.

Results: the principal peak in the chromatogram obtained with test solution (b) is similar in position and approximate dimensions to the principal peak in the chromatogram obtained with reference solution (c).

D. Dissolve 0.20 g in 0.5 mL of *anhydrous pyridine R*. Add 3 mL of a 150 g/L solution of *dinitrobenzoyl chloride R* in *anhydrous pyridine R*. Heat on a water-bath for 10 min. Add 7.0 mL of *water R* in small quantities with stirring and allow to stand in iced water for 30 min. A precipitate is formed. Allow to stand and decant the supernatant liquid. Wash the precipitate with 2 quantities, each of 5 mL, of iced *water R*, recrystallise from 10 mL of *acetone R*, wash with iced *acetone R* and dry at 75 °C at a pressure not exceeding 2.7 kPa for 30 min. The crystals melt (*2.2.14*) at 130 °C to 131 °C.

TESTS

Solution S. Dissolve 2.50 g in 10 mL of *ethanol (96 per cent) R* and dilute to 25.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Acidity or alkalinity. Dissolve 1.0 g in *ethanol (96 per cent) R* and dilute to 10 mL with the same solvent. Add 0.1 mL of *phenolphthalein solution R*. The solution is colourless. Not more than 0.5 mL of *0.01 M sodium hydroxide* is required to change the colour of the indicator to pink.

Optical rotation (*2.2.7*): – 0.2° to + 0.2°, determined on solution S.

Related substances. Gas chromatography (*2.2.28*).

Test solution (a). Dissolve 0.20 g of the substance to be examined in *methylene chloride R* and dilute to 50.0 mL with the same solvent.

Test solution (b). Dilute 1.0 mL of test solution (a) to 10.0 mL with *methylene chloride R*.

Reference solution (a). Dissolve 40.0 mg of the substance to be examined and 40.0 mg of *isomenthol R* in *methylene chloride R* and dilute to 100.0 mL with the same solvent.

Reference solution (b). Dilute 0.10 mL of test solution (a) to 100.0 mL with *methylene chloride R*.

Reference solution (c). Dissolve 40.0 mg of *menthol CRS* in *methylene chloride R* and dilute to 100.0 mL with the same solvent.

Column:

– *material*: glass;
– *size*: *l* = 2.0 m, Ø = 2 mm;
– *stationary phase*: *diatomaceous earth for gas chromatography R* impregnated with 15 per cent *m/m* of *macrogol 1500 R*.

Carrier gas: *nitrogen for chromatography R*.

Flow rate: 30 mL/min.

Temperature:

– *column*: 120 °C;
– *injection port*: 150 °C;
– *detector*: 200 °C.

Detection: flame ionisation.

Injection: 1 µL.

Run time: twice the retention time of menthol.

System suitability:

– *resolution*: minimum 1.4 between the peaks due to menthol and isomenthol in the chromatogram obtained with reference solution (a);

Monographs M