solution of *chromotropic acid, sodium salt R* and, carefully, 2 ml of *sulphuric acid R*. An intense violet colour is produced.

TESTS

Related substances. Thin-layer chromatography (*2.2.27*).

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

Reference solution. Dilute 0.3 ml of the test solution to 100 ml with *alcohol R*.

Plate: *TLC silica gel F_{254} plate R*.

Mobile phase: *glacial acetic acid R, ethyl acetate R, methylene chloride R* (20:50:60 *V/V/V*).

Application: 10 µl.

Development: over 2/3 of the plate.

Drying: in air.

Detection: examine in ultraviolet light at 254 nm.

Limits:

– *any impurity*: any spots, apart from the principal spot, are not more intense than the spot in the chromatogram obtained with the reference solution (0.3 per cent).

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

1.0 g complies with limit test F. Prepare the standard using 2 ml of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 2.000 g by drying at 60 °C over *diphosphorus pentoxide R* at a pressure of 0.1-0.5 kPa.

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

ASSAY

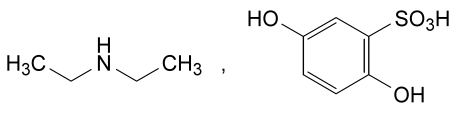
Dissolve 0.250 g in 100 ml of *methanol R* and add 5 ml of *water R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M sodium hydroxide* is equivalent to 30.31 mg of $C_{13}H_{12}Cl_2O_4$.

01/2008:1204

ETAMSYLATE

Etamsylatum



$C_{10}H_{17}NO_5S$ M_r 263.3
[2624-44-4]

DEFINITION

Etamsylate contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of *N*-ethylethanamine 2,5-dihydroxybenzenesulphonate, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder, very soluble in water, freely soluble in methanol, soluble in ethanol, practically insoluble in methylene chloride.

It shows polymorphism (*5.9*).

IDENTIFICATION

First identification: B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 127 °C to 134 °C.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *etamsylate CRS*. Examine the substances prepared as discs.

C. Dissolve 0.100 g in *water R* and dilute to 200.0 ml with the same solvent. Dilute 5.0 ml of the solution to 100.0 ml with *water R*. Examined immediately between 210 nm and 350 nm (*2.2.25*), the solution shows two absorption, maxima at 221 nm and 301 nm. The specific absorbance at the maximum at 301 nm is 145 to 151.

D. In a test-tube, introduce 2 ml of freshly prepared solution S (see Tests) and 0.5 g of *sodium hydroxide R*. Warm the mixture and place near the open end of the tube a wet strip of *red litmus paper R*. The colour of the paper becomes blue.

TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* and dilute to 100 ml with the same solvent.

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

pH (*2.2.3*). The pH of solution S is 4.5 to 5.6.

Hydroquinone. Examine by thin-layer chromatography (*2.2.27*), using as the coating substance a suitable silica gel with a fluorescent indicator having an optimal intensity at 254 nm.

Test solution. Dissolve 2.0 g of the substance to be examined in *water R* and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 10 mg of *hydroquinone R* in *water R* and dilute to 50 ml with the same solvent.

Apply to the plate 10 µl of each solution and dry the starting points in a current of cool air. Develop over a path of 15 cm using a mixture of 20 volumes of *methylene chloride R*, 30 volumes of *methyl acetate R* and 50 volumes of *ethyl acetate R*. Dry the plate in a current of hot air and examine in ultraviolet light at 254 nm. Any spot corresponding to hydroquinone in the chromatogram obtained with the test solution is not more intense than the principal spot in the chromatogram obtained with the reference solution (0.1 per cent).

Heavy metals (*2.4.8*). 1.0 g complies with limit test C for heavy metals (15 ppm). Prepare the standard using 1.5 ml of *lead standard solution (10 ppm Pb) R*.

Iron (*2.4.9*). 10 ml of solution S complies with the limit test for iron (10 ppm).

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying in an oven *in vacuo* at 60 °C.

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

ASSAY

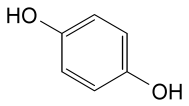
Dissolve 0.200 g in a mixture of 10 ml of *water R* and 40 ml of *dilute sulphuric acid R*. Titrate with *0.1 M cerium sulphate*, determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M cerium sulphate* is equivalent to 13.16 mg of $C_{10}H_{17}NO_5S$.

STORAGE

Store in an airtight container, protected from light.

IMPURITIES

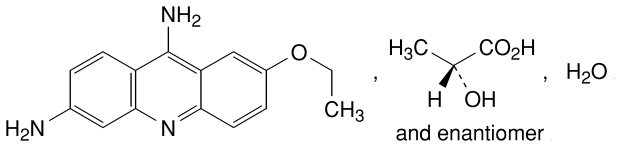


A. benzene-1,4-diol (hydroquinone).

01/2008:1591
corrected 6.0

ETHACRIDINE LACTATE MONOHYDRATE

Ethacridini lactas monohydricus



$C_{18}H_{21}N_3O_4,H_2O$ M_r 361.4
[1837-57-6]

DEFINITION

7-Ethoxyacridine-3,9-diamine (2*RS*)-2-hydroxypropanoate.

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

CHARACTERS

Appearance: yellow crystalline powder.

Solubility: sparingly soluble in water, very slightly soluble in alcohol, practically insoluble in methylene chloride.

IDENTIFICATION

First identification: A.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *ethacridine lactate monohydrate CRS.*

B. Mix 0.1 ml of solution S (see Tests) and 100 ml of *water R*. The solution is greenish-yellow and shows a strong green fluorescence in ultraviolet light at 365 nm. Add 5 ml of *1 M hydrochloric acid*. The fluorescence remains.

C. To 0.5 ml of solution S add 1.0 ml of *water R*, 0.1 ml of a 10 g/l solution of *cobalt chloride R* and 0.1 ml of a 50 g/l solution of *potassium ferrocyanide R*. The solution is green.

D. To 50 ml of solution S add 10 ml of *dilute sodium hydroxide solution R*. Filter. To 5 ml of the filtrate, add 1 ml of *dilute sulphuric acid R*. 5 ml of the solution obtained gives the reaction of lactates (*2.3.1*).

TESTS

Solution S. Dissolve 2.0 g in *carbon dioxide-free water R* and dilute to 100.0 ml with the same solvent.

pH (*2.2.3*): 5.5 to 7.0 for solution S.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 10.0 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 test solution to 100.0 ml with the mobile phase.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 10.0 ml with the mobile phase.

Column:
- *size*: *l* = 0.25 m, Ø = 4.6 mm,
- *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: dissolve 1.0 g of *sodium octanesulphonate R* in a mixture of 300 ml of *acetonitrile R* and 700 ml of *phosphate buffer solution pH 2.8 R*.

Flow rate: 1 ml/min.

Detection: spectrophotometer at 268 nm.

Injection: 10 µl.

Run time: 3 times the retention time of ethacridine.

Retention time: ethacridine = about 15 min.

Limits:
- *any impurity*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent),
- *total*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (1 per cent),
- *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 50 ppm.

1.0 g complies with limit test F. Prepare the standard using 5.0 ml of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): 4.5 per cent to 5.5 per cent, determined on 1.000 g by drying in an oven *in vacuo* at 105 °C.

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

ASSAY

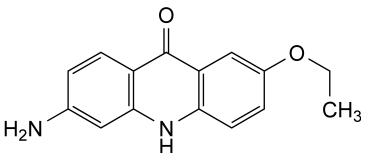
Dissolve 0.270 g in 5.0 ml of *anhydrous formic acid R*. Add 60.0 ml of *acetic anhydride R* and titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M perchloric acid* is equivalent to 34.34 mg of $C_{18}H_{21}N_3O_4$.

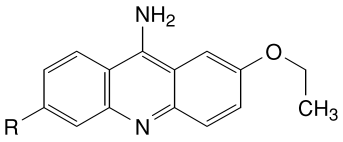
STORAGE

Protected from light.

IMPURITIES



A. 6-amino-2-ethoxyacridin-9(10*H*)-one,



B. R = Cl: 6-chloro-2-ethoxyacridin-9-amine,

C. R = O-CH_2-CH_2-OH: 2-[(9-amino-7-ethoxyacridin-3-yl)oxy]ethanol.