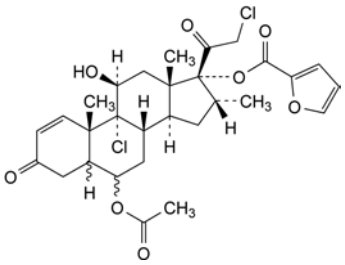
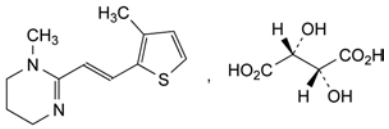


I. 9,21-dichloro-11β-hydroxy-16α-methyl-3,20-dioxo-5ξ-pregn-1-ene-6ξ,17-diyl 6-acetate 17-(furan-2-carboxylate).

01/2008:1546
corrected 6.0

MORANTEL HYDROGEN TARTRATE FOR VETERINARY USE

Moranteli hydrogenotartras ad usum veterinarium



$C_{16}H_{22}N_2O_6S$ M_r 370.4
[26155-31-7]

DEFINITION

1-Methyl-2-[(*E*)-2-(3-methylthiophen-2-yl)ethenyl]-1,4,5,6-tetrahydropyrimidine hydrogen tartrate.

Content: 98.5 per cent to 101.5 per cent (dried substance).

CHARACTERS

Appearance: white or pale yellow, crystalline powder.

Solubility: very soluble in water and in ethanol (96 per cent), practically insoluble in ethyl acetate.

IDENTIFICATION

First identification: B.

Second identification: A, C, D.

A. Melting point (*2.2.14*): 167 °C to 172 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *morantel hydrogen tartrate CRS.*

C. Dissolve about 10 mg in 1 mL of a 5 g/L solution of *ammonium vanadate R*. Evaporate to dryness. Add 0.1 mL of *sulfuric acid R*. A purple colour is produced.

D. Dissolve about 10 mg in 1 mL of *0.1 M sodium hydroxide*. Transfer to a separating funnel and shake with 5 mL of *methylene chloride R*. Discard the organic layer. Neutralise the aqueous layer with a few drops of *dilute hydrochloric acid R*. The solution gives reaction (b) of tartrates (*2.3.1*).

TESTS

Solution S. Dissolve 0.25 g in *carbon dioxide-free water R* and dilute to 25.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution GY_6 or Y_6 (*2.2.2, Method II*).

pH (*2.2.3*): 3.3 to 3.9 for solution S.

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

Test solution. Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

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

Reference solution (b). Dilute 2.0 mL of reference solution (a) to 100.0 mL with the mobile phase.

Reference solution (c). Expose 10 mL of reference solution (a) to daylight for 15 min before injection.

Reference solution (d). Dissolve 15.0 mg of *tartaric acid R* in the mobile phase and dilute to 100.0 mL with the mobile phase.

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

Mobile phase: to a mixture of 0.35 volumes of *triethylamine R* and 85 volumes of *water R* adjusted to pH 2.5 with *phosphoric acid R*, add 5 volumes of *tetrahydrofuran R* and 10 volumes of *methanol R*.

Flow rate: 0.75 mL/min.

Detection: spectrophotometer at 226 nm.

Injection: 20 μL.

Run time: twice the retention time of morantel.

System suitability: reference solution (c):
- *resolution*: minimum of 2 between the principal peak and the preceding peak ((*Z*)-isomer).

Limits:
- *any impurity apart from the peak due to tartaric acid*: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 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*: the area of the principal peak in the chromatogram obtained with reference solution (b) (0.02 per cent).

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

1.0 g complies with test C. Prepare the reference solution using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 1.5 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

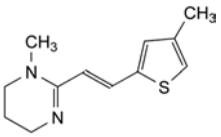
Dissolve 0.280 g in 40 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 37.04 mg of $C_{16}H_{22}N_2O_6S$.

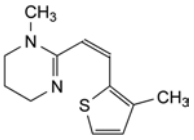
STORAGE

Protected from light.

IMPURITIES

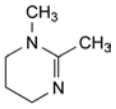


A. 1-methyl-2-[(*E*)-2-(4-methylthiophen-2-yl)ethenyl]-1,4,5,6-tetrahydropyrimidine,

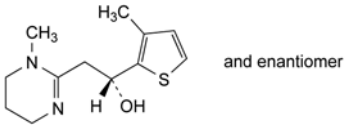


B. 1-methyl-2-[(*Z*)-2-(3-methylthiophen-2-yl)ethenyl]-1,4,5,6-tetrahydropyrimidine,

Monographs M

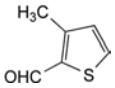


C. 1,2-dimethyl-1,4,5,6-tetrahydropyrimidine,



and enantiomer

D. (1*RS*)-2-(1-methyl-1,4,5,6-tetrahydropyrimidin-2-yl)-1-(3-methylthiophen-2-yl)ethanol,

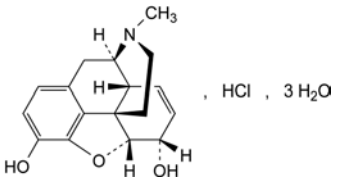


E. 3-methylthiophene-2-carbaldehyde.

04/2008:0097
corrected 6.7

MORPHINE HYDROCHLORIDE

Morphini hydrochloridum



$C_{17}H_{20}ClNO_3,3H_2O$ M_r 375.8
[6055-06-7]

DEFINITION

7,8-Didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol hydrochloride trihydrate.

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

CHARACTERS

Appearance: white or almost white, crystalline powder or colourless, silky needles or cubical masses, efflorescent in a dry atmosphere.

Solubility: soluble in water, slightly soluble in ethanol (96 per cent), practically insoluble in toluene.

IDENTIFICATION

First identification: A, E.

Second identification: B, C, D, E.

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *morphine hydrochloride CRS*.

B. Ultraviolet and visible absorption spectrophotometry (*2.2.25*).
Solution A. Dissolve 25.0 mg in *water R* and dilute to 25.0 mL with the same solvent.
Test solution (a). Dilute 10.0 mL of solution A to 100.0 mL with *water R*.
Test solution (b). Dilute 10.0 mL of solution A to 100.0 mL with *0.1 M sodium hydroxide*.
Spectral range: 250-350 nm for test solutions (a) and (b).
Absorption maximum: at 285 nm for test solution (a); at 298 nm for test solution (b).
Specific absorbance at the absorption maximum: 37 to 43 for test solution (a); 64 to 72 for test solution (b).

C. To about 1 mg of powdered substance in a porcelain dish add 0.5 mL of *sulfuric acid-formaldehyde reagent R*. A purple colour develops and becomes violet.

D. It gives the reaction of alkaloids (*2.3.1*).

E. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 0.500 g in *carbon dioxide-free water R* and dilute to 25.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_6 or BY_6 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.05 mL of *methyl red solution R*. Not more than 0.2 mL of *0.02 M sodium hydroxide* or *0.02 M hydrochloric acid* is required to change the colour of the indicator.

Specific optical rotation (*2.2.7*): – 110 to – 115 (anhydrous substance), determined on solution S.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.125 g of the substance to be examined in a 1 per cent *V/V* solution of *acetic acid R* and dilute to 50 mL with the same solution.

Reference solution (a). Dilute 1.0 mL of the test solution to 100.0 mL with a 1 per cent *V/V* solution of *acetic acid R*. Dilute 2.0 mL of this solution to 10.0 mL with a 1 per cent *V/V* solution of *acetic acid R*.

Reference solution (b). Dissolve 5 mg of *morphine for system suitability CRS* (containing impurities B, C, E and F) in a 1 per cent *V/V* solution of *acetic acid R* and dilute to 2 mL with the same solution.

Column:
- *size*: *l* = 0.15 m, Ø = 4.6 mm;
- *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (5 μm);
- *temperature*: 35 °C.

Mobile phase:
- *mobile phase A*: 1.01 g/L solution of *sodium heptanesulfonate R* adjusted to pH 2.6 with a 50 per cent *V/V* solution of *phosphoric acid R*;
- *mobile phase B*: *methanol R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	85	15
2 - 35	85 → 50	15 → 50
35 - 40	50	50

Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 230 nm.

Injection: 10 μL.

Identification of impurities: use the chromatogram supplied with *morphine for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities B, C, E and F.

Relative retention with reference to morphine (retention time = about 12.5 min): impurity F = about 0.95; impurity E = about 1.1; impurity C = about 1.6; impurity B = about 1.9.

System suitability: reference solution (b):
- *peak-to-valley ratio*: minimum 2, where H_p = height above the baseline of the peak due to impurity F and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to morphine.

Limits:
- *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity B = 0.25; impurity C = 0.4; impurity E = 0.5;
- *impurity B*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.4 per cent);