TESTS

pH (*2.2.3*): 2.0 to 8.0.

Disperse 5.0 g in 100 ml of *carbon dioxide-free water R*.

Chlorides: maximum 0.2 per cent.

Dissolve 2.5 g in 50 ml of boiling *water R*, dilute to 100 ml with *water R* and filter. Dilute 1 ml of the filtrate to 15 ml, add 1 ml of *dilute nitric acid R*, pour the mixture as a single addition into 1 ml of *silver nitrate solution R2* and allow to stand for 5 min protected from light. When viewed transversely against a black background any opalescence produced is not more intense than that obtained by treating a mixture of 10 ml of *chloride standard solution (5 ppm Cl) R* and 5 ml of *water R*, prepared in the same manner.

Reducing sugars: maximum 10 per cent, calculated as glucose $C_6H_{12}O_6$.

To a quantity of dextrin equivalent to 2.0 g (dried substance) add 100 ml of *water R*, shake for 30 min, dilute to 200.0 ml with *water R* and filter. To 10.0 ml of alkaline *cupri-tartaric solution R* add 20.0 ml of the filtrate, mix, and heat on a hot plate adjusted to bring the solution to boil within 3 min. Boil for 2 min, and cool immediately. Add 5 ml of a 300 g/l solution of *potassium iodide R* and 10 ml of *1 M sulphuric acid*, mix, and titrate immediately with *0.1 M sodium thiosulphate*, using *starch solution R*, added towards the end of the titration, as indicator. Repeat the procedure beginning with "To 10.0 ml of...", using, in place of the filtrate, 20.0 ml of a 1 g/l solution of *glucose R*, accurately prepared. Perform a blank titration. ($V_B - V_U$) is not greater than ($V_B - V_S$), in which V_B, V_U and V_S are the number of millilitres of *0.1 M sodium thiosulphate* consumed in the titrations of the blank, the dextrin and the glucose, respectively.

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*.

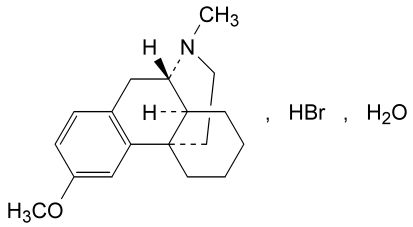
Loss on drying (*2.2.32*): maximum 13.0 per cent, determined on 1.000 g by drying at 130-135 °C for 90 min.

Sulphated ash (*2.4.14*): maximum 0.5 per cent, determined on 1.0 g.

01/2008:0020

DEXTROMETHORPHAN HYDROBROMIDE

Dextromethorphani hydrobromidum



$C_{18}H_{26}BrNO,H_2O$ M_r 370.3

[6700-34-1]

DEFINITION

ent-3-Methoxy-17-methylmorphinan hydrobromide monohydrate.

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

CHARACTERS

Appearance: almost white, crystalline powder.

Solubility: sparingly soluble in water, freely soluble in alcohol.

mp: about 125 °C, with decomposition.

IDENTIFICATION

First identification: A, B, D.

Second identification: A, C, D.

A. It complies with the test for specific optical rotation (see Tests).

B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *dextromethorphan hydrobromide CRS*.

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

Test solution. Dissolve 25 mg of the substance to be examined in *methanol R* and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 25 mg of *dextromethorphan hydrobromide CRS* in *methanol R* and dilute to 10 ml with the same solvent.

Plate: *TLC silica gel G plate R*.

Mobile phase: *concentrated ammonia R, methylene chloride R, methanol R, ethyl acetate R, toluene R* (2:10:13:20:55 *V/V/V/V/V*).

Application: 5 µl.

Development: over 2/3 of the plate.

Drying: in air.

Detection: spray with *potassium iodobismuthate solution R2*.

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

D. It gives reaction (a) of bromides (*2.3.1*).

TESTS

Solution S. Dissolve 1.0 g in *alcohol R* and dilute to 20 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 0.4 g in *carbon dioxide-free water R* with gentle heating, cool and dilute to 20 ml with the same solvent. Add 0.1 ml of *methyl red solution R* and 0.2 ml of *0.01 M sodium hydroxide*. The solution is yellow. Not more than 0.4 ml of *0.01 M hydrochloric acid* is required to change the colour of the indicator to red.

Specific optical rotation (*2.2.7*). + 28 to + 30 (anhydrous substance).

Dissolve 0.200 g in *0.1 M hydrochloric acid* and dilute to 10.0 ml with the same acid.

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 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 2 mg of *dextromethorphan impurity A CRS* in 2 ml of the test solution and dilute to 25.0 ml with the mobile phase.

Reference solution (b). Dilute 1.0 ml of the test solution to 200.0 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 3.11 g of *docusate sodium R* in a mixture of 400 ml of *water R* and 600 ml of *acetonitrile R*. Add 0.56 g of *ammonium nitrate R*. Adjust to apparent pH 2.0 with *glacial acetic acid R*.

Flow rate: 1.0 ml/min.

Detection: spectrophotometer at 280 nm.

Injection: 20 µl.

Run time: twice the retention time of dextromethorphan.

Relative retention with reference to dextromethorphan (retention time = about 21.9 min): impurity B = about 0.44; impurity C = about 0.85; impurity D = about 0.90; impurity A = about 1.13.

System suitability: reference solution (a):

– *resolution*: minimum 1.5 between the peaks due to impurity A and dextromethorphan.

Limits:

– *correction factor*: for the calculation of content, multiply the peak area of impurity C by 0.2,
– *any impurity*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent), and not more than 1 such peak has an area greater than half the area of the principal peak in the chromatogram obtained with reference solution (b) (0.25 per cent),
– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (1 per cent),
– *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

***N,N*-Dimethylaniline**: maximum 10 ppm.

Dissolve 0.5 g with heating in 20 ml of *water R*. Allow to cool, add 2 ml of *dilute acetic acid R* and 1 ml of a 10 g/l solution of *sodium nitrite R* and dilute to 25 ml with *water R*. The solution is not more intensely coloured than a reference solution prepared at the same time in the same manner using 20 ml of a 0.25 mg/l solution of *dimethylaniline R*.

Water (*2.5.12*): 4.0 per cent to 5.5 per cent, determined on 0.200 g.

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

ASSAY

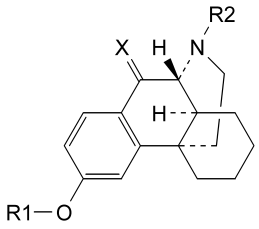
Dissolve 0.300 g in a mixture of 5.0 ml of *0.01 M hydrochloric acid* and 20 ml of *alcohol R*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*). Read the volume added between the 2 points of inflexion.

1 ml of *0.1 M sodium hydroxide* is equivalent to 35.23 mg of $C_{18}H_{26}BrNO$.

STORAGE

Protected from light.

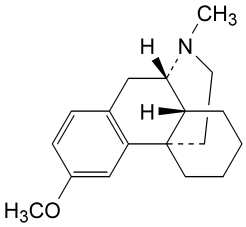
IMPURITIES



A. R1 = CH_3, R2 = H, X = H_2: *ent*-3-methoxymorphinan,

B. R1 = H, R2 = CH_3, X = H_2: *ent*-17-methylmorphinan-3-ol,

C. R1 = R2 = CH_3, X = O: *ent*-3-methoxy-17-methylmorphinan-10-one,

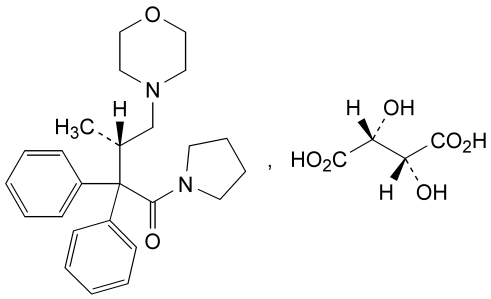


D. *ent*-(14*S*)-3-methoxy-17-methylmorphinan.

01/2008:0021
corrected 6.0

DEXTROMORAMIDE TARTRATE

Dextromoramidi tartras



$C_{29}H_{38}N_2O_8$ M_r 542.6
[2922-44-3]

DEFINITION

Dextromoramide tartrate contains not less than 98.0 per cent and not more than the equivalent of 101.0 per cent of 1-[(3*S*)-3-methyl-4-(morpholin-4-yl)-2,2-diphenylbutanoyl]pyrrolidine hydrogen (2*R*,3*R*)-2,3-dihydroxybutanedioate, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, amorphous or crystalline powder, soluble in water, sparingly soluble in alcohol.

It melts at about 190 °C, with slight decomposition.

IDENTIFICATION

A. Dissolve 75 mg in *1 M hydrochloric acid* and dilute to 100.0 ml with the same acid. Examined between 230 nm and 350 nm (*2.2.25*), the solution shows 3 absorption maxima, at 254 nm, 259 nm and 264 nm. The specific absorbances at the maxima are about 6.9, 7.7 and 6.5, respectively.

B. Dissolve about 50 mg in *water R* and dilute to 10 ml with the same solvent. To 2 ml of the solution add 3 ml of *ammoniacal silver nitrate solution R* and heat on a water-bath. A grey or black precipitate is formed.

C. It gives reaction (b) of tartrates (*2.3.1*).

TESTS

pH (*2.2.3*). Dissolve 0.2 g in *carbon dioxide-free water R* and dilute to 20 ml with the same solvent. The pH of the solution is 3.0 to 4.0.

Specific optical rotation (*2.2.7*). Dissolve 0.50 g in *0.1 M hydrochloric acid* and dilute to 10.0 ml with the same acid. The specific optical rotation is + 21 to + 23.