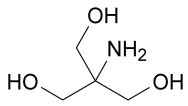
01/2008:1053
corrected 6.0

TROMETAMOL

Trometamolum



$C_4H_{11}NO_3$ M_r 121.1
[77-86-1]

DEFINITION

Trometamol contains not less than 99.0 per cent and not more than the equivalent of 100.5 per cent of aminomethylidynetri(methanol), calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder, or colourless crystals, freely soluble in water, sparingly soluble in alcohol, very slightly soluble in ethyl acetate.

IDENTIFICATION

First identification: B, C.

Second identification: A, B, D.

A. Solution S (see Tests) is strongly alkaline (*2.2.4*).

B. Melting point (*2.2.14*): 168 °C to 174 °C.

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

D. Examine the chromatograms obtained in the test for related substances. The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 50 ml with the same solvent.

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

pH (*2.2.3*). The pH of freshly prepared solution S is 10.0 to 11.5.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel G R* as the coating substance. Wash the plate with *methanol R* before applying the solutions.

Test solution (a). Dissolve 0.20 g in 1 ml of *water R*, with heating, and dilute to 10 ml with *methanol R*.

Test solution (b). Dilute 1 ml of test solution (a) to 10 ml with *methanol R*.

Reference solution (a). Dissolve 20 mg of *trometamol CRS* in *methanol R* and dilute to 10 ml with the same solvent.

Reference solution (b). Dilute 1 ml of test solution (a) to 100 ml with *methanol R*.

Apply to the plate 10 µl of each solution. Develop over a path of 10 cm using a mixture of 10 volumes of *dilute ammonia R1* and 90 volumes of *2-propanol R*. Dry the plate at 100 °C to 105 °C. Spray with a 5 g/l solution of *potassium permanganate R* in a 10 g/l solution of *sodium carbonate R*. After about 10 min examine in daylight. Any spot in the chromatogram obtained with test solution (a), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (b) (1.0 per cent).

Chlorides (*2.4.4*). To 10 ml of solution S add 2.5 ml of *dilute nitric acid R* and dilute to 15 ml with *water R*. The solution complies with the limit test for chlorides (100 ppm).

Heavy metals (*2.4.8*). Dissolve 2.0 g in 10 ml of *water R*. Neutralise the solution with *hydrochloric acid R1* and dilute to 20 ml with *water R*. 12 ml of the solution complies with limit test A for heavy metals (10 ppm). Prepare the standard using *lead standard solution (1 ppm Pb) R*.

Iron (*2.4.9*). Dissolve 1.0 g in *water R* and dilute to 10 ml with the same solvent. The solution 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 at 105 °C.

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

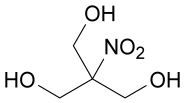
Bacterial endotoxins (*2.6.14*): less than 0.03 IU/mg, if intended for use in the manufacture of parenteral dosage forms without a further appropriate procedure for the removal of bacterial endotoxins.

ASSAY

Dissolve 0.100 g in 20 ml of *water R*. Add 0.2 ml of *methyl red solution R*. Titrate with *0.1 M hydrochloric acid* until the colour changes from yellow to red.

1 ml of *0.1 M hydrochloric acid* is equivalent to 12.11 mg of $C_4H_{11}NO_3$.

IMPURITIES

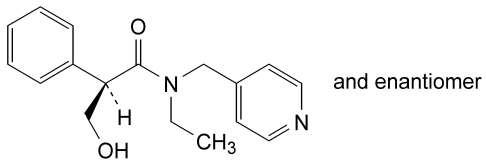


A. nitromethylidynetri(methanol).

01/2008:1159

TROPICAMIDE

Tropicamidum



$C_{17}H_{20}N_2O_2$ M_r 284.4
[1508-75-4]

DEFINITION

Tropicamide contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of (2*RS*)-*N*-ethyl-3-hydroxy-2-phenyl-*N*-(pyridin-4-ylmethyl)propanamide, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder, slightly soluble in water, freely soluble in alcohol and in methylene chloride.

IDENTIFICATION

First identification: C.

Second identification: A, B, D, E.

A. Melting point (*2.2.14*): 95 °C to 98 °C.

B. Dissolve 20.0 mg in *0.1 M hydrochloric acid* and dilute to 50.0 ml with the same acid. Dilute 2.0 ml of the solution to 20.0 ml with *0.1 M hydrochloric acid*. Examined between 230 nm and 350 nm (*2.2.25*), the solution shows an absorption maximum at 254 nm. The specific absorbance at the maximum is 170 to 190.

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

D. Examine the chromatograms obtained in the test for related substances. The principal spot in the chromatogram obtained with test solution (b) is similar in position and size to the spot in the chromatogram obtained with reference solution (a).

E. Dissolve about 5 mg in 3 ml of a mixture of 9 ml of *acetic anhydride R*, 1 ml of *acetic acid R* and 0.1 g of *citric acid R*. Heat on a water-bath for 5 min to 10 min. A reddish-yellow colour is produced.

TESTS

Appearance of solution. Dissolve 0.1 g in *alcohol R* and dilute to 10 ml with the same solvent. The solution is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Optical rotation (*2.2.7*). Dissolve 2.5 g in *ethanol R* and dilute to 25.0 ml with the same solvent. The angle of optical rotation is – 0.1° to + 0.1°.

Related substances. 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 (a). Dissolve 0.10 g of the substance to be examined in *methylene chloride R* and dilute to 5 ml with the same solvent.

Test solution (b). Dilute 1 ml of test solution (a) to 20 ml with *methylene chloride R*.

Reference solution (a). Dissolve 10 mg of *tropicamide CRS* in *methylene chloride R* and dilute to 10 ml with the same solvent.

Reference solution (b). Dilute 1 ml of test solution (b) to 10 ml with *methylene chloride R*.

Reference solution (c). Dilute 2 ml of reference solution (b) to 5 ml with *methylene chloride R*.

Reference solution (d). Dissolve 20 mg of *4-[(ethylamino)methyl]pyridine R* in *methylene chloride R* and dilute to 20 ml with the same solvent. Dilute 1 ml of the solution and 1 ml of reference solution (a) to 10 ml with *methylene chloride R*.

Apply separately to the plate 10 µl of each solution. Develop over a path of 15 cm using a mixture of 0.5 volumes of *concentrated ammonia R*, 5 volumes of *methanol R* and 95 volumes of *methylene chloride R*. Allow the plate to dry in air and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with test solution (a), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.5 per cent) and at most one such spot is more intense than the spot in the chromatogram obtained with reference solution (c) (0.2 per cent). The test is not valid unless the chromatogram obtained with reference solution (d) shows two clearly separated spots.

Tropic acid. To 10.0 mg add 5 mg of *disodium tetraborate R* and 0.35 ml of a freshly prepared 100 g/l solution of *dimethylaminobenzaldehyde R* in a mixture of 1 volume of *water R* and 9 volumes of *sulphuric acid R*. Heat on a water-bath for 3 min. Cool in ice water and add 5 ml of *acetic anhydride R*. No violet-red colour develops (0.05 per cent).

Chlorides (*2.4.4*). Dissolve 1.0 g with heating in 8 ml of *acetic acid R*, cool and dilute to 10 ml with the same acid. Dilute 5 ml of the solution to 15 ml with *water R*. The solution complies with the limit test for chlorides (100 ppm).

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 80 °C at a pressure not exceeding 0.7 kPa for 4 h.

Sulphated ash (*2.2.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

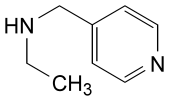
Dissolve 0.200 g in 50 ml of *anhydrous acetic acid R*. Add 0.2 ml of *naphtholbenzein solution R* and titrate with *0.1 M perchloric acid* until the colour changes from orange to green.

1 ml of *0.1 M perchloric acid* is equivalent to 28.44 mg of $C_{17}H_{20}N_2O_2$.

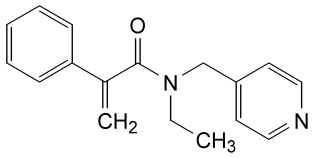
STORAGE

Store protected from light.

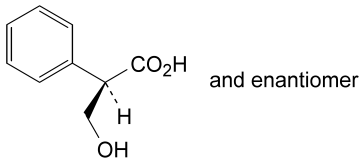
IMPURITIES



A. *N*-(pyridin-4-ylmethyl)ethanamine,



B. *N*-ethyl-2-phenyl-*N*-(pyridin-4-ylmethyl)propenamide,

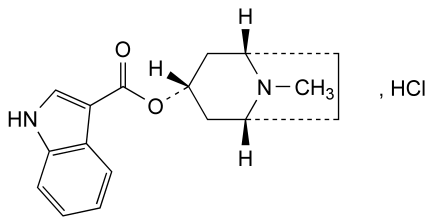


C. (2*RS*)-3-hydroxy-2-phenylpropanoic acid (tropic acid).

01/2008:2102
corrected 6.0

TROPISETRON HYDROCHLORIDE

Tropisetroni hydrochloridum



$C_{17}H_{21}ClN_2O_2$ M_r 320.8
[105826-92-4]