Reference solution (a). Dissolve 10.0 mg of *tramazoline impurity A CRS* and 10.0 mg of *tramazoline impurity B CRS* in 10 ml of a mixture of 50 volumes of *acetonitrile R* and 50 volumes of *water R* and add 10 ml of the test solution.

Reference solution (b). Dilute 0.2 ml of reference solution (a) to 100 ml with a mixture of 50 volumes of *acetonitrile R* and 50 volumes of *water R*.

Column:

– *size*: *l* = 0.125 m, Ø = 4 mm,

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: 2.0 g/l solution of *sodium dodecyl sulphate R* in a mixture of 6 volumes of *2-propanol R*, 42 volumes of *acetonitrile R* and 52 volumes of *water R*.

Flow rate: 1.2 ml/min.

Detection: spectrophotometer at 215 nm.

Injection: 5 µl.

Run time: 3 times the retention time of tramazoline.

Relative retentions with reference to tramazoline (retention time = about 6.5 min): impurity A = about 0.71; impurity B = about 0.86.

System suitability: reference solution (a):

– the chromatogram obtained shows 3 clearly separated peaks,

– *resolution*: minimum 1.5 between tramazoline and impurity B.

Limits:

– *impurity A*: not more than 3 times the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.3 per cent),

– *impurity B*: not more than 3 times the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.3 per cent),

– *any other impurity*: not more than the area of the peak due to impurity B in the chromatogram obtained with reference solution (b) (0.1 per cent),

– *total of other impurities*: not more than 2 times the area of the peak due to impurity B in the chromatogram obtained with reference solution (b) (0.2 per cent),

– *disregard limit*: 0.2 times the area of the peak due to impurity B in the chromatogram obtained with reference solution (b) (0.02 per cent).

Water (*2.5.12*): 6.2 per cent to 7.2 per cent, determined on 0.500 g.

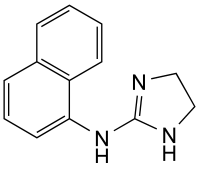
Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

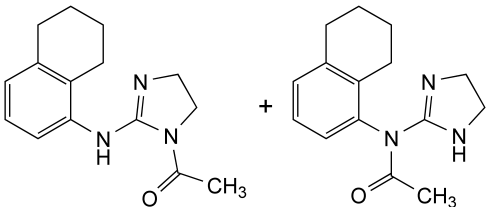
Dissolve 2.000 g in a mixture of 5 ml of *0.1 M hydrochloric acid* and 75 ml of *alcohol R*. Carry out a potentiometric titration (*2.2.20*) using *1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 ml of *1 M sodium hydroxide* is equivalent to 251.8 mg of $C_{13}H_{18}ClN_3$.

IMPURITIES



A. *N*-(naphthalen-1-yl)-4,5-dihydro-1*H*-imidazol-2-amine,



B. mixture of 1-acetyl-2-[(5,6,7,8-tetrahydronaphthalen-1-yl)amino]-4,5-dihydro-1*H*-imidazole and *N*-(4,5-dihydro-1*H*-imidazol-2-yl)-*N*-(5,6,7,8-tetrahydronaphthalen-1-yl)acetamide.

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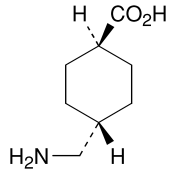
TRANEXAMIC ACID

Acidum tranexamicum



$C_8H_{15}NO_2$ M_r 157.2

DEFINITION

Trans-4-(aminomethyl)cyclohexanecarboxylic acid.

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

CHARACTERS

Appearance: white, crystalline powder.

Solubility: freely soluble in water and in glacial acetic acid, practically insoluble in acetone and in alcohol.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *tranexamic acid CRS*.

TESTS

pH (*2.2.3*): 7.0 to 8.0.

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

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.20 g of the substance to be examined in *water R* and dilute to 20.0 ml with the same solvent.

Reference solution (a). Dilute 5.0 ml of the test solution to 100.0 ml with *water R*. Dilute 1.0 ml of this solution to 10.0 ml with *water R*.

Reference solution (b). Dissolve 5 mg of *tranexamic acid impurity C CRS* in *water R* and dilute to 50.0 ml with the same solvent. To 1.0 ml of this solution add 1.0 ml of the test solution and dilute to 50.0 ml with *water R*.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm or *l* = 0.25 m, Ø = 6.0 mm,

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: dissolve 11.0 g of *anhydrous sodium dihydrogen phosphate R* in 500 ml of *water R*, add 5 ml of *triethylamine R* and 1.4 g of *sodium laurilsulfate R*. Adjust to pH 2.5 with *dilute phosphoric acid R* and dilute to 600 ml with *water R*. Add 400 ml of *methanol R* and mix.

Flow rate: 0.9 ml/min.

Detection: spectrophotometer at 220 nm.

Injection: 20 µl.

Run time: 3 times the retention time of tranexamic acid.

Relative retentions with reference to tranexamic acid (retention time = about 13 min): impurity C = about 1.1; impurity D = about 1.3; impurity B = about 1.5; impurity A = about 2.1.

System suitability: reference solution (b):

– *resolution*: minimum of 2.0 between the peaks due to tranexamic acid and to impurity C.

Limits:

– *correction factors*: for the calculation of contents, multiply the peak areas of the following impurities by the corresponding correction factor: impurity B = 1.2; impurity C = 0.005; impurity D = 0.006;

– *impurity A*: not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);

– *impurity B*: not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

– *any other impurity*: not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);

– *total of other impurities*: not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

– *disregard limit*: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.025 per cent).

Halides expressed as chlorides (*2.4.4*): maximum 140 ppm.

Dissolve 1.2 g in *water R* and dilute to 50 ml with the same solvent. 15 ml of this solution complies with the limit test for chlorides.

Heavy metals (*2.4.8*): maximum 10 ppm.

Dissolve 2.0 g in *water R* and dilute to 20 ml with the same solvent. 12 ml of this solution complies with limit test A. Prepare the standard using *lead standard solution (1 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 100-105 °C for 2 h.

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

ASSAY

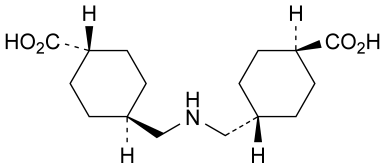
Dissolve 0.140 g in 20 ml of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M perchloric acid* is equivalent to 15.72 mg of $C_8H_{15}NO_2$.

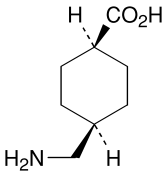
IMPURITIES

Specified impurities: A, B.

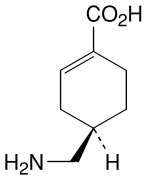
Other detectable impurities: C, D.



A. *trans,trans*-4,4′-(iminodimethylene)di(cyclohexanecarboxylic) acid,

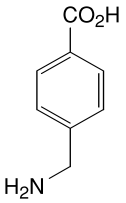


B. *cis*-4-(aminomethyl)cyclohexanecarboxylic acid,



and enantiomer

C. (*RS*)-4-(aminomethyl)cyclohex-1-enecarboxylic acid,



D. 4-aminomethylbenzoic acid.

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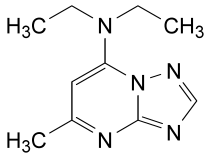
TRAPIDIL

Trapidilum



$C_{10}H_{15}N_5$ M_r 205.3

DEFINITION

N,N-Diethyl-5-methyl-[1,2,4]triazolo[1,5-*a*]pyrimidin-7-amine.

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

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water, soluble in ethanol and in methylene chloride.

mp: about 102 °C.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *trapidil CRS*.

TESTS

Solution S. Dissolve 2.0 g in *carbon dioxide-free water R* and dilute to 100 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. To 10 ml of solution S add 0.2 ml of *methyl red solution R* and 0.2 ml of *0.01 M hydrochloric acid*. The solution is red. Add 0.4 ml of *0.01 M sodium hydroxide*. The solution is yellow.