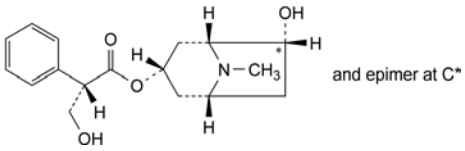
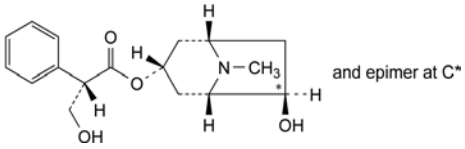
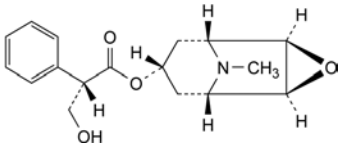


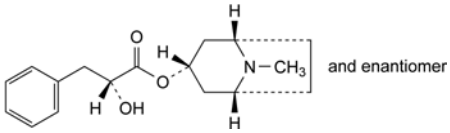
D. (1*R*,3*S*,5*R*,6*RS*)-6-hydroxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2*S*)-3-hydroxy-2-phenylpropanoate (6-hydroxyhyoscyamine),



E. (1*S*,3*R*,5*S*,6*RS*)-6-hydroxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2*S*)-3-hydroxy-2-phenylpropanoate (7-hydroxyhyoscyamine),



F. (1*R*,2*R*,4*S*,5*S*,7*s*)-9-methyl-3-oxa-9-azatricyclo[3.3.1.$0^{2,4}$]non-7-yl (2*S*)-3-hydroxy-2-phenylpropanoate (hyoscine),



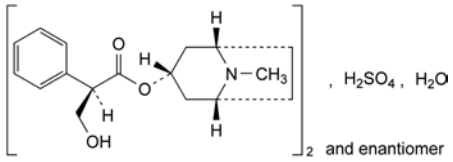
G. (1*R*,3*r*,5*S*)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2*RS*)-2-hydroxy-3-phenylpropanoate (littorine),

H. unknown structure.

04/2008:0068
corrected 7.0

ATROPINE SULFATE

Atropini sulfas



$C_{34}H_{48}N_2O_{10}S,H_2O$ M_r 695
[5908-99-6]

DEFINITION

Bis[(1*R*,3*r*,5*S*)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2*RS*)-3-hydroxy-2-phenylpropanoate] sulfate monohydrate.

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

CHARACTERS

Appearance: white or almost white, crystalline powder or colourless crystals.

Solubility: very soluble in water, freely soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: A, B, E.

Second identification: C, D, E, F.

A. Optical rotation (see Tests).

B. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *atropine sulfate CRS.*

C. Dissolve about 50 mg in 5 mL of *water R* and add 5 mL of *picric acid solution R*. The precipitate, washed with *water R* and dried at 100-105 °C for 2 h, melts (*2.2.14*) at 174 °C to 179 °C.

D. To about 1 mg add 0.2 mL of *fuming nitric acid R* and evaporate to dryness in a water-bath. Dissolve the residue in 2 mL of *acetone R* and add 0.1 mL of a 30 g/L solution of *potassium hydroxide R* in *methanol R*. A violet colour develops.

E. It gives the reactions of sulfates (*2.3.1*).

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

TESTS

pH (*2.2.3*): 4.5 to 6.2.

Dissolve 0.6 g in *carbon dioxide-free water R* and dilute to 30 mL with the same solvent.

Optical rotation (*2.2.7*): – 0.50° to + 0.05° (measured in a 2 dm tube).

Dissolve 2.50 g in *water R* and dilute to 25.0 mL with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 24 mg of the substance to be examined in mobile phase A and dilute to 100.0 mL with mobile phase A.

Reference solution (a). Dilute 1.0 mL of the test solution to 100.0 mL with mobile phase A. Dilute 1.0 mL of this solution to 10.0 mL with mobile phase A.

Reference solution (b). Dissolve 5 mg of *atropine impurity B CRS* in the test solution and dilute to 20 mL with the test solution. Dilute 5 mL of this solution to 25 mL with mobile phase A.

Reference solution (c). Dissolve the contents of a vial of *atropine for peak identification CRS* (containing impurities A, D, E, F, G and H) in 1 mL of mobile phase A.

Reference solution (d). Dissolve 5 mg of *tropic acid R* (impurity C) in mobile phase A and dilute to 10 mL with mobile phase A. Dilute 1 mL of the solution to 100 mL with mobile phase A. Dilute 1 mL of this solution to 10 mL with mobile phase A.

Column:

– *size*: *l* = 0.10 m, Ø = 4.6 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase:

– *mobile phase A*: dissolve 3.5 g of *sodium dodecyl sulfate R* in 606 mL of a 7.0 g/L solution of *potassium dihydrogen phosphate R* previously adjusted to pH 3.3 with *0.05 M phosphoric acid*, and mix with 320 mL of *acetonitrile R1*;
– *mobile phase B*: *acetonitrile R1*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 2	95	5
2 - 20	95 → 70	5 → 30

Flow rate: 1 mL/min.

Detection: spectrophotometer at 210 nm.

Injection: 10 µL.

Identification of impurities: use the chromatogram supplied with *atropine for peak identification CRS* and the chromatogram obtained with reference solution (c) to identify the peaks due to impurities A, D, E, F, G and H. Use the chromatogram obtained with reference solution (b) to identify the peak due to impurity B, and use the chromatogram obtained with reference solution (d) to identify the peak due to impurity C.

Relative retention with reference to atropine (retention time = about 11 min): impurity C = about 0.2; impurity E = about 0.67; impurity D = about 0.73;

impurity F = about 0.8; impurity B = about 0.89; impurity H = about 0.93; impurity G = about 1.1; impurity A = about 1.7.

System suitability: reference solution (b):

– *resolution*: minimum 2.5 between the peaks due to impurity B and atropine.

Limits:

– *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 0.6; impurity C = 0.6;
– *impurities E, H*: for each impurity, not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent);
– *impurities A, B, C, D, F, G*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);
– *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);
– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Water (*2.5.12*): 2.0 per cent to 4.0 per cent, determined on 0.500 g.

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

ASSAY

Dissolve 0.500 g in 30 mL of *anhydrous acetic acid R*, warming if necessary. Cool the solution. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

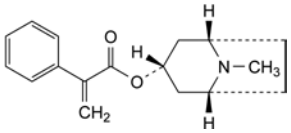
1 mL of *0.1 M perchloric acid* is equivalent to 67.68 mg of $C_{34}H_{48}N_2O_{10}S$.

STORAGE

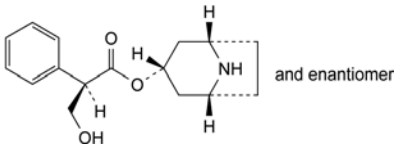
Protected from light.

IMPURITIES

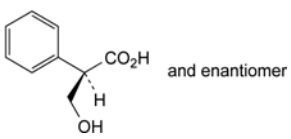
Specified impurities: A, B, C, D, E, F, G, H.



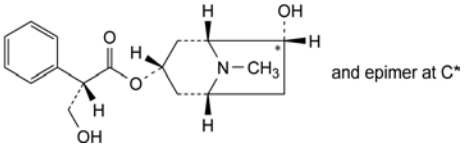
A. (1*R*,3*r*,5*S*)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl 2-phenylpropenoate (apoatropine),



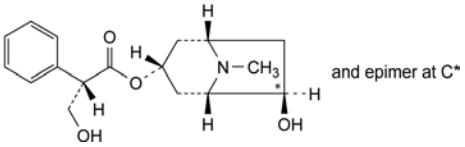
B. (1*R*,3*r*,5*S*)-8-azabicyclo[3.2.1]oct-3-yl (2*RS*)-3-hydroxy-2-phenylpropanoate (noratropine),



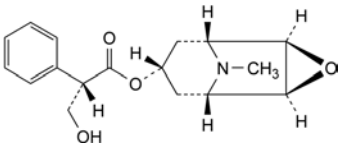
C. (2*RS*)-3-hydroxy-2-phenylpropanoic acid (tropic acid),



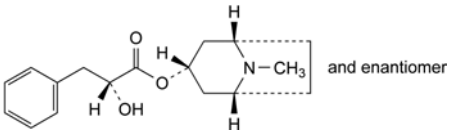
D. (1*R*,3*S*,5*R*,6*RS*)-6-hydroxy-8-methyl-8-azabicyclo-[3.2.1]oct-3-yl (2*S*)-3-hydroxy-2-phenylpropanoate (6-hydroxyhyoscyamine),



E. (1*S*,3*R*,5*S*,6*RS*)-6-hydroxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2*S*)-3-hydroxy-2-phenylpropanoate (7-hydroxyhyoscyamine),



F. (1*R*,2*R*,4*S*,5*S*,7*s*)-9-methyl-3-oxa-9-azatricyclo[3.3.1.0^{2,4}]non-7-yl (2*S*)-3-hydroxy-2-phenylpropanoate (hyoscine),



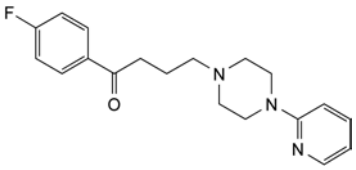
G. (1*R*,3*r*,5*S*)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl (2*RS*)-2-hydroxy-3-phenylpropanoate (littorine).

H. unknown structure.

04/2010:1708
corrected 7.0

AZAPERONE FOR VETERINARY USE

Azaperonum ad usum veterinarium



$C_{19}H_{22}FN_3O$ M_r 327.4
[1649-18-9]

DEFINITION

1-(4-Fluorophenyl)-4-[4-(pyridin-2-yl)piperazin-1-yl]butan-1-one.

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

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water, freely soluble in acetone and in methylene chloride, soluble in ethanol (96 per cent).

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *azaperone CRS*.

If the spectra obtained show differences, dissolve the substance to be examined and the reference substance separately in *acetone R*, evaporate to dryness and record new spectra using the residues.