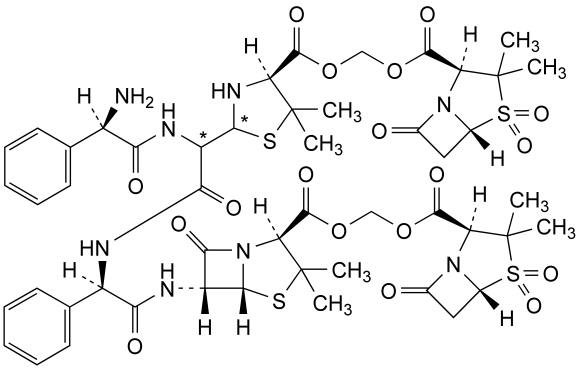
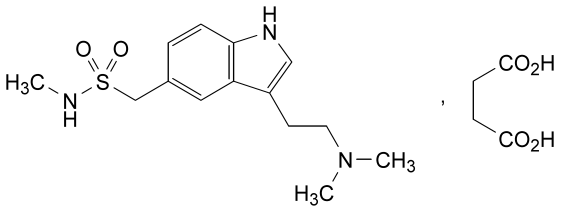


G. methylene (2*S*,5*R*,6*R*)-6-[[(2*R*)-[[[[(2*R*)-amino-phenylacetyl]amino][(4*S*)-4-[[[[[(2*S*,5*R*)-3,3-dimethyl-4,4,7-trioxo-4λ⁶-thia-1-azabicyclo[3.2.0]hept-2-yl] carbonyl]oxy]methoxy]carbonyl]-5,5-dimethylthiazolidin-2-yl]acetyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate (2*S*,5*R*)-3,3-dimethyl-4,4,7-trioxo-4λ⁶-thia-1-aza-bicyclo[3.2.0]heptane-2-carboxylate (sultamicillin dimer).

01/2008:1573

SUMATRIPTAN SUCCINATE

Sumatriptani succinas



$C_{18}H_{27}N_3O_6S$ M_r 413.5
[103628-48-4]

DEFINITION

[3-[2-(Dimethylamino)ethyl]-1*H*-indol-5-yl]-*N*-methylmethanesulphonamide hydrogen butanedioate.

Content: 97.5 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white powder.

Solubility: freely soluble in water, sparingly soluble in methanol, practically insoluble in methylene chloride.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *sumatriptan succinate CRS*.

TESTS

Solution S. Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 25.0 ml with the same solvent.

pH (*2.2.3*): 4.5 to 5.3.

Dilute 2.5 ml of solution S to 10 ml with *carbon dioxide-free water R*.

Absorbance (*2.2.25*): maximum 0.10, measured at 440 nm on solution S.

Impurities A and H. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 30.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 ml with the mobile phase.

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

Reference solution (b). Dissolve the contents of a vial of *sumatriptan for system suitability CRS* (containing impurities A and H) in the mobile phase and dilute to 1 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;
– *stationary phase*: *silica gel for chromatography R* (5 µm).

Mobile phase: mix 10 volumes of a 771 g/l solution of *ammonium acetate R* and 90 volumes of *methanol R*.

Flow rate: 2.0 ml/min.

Detection: spectrophotometer at 282 nm.

Injection: 20 µl.

Run time: 5 times the retention time of sumatriptan.

System suitability: reference solution (b):

– *resolution*: minimum 1.5 between the peaks due to sumatriptan and impurity A;
– the chromatogram is similar to the chromatogram supplied with *sumatriptan for system suitability CRS*.

Limits:

– *impurity A*: not more than 6 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.6 per cent);
– *impurity H*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent).

Related substances. Liquid chromatography (*2.2.29*).

Solution A. Dissolve 2.925 g of *sodium dihydrogen phosphate R* in 600 ml of *water R*, adjust to pH 6.5 with *strong sodium hydroxide solution R*, dilute to 750 ml with *water R*, add 250 ml of *acetonitrile R* and mix.

Test solution (a). Dissolve 30.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 ml with the mobile phase.

Test solution (b). Dissolve 15.0 mg of the substance to be examined in solution A and dilute to 100.0 ml with solution A.

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

Reference solution (b). Dissolve the contents of a vial of *sumatriptan impurity mixture CRS* (containing impurities B, C, D and E) in the mobile phase and dilute to 1 ml with the mobile phase.

Reference solution (c). Dissolve 15.0 mg of *sumatriptan succinate CRS* in solution A and dilute to 100.0 ml with solution A.

Column:

– *size*: *l* = 0.25 m, Ø = 4 mm;
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: mix 25 volumes of *acetonitrile R* with 75 volumes of a solution prepared as follows: dissolve 0.970 g of *dibutylamine R*, 0.735 g of *phosphoric acid R*

and 2.93 g of *sodium dihydrogen phosphate R* in 750 ml of *water R*, adjust to pH 6.5 with *strong sodium hydroxide solution R* and dilute to 1000 ml with *water R*.

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 282 nm.

Injection: 10 µl of test solution (a) and reference solutions (a) and (b).

Run time: 4 times the retention time of sumatriptan.

Identification of impurities: use the chromatogram obtained with reference solution (b) and the chromatogram supplied with *sumatriptan impurity mixture CRS* to identify the peaks due to impurities B, C, D and E.

System suitability: reference solution (b):

– *resolution*: minimum 1.5 between the peaks due to sumatriptan and impurity C;

– the chromatogram shows 5 clearly separated peaks.

Limits:

– *impurities B, C, D*: for each impurity, not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

– *impurity E*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 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 6 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.6 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*): maximum 1.0 per cent, determined on 0.500 g.

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

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

Injection: test solution (b) and reference solution (c).

Calculate the percentage content of $C_{18}H_{27}N_3O_6S$ from the declared content of *sumatriptan succinate CRS*.

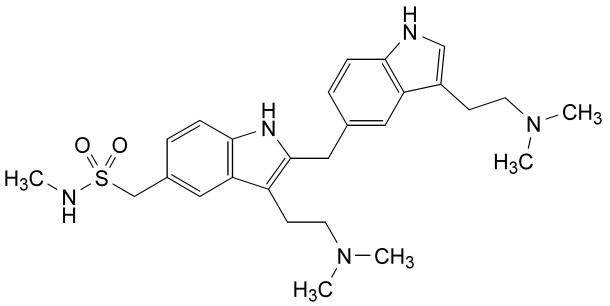
STORAGE

Protected from light.

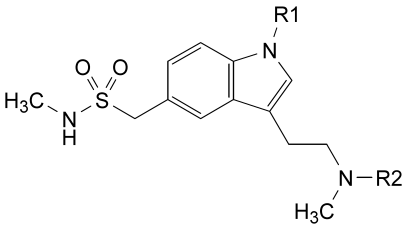
IMPURITIES

Specified impurities: *A, B, C, D, E, H.*

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. It is therefore not necessary to identify these impurities for demonstration of compliance. See also *5.10. Control of impurities in substances for pharmaceutical use*): *F, G.*

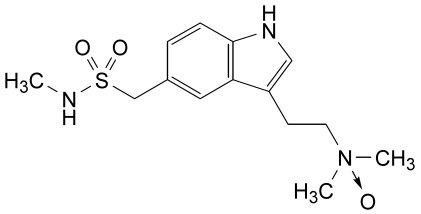


A. [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1*H*-indol-5-yl]methyl]-1*H*-indol-5-yl]-*N*-methylmethanesulphonamide,

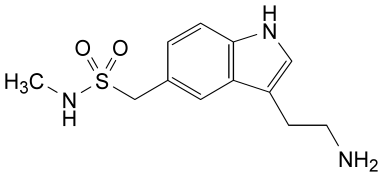


B. R1 = R2 = H: *N*-methyl[3-[2-(methylamino)ethyl]-1*H*-indol-5-yl]methanesulphonamide,

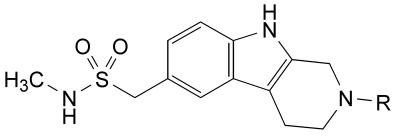
C. R1 = CH_2-OH, R2 = CH_3: [3-[2-(dimethylamino)ethyl]-1-(hydroxymethyl)-1*H*-indol-5-yl]-*N*-methylmethanesulphonamide,



D. *N*,*N*-dimethyl-2-[5-[(methylsulphamoyl)methyl]-1*H*-indol-3-yl]ethanamine *N*-oxide,

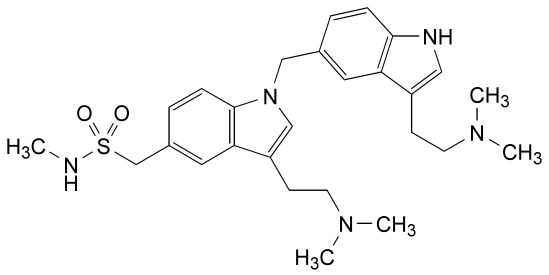


E. [3-(2-aminoethyl)-1*H*-indol-5-yl]-*N*-methylmethanesulphonamide,



F. R = H: *N*-methyl(2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-6-yl)methanesulphonamide,

G. R = CH_3: *N*-methyl(2-methyl-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-6-yl)methanesulphonamide,



H. [3-[2-(dimethylamino)ethyl]-1-[[3-[2-(dimethylamino)ethyl]-1*H*-indol-5-yl]methyl]-1*H*-indol-5-yl]-*N*-methylmethanesulphonamide.

01/2008:1371

SUNFLOWER OIL, REFINED

Helianthi annui oleum raffinatum

DEFINITION

Sunflower oil is the fatty oil obtained from the seeds of *Helianthus annuus* L. by mechanical expression or by extraction. It is then refined. A suitable antioxidant may be added.

CHARACTERS

A clear, light yellow liquid, practically insoluble in water and in alcohol, miscible with light petroleum (bp: 40 °C to 60 °C).

It has a relative density of about 0.921 and a refractive index of about 1.474.

IDENTIFICATION

Carry out the identification of fatty oils by thin-layer chromatography (*2.3.2*). The chromatogram obtained is similar to the typical chromatogram for sunflower oil.

TESTS

Acid value (*2.5.1*). Not more than 0.5, determined on 10.0 g.

Peroxide value (*2.5.5*). Not more than 10.0.

Unsaponifiable matter (*2.5.7*). Not more than 1.5 per cent, determined on 5.0 g.

Alkaline impurities (*2.4.19*). It complies with the test for alkaline impurities in fatty oils.

Composition of fatty acids (*2.4.22, Method A*). The fatty-acid fraction of the oil has the following composition:

– *palmitic acid*: 4.0 per cent to 9.0 per cent,

– *stearic acid*: 1.0 per cent to 7.0 per cent,

– *oleic acid*: 14.0 per cent to 40.0 per cent,

– *linoleic acid*: 48.0 per cent to 74.0 per cent.

STORAGE

Store in an airtight, well-filled container, protected from light.

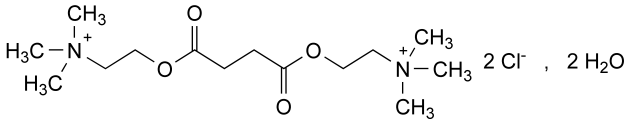
LABELLING

The label states whether the oil is obtained by mechanical expression or by extraction.

01/2008:0248

SUXAMETHONIUM CHLORIDE

Suxamethonii chloridum



$C_{14}H_{30}Cl_2N_2O_4,2H_2O$ M_r 397.3
[6101-15-1]

DEFINITION

Suxamethonium chloride contains not less than 98.0 per cent and not more than the equivalent of 102.0 per cent of 2,2′-[butanedioylbis(oxy)]bis(*N,N,N*-trimethylethanaminium) dichloride, calculated with reference to the anhydrous substance.

CHARACTERS

A white or almost white, crystalline powder, hygroscopic, freely soluble in water, slightly soluble in alcohol.

It melts at about 160 °C, determined without previous drying.

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

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

B. To 1 ml of solution S (see Tests) add 9 ml of *water R*, 10 ml of *dilute sulphuric acid R* and 30 ml of *ammonium reineckate solution R*. A pink precipitate is formed. Allow to stand for 30 min, filter, wash with *water R*, with *alcohol R* and then with *ether R* and dry at 80 °C. The melting point (*2.2.14*) of the precipitate is 180 °C to 185 °C.

C. Dissolve about 25 mg in 1 ml of *water R* and add 0.1 ml of a 10 g/l solution of *cobalt chloride R* and 0.1 ml of *potassium ferrocyanide solution R*. A green colour is produced.

D. About 20 mg gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 20 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*). Dilute 4 ml of solution S to 10 ml with *water R*. The solution is colourless (*2.2.2, Method II*).

pH (*2.2.3*). Dilute 1 ml of solution S to 10 ml with *carbon dioxide-free water R*. The pH of the solution is 4.0 to 5.0.

Choline chloride. Examine by thin-layer chromatography (*2.2.27*), using *cellulose for chromatography R1* as the coating substance.

Test solution. Dissolve 0.4 g of the substance to be examined in *methanol R* and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 0.4 g of *suxamethonium chloride CRS* and 2 mg of *choline chloride R* in *methanol R* and dilute to 10 ml with the same solvent.