Reference solution (c). Dilute 1.0 mL of the test solution to 10.0 mL with the mobile phase.

Reference solution (d). Mix 1.0 mL of reference solution (a), 1.0 mL of reference solution (b) and 1.0 mL of reference solution (c) and dilute to 100.0 mL with the mobile phase.

Column:

– *size*: *l* = 0.15 m, Ø = 3.9 mm;
– *stationary phase*: *end-capped polar-embedded octadecylsilyl amorphous organosilica polymer R* (5 µm);
– *temperature*: 30 °C.

Mobile phase: mix 30 volumes of *acetonitrile for chromatography R* and 70 volumes of a 4.85 g/L solution of *potassium dihydrogen phosphate R* adjusted to pH 8.0 with *strong sodium hydroxide solution R*.

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 230 nm.

Injection: 20 µL.

Run time: 3.5 times the retention time of lidocaine.

Relative retention with reference to lidocaine (retention time = about 17 min): impurity H = about 0.37; impurity A = about 0.40.

System suitability: reference solution (d):

– *resolution*: minimum 1.5 between the peaks due to impurities H and A.

Limits:

– *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (d) (0.01 per cent);
– *unspecified impurities*: for each impurity, not more than the area of the peak due to lidocaine in the chromatogram obtained with reference solution (d) (0.10 per cent);
– *total*: not more than 5 times the area of the peak due to lidocaine in the chromatogram obtained with reference solution (d) (0.5 per cent);
– *disregard limit*: 0.5 times the area of the peak due to lidocaine in the chromatogram obtained with reference solution (d) (0.05 per cent).

Heavy metals (*2.4.8*): maximum 5 ppm.

Dissolve 1.0 g in *water R* and dilute to 25 mL with the same solvent. Carry out the prefiltration. 10 mL of the prefiltrate complies with test E. Prepare the reference solution using 2 mL of *lead standard solution (1 ppm Pb) R*.

Water (*2.5.12*): 5.5 per cent to 7.0 per cent, determined on 0.25 g.

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

ASSAY

Dissolve 0.220 g in 50 mL of *ethanol (96 per cent) R* and add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 mL of *0.1 M sodium hydroxide* is equivalent to 27.08 mg of $C_{14}H_{23}ClN_2O$.

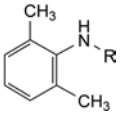
STORAGE

Protected from light.

IMPURITIES

Specified impurities: *A*.

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*): *B, C, D, E, F, G, H, I, J, K*.



A. R = H: 2,6-dimethylaniline,

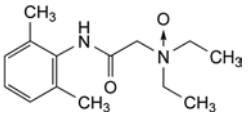
C. R = CO-CH_3: *N*-(2,6-dimethylphenyl)acetamide,

D. R = CO-CH_2-NH-C_2H_5: *N*-(2,6-dimethylphenyl)-2-(ethylamino)acetamide,

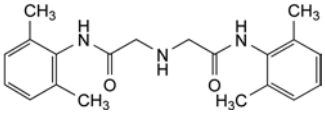
G. R = CO-CH_2-NH-$CH(CH_3)_2$: *N*-(2,6-dimethylphenyl)-2-[(1-methylethyl)amino]acetamide,

H. R = CO-CH_2-Cl: 2-chloro-*N*-(2,6-dimethylphenyl)acetamide,

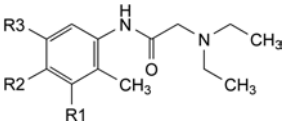
K. R=CO-CH_2-$N(CH_3)C_2H_5$: *N*-(2,6-dimethylphenyl)-2-(ethylmethylamino)acetamide,



B. 2-(diethylazinoyl)-*N*-(2,6-dimethylphenyl)acetamide (lidocaine N^2-oxide),



E. 2-2′-(azanediyl)bis[*N*-(2,6-dimethylphenyl)acetamide],



F. R1 = CH_3, R2 = R3 = H: 2-(diethylamino)-*N*-(2,3-dimethylphenyl)acetamide,

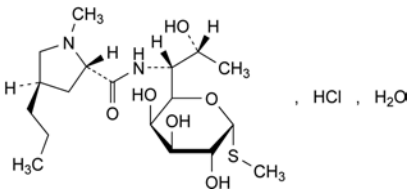
I. R1 = R3 = H, R2 = CH_3: 2-(diethylamino)-*N*-(2,4-dimethylphenyl)acetamide,

J. R1 = R2 = H, R3 = CH_3: 2-(diethylamino)-*N*-(2,5-dimethylphenyl)acetamide.

01/2008:0583

LINCOMYCIN HYDROCHLORIDE

Lincomycini hydrochloridum



$C_{18}H_{35}ClN_2O_6S,H_2O$ M_r 461.0

[7179-49-9]

DEFINITION

Lincomycin hydrochloride consists mainly of the methyl 6,8-dideoxy-6-[[[(2*S*,4*R*)-1-methyl-4-propylpyrrolidin-2-yl]carbonyl]amino]-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside hydrochloride, an antimicrobial substance produced by *Streptomyces lincolnensis* var. *lincolnensis* or by any other means. It contains not less than 89.5 per cent and not more than 102.0 per cent of lincomycin hydrochloride ($C_{18}H_{35}ClN_2O_6S$), calculated with reference to the anhydrous substance.

CHARACTERS

A white or almost white, crystalline powder, very soluble in water, slightly soluble in ethanol (96 per cent), very slightly soluble in acetone.

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 *lincomycin hydrochloride CRS*.

B. Examine by thin-layer chromatography (*2.2.27*), using *silica gel G R* as the coating substance.

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

Reference solution (a). Dissolve 10 mg of *lincomycin hydrochloride CRS* in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution (b). Dissolve 10 mg of *lincomycin hydrochloride CRS* and 10 mg of *clindamycin hydrochloride CRS* in *methanol R* and dilute to 10 mL with the same solvent.

Apply separately to the plate 5 µL of each solution. Develop over a path of 15 cm using the upper layer from a mixture of 20 volumes of *2-propanol R*, 40 volumes of a 150 g/L solution of *ammonium acetate R* previously adjusted to pH 9.6 with *ammonia R* and 45 volumes of *ethyl acetate R*. Allow the plate to dry in air and spray with a 1 g/L solution of *potassium permanganate R*. The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a). The test is not valid unless the chromatogram obtained with reference solution (b) shows two clearly separated spots.

C. Dissolve about 10 mg in 2 mL of *dilute hydrochloric acid R* and heat in a water-bath for 3 min. Add 3 mL of *sodium carbonate solution R* and 1 mL of a 20 g/L solution of *sodium nitroprusside R*. A violet-red colour develops.

D. Dissolve 0.1 g in *water R* and dilute to 10 mL with the same solvent. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 2.0 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*) and not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*).

pH (*2.2.3*). The pH of solution S is 3.5 to 5.5.

Specific optical rotation (*2.2.7*). Dissolve 1.000 g in *water R* and dilute to 25.0 mL with the same solvent. The specific optical rotation is + 135 to + 150, calculated with reference to the anhydrous substance.

Lincomycin B. Examine the chromatogram obtained in the assay with test solution (a). The area of the peak due to lincomycin B, which is eluted just before lincomycin, is not more than 5 per cent of the area of the peak due to lincomycin.

Heavy metals (*2.4.8*). 2.0 g complies with test C for heavy metals (5 ppm). Prepare the reference solution using 1.0 mL of *lead standard solution (10 ppm Pb) R*.

Water (*2.5.12*). 3.1 per cent to 4.6 per cent, determined on 0.500 g by the semi-micro determination of water.

Sulfated ash (*2.4.14*). Not more than 0.5 per cent, determined on 1.0 g.

Bacterial endotoxins (*2.6.14*): less than 0.50 IU/mg, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for removal of bacterial endotoxins.

ASSAY

Examine by gas chromatography (*2.2.28*), using *dotriacontane R* as the internal standard.

Internal standard solution. Dissolve 0.200 g of *dotriacontane R* in *chloroform R* and dilute to 25.0 mL with the same solvent.

Test solution (a). Dissolve 0.100 g of the substance to be examined in a 20 g/L solution of *imidazole R* in *chloroform R* and dilute to 100.0 mL with the same solution. Shake until dissolution is complete. Place 4.0 mL of the solution in a ground-glass-stoppered 15 mL centrifuge tube. Add 1.0 mL of a mixture of 1 volume of *chlorotrimethylsilane R* and 99 volumes of *N,O-bis(trimethylsilyl)acetamide R* and swirl gently. Position the glass stopper loosely in the tube and heat at 65 °C for 30 min.

Test solution (b). Prepare as described for test solution (a) but add 10.0 mL of the internal standard solution before dissolution of the substance to be examined.

Reference solution. Prepare as described for test solution (a) using 0.100 g of *lincomycin hydrochloride CRS* instead of the substance to be examined and adding 10.0 mL of the internal standard solution before dissolution of the reference substance.

The chromatographic procedure may be carried out using:

– a glass column 1.5 m long and 3 mm in internal diameter packed with *silanised diatomaceous earth for gas chromatography R* impregnated with 3 per cent *m/m* of *poly(methylphenylsiloxane) R*,
– *helium for chromatography R* as the carrier gas at a flow rate of about 45 mL/min,
– a flame-ionisation detector,

maintaining the temperature of the column at 260 °C and that of the injection port and of the detector between 260 °C and 290 °C. Inject the chosen volume of the test solutions and the reference solution.

STORAGE

Store in an airtight container at a temperature not exceeding 30 °C. If the substance is sterile, store in a sterile, airtight, tamper-proof container.

01/2008:1232

LINOLEOYL MACROGOLGLYCERIDES

Macrogolglyceridorum linoleates

DEFINITION

Mixtures of monoesters, diesters and triesters of glycerol and monoesters and diesters of macrogols.

They are obtained by partial alcoholysis of an unsaturated oil mainly containing triglycerides of linoleic (*cis,cis*-9,12-octadecadienoic) acid, using macrogol with a mean relative molecular mass between 300 and 400, or by esterification of glycerol and macrogol with unsaturated fatty acids, or by mixing glycerol esters and condensates of ethylene oxide with the fatty acids of this unsaturated oil.

CHARACTERS

Appearance: amber, oily liquid which may give rise to a deposit after prolonged periods at 20 °C.

Solubility: practically insoluble but dispersible in water, freely soluble in methylene chloride.

Viscosity: about 35 mPa·s at 40 °C.

Relative density: about 0.95 at 20 °C.

Refractive index: about 1.47 at 20 °C.

IDENTIFICATION

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

Test solution. Dissolve 1.0 g of the substance to be examined in *methylene chloride R* and dilute to 20 mL with the same solvent.