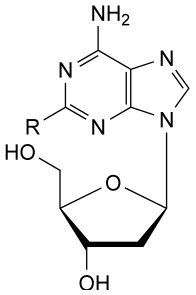
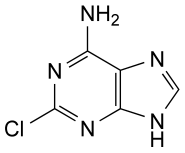
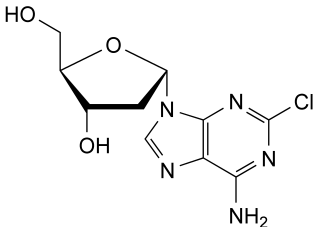


A. R = NH_2: 9-(2-deoxy-β-D-*erythro*-pentofuranosyl)-9*H*-purin-2,6-diamine,

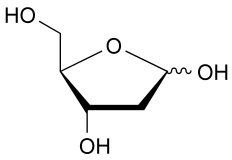
B. R = OCH_3: 9-(2-deoxy-β-D-*erythro*-pentofuranosyl)-2-methoxy-9*H*-purin-6-amine,



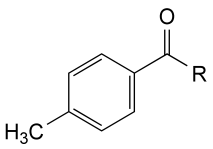
C. 2-chloro-7*H*-purin-6-amine (2-chloroadenine),



D. 2-chloro-9-(2-deoxy-α-D-*erythro*-pentofuranosyl)-9*H*-purin-6-amine,



E. 2-deoxy-D-*erythro*-pentofuranose (2-deoxy-D-ribose),



F. R = NH_2: 4-methylbenzamide,

G. R = OCH_3: methyl 4-methylbenzoate.

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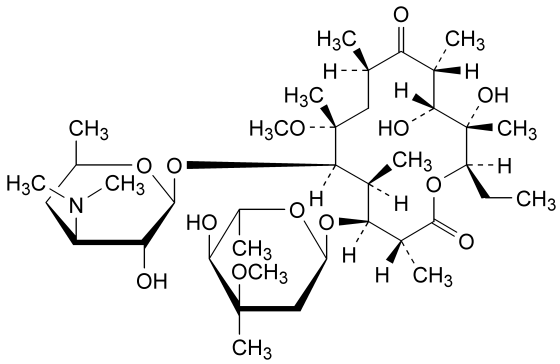
corrected 6.0

CLARITHROMYCIN

Clarithromycinum



$C_{38}H_{69}NO_{13}$ M_r 748
[81103-11-9]

DEFINITION

(3*R*,4*S*,5*S*,6*R*,7*R*,9*R*,11*R*,12*R*,13*S*,14*R*)-4-[(2,6-Dideoxy-3-*C*-methyl-3-*O*-methyl-α-L-*ribo*-hexopyranosyl)oxy]-14-ethyl-12,13-dihydroxy-7-methoxy-3,5,7,9,11,13-hexamethyl-6-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexopyranosyl]oxy]oxacyclotetradecane-2,10-dione (6-*O*-methylerythromycin A).

Semi-synthetic product derived from a fermentation product.

Content: 96.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: practically insoluble in water, soluble in acetone and in methylene chloride, slightly soluble in methanol.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *clarithromycin CRS*.

TESTS

Solution S. Dissolve 0.500 g in *methylene chloride R* and dilute to 50.0 ml with the same solvent.

Appearance of solution. Solution S is clear or not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution Y_7 (*2.2.2, Method II*).

Specific optical rotation (*2.2.7*): – 94 to – 102 (anhydrous substance), determined on solution S.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 75.0 mg of the substance to be examined in 25 ml of *acetonitrile R1* and dilute to 50.0 ml with *water R*.

Reference solution (a). Dissolve 75.0 mg of *clarithromycin CRS* in 25 ml of *acetonitrile R1* and dilute to 50.0 ml with *water R*.

Reference solution (b). Dilute 5.0 ml of reference solution (a) to 100.0 ml with a mixture of equal volumes of *acetonitrile R1* and *water R*.

Reference solution (c). Dilute 1.0 ml of reference solution (b) to 10.0 ml with a mixture of equal volumes of *acetonitrile R1* and *water R*.

Reference solution (d). Dissolve 15.0 mg of *clarithromycin for peak identification CRS* in 5.0 ml of *acetonitrile R1* and dilute to 10.0 ml with *water R*.

Blank solution. Dilute 25.0 ml of *acetonitrile R1* to 50.0 ml with *water R* and mix.

Column:

– *size*: *l* = 0.10 m, Ø = 4.6 mm,

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (3.5 µm),

– *temperature*: 40 °C.

Mobile phase:

– *mobile phase A*: a 4.76 g/l solution of *potassium dihydrogen phosphate R* adjusted to pH 4.4 with *dilute phosphoric acid R* or a 45 g/l solution of *potassium hydroxide R*, filtered through a C18 filtration kit,

– *mobile phase B*: *acetonitrile R1*,

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 32	75 → 40	25 → 60
32 - 34	40	60
34 - 36	40 → 75	60 → 25
36 - 42	75	25

Flow rate: 1.1 ml/min.

Detection: spectrophotometer at 205 nm.

Injection: 10 µl of the blank solution, the test solution and reference solutions (b), (c) and (d).

Relative retention r (not r_G) with reference to clarithromycin (retention time = about 11 min): impurity I = about 0.38; impurity A = about 0.42; impurity J = about 0.63; impurity L = about 0.74; impurity B = about 0.79; impurity M = about 0.81; impurity C = about 0.89; impurity D = about 0.96; impurity N = about 1.15; impurity E = about 1.27; impurity F = about 1.33; impurity P = about 1.35; impurity O = about 1.41; impurity K = about 1.59; impurity G = about 1.72; impurity H = about 1.82.

System suitability:

– *symmetry factor*: maximum 1.7 for the peak due to clarithromycin in the chromatogram obtained with reference solution (b),

– *peak-to-valley ratio*: minimum 3.0, where H_p = height above the baseline of the peak due to impurity D and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to clarithromycin in the chromatogram obtained with reference solution (d).

Limits:

– *correction factors*: for the calculation of contents, multiply the peak areas of the following impurities by the corresponding correction factor: impurity G = 0.27; impurity H = 0.15; use the chromatogram supplied with *clarithromycin for peak identification CRS* to identify the peaks;

– *any impurity*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (c) (1.0 per cent), and not more than 4 such peaks have an area greater than 0.8 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.4 per cent);

– *total*: not more than 7 times the area of the principal peak in the chromatogram obtained with reference solution (c) (3.5 per cent);

– *disregard limit*: 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent); disregard the peaks eluting before impurity I and after impurity H.

Heavy metals (*2.4.8*): maximum 20 ppm.

Dissolve 1.0 g in a mixture of 15 volumes of *water R* and 85 volumes of *dioxan R* and dilute to 20 ml with the same mixture of solvents. 12 ml of the solution complies with limit test B. Prepare the reference solution using lead standard solution (1 ppm Pb) obtained by diluting *lead standard solution (100 ppm Pb) R* with a mixture of 15 volumes of *water R* and 85 volumes of *dioxan R*.

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

Sulphated ash (*2.4.14*): maximum 0.2 per cent, determined on 0.5 g.

ASSAY

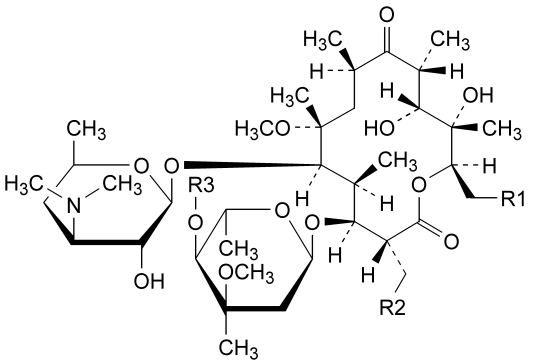
Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modifications.

Injection: test solution and reference solution (a).

Calculate the percentage content of $C_{38}H_{69}NO_{13}$.

IMPURITIES

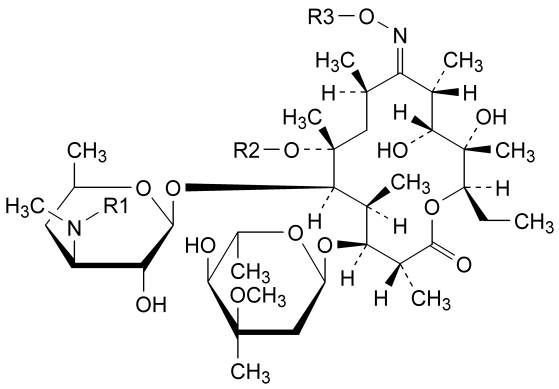
Specified impurities: A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P.



A. R1 = CH_3, R2 = OH, R3 = H: 2-demethyl-2-(hydroxymethyl)-6-*O*-methylerythromycin A (clarithromycin F),

B. R1 = R2 = R3 = H: 6-*O*-methyl-15-norerythromycin A,

P. R1 = R3 = CH_3, R2 = H: 4′,6-di-*O*-methylerythromycin A,

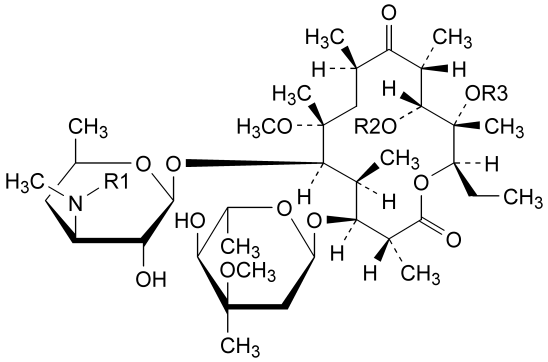


C. R1 = R2 = CH_3, R3 = H: 6-*O*-methylerythromycin A (*E*)-9-oxime,

G. R1 = R2 = R3 = CH_3: 6-*O*-methylerythromycin A (*E*)-9-(*O*-methyloxime),

J. R1 = CH_3, R2 = R3 = H: erythromycin A (*E*)-9-oxime,

M. R1 = R3 = H, R2 = CH_3: 3″-*N*-demethyl-6-*O*-methylerythromycin A (*E*)-9-oxime,

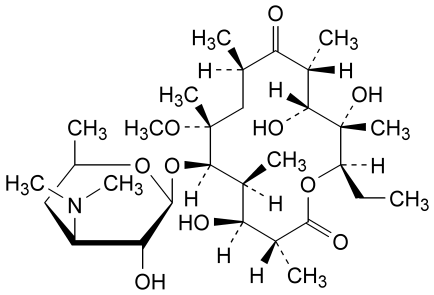


D. R1 = R2 = R3 = H: 3″-*N*-demethyl-6-*O*-methylerythromycin A,

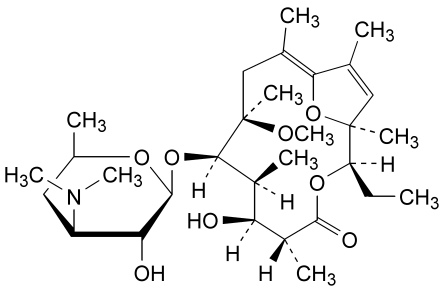
E. R1 = R2 = CH_3, R3 = H: 6,11-di-*O*-methylerythromycin A,

F. R1 = R3 = CH_3, R2 = H: 6,12-di-*O*-methylerythromycin A,

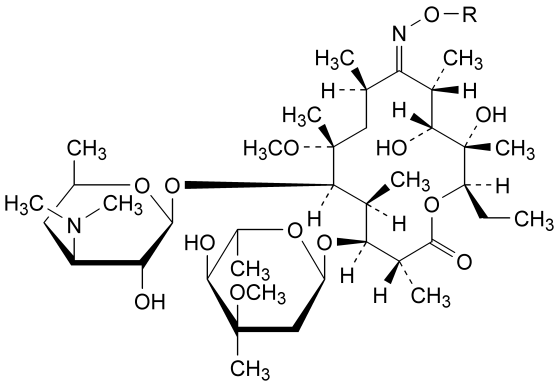
H. R1 = CHO, R2 = R3 = H: 3″-*N*-demethyl-3′-*N*-formyl-6-*O*-methylerythromycin A,



I. 3-*O*-decladinosyl-6-*O*-methylerythromycin A,

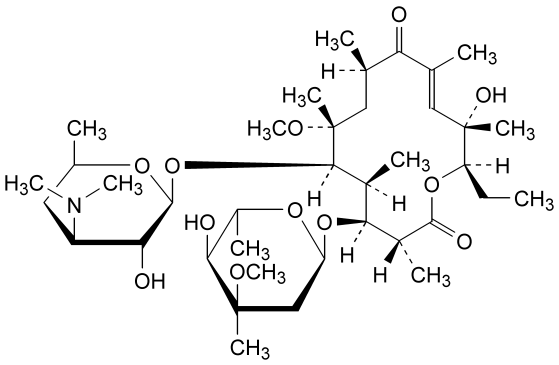


K. (1*S*,2*R*,5*R*,6*S*,7*S*,8*R*,9*R*,11*Z*)-2-ethyl-6-hydroxy-9-methoxy-1,5,7,9,11,13-hexamethyl-8-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexopyranosyl]oxy]-3,15-dioxabicyclo[10.2.1]pentadeca-11,13-dien-4-one (3-*O*-decladinosyl-8,9:10,11-dianhydro-6-*O*-methylerythromycin A-9,12-hemiketal,



L. R = H: 6-*O*-methylerythromycin A (*Z*)-9-oxime,

O. R = CH_3: 6-*O*-methylerythromycin A (*Z*)-9-(*O*-methyloxime),



N. (10*E*)-10,11-didehydro-11-deoxy-6-*O*-methylerythromycin A.

01/2008:1850

CLARY SAGE OIL

Salviae sclareae aetheroleum

DEFINITION

Essential oil obtained by steam distillation from the fresh or dried flowering stems of *Salvia sclarea* L.

CHARACTERS

Appearance: colourless to brownish-yellow liquid, usually pale yellow, with a characteristic odour.

IDENTIFICATION

First identification: B.