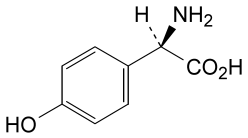
Calculate the percentage content of cefadroxil.

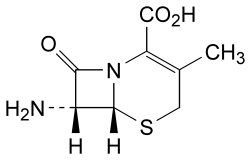
STORAGE

Protected from light.

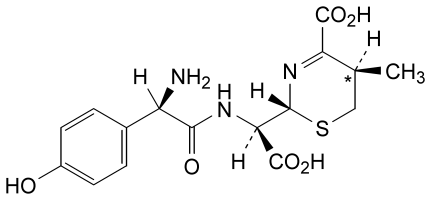
IMPURITIES



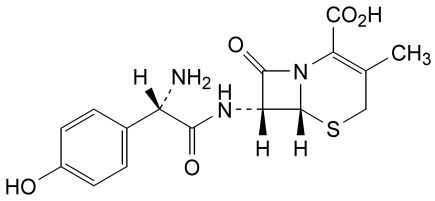
A. (2*R*)-2-amino-2-(4-hydroxyphenyl)acetic acid,



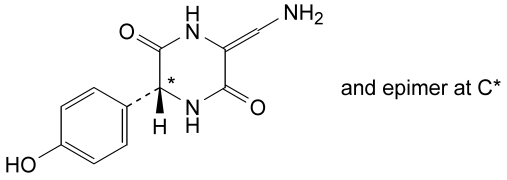
B. (6*R*,7*R*)-7-amino-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (7-ADCA),



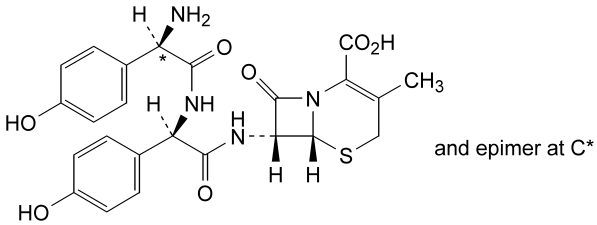
C. (2*R*,5*RS*)-2-[(*R*)-[[(2*R*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]carboxymethyl]-5-methyl-5,6-dihydro-2*H*-1,3-thiazine-4-carboxylic acid,



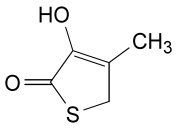
D. (6*R*,7*R*)-7-[[(2*S*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (L-cefadroxil),



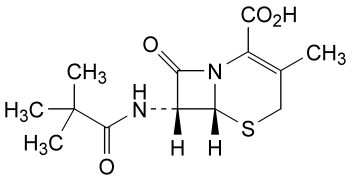
E. (6*RS*)-3-(aminomethylene)-6-(4-hydroxyphenyl)piperazine-2,5-dione,



F. (6*R*,7*R*)-7-[[(2*R*)-2-[[(2*RS*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-2-(4-hydroxyphenyl)acetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,



G. 3-hydroxy-4-methylthiophen-2(5*H*)-one,

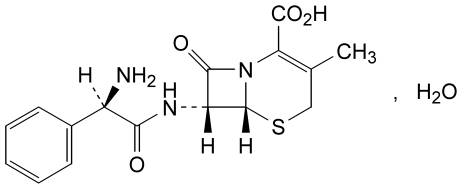


H. (6*R*,7*R*)-7-[(2,2-dimethylpropanoyl)amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (7-ADCA pivalamide).

01/2008:0708
corrected 6.0

CEFALEXIN MONOHYDRATE

Cefalexinum monohydricum



$C_{16}H_{17}N_3O_4S,H_2O$ M_r 365.4
[23325-78-2]

DEFINITION

(6*R*,7*R*)-7-[[(2*R*)-2-Amino-2-phenylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate.

Semi-synthetic product derived from a fermentation product.

Content: 95.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: sparingly soluble in water, practically insoluble in alcohol.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *cefalexin monohydrate CRS*.

TESTS

pH (*2.2.3*): 4.0 to 5.5.

Dissolve 50 mg in *carbon dioxide-free water R* and dilute to 10 ml with the same solvent.

Specific optical rotation (*2.2.7*): + 149 to + 158 (anhydrous substance).

Dissolve 0.125 g in *phthalate buffer solution pH 4.4 R* and dilute to 25.0 ml with the same solvent.

Absorbance (*2.2.25*). Dissolve 50 mg in *water R* and dilute to 100.0 ml with the same solvent. The absorbance of the solution determined at 330 nm is not greater than 0.05. Dilute 2.0 ml of the solution to 50.0 ml with *water R*. Examined between 220 nm and 300 nm, the diluted solution

shows an absorption maximum at 262 nm. The specific absorbance at this maximum is 220 to 245, calculated with reference to the anhydrous substance.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 50.0 mg of the substance to be examined in mobile phase A and dilute to 50.0 ml with mobile phase A.

Reference solution (a). Dissolve 10.0 mg of *D-phenylglycine R* in mobile phase A and dilute to 10.0 ml with mobile phase A.

Reference solution (b). Dissolve 10.0 mg of *7-aminodesacetoxycephalosporanic acid CRS* in *phosphate buffer solution pH 7.0 R5* and dilute to 10.0 ml with mobile phase A.

Reference solution (c). Dilute 1.0 ml of reference solution (a) and 1.0 ml of reference solution (b) to 100.0 ml with mobile phase A.

Reference solution (d). Dissolve 10 mg of *dimethylformamide R* and 10 mg of *dimethylacetamide R* in mobile phase A and dilute to 10.0 ml with mobile phase A. Dilute 1.0 ml to 100.0 ml with mobile phase A.

Reference solution (e). Dilute 1.0 ml of reference solution (c) to 20.0 ml with mobile phase A.

Reference solution (f). Dissolve 10 mg of *cefotaxime sodium CRS* in mobile phase A and dilute to 10.0 ml with mobile phase A. To 1.0 ml of the solution add 1.0 ml of the test solution and dilute to 100 ml with mobile phase A.

Column:

– *size*: *l* = 0.10 m, Ø = 4.6 mm,

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

Mobile phase:

– *mobile phase A*: *phosphate buffer solution pH 5.0 R,*

– *mobile phase B*: *methanol R2,*

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 1	98	2
1 - 20	98 → 70	2 → 30
20 - 23	70 → 98	30 → 2
23 - 30	98	2

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 220 nm.

Injection: 20 µl; inject the test solution and reference solutions (c), (d), (e) and (f).

System suitability:

– *resolution*: minimum of 2.0 between the peaks due to impurity A and to impurity B in the chromatogram obtained with reference solution (c) and minimum of 1.5 between the peaks due to cefalexin and to cefotaxime in the chromatogram obtained with reference solution (f).

Limits:

– *impurity B*: not more than the area of the second peak in the chromatogram obtained with reference solution (c) (1.0 per cent),

– *any other impurity* (disregard the peaks due to dimethylformamide and dimethylacetamide): not more than the area of the first peak in the chromatogram obtained with reference solution (c) (1.0 per cent),

– *total*: not more than 3 times the area of the first peak in the chromatogram obtained with reference solution (c) (3.0 per cent),

– *disregard limit*: the area of the second peak in the chromatogram obtained with reference solution (e) (0.05 per cent).

***N,N*-Dimethylaniline** (*2.4.26, Method B*): maximum 20 ppm.

Water (*2.5.12*): 4.0 per cent to 8.0 per cent, determined on 0.300 g.

Sulphated ash (*2.4.14*): maximum 0.2 per cent, determined on 1.0 g.

ASSAY

Liquid chromatography (*2.2.29*).

Test solution. Dissolve 50.0 mg of the substance to be examined in *water R* and dilute to 100.0 ml with the same solvent.

Reference solution (a). Dissolve 50.0 mg of *cefalexin monohydrate CRS* in *water R* and dilute to 100.0 ml with the same solvent.

Reference solution (b). Dissolve 10 mg of *cefradine CRS* in 20 ml of reference solution (a) and dilute to 100 ml with *water R*.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm,

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

Mobile phase: *methanol R, acetonitrile R*, a 13.6 g/l solution of *potassium dihydrogen phosphate R, water R* (2:5:10:83 *V/V/V/V*).

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 254 nm.

Injection: 20 µl.

System suitability: reference solution (b):

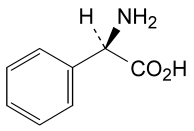
– *resolution*: minimum 4.0 between the peaks due to cefalexin and to cefradine.

Calculate the percentage content of cefalexin monohydrate.

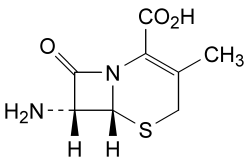
STORAGE

Protected from light.

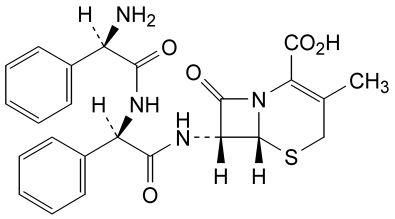
IMPURITIES



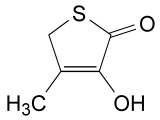
A. (2*R*)-2-amino-2-phenylacetic acid (D-phenylglycine),



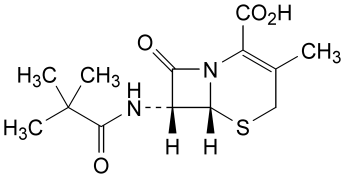
B. (6*R*,7*R*)-7-amino-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (7-aminodesacetoxycephalosporanic acid, 7-ADCA),



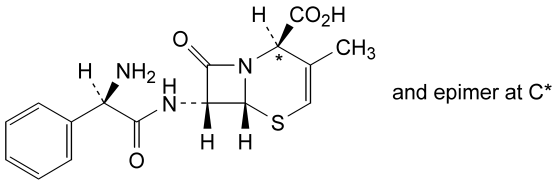
C. (6*R*,7*R*)-7-[[(2*R*)-2-[[(2*R*)-2-amino-2-phenylacetyl]amino]-2-phenylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,



D. 3-hydroxy-4-methylthiophen-2(5*H*)-one,



E. (6*R*,7*R*)-7-[(2,2-dimethylpropanoyl)amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (7-ADCA pivalamide),

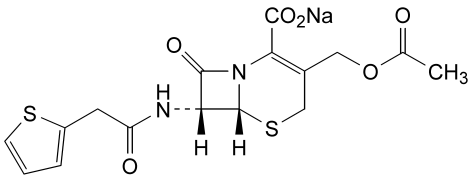


F. (2*RS*,6*R*,7*R*)-7-[[(2*R*)-2-amino-2-phenylacetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid (delta-2-cefalexin).

01/2008:0987

CEFALOTIN SODIUM

Cefalotinum natricum



$C_{16}H_{15}N_2NaO_6S_2$ M_r 418.4
[58-71-9]

DEFINITION

Sodium (6*R*,7*R*)-3-[(acetyloxy)methyl]-8-oxo-7-[(thiophen-2-ylacetyl)amino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate.

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 powder.

Solubility: freely soluble in water, slightly soluble in anhydrous ethanol.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *cefalotin sodium CRS*.

B. It gives reaction (a) of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 2.50 g in *carbon dioxide-free water R* and dilute to 25.0 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and its absorbance (*2.2.25*) at 450 nm is not greater than 0.20.

pH (*2.2.3*): 4.5 to 7.0 for solution S.

Specific optical rotation (*2.2.7*): + 124 to + 134 (anhydrous substance).

Dissolve 1.25 g in *water R* and dilute to 25.0 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).
Prepare the solutions immediately before use.

Test solution (a). Dissolve 75.0 mg of the substance to be examined in *water R* and dilute to 25.0 ml with the same solvent.

Test solution (b). Dilute 5.0 ml of test solution (a) to 50.0 ml with *water R*.

Reference solution (a). Dissolve 75.0 mg of *cefalotin sodium CRS* in *water R* and dilute to 25.0 ml with the same solvent. Dilute 5.0 ml of this solution to 50.0 ml with *water R*.

Reference solution (b). Dilute 1.0 ml of test solution (a) to 100.0 ml with *water R*.

Reference solution (c). Mix 1 ml of test solution (a), 1 ml of *hydrochloric acid R1* and 8 ml of *water R*. Heat at 60 °C for 12 min and cool to room temperature in iced water. Inject immediately.

Reference solution (d). Dissolve 5 mg of *cefalotin for impurity B identification CRS* in *water R* and dilute to 5 ml with the same solvent.

Column:
- *size*: *l* = 0.25 m, Ø = 4.6 mm;
- *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (5 µm);
- *temperature*: 40 °C.

Mobile phase:
- *mobile phase A*: mix 3 volumes of *acetonitrile R1* and 97 volumes of a 1.742 g/l solution of *dipotassium hydrogen phosphate R* previously adjusted to pH 2.5 with *phosphoric acid R*;
- *mobile phase B*: mix 40 volumes of *acetonitrile R1* and 60 volumes of a 1.742 g/l solution of *dipotassium hydrogen phosphate R* previously adjusted to pH 2.5 with *phosphoric acid R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 30	100 → 0	0 → 100
30 - 35	0	100
35 - 36	0 → 100	100 → 0
36 - 41	100	0

Flow rate: 1.0 ml/min.

Detection: spectrophotometer at 220 nm.

Injection: 20 µl of test solution (a) and reference solutions (b), (c) and (d).