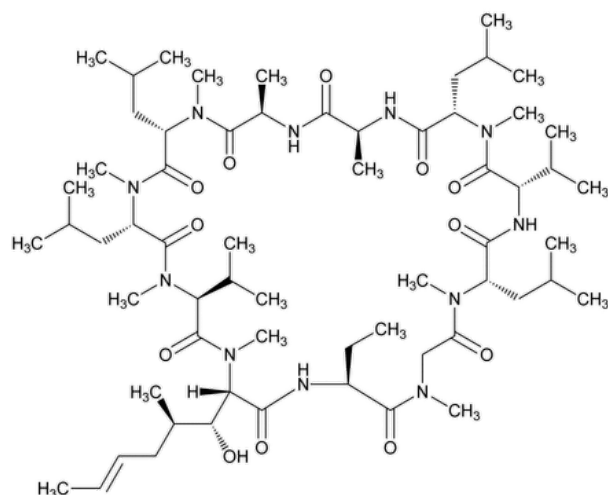


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Cyclosporine



$C_{62}H_{111}N_{11}O_{12}$ 1202.61

Cyclo[[*(E)*-(2*S*,3*R*,4*R*)-3-hydroxy-4-methyl-2-(methylamino)oct-6-enoyl]-*L*-2-aminobutyryl-*N*-methylglycyl-*N*-methyl-*L*-leucyl-*L*-valyl-*N*-methyl-*L*-leucyl-*L*-alanyl-*D*-alanyl-*N*-methyl-*L*-leucyl-*N*-methyl-*L*-leucyl-*N*-methyl-*L*-valyl]; [*R*-(*R**,*R**-(*E*))]—Cyclic(*L*-alanyl-*D*-alanyl-*N*-methyl-*L*-leucyl-*N*-methyl-*L*-leucyl-*N*-methyl-*L*-valyl-3-hydroxy-*N*,4-dimethyl-*L*-2-amino-6-octenoyl-*L*- α -aminobutyryl-*N*-methylglycyl-*N*-methyl-*L*-leucyl-*L*-valyl-*N*-methyl-*L*-leucyl) CAS RN®: 59865-13-3; UNII: 83HN0GTJ6D.

DEFINITION

Cyclosporine contains NLT 97.0% and NMT 101.5% of cyclosporine A ($C_{62}H_{111}N_{11}O_{12}$), calculated on the dried basis.

IDENTIFICATION

Add the following:

- ▲ **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), [Infrared Spectroscopy](#): 197A or 197K▲ (USP 1-Dec-2021)

Change to read:

- **▲B.**▲ (USP 1-Dec-2021) The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

Change to read:

PROCEDURE

Mobile phase: [Acetonitrile](#), [tert-butyl methyl ether](#), [water](#), and [phosphoric acid](#) (430:50:520:1)

Diluent: [Acetonitrile](#) and [water](#) (1:1)

System suitability solution: 1.25 mg/mL of [USP Cyclosporine Resolution Mixture RS](#) in *Diluent*

Standard solution: 1.25 mg/mL of [USP Cyclosporine RS](#) in *Diluent*

Sample solution: 1.25 mg/mL of Cyclosporine in *Diluent*

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 210 nm

Column: 4-mm × 25-cm; 3- to 5-μm packing [L1](#). ▲If needed, tubing may be ▲(USP 1-Dec-2021) connected to the column inlet ▲to support the Column temperature. ▲(USP 1-Dec-2021)

Column temperature: 80°. ▲If used, ▲(USP 1-Dec-2021) the tubing ▲may be ▲(USP 1-Dec-2021) maintained at 80°, to ensure that the *Mobile phase* entering the column is heated to 80°.

Flow rate: 1.2 mL/min

Injection volume: 20 μL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for cyclosporine U and cyclosporine are 0.95 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.0 between cyclosporine U and cyclosporine, *System suitability solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of cyclosporine ($C_{62}H_{111}N_{11}O_{12}$) in the portion of Cyclosporine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times 100$$

r_U = peak area of cyclosporine from the *Sample solution*

r_S = peak area of cyclosporine from the *Standard solution*

C_S = concentration of ▲[USP Cyclosporine RS](#) in ▲(USP 1-Dec-2021) the *Standard solution* (mg/mL)

C_U = concentration of ▲Cyclosporine in ▲(USP 1-Dec-2021) the *Sample solution* (mg/mL)

P = potency of cyclosporine in [USP Cyclosporine RS](#) (mg/mg)

Acceptance criteria: 97.0%–101.5% on the dried basis

IMPURITIES

Change to read:

• ORGANIC IMPURITIES

Mobile phase, Diluent, System suitability solution, Sample solution, and Chromatographic system: Proceed as directed in the Assay.

Standard solution: 0.01 mg/mL of [USP Cyclosporine RS](#) in *Diluent*

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The relative retention times for cyclosporine U and cyclosporine are 0.95 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.0 between cyclosporine U and cyclosporine, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ▲any individual ▲(USP 1-Dec-2021) impurity in the portion of Cyclosporine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times 100$$

r_U = peak area of ▲each ▲(USP 1-Dec-2021) individual impurity from the *Sample solution*

r_S = peak area of cyclosporine from the *Standard solution*

C_S = concentration of ▲[USP Cyclosporine RS](#) in ▲(USP 1-Dec-2021) the *Standard solution* (mg/mL)

C_U = concentration of ▲Cyclosporine in ▲(USP 1-Dec-2021) the *Sample solution* (mg/mL)

P = potency of cyclosporine in [USP Cyclosporine RS](#) (mg/mg)

Acceptance criteria: The reporting threshold is 0.05%.