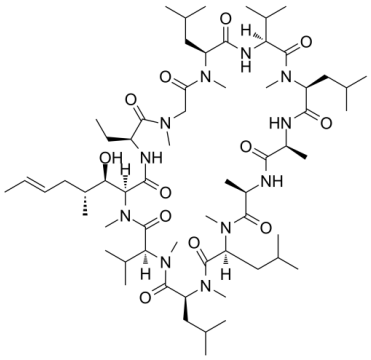
Data Sheet

Product Name:	Cyclosporin A
Cat. No.:	CS-2761
CAS No.:	59865-13-3
Molecular Formula:	C62H111N11O12
Molecular Weight:	1202.61
Target:	Complement System
Pathway:	Immunology/Inflammation
Solubility:	DMSO : 62.5 mg/mL (51.97 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

Cyclosporin A is an immunosuppressant which binds to the cyclophilin and inhibits phosphatase activity of **calcineurin** with an **IC_{50}** of 5 nM. Cyclosporin A also inhibits **CD11a/CD18** adhesion. IC50 & Target: IC50: 7 nM (calcineurin) **In Vitro:** Cyclosporin A is able to bind with the cyclophilin in T cells[1]. Cyclosporin A works by forming a Cyclophilin-Cyclosporin A complex to inhibit calcineurin[2]. Cyclosporin A exhibits inhibitory effect on calcineurin with an IC_{50} of 7 nM[3]. Cyclosporin A suppresses the nuclear translocation of NF-AT[4]. Cyclosporin A shows an effect on mitochondria via preventing the MTP from opening with an IC_{50} of 39 nM[5]. **In Vivo:** Cyclosporin A has immunosuppressive activity, and is active via parenteral and p.o. administration in mice, rat and guinea pigs[6]. Cyclosporin A can be used in organ transplantation to prevent rejection[7].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [3]Reaction mixtures with purified enzyme contains 100 nM calcineurin, 100 nM calmodulin, and 5 μM ^{32}P-labeled phosphopeptide, in 60 μL (total volume) of assay buffer containing 20 mM Tris (pH 8), 100 mM NaCl, 6 mM $MgCl_2$, 0.5 mM dithiothreitol, 0.1 mg of bovine serum albumin per mL, and either 0.1 mM $CaCl_2$ or 5 mM EGTA. Reaction mixtures with cell lysates contains 20 μL of undiluted lysate, 5 μM ^{32}P-labeled phosphopeptide, and 40 μL of assay buffer. Reaction mixtures contains 50 μM peptide 412 or 413 and/or 500 nM okadaic acid, a specific inhibitor of phosphatases 1 and 2A; 500 nM okadaic acid is sufficient for inhibition of Ca^{2+}-independent phosphatases, whereas higher concentrations partially inhibit Ca^{2+}-dependent activity as well. After 15 min at 30°C, reactions are terminated by the addition of 0.5 mL of 100 mM potassium phosphate buffer (pH 7.0) containing 5% trichloroacetic acid. Free inorganic phosphate is isolated by Dowex cation-exchange chromatography and quantitated by scintillation counting as described. **Cell Assay:** Cyclosporin A is dissolved in ethanol.[3]Immunosuppressive agents are dissolved in ethanol at concentrations 1000-fold more than the concentration desired for cell treatments. Cells (10^6) are suspended in 1 mL of complete medium in microcentrifuge tubes; 1 μL of ethanol or of the ethanolic solution of Cyclosporin A is added, and the cells are incubated at 37°C for 1 hr. Cells are washed twice with 1 mL of PBS on ice and lysed in 50 μL of hypotonic buffer containing 50 mM Tris (pH 7.5); 0.1 mM EGTA; 1 mM EDTA; 0.5 mM dithiothreitol; and 50 μg of phenylmethylsulfonyl fluoride, 50 μg of soybean trypsin inhibitor, 5 μg of leupeptin, and 5 μg of aprotinin per mL. Lysates are subjected to three cycles of freezing in liquid nitrogen followed by thawing at 30°C and then are centrifuged at 4°C for 10 min at 12,000×g. **Animal Administration:** Cyclosporin A is suspended in 0.5% solution of tragacanth.[6]Rats are immunized on day 0 i.p. with 0 5 mL and mice i.v. with 0 2 mL of a 10% suspension of washed sheep erythrocytes (SE). To elicit a secondary response, mice are boosted 8-11 weeks after the primary immunization with an i.v. injection of 0-2 mL of 0 25% washed SE (10^7 cells). For prolonged treatment the animals receive on the average 45 mg/kg cyclosporin A daily in the food during 13 weeks. These rats are immunized 5 days before killing.

References:

[1]. Handschumacher RE, et al. Cyclophilin: a specific cytosolic binding protein for cyclosporin A. Science. 1984 Nov 2;226(4674):544-7.

[2]. Liu J, et al. Calcineurin is a common target of cyclophilin-cyclosporin A and FKBP-FK506 complexes. Cell. 1991 Aug 23;66(4):807-15.

[3]. Fruman DA, et al. Calcineurin phosphatase activity in T lymphocytes is inhibited by FK 506 and cyclosporin A. Proc Natl Acad Sci U S A. 1992 May 1;89(9):3686-90.

[4]. Flanagan WM, et al. Nuclear association of a T-cell transcription factor blocked by FK-506 and cyclosporin A. Nature. 1991 Aug 29;352(6338):803-7.

[5]. Nicolli A, et al. Interactions of cyclophilin with the mitochondrial inner membrane and regulation of the permeability transition pore, and cyclosporin A-sensitive channel. J Biol Chem. 1996 Jan 26;271(4):2185-92.

[6]. Borel JF, et al. Effects of the new anti-lymphocytic peptide cyclosporin A in animals. Immunology. 1977 Jun;32(6):1017-25.

[7]. Williams, R, et al. Randomised trial comparing tacrolimus (FK506) and cyclosporin in prevention of liver allograft rejection. European FK506 Multicentre Liver Study Group. Lancet, 1994, 344(8920), 423-428.

[8]. Dalmarco EM, et al. Cyclosporin A inhibits CD11a/CD18 adhesion molecules due to inhibition of TNFalpha and IL-1 beta levels in the mouse model of pleurisy induced by carrageenan. Cell Adh Migr. 2008 Oct-Dec;2(4):231-5.

CAIndexNames:

Cyclosporin A

SMILES:

C/C=C/C[C@H]([C@@H](O)[C@@]1(N(C)C([C@]([H])(C(C)C)N(C)C([C@H](CC(C)C)N(C)C([C@]([H])(CC(C)C)N(C)C([C@@H](C)NC([C@H](C)NC([C@@H](N(C([C@@]([H])(NC([C@@H](N(C(CN(C([C@@H](NC1=O)CC)=O)C)=O)C)CC(C)C)=O)C(C)C)=O)CC(C)C)=O)=O)=O)=O)=O)[H])C

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