Cyclosporin A

Cat. No.: HY-B0579

CAS No.: 59865-13-3

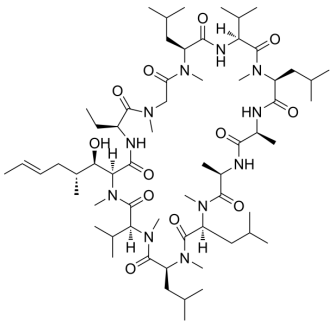
Molecular Formula: $C_{62}H_{111}N_{11}O_{12}$

Molecular Weight: 1202.61

Target: Complement System; Phosphatase; Antibiotic; Molecular Glues

Pathway: Immunology/Inflammation; Metabolic Enzyme/Protease; Anti-infection; PROTAC

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 62.5 mg/mL (51.97 mM; Need ultrasonic)
Ethanol : 50 mg/mL (41.58 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	0.8315 mL	4.1576 mL	8.3152 mL
	5 mM	0.1663 mL	0.8315 mL	1.6630 mL
	10 mM	0.0832 mL	0.4158 mL	0.8315 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: corn oil
   Solubility: 20 mg/mL (16.63 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.62 mg/mL (2.18 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.08 mg/mL (1.73 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (1.73 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (1.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cyclosporin A (Cyclosporine A) is an immunosuppressant which binds to the cyclophilin and inhibits phosphatase activity of protein phosphatase 2B (PP2B/calcineurin) with an IC_{50} of 5 nM[3]. Cyclosporin A also inhibits CD11a/CD18 adhesion[8].

IC_{50} & 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 inhibits calcineurin in stimulated cells with an IC_{50} value 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. Pharmacokinetic parameters of blood showed area under the curve of 27.3 μg·h·mL^{-1}, half-life of 6.9 h, volune of distribution of 3.7 L/kg in 140-200 g, 5-6 weeks, twelve adult male Wistar rats (Cyclosporin A 10 mg/kg; iv)[9].Blood pharmacokinetic parameters shows: Cyclosporin A (10 mg/kg; iv) has an area of the curve of 27.3 μg·h·mL^{-1} and a half-life of 6.9 h, and the distribution volume of 3.7 L/kg in male Wistar rats (140-200 g, 5-6 weeks)[9]. Induction of uraemia[10][11] • Background Cyclosporin A administration induces interstitial deposition of collagen type III and fibrosis via stimulation of the Transforming Growth Factor beta (TGF-β)-signalling pathway, while inhibiting extracellular matrix (ECM) degradation via modulation of matrix metallopeptidase 9, thus leading to an imbalance in ECM turn over[2]. • Specific Mmodeling Methods Mice: Six-to-eight weeks old C57BL/6 mice Administration: 30 mg/kg • SC • daily for 16 weeks. • Modeling Indicators Molecular changes: Upregulated mRNA expression of both LOX, LOXL2, TNFα, MCP-1, (NOX)4; significantly downregulated SOD2 mRNA expression; increased the urea nitrogen (BUN) level, increased tubular injury, interstitial inflammation and fibrosis scores, PAS scores, increased the level the deposition of collagen type I (COL1) and type III (COL3) in the renal ECM,increased the expression of alpha-smooth-muscle actin (α-SMA), fibronectin (FN), COL1A, MCP-1[10][11]. • Opposite Product(s): Lipoxygenase, general (HY-P2976); Anti-Mouse/Human/Rat/Monkey/Hamster/Canine/Bovine TGF-β Antibody (1D11) (HY-P990107) MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [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 Kiker 52G 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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Metab. 2023 Mar 6.
- Bioact Mater. 2023, 23:300-313
- Nat Commun. 2021 May 18;12(1):2915.
- Adv Sci (Weinh). 2023 Mar 8;e2201164.
- Adv Sci (Weinh). 2023 Jan 15;e2203869.

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REFERENCES

[1]. Medeiros M, et al. Increased cyclosporine bioavailability induced by experimental nephrotic syndrome in rats. Can J Physiol Pharmacol. 2007 May;85(5):502-6.

[2]. Nguyen LT, et al. Lysyl oxidase inhibitors attenuate cyclosporin A-induced nephropathy in mouse. Sci Rep. 2021 Jun 14;11(1):12437.

[3]. Ling H, et al. Therapeutic role of TGF-beta-neutralizing antibody in mouse cyclosporin A nephropathy: morphologic improvement associated with functional preservation. J Am Soc Nephrol. 2003 Feb;14(2):377-88.

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

[5]. 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.

[6]. 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.

[7]. 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.

[8]. 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.

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

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

[11]. 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.

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