Product Data Sheet

Product Name: Tacrolimus (FK506)
Cat. No.: GC16233

Chemical Properties

Cas. No.	104987-11-3		
SMILES	CO[C@@H]1C[C@H](/C=C(C)/[C@@H](OC([C@]2([H])CCCCN2C(C([C@]3(O)O[C@H]([C@@H](OC)C[C@H](C/C(C)=C/4)C)[C@@H](OC)C[C@H]3C)=O)=O)=O)[C@H](C)[C@H](CC([C@@H]4CC=C)=O)O)CC[C@H]1O		
Formula	$C_{44}H_{69}NO_{12}$	M.Wt	804.02
Solubility	≥ 26.6mg/mL in DMSO, ≥ 84.5 mg/mL in EtOH	Storage	Store at -20°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Caution: Product has not been fully validated for medical applications. For research use only.
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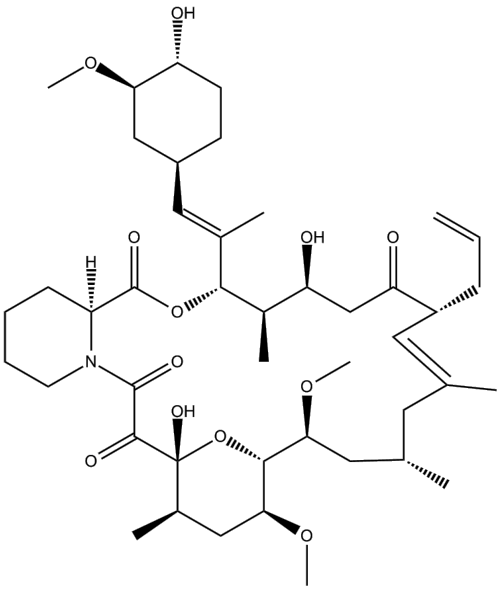
Structure



Protocol

Cell experiment [1]:

Cell lines Human lung fibroblasts (HLFs)

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Preparation Method	Cells were incubated with the indicated concentrations of FK506 for 24 h. The cells were then washed 3 times with PBS and incubated for 3 h in serum free medium to accumulate secreted collagen.
Reaction Conditions	0-2 μM Tacrolimus (FK506);24 h
Applications	Tacrolimus (FK506) reduces synthesis of type I collagen protein.

Animal experiment [1]:

Animal models	Male inbred alki Wistar rats weighing 150-200 g
Preparation Method	At the start of the study, drinking water was replaced by 5% ethanol as the only source of liquid and the rats were allowed to drink at will. Carbon tetrachloride (CCl4) was administered intraperitoneally (i.p.) at 0.5 μl/g of CCl4 in mineral oil twice a week for 4 weeks. Tacrolimus (FK506) was dissolved in 200 μL of Cremaphor and injected at daily dose of 4 mg/kg for 4 weeks (28 days). Control animals received by i.p. injections the Cremaphor vehicle. The groups were as follows: group 1:5% ethanol liquid+CCl4 injections; group 2:5% ethanol liquid+CCl4 injections+FK506 treatment; group 3: FK506 treatment only; group 4: vehicle only.
Dosage form	4 mg/kg;4 weeks (28 days);i.p.

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Applications	Tacrolimus (FK506) treatment inhibited activation of hepatic stellate cells (HSC) or reduced their number in the liver. In vivo, administration of FK506 at a dose of 4 mg/kg completely prevented development of alcohol/carbon tetrachloride induced liver fibrosis in rats.

References:

[1].Manojlovic Z, Blackmon J, et,al. Tacrolimus (FK506) prevents early stages of ethanol induced hepatic fibrosis by targeting LARP6 dependent mechanism of collagen synthesis. PLoS One. 2013 Jun 3;8(6):e65897. doi: 10.1371/journal.pone.0065897. PMID: 23755290; PMCID: PMC3670911.

Background

Tacrolimus (FK506), a macrolide antibiotic with potent immunosuppressive effects was isolated from Streptomyces tsukubaensis and has been previously used to prevent allograft and for treatment of autoimmune disorders in humans[1-3].

Tacrolimus(FK506) (0-2 μM;24 h)reduces synthesis of type I collagen protein without affecting expression of collagen mRNAs in Human lung fibroblasts (HLFs)[8]. T cell proliferation in response to ligation of the T cell receptor is inhibited by tacrolimus(FK506) [4]. Ttacrolimus(FK506) (concentration gradient;48 h)inhibited oral squamous cell carcinoma (OSCC) progression in vitro [9].

Tacrolimus (FK506) was given intramuscularly at the dose of 0.5 and 1.0 mg/kg for three days before burn injury. Thermal trauma to the skin caused a statistically significant increase in MPO activity and MDA content in remote organs. Tacrolimus (FK506) was effective in reducing lipid peroxidation and neutrophil infiltration especially at 24 h postinjury in lung, liver and kidney[5]. Tacrolimus (FK506) has the ability to down-regulate free radical levels in severe ischemia-reperfusion liver, and tachlimus has also been shown to be an effective inhibitor of cytokine response[6]. A study on pulmonary fibrosis in mice suggested that FK506 can be a potent antifibrotic agent [7]. Tacrolimus (FK506) treatment inhibited activation of HSCs or reduced their number in the liver. In vivo, administration of Tacrolimus (FK506) at a dose of 4 mg/kg(i.p.; 4 weeks) completely prevented development of alcohol/carbon tetrachloride induced liver fibrosis in rats[8].

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References:

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[2]. Kino T, Hatanaka H, et,al. FK-506, a novel immunosuppressant isolated from a Streptomyces. II. Immunosuppressive effect of FK-506 in vitro. J Antibiot (Tokyo). 1987 Sep;40(9):1256-65. doi: 10.7164/antibiotics.40.1256. PMID: 2445722.
[3]. Kondo H, Abe T, et,al. Efficacy and safety of tacrolimus (FK506) in treatment of rheumatoid arthritis: a randomized, double blind, placebo controlled dose-finding study. J Rheumatol. 2004 Feb;31(2):243-51. PMID: 14760792.
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[5]. Cetinkale O, Konukoğlu D, et,al. Modulating the functions of neutrophils and lipid peroxidation by FK506 in a rat model of thermal injury. Burns. 1999 Mar;25(2):105-12. doi: 10.1016/s0305-4179(98)00147-8. PMID: 10208383.
[6]. Garcia-Criado FJ, Palma-Vargas JM, et,al.Tacrolimus (FK506) down-regulates free radical tissue levels, serum cytokines, and neutrophil infiltration after severe liver ischemia. Transplantation. 1997 Aug 27;64(4):594-8. doi: 10.1097/00007890-199708270-00008. PMID: 9293871.
[7]. Nagano J, Iyonaga K, et,al.Use of tacrolimus, a potent antifibrotic agent, in bleomycin-induced lung fibrosis. Eur Respir J. 2006 Mar;27(3):460-9. doi: 10.1183/09031936.06.00070705. PMID: 16507844.
[8]. Manojlovic Z, Blackmon J, et,al.Tacrolimus (FK506) prevents early stages of ethanol induced hepatic fibrosis by targeting LARP6 dependent mechanism of collagen synthesis. PLoS One. 2013 Jun 3;8(6):e65897. doi: 10.1371/journal.pone.0065897. PMID: 23755290; PMCID: PMC3670911.
[9]: Li Y, Wang Y, et,al. Tacrolimus inhibits oral carcinogenesis through cell cycle control. Biomed Pharmacother. 2021 Jul;139:111545. doi: 10.1016/j.biopha.2021.111545. Epub 2021 Apr 16. PMID: 33873145.

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