产品名称：他克莫司一水合物
产品别名：Tacrolimus monohydrate；FK506 monohydrate

生物活性：

Description	Tacrolimus monohydrate (FK506 monohydrate; Fujimycin monohydrate; FR900506 monohydrate) is a macrocyclic lactone with potent immunosuppressive properties, an immunosuppressant. Tacrolimus monohydrate binds to FK506 binding protein (FKBP) to form a complex and inhibits calcineurin phosphatase, which inhibits T-lymphocyte signal transduction and IL-2 transcription[1].
IC_{50} & Target	PP2B (calcineurin phosphatase)[1] Autophagy inducer[2]
In Vitro	Tacrolimus monohydrate (FK506 monohydrate; Fujimycin monohydrate; FR900506 monohydrate) inhibits calcium-dependent events, such as IL-2 gene transcription, NO synthase activation, cell degranulation, and apoptosis. Tacrolimus also potentiates the actions of glucocorticoids and progesterone by binding to FKBPs contained within the hormone receptor complex, preventing degradation. The agent may enhance expression of the TGFβ-1 gene in a fashion analogous to that demonstrated for CsA. T cell proliferation in response to ligation of the T cell receptor is inhibited by Tacrolimus[1]. Treatment with a low concentration of Tacrolimus (FK506,10 μg/L) does not significantly affect the proliferation of MH3924A cells (P=0.135). Upon treatment with higher concentrations of Tacrolimus (100-1,000 μg/L), the proliferation of MH3924A cells is significantly enhanced (P<0.01). Treatment with AMD3100 at any concentration (10, 50 or 100 μg/L), has no obvious effect on MH3924A cell proliferation (P>0.05). However, when different concentrations of AMD3100 are combined with 100 μg/L Tacrolimus, the in vitro proliferation of MH3924A cells is increased (P<0.01)[3].
In Vivo	The therapeutic effect of Tacrolimus is investigated on progression and perpetuation of colitis by administering Tacrolimus to Dextran sulfate sodium (DSS)-treated mice from Days 10 to 16 or to 23. At Days 17 and 24, colon length is significantly shortened, and colon weight is significantly higher in DSS-treated control animals than in normal animals. In addition, colon weight per unit length in the control group is more than twice that in the normal group. While both 7 and 14 d treatment with Tacrolimus significantly suppresses increases in colon weight per unit length in DSS-treated animals compared with the control group, this treatment does not actually restore the colon shortening. In addition, this inhibitory effect of Tacrolimus on increases in colon weight per unit length is more pronounced with 14-d than 7-d treatment, as shown by the inhibitory percentages (59% vs. 28%)[4].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL** (**121.65 mM**) **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2165 mL	6.0825 mL	12.1650 mL
	5 mM	0.2433 mL	1.2165 mL	2.4330 mL
	10 mM	0.1217 mL	0.6083 mL	1.2165 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

	In Vivo: 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (3.04 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.04 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (3.04 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.04 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Thomson AW, et al. Mode of action of Tacrolimus (FK506): molecular and cellular mechanisms. Ther Drug Monit. 1995 Dec;17(6):584-91. [2]. Okada Y, et al. Tacrolimus ameliorates dextran sulfate sodium-induced colitis in mice: implication of interferon-γ and interleukin-1β suppression. Biol Pharm Bull. 2011;34(12):1823-7. [3]. Vogel KR, et al. mTOR inhibitors rescue premature lethality and attenuate dysregulation of GABAergic/glutamatergic transcription in murine succinate semialdehyde dehydrogenase deficiency (SSADHD), a disorder of GABA metabolism. J Inherit Metab Dis. 2016 Nov;39(6):877-886. [4]. Zhu H, et al. Tacrolimus promotes hepatocellular carcinoma and enhances CXCR4/SDF 1α expression in vivo. Mol Med Rep. 2014 Aug;10(2):585-92.

实验参考：

Cell Assay	Tumor cell proliferation is determined by the MTT assay. Briefly, after MH3924A cells have reached the logarithmic growth phase, a 0.2-mL cell suspension at 1×10^4 cells/mL is added into each well of a 96-well plate and cultured in DMEM with 10% FBS, 10 μg/L vascular endothelial growth factor and 0.1 g/L heparin for 24 h. When adherent growth is established, different concentrations of Tacrolimus (10, 100 and 1,000 μg/L) , AMD3100 (10, 50 and 100 μg/L) and Tacrolimus (0 and 100 μg/L)+AMD3100 (0, 10, 50 and 100 μg/L) are added into the plates. Untreated cells cultured in medium alone are used as controls. After culturing for 48 h, 10 μL MTT (5 g/L) are added, and each well is incubated for 6 h; next, 150 μL/well DMSO are added, followed by measurements of the absorbance at 570 mm on a spectrophotometer reader. Each well is measured three times, and each sample is assayed in triplicate[3].
Animal Administration	Mice[4] Six-week-old male C57BL/6J mice are maintained in a temperature- and humidity-controlled room with a 12-h light-dark cycle. For the multiple dosing study, colitic mice (n=10) are orally administered Tacrolimus at 30 mg/kg for 7 d (Days 10 to 16) or 14 d (Days 10 to 23). Control (n=10) and normal groups (n=5) are administered placebo using the same regimen. Tacrolimus or placebo is

	administered at 10 mL/kg. Mice are euthanized by CO_2 inhalation on the day following the final dosing. For the single dosing study, colitic mice are orally administered Tacrolimus at 30 mg/kg or placebo (n=8) once on Day 7, 10, 17, or 24. Normal mice (n=4) are administered placebo using the same regimen. Mice are euthanized by CO_2 inhalation eight hours after dosing[4].
References	[1]. Thomson AW, et al. Mode of action of Tacrolimus (FK506): molecular and cellular mechanisms. Ther Drug Monit. 1995 Dec;17(6):584-91. [2]. Okada Y, et al. Tacrolimus ameliorates dextran sulfate sodium-induced colitis in mice: implication of interferon-γ and interleukin-1β suppression. Biol Pharm Bull. 2011;34(12):1823-7. [3]. Vogel KR, et al. mTOR inhibitors rescue premature lethality and attenuate dysregulation of GABAergic/glutamatergic transcription in murine succinate semialdehyde dehydrogenase deficiency (SSADHD), a disorder of GABA metabolism. J Inherit Metab Dis. 2016 Nov;39(6):877-886. [4]. Zhu H, et al. Tacrolimus promotes hepatocellular carcinoma and enhances CXCR4/SDF 1α expression in vivo. Mol Med Rep. 2014 Aug;10(2):585-92.