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产品名称：T-5224
产品别名：T-5224

生物活性：

Description	T-5224 is a transcription factor c-Fos/activator protein (AP)-1 inhibitor with anti-inflammatory effects, which specifically inhibits the DNA binding activity of c-Fos/c-Jun without affecting other transcription factors. T-5224 inhibits the IL-1β-induced up-regulation of Mmp-3, Mmp-13 and Adamts-5 transcription[1][2].
IC_{50} & Target	c-Fos/activator protein (AP)-1[1]
In Vitro	T-5224 inhibits in-vitro production of the mediators MMP-1, MMP-3, IL-6 and TNF-α by IL-1β-stimulated human synovial SW982 cells with the mean IC50 of about 10 μM[2]. T-5224 (0-80 μM) significantly inhibits the invasion, migration, and MMP activity of HSC-3-M3 cells in a dose-dependent manner[3].
In Vivo	Administration of T-5224 (300 mg/kg, p.o.) after intraperitoneal injection of LPS impartes appreciable protection against acute elevations in serum levels of TNFα, HMGB1, ALT/AST as well as in liver tissue levels of MIP-1α and MCP-1, and reduces the lethality (27%)[4]. G2 is observed in rat and monkey liver microsomes as a major metabolite of T-5224, suggesting that G2 is not a human-specific metabolite[5]. T-5224 (300 mg/kg, p.o.) inhibits the production of TNF-alpha and other downstream effectors in C57BL/6 mice[6].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 31 mg/mL (59.90 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	1.9323 mL	9.6613 mL	19.3225 mL
	5 mM	0.3865 mL	1.9323 mL	3.8645 mL
	10 mM	0.1932 mL	0.9661 mL	1.9323 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: ≥ 2.08 mg/mL (4.02 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (4.02 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 20.8 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% (20% SBE-β-CD in saline) Solubility: 2.08 mg/mL (4.02 mM); Suspended solution; Need ultrasonic 此方案可获得 2.08 mg/mL (4.02 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.08 mg/mL (4.02 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.02 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Makino H, et al. A selective inhibition of c-Fos/activator protein-1 as a potential therapeutic target for intervertebraldisc degeneration and associated pain. Sci Rep. 2017 Dec 5;7(1):16983. [2]. Aikawa Y, et al. Treatment of arthritis with a selective inhibitor of c-Fos/activator protein-1. Nat Biotechnol. 2008 Jul;26(7):817-23. [3]. Kamide D, et al. Selective activator protein-1 inhibitor T-5224 prevents lymph node metastasis in an oral cancer model. Cancer Sci.?2016 May;107(5):666-73. [4]. Izuta S, et al. T-5224, a selective inhibitor of c-Fos/activator protein-1, attenuates lipopolysaccharide-induced liver injury in mice. Biotechnol Lett. 2012 Dec;34(12):2175-82. [5]. Uchihashi S, et al. Metabolism of the c-Fos/activator protein-1 inhibitor T-5224 by multiple human UDP-glucuronosyltransferase isoforms. Drug Metab Dispos. 2011 May;39(5):803-13. [6]. Miyazaki H, et al. The effects of a selective inhibitor of c-Fos/activator protein-1 on endotoxin-induced acute kidney injury in mice. BMC Nephrol. 2012 Nov 23;13:153.

实验参考：

Cell Assay	HSC-3-M3 cells are starved for 24 h with DMEM containing 0.5% FBS. The top chamber of the cell invasion device is coated with 50 μL of 0.1 × basement membrane extract solution and incubataed overnight. HSC-3-M3 cells (5.0×10^4 cells/well) are added to the top chamber with DMEM containing 0.5% FBS mixed with 0-80 μM T-5224; DMEM with 10% FBS is added to the bottom chamber and incubated for 48 h. The bottom plate is read using a multilabel plate reader. The data are compared with the standard curve to determine the fraction of invaded cells. [4]
Animal Administration	Mice in LPS group are administered orally with polyvinylpyrrolidone solution in the same volume of T-5224 solution immediately after LPS injection, while in the T-5224 group, mice are administered orally with T-5224 (300 mg/kg, p.o.) in the same manner. In the control group, mice receives polyvinylpyrrolidone solution orally soon after intraperitoneal saline injection. Blood samples are collected for each measurement at the optimal time. [2]
	[1]. Makino H, et al. A selective inhibition of c-Fos/activator protein-1 as a potential therapeutic

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