上海源叶生物科技有限公司
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产品名称：PF-3644022
CAS 号：1276121-88-0
产品货号： S89175

生物活性：

Description

PF-3644022 是一种有效的，选择性的，口服活性的，具有 ATP 竞争性的 MAPKAPK2 (MK2) 抑制剂，IC50 为 5.2 nM，Ki 为 3 nM。PF-3644022 还抑制 MK3 和 p38 调节/激活激酶 (PRAK)，IC50 分别为 53 nM 和 5.0 nM。PF-3644022 有效抑制 TNFα 的产生并具有抗炎作用。

IC50 & Target

IC50: 5.2 nM (MK2), 5.0 nM (PRAK) and 53 nM (MK3)[1].

Ki: 3 nM (MK2)[1]

Cellular Effect

Cell Line	Type	Value	Description
MDCK	IC_{50}	7 μM	Inhibition of MRP2 in MDCK cells after 15 mins by Calcein-AM assay
PBMC	IC_{50}	0.16 μM	Inhibition of TNF alpha production in LPS induced human PBMC cells preincubated with compound for 1 hr followed by LPS induction and measured after 16 hrs by MSD analysis
PBMC	IC_{50}	0.214 μM	Antiinflammatory activity in human PBMC cells assessed as inhibition of LPS induced TNF alpha production preincubated for 1 hr followed by LPS stimulation and measured after 16 hrs by MSD analysis
PBMC	IC_{50}	1.26 μM	Inhibition of IL-6 production in LPS induced human PBMC cells preincubated with compound for 1 hr followed by LPS induction and measured after 16 hrs by MSD analysis
PBMC	IC_{50}	1.4 μM	Antiinflammatory activity in human PBMC cells assessed as inhibition of LPS induced IL-6 production preincubated for 1 hr followed by LPS stimulation and measured after 16 hrs by MSD analysis
PBMC	IC_{50}	2.09 μM	Inhibition of IL-8 production in LPS induced human PBMC cells preincubated with compound for 1 hr followed by LPS induction and measured after 16 hrs by MSD analysis
PBMC	IC_{50}	2.59 μM	Antiinflammatory activity in human PBMC cells assessed as inhibition of LPS induced IL-8 production preincubated for 1 hr followed by LPS stimulation and measured after 16 hrs by MSD analysis
PBMC	IC_{50}	2.71 μM	Antiinflammatory activity in human PBMC cells assessed as inhibition of LPS induced IL-1 beta production preincubated for 1 hr followed by LPS stimulation and measured after 16 hrs by MSD analysis
PBMC	IC_{50}	2.78 μM	Inhibition of IL-1 beta production in LPS induced human PBMC cells preincubated with compound for 1 hr followed by LPS induction and measured after 16 hrs by MSD analysis
Sf9	IC_{50}	7 μM	Inhibition of human BSEP expressed in recombinant baculovirus infected insect Sf9 cell membrane vesicles assessed as [3H]-taurocholate transport preincubated for 5 mins followed by

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				ATP or AMP addition measured after 5 mins by scintillation counting method
	U-937	IC_{50}	0.159 μM	Inhibition of TNF-alpha production in LPS-induced human U-937 cells preincubated with compound for 1 hr followed by LPS induction and measured after 4 hrs by MSD analysis
	U-937	IC_{50}	0.201 μM	Inhibition of MK2 activity in LPS induced human U937 cells preincubated with compound for 1 hr followed by LPS induction and measured after 30 mins by Western blot analysis
	U-937	IC_{50}	150 nM	Inhibition of LPS-induced TNFalpha production in human U937 cells preincubated for 1 hr followed by LPS addition measured after 4 hrs by electro-chemiluminescence method
	U-937	IC_{50}	201 nM	Inhibition of MK2 in human U937 cells assessed as reduction in LPS-stimulated HSP27 phosphorylation at Ser82 preincubated for 1 hr followed by LPS addition measured after 30 mins by Western blot analysis

In Vitro

PF-3644022 对其他 MAPKAP 激酶家族成员的抑制活性评估显示：除对 MNK2 的 IC50 值为 148 nM 外，PF-3644022 对其他家族成员基本无抑制活性，相较于 MK2 表现出至少数百倍的选择性[1]。

在人源 U937 单核细胞系或外周血单个核细胞中，PF-3644022 能有效抑制 TNFα 生成(IC50=160 nM)。在 LPS 刺激的人全血实验中，该化合物对 TNFα 和 IL-6 生成的 IC50 值分别为 1.6 μM 和 10.3 μM。其在 U937 细胞和全血中对 TNFα 的抑制效应，与对磷酸化热休克蛋白 27 (MK2 活性的靶标生物标志物)的抑制程度高度相关[1].

In Vivo

PF-3644022 (3-100 mg/kg；灌胃给药；每日两次；持续 12 天) 对 Lewis 大鼠慢性爪肿胀具有剂量依赖性抑制作用，其半数有效剂量 (ED50) 值为 20 mg/kg[1]。

Animal Model:	Female Lewis rats (125-140 g) injected with streptococcal cell wall[1]
Dosage:	3 mg/kg, 10 mg/kg, 30 mg/kg, 50 mg/kg, 100 mg/kg
Administration:	Oral gavage; twice a day; for 12 days
Result:	Showed dose-dependent inhibition of chronic paw swelling measured on day 21 after 12 days of oral dosing.

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 : 41.67 mg/mL (111.28 mM; 超声助溶 (<80° C); 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO）

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.6705 mL	13.3526 mL	26.7051 mL
	5 mM	0.5341 mL	2.6705 mL	5.3410 mL
	10 mM	0.2671 mL	1.3353 mL	2.6705 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。

动物实验：

请根据您的 实验动物和给药方式 选择适当的溶解方案。

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	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 方案 一 请依序添加每种溶剂： 10% DMSO → 90% (20% SBE-β-CD in Saline) Solubility: 2.08 mg/mL (5.55 mM); 悬浊液; 超声助溶 此方案可获得 2.08 mg/mL 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。 2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。
参考文献	[1]. Mourey RJ, et al. A benzothiophene inhibitor of mitogen-activated protein kinase-activated protein kinase 2 inhibits tumor necrosis factor alpha production and has oral anti-inflammatory efficacy in acute and chronic models of inflammation. J Pharmacol Exp Ther. 2010 Jun;333(3):797-807.

完整储备液配制表：

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。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	2.6705 mL	13.3526 mL	26.7051 mL	66.7628 mL
	5 mM	0.5341 mL	2.6705 mL	5.3410 mL	13.3526 mL
	10 mM	0.2671 mL	1.3353 mL	2.6705 mL	6.6763 mL
	15 mM	0.1780 mL	0.8902 mL	1.7803 mL	4.4509 mL
	20 mM	0.1335 mL	0.6676 mL	1.3353 mL	3.3381 mL
	25 mM	0.1068 mL	0.5341 mL	1.0682 mL	2.6705 mL
	30 mM	0.0890 mL	0.4451 mL	0.8902 mL	2.2254 mL
	40 mM	0.0668 mL	0.3338 mL	0.6676 mL	1.6691 mL
	50 mM	0.0534 mL	0.2671 mL	0.5341 mL	1.3353 mL
	60 mM	0.0445 mL	0.2225 mL	0.4451 mL	1.1127 mL
	80 mM	0.0334 mL	0.1669 mL	0.3338 mL	0.8345 mL
	100 mM	0.0267 mL	0.1335 mL	0.2671 mL	0.6676 mL