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产品名称：Pyridone 6
产品别名：Pyridone 6

生物活性：

Description	Pyridone 6 is a pan-JAK inhibitor, which potently inhibits the JAK kinase family, with IC_{50}s of 1 nM for JAK2 and TYK2, 5 nM for JAK3, and 15 nM for JAK1, while displaying significantly weaker affinities (130 nM to >10 mM) for other protein tyrosine kinases.			
IC_{50} & Target	JAK2	Tyk2	JAK3	Murine JAK1
	1 nM (IC_{50})	1 nM (IC_{50})	5 nM (IC_{50})	15 nM (IC_{50})
	CDK2	cAMP-dependent kinase	Csk	Hck
	3.3 μM (IC_{50})	7.1 μM (IC_{50})	2.1 μM (IC_{50})	7.7 μM (IC_{50})
	Fyn T	p38	MAPK	Mek
	0.5 μM (IC_{50})	11 μM (IC_{50})	1.78 μM (IC_{50})	0.16 μM (IC_{50})
	IκB Kinase 2	KDR	Flt-1	Flt-4
	0.3 μM (IC_{50})	1.4 μM (IC_{50})	1.52 μM (IC_{50})	0.69 μM (IC_{50})
	FGFR	FGFR2	Tek	PDGFR
	1.48 μM (IC_{50})	0.94 μM (IC_{50})	24 μM (IC_{50})	1.49 μM (IC_{50})
	PKC(α)			
	1.2 μM (IC_{50})			
In Vitro	Pyridone 6 is tested as an inhibitor of 21 other protein kinases; Pyridone 6 inhibits these kinases with IC50s ranging from 130 nM to >10 μM. Pyridone 6 inhibits IL2 driven proliferation of CTLL cells with IC50=0.1 μM and IL4 driven proliferation with IC50=0.052 μM[1]. Pyridone 6 (P6) is shown to inhibit kinase by interacting within the ATP-binding cleft of each JAK. The IC50 of Pyridone 6 is 3 nM for all of these cytokines; this is comparable to the reported IC50s of Pyridone 6 for JAK2, Tyk2, and JAK3. Pyridone 6 strongly inhibits Th2 and modestly inhibits Th1, whereas it enhances Th17 development when present within a certain range of concentrations. Pyridone 6 reduces IFN-γ and IL-13, whereas it enhances IL-17 and IL-22 expression. Pyridone 6 also inhibits both Th1 and Th2 development, whereas it promotes Th17 differentiation from naive T cells when present within a certain range of concentrations[2].			
In Vivo	Pyridone 6 (P6) delays the onset and reduced the magnitude of skin disease in an AD-like skin-disease model of NC/Nga mice. P6-nano strongly ameliorates atopic dermatitis (AD) in NC/Nga mice, exerting an effect comparable to that of betamethasone ointment, a commonly used drug, which also tested as a positive control. In contrast, empty polylactic acid with glycolic acid (PLGA) nanoparticles (C-nano) seemed to have no effect[2].			
	In Vitro: **DMSO : ≥ 100 mg/mL (323.27 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.			
		Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**

<table>
<tr><td rowspan="4">Solvent&Solubility</td><td rowspan="3">Preparing Stock Solutions</td><td>1 mM</td><td>3.2327 mL</td><td>16.1634 mL</td><td>32.3269 mL</td></tr>
<tr><td>5 mM</td><td>0.6465 mL</td><td>3.2327 mL</td><td>6.4654 mL</td></tr>
<tr><td>10 mM</td><td>0.3233 mL</td><td>1.6163 mL</td><td>3.2327 mL</td></tr>
<tr><td colspan="5">*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 (8.08 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (8.08 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% (20% SBE-β-CD in saline)
Solubility: 2.5 mg/mL (8.08 mM); Suspended solution; Need ultrasonic
此方案可获得 2.5 mg/mL (8.08 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 25.0 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: ≥ 2.5 mg/mL (8.08 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (8.08 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。</td></tr>
<tr><td>References</td><td colspan="5">[1]. Thompson JE, et al. Photochemical preparation of a pyridone containing tetracycle: a Jak protein kinase inhibitor. Bioorg Med Chem Lett. 2002 Apr 22;12(8):1219-23.
[2]. Nakagawa R, et al. Pyridone 6, a pan-JAK inhibitor, ameliorates allergic skin inflammation of NC/Nga mice via suppression of Th2 and enhancement of Th17. J Immunol. 2011 Nov 1;187(9):4611-20.</td></tr>
<tr><td colspan="6">实验参考：</td></tr>
<tr><td>Cell Assay</td><td colspan="5">Naive CD4+ T cells are treated with various concentrations of Pyridone 6 (10 and 30 nM) in RPMI 1640 medium 1 h before the appropriate cytokines are added to create each Th-differentiating condition. Immunoblotting is performed using antiphospho-STAT protein Abs or anti-total STAT protein Abs[2].</td></tr>
<tr><td></td><td colspan="5">Mice[2]</td></tr>
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Animal Administration	NC/Nga mice are used at the age of 10-15 wk. To assess the effect of Pyridone 6 treatment on AD symptoms, nanoparticles containing Pyridone 6 (2 mg/body) or empty nanoparticles as a negative control (C-nano) are dissolved in 0.1 mL saline and administered s.c. 1 d after Dfb ointment application; this treatment is repeated twice a week. To assess the effects of recombinant murine IL-17 and IL-22, these cytokines (50 μg/kg) or 100 μL PBS is administered for the same duration as the nanoparticles. Twenty milligrams of 0.064% betamethasone ointment are applied to the dorsal lesion of mice once a week[2].
References	[1]. Thompson JE, et al. Photochemical preparation of a pyridone containing tetracycle: a Jak protein kinase inhibitor. Bioorg Med Chem Lett. 2002 Apr 22;12(8):1219-23. [2]. Nakagawa R, et al. Pyridone 6, a pan-JAK inhibitor, ameliorates allergic skin inflammation of NC/Nga mice via suppression of Th2 and enhancement of Th17. J Immunol. 2011 Nov 1;187(9):4611-20.