Pyridone 6

Cat. No.: HY-14435

CAS No.: 457081-03-7

Molecular Formula: $C_{18}H_{16}FN_3O$

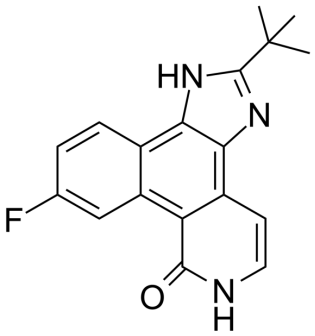
Molecular Weight: 309.34

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (323.27 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.2327 mL	16.1634 mL	32.3269 mL
5 mM	0.6465 mL	3.2327 mL	6.4654 mL
10 mM	0.3233 mL	1.6163 mL	3.2327 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (8.08 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (8.08 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.08 mM); Clear solution

BIOLOGICAL ACTIVITY

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 3.3 μM (IC_{50})	cAMP-dependent kinase 7.1 μM (IC_{50})	Csk 2.1 μM (IC_{50})	Hck 7.7 μM (IC_{50})
	Fyn T 0.5 μM (IC_{50})	p38 11 μM (IC_{50})	MAPK 1.78 μM (IC_{50})	Mek 0.16 μM (IC_{50})
	IκB Kinase 2 0.3 μM (IC_{50})	KDR 1.4 μM (IC_{50})	Flt-1 1.52 μM (IC_{50})	Flt-4 0.69 μM (IC_{50})
	FGFR 1.48 μM (IC_{50})	FGFR2 0.94 μM (IC_{50})	Tek 24 μM (IC_{50})	PDGFR 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 IC_{50}s ranging from 130 nM to >10 μM. Pyridone 6 inhibits IL2 driven proliferation of CTLL cells with IC_{50}=0.1 μM and IL4 driven proliferation with IC_{50} =0.052 μM[1]. Pyridone 6 (P6) is shown to inhibit kinase by interacting within the ATP-binding cleft of each JAK. The IC_{50} of Pyridone 6 is 3 nM for all of these cytokines; this is comparable to the reported IC_{50}s 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].

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PROTOCOL

Cell Assay [2]

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [2]

Mice[2]

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Leukemia. 2012 Oct;26(10):2233-44.

- Viruses. 2021, 13(6), 976.
- bioRxiv. July 29, 2021.
- Cell Regen. 2021 Mar 3;10(1):8.
- Patent. US20160368910A1.

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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.

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