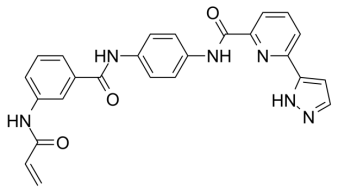
JH-X-119-01

Cat. No.:	HY-103017A
CAS No.:	2227368-54-7
Molecular Formula:	$C_{25}H_{20}N_6O_3$
Molecular Weight:	452.46
Target:	IRAK
Pathway:	Immunology/Inflammation
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 : 125 mg/mL (276.27 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2101 mL	11.0507 mL	22.1014 mL
5 mM	0.4420 mL	2.2101 mL	4.4203 mL
10 mM	0.2210 mL	1.1051 mL	2.2101 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: ≥ 1.98 mg/mL (4.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

JH-X-119-01 is a potent and selective interleukin-1 receptor-associated kinases 1 (IRAK1) inhibitor. JH-X-119-01 ameliorates LPS-induced sepsis in mice[1]. JH-X-119-01 inhibits IRAK1 biochemically with an apparent IC_{50} of 9 nM while exhibiting no inhibition of IRAK4 at concentrations up to 10 μM[2].

IC_{50} & Target

IRAK-1
9 nM (IC_{50})

In Vitro

JH-X-119-01 (10 μM) decreases phosphorylation of NF-κB and mRNA levels of IL-6 and TNFα in LPS-treated macrophages in vitro. JH-X-119-01 selectively inhibits IRAK1 phosphorylation[1].JH-X-119-01 exhibits off-target inhibition of only two additional kinases, YSK4 and MEK3. Dose response analysis reveals an IC_{50} of 57 nM for YSK4[2].JH-X-119-01 shows moderate cell killing effects in a panel of Waldenström's macroglobulinemia (WM) cells, Diffused Large B-cell Lymphoma (DLBCL) cells, and lymphoma cells expressing mutant MYD88, with EC_{50}s ranging from 0.59 to 9.72 μM[2].

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

Western Blot Analysis[1]

Cell Line:	RAW 264.7 cells and THP-1 cells
Concentration:	10 μM
Incubation Time:	15 minutes
Result:	Decreased LPS (100 ng/mL)-induced phosphorylation of IκBα and NF-κB-P65.

In Vivo

JH-X-119-01 improves survival and decreases immunopathies of LPS-challenged mice. JH-X-119-01 increases survival of mice at the dose of 5 mg/kg body weight. Survival is further improved when the dose is increased to 10 mg/kg[1].

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

Animal Model:	C57BL/6 (20-22 g, male) mice[1]
Dosage:	5 mg/kg and 10 mg/kg
Administration:	Intraperitoneally injected; 5 days
Result:	Protected mice from LPS (20 mg/kg)-induced sepsis. Survival at day 5 was 13.3% in control group where septic mice were treated by vehicle, while the values were 37.5% and 56.3% for 5 mg/kg and 10 mg/kg.

CUSTOMER VALIDATION

- JCI Insight. 2022 Jul 8;7(13):e149825.
- University of Louisville. 2023 May 24.

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REFERENCES

[1]. Bin Pan, et al. Selective inhibition of interleukin-1 receptor-associated kinase 1 ameliorates lipopolysaccharide-induced sepsis in mice. Int Immunopharmacol. 2020 Aug;85:106597.

[2]. John M Hatcher, et al. Discovery of a Selective, Covalent IRAK1 Inhibitor with Antiproliferative Activity in MYD88 Mutated B-Cell Lymphoma. ACS Med Chem Lett. 2020 Oct 9;11(11):2238-2243.

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