LP-935509

Cat. No.: HY-117626

CAS No.: 1454555-29-3

Molecular Formula: $C_{20}H_{24}N_6O_3$

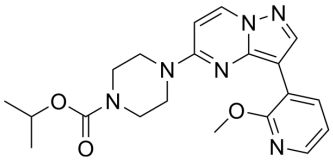
Molecular Weight: 396.44

Target: AAK1; Cyclin G-associated Kinase (GAK); SARS-CoV

Pathway: Neuronal Signaling; Cell Cycle/DNA Damage; Anti-infection

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (126.12 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5224 mL	12.6122 mL	25.2245 mL
	5 mM	0.5045 mL	2.5224 mL	5.0449 mL
	10 mM	0.2522 mL	1.2612 mL	2.5224 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: ≥ 2.08 mg/mL (5.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.25 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LP-935509 is an orally active, potent, selective, ATP-competitive and brain-penetrant inhibitor of adaptor protein-2 associated kinase 1 (AAK1) with an IC_{50} of 3.3 nM and a K_i of 0.9 nM, respectively. LP-935509 is also a potent inhibitor of BIKE (IC_{50}=14 nM) and a modest inhibitor of GAK (IC_{50}=320 nM). LP-935509 shows antinociceptive activity. LP-935509 can be used for neuropathic pain and SARS-CoV-2 research[1].

IC_{50} & Target

IC50: 3.3 ± 0.7 nM (AAK1), 14 nM (BIKE), 320 ± 40 nM (GAK)[1]

In Vitro

LP-935509 inhibits μ2 phosphorylation with an IC_{50} value of 2.8 ± 0.4 nM, inhibits phosphorylation of a peptide derived from the μ2 protein with an IC_{50} value of 3.3 ± 0.7 nM[1].

?LP-935509 exhibits a dose-dependent inhibition of the SARS-CoV-2 S-RBD internalization into host cells[2].

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

In Vivo

LP-935509 (0-60 mg/kg; PO, single) causes a robust reduction in pain behavior[1].

?LP-935509 (0.1-30 mg/kg; PO, single dosage) causes a dose-dependent reversal of thermal hyperalgesia in CCI model[1].

?LP-935509 (IV (1 mg/kg) or orally (10 mg/kg); once) has 100% oral bioavailability and a plasma half life of 3.6 hours[1].

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

Animal Model:	Male C57BL/6J mice (with SNL(spinal nerve ligation) injury, n=8-10 male mice per group)[1]
Dosage:	0, 10, 30 and 60 mg/kg (10 ml/kg)
Administration:	PO, single
Result:	Caused a dose-dependent reduction in phase II paw flinches that was significantly lower than the vehicle-treated animals; exhibited a dose-dependent reversal of the mechanical allodynia; Caused a robust reduction in pain behavior.

Animal Model:	Male Sprague-Dawley rats (CCI (chronic constriction injury)-operated rats)[1]
Dosage:	0, 0.1, 0.3, 1, 3, 10, or 30 mg/kg
Administration:	PO, two daily, for 5 days
Result:	Caused a dose-dependent reversal of thermal hyperalgesia, cold allodynia, mechanical allodynia, and mechanical hyperalgesia in CCI animals. Reversed the behavioral deficits, with ED_{50} values ranging from 2 mg/kg to 10 mg/kg.

Animal Model:	Male Sprague-Dawley rats[1]
Dosage:	1 mg/kg (IV), 10 mg/kg (PO)
Administration:	IV, PO; once (Pharmacokinetic Analysis)
Result:	Had 100% oral bioavailability and a plasma half life of 3.6 hours; The Cmax for the 10 mg/kg oral dose was 5.2 μM at 0.5-hour postdose; had a plasma-free fraction of 2.6% in mice. Brain drug levels exceeded plasma drug levels with a brain/plasma drug ratio typically between 3 and 4, showing that LP-935509 was highly brain-penetrant.

REFERENCES

[1]. Mushtaq, et al. Role Of Endocytic Machinery Regulators in EGFR Traffic and Viral Entry (2021). Theses & Dissertations. 532.

[2]. Kostich W, et al. Inhibition of AAK1 Kinase as a Novel Therapeutic Approach to Treat Neuropathic Pain. J Pharmacol Exp Ther. 2016 Sep;358(3):371-86.

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