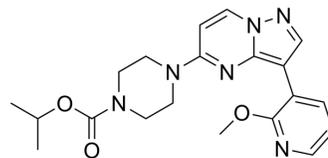


LP-935509

Cat. No.:	HY-117626		
CAS No.:	1454555-29-3		
Molecular Formula:	C ₂₀ H ₂₄ N ₆ O 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)			
		Solvent Concentration	Mass	
			1 mg	5 mg
			10 mg	
Preparing Stock Solutions	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	<ol style="list-style-type: none"> 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 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 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] .
IC₅₀ & Target	IC ₅₀ : 3.3 ± 0.7 nM (AAK1), 14 nM (BIKE), 320 ± 40 nM (GAK) ^[1]

In Vitro	<p>LP-935509 inhibits $\mu 2$ phosphorylation with an IC_{50} value of 2.8 ± 0.4 nM, inhibits phosphorylation of a peptide derived from the $\mu 2$ protein with an IC_{50} value of 3.3 ± 0.7 nM^[1].</p> <p>?LP-935509 exhibits a dose-dependent inhibition of the SARS-CoV-2 S-RBD internalization into host cells^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>																								
In Vivo	<p>LP-935509 (0-60 mg/kg; PO, single) causes a robust reduction in pain behavior^[1].</p> <p>?LP-935509 (0.1-30 mg/kg; PO, single dosage) causes a dose-dependent reversal of thermal hyperalgesia in CCI model^[1].</p> <p>?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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1" data-bbox="347 449 1515 758"> <tr> <td>Animal Model:</td> <td>Male C57BL/6J mice (with SNL(spinal nerve ligation) injury, n=8-10 male mice per group)^[1]</td> </tr> <tr> <td>Dosage:</td> <td>0, 10, 30 and 60 mg/kg (10 ml/kg)</td> </tr> <tr> <td>Administration:</td> <td>PO, single</td> </tr> <tr> <td>Result:</td> <td>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.</td> </tr> </table> <table border="1" data-bbox="347 793 1515 1102"> <tr> <td>Animal Model:</td> <td>Male Sprague-Dawley rats (CCI (chronic constriction injury)-operated rats)^[1]</td> </tr> <tr> <td>Dosage:</td> <td>0, 0.1, 0.3, 1, 3, 10, or 30 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>PO, two daily, for 5 days</td> </tr> <tr> <td>Result:</td> <td>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.</td> </tr> </table> <table border="1" data-bbox="347 1138 1515 1480"> <tr> <td>Animal Model:</td> <td>Male Sprague-Dawley rats^[1]</td> </tr> <tr> <td>Dosage:</td> <td>1 mg/kg (IV), 10 mg/kg (PO)</td> </tr> <tr> <td>Administration:</td> <td>IV, PO; once (Pharmacokinetic Analysis)</td> </tr> <tr> <td>Result:</td> <td>Had 100% oral bioavailability and a plasma half life of 3.6 hours; The C_{max} 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.</td> </tr> </table>	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 C_{max} for the 10 mg/kg oral dose was 5.2 μ M 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.
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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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA