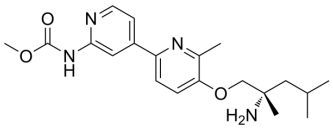
AAK1-IN-4

Cat. No.:	HY-145838
CAS No.:	1815612-79-3
Molecular Formula:	$C_{20}H_{28}N_4O_3$
Molecular Weight:	372.46
Target:	AAK1
Pathway:	Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AAK1-IN-4 is a highly selective, CNS-penetrable, and orally active adaptor protein-2-associated kinase 1 (AAK1) inhibitor (AAK1 IC_{50} of 4.6 nM, Filt K_i of 0.9 nM, and cell IC_{50} of 8.6 nM). AAK1-IN-4 has the potential for the research for neuropathic pain[1].
IC_{50} & Target	IC_{50}: 4.6 nM (AAK1)[1]. K_i: 0.9 nM (AAK1)[1]
In Vitro	AAK1-IN-4 (compound 43) (0.5 μM, 0-10 min) has good cell potencies of 2.4 in liver microsomes, as well as good metabolic stability (value of 95, 95, 93 for human, rat, and mouse microsomes, respectively) and no issue with CYP inhibitions[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AAK1-IN-4 (3 mg/kg; p.o; single) can significantly reduce tactile allodynia with close to 80% inhibition of the pain response in the rat CCI-induced pain model[1]. AAK1-IN-4 (3 mg/kg; p.o; 0-7.5 hours) has good spinal cord penetration and spinal-cord-to-plasma-concentration ratios of 8.8[1]. AAK1-IN-4 (1-10 mg/kg; p.o.; 0-24.5 hours) can significantly reduces mechanical allodynia with over 80% peak inhibition of the pain response achieved at an oral dose of 10 mg/kg, and over 60% peak inhibition of the pain response at 3 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague-Dawley rats (chronic constriction injury, CCI)[1]
Dosage:	3 mg/kg
Administration:	p.o, 0-7.5 hours
Result:	Significantly reduced tactile allodynia with close to 80% inhibition of the pain response, as well as showed good spinal cord penetration and spinal-cord-to-plasma-concentration ratios of 8.8.

Animal Model:	Male Sprague-Dawley rats (STZ-induced diabetic peripheral neuropathic pain, DPNP) [1]
Dosage:	1-10 mg/kg

Administration:	p.o., 0-24.5 hours
Result:	Significantly reduced mechanical allodynia with over 80% peak inhibition of the pain response achieved at an oral dose of 10 mg/kg, and over 60% peak inhibition of the pain response at 3 mg/kg.

REFERENCES

[1]. Luo G, et al. Discovery and Optimization of Biaryl Alkyl Ethers as a Novel Class of Highly Selective, CNS-Penetrable, and Orally Active Adaptor Protein-2-Associated Kinase 1 (AAK1) Inhibitors for the Potential Treatment of Neuropathic Pain. J Med Chem. 2022;65(6):4534-4564.

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