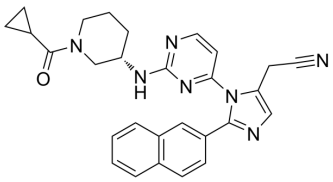
JNK3 inhibitor-4

Cat. No.:	HY-151929
CAS No.:	2409109-65-3
Molecular Formula:	$C_{28}H_{27}N_7O$
Molecular Weight:	477.56
Target:	JNK
Pathway:	MAPK/ERK Pathway
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

JNK3 inhibitor-4 is a potent inhibitor of JNK3 (IC_{50}=1.0 nM) based on 2-aryl-1-pyrimidinyl-1H-imidazole-5-yl acetonitrile. JNK3 inhibitor-4 shows excellent selectivity over other protein kinases including isoforms JNK1 (IC_{50}=143.9 nM) and JNK2 (IC_{50}=298.2 nM)[1]. JNK3 inhibitor-4 has neuroprotective effect and predicated blood-brain barrier permeability[1].

IC_{50} & Target

JNK3	JNK1	JNK2
1.0 nM (IC_{50})	143.9 nM (IC_{50})	298.2 nM (IC_{50})

In Vitro

JNK3 inhibitor-4 (compound 15d) (1, 5, 10, 20 μM; 24 h and 48 h) inhibits $Aβ_{1-42}$ induced Aβ1-42-induced cellular toxicity in primary rat cortex neuron[1].

JNK3 inhibitor-4 (10 μM and 20 μM; 24 h and 48 h) inhibits c-jun phosphorylation and APP phosphorylation induced by 10 μM $Aβ_{1-42}$ or 0.5 μM Anisomycin (HY-18982) in primary rat cortex neuron[1].

JNK3 inhibitor-4 (50 μM; 4 h) shows high permeability in Caco-2 assay and is predicted as BBB permeable (CNS+) based on effective permeability coefficient (Pe) value > 4 in PAMPA assay[1].

JNK3 inhibitor-4 also shows inhibitory potency on GSK3α (h), GSK3β (h), JNK1, 2, MKK6, MOK, SAPK2a (h), SAPK2a (T106 M) (h), SAPK2b (h), MKK4, JNK1α1 (h), and JNK2α1 (h). These shows IC_{50} values of 5.78, 11.7, 15.1, 1.18, 3.10, 1.19, 0.280, 0.970, 0.860, and 0.340 μM, respectively[1].

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

Western Blot Analysis[1]

Cell Line:	Primary rat cortex neuron
Concentration:	10 μM and 20 μM
Incubation Time:	24 hours
Result:	Monomeric Aβ1-42 induced c-jun phosphorylation dose-dependently and that was inhibited by JNK3 inhibitor-4 in concentration-dependent manner.

Cell Viability Assay[1]

Cell Line:	Primary rat cortex neuron
Concentration:	1, 5, 10, 20 μM

Incubation Time:	24 hours and 48 hours
Result:	Showed neuroprotective effect and increased cell viability under $A\beta_{1-42}$ treatment.

In Vivo

JNK3 inhibitor-4 improves memory for the Alzheimer's disease mouse model. JNK3 inhibitor-4 (compound 15d) (10 or 30 mg/kg; i.v.; 3 times/week for 1 month in 9-month-old APP/PS1 3Tx3Tg mice) results significantly higher spontaneous alteration and response latency of mouse (at 27th or 30th days) compared to the APP/PS1vehicle groups in Y-maze test and passive avoidance test, with a dose correlation[1].

JNK3 inhibitor-4 (30 mg/kg; p.o.; single dose) shows blood-brain barrier permeability with brain to plasma ratio of 0.02 in SD rats[1].

Pharmacokinetics in rats[1]

Route	Dose (mg/kg)	AUC_{0-t} (ng·h/mL)	C_{max} (ng/mL)	T_{max} (h)	$T_{1/2}$ (h)	BA (%)
IV	1	718.0			0.22	
PO	3	337.5	377.82	0.63	0.34	15.67

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

REFERENCES

[1]. Jun J, et al. Discovery of novel imidazole chemotypes as isoform-selective JNK3 inhibitors for the treatment of Alzheimer's disease. Eur J Med Chem. 2023 Jan 5;245(Pt 1):114894.

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