JNK3 inhibitor-8

Cat. No.: HY-149280

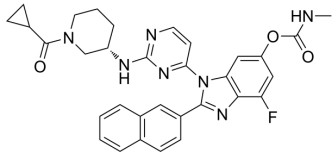
Molecular Formula: $C_{32}H_{30}FN_7O_3$

Molecular Weight: 579.62

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-8 is a potent, delective, orally active and cross the blood-brain barrier JNK3 inhibitor with IC_{50} values of 21, 2203, >10000 nM for JNK3, JNK2, JNK1, respectively. JNK3 inhibitor-8 shows significant neuroprotective effects. JNK3 inhibitor-8 has the potential for the research of Alzheimer's disease (AD)[1].

IC_{50} & Target

JNK3	JNK2	JNK1
21 nM (IC_{50})	2203 nM (IC_{50})	>10000 nM (IC_{50})

In Vitro

JNK3 inhibitor-8 (compound 3h; 10, 20 μM; 24, 48 h) increases primary rat cortex neuron cell viability when treatment with 10 μM amyloid-β_{1-42}[1].

JNK3 inhibitor-8 (10, 20 μM) decreases the expression of p-c-jun (S63), p-c-jun (S73), PARP and p-Tau 10 μM amyloid-β_{1-42} stitumed[1].

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

Cell Viability Assay[1]

Cell Line:	primary rat cortex neuron cells
Concentration:	10, 20 μM
Incubation Time:	24, 48 h
Result:	Increased cell viability when treatment with 10 μM amyloid-β_{1-42}.

Western Blot Analysis[1]

Cell Line:	primary rat cortex neuron cells
Concentration:	10, 20 μM
Incubation Time:	
Result:	Decreased the expression of p-c-jun (S63) and p-c-jun (S73) in 0.5 μM anisomycin or 10 μM amyloid-β_{1-42} stitumed, and decreased the expression of PARP and p-Tau expression when treatment with 10 μM amyloid-β_{1-42}.

In Vivo

JNK3 inhibitor-8 (30, 60 mg/kg; p.o.; daily for 4 weeks) shows significant neuroprotective effects in mice[1].

Pharmacokinetic Parameters of JNK3 inhibitor-8 in Sprague-Dawley rats[1].

compound	2h
admin.	PO
dose (mg/kg)	3
AUC_{last} (h ng/ml)	727.09
C_0 or C_{max} (ng/mL)	423.17
T_{max} (h)	0.39
$T_{1/2}$ (h)	0.97

Sprague-Dawley rats, 3 mg/kg p.o.[1]

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

Animal Model:	6 month-old APP/PS1 AD mice[1]
Dosage:	30, 60 mg/kg
Administration:	P.o.; daily for 4 weeks
Result:	Decrease in escape time and distance traveled, showed a significantly higher level of altered behavioral ability compared to APP/PS1 and vehicle control in the Y-maze test, improved memory and cognitive function.

Animal Model:	10 month-old 3xTg AD mice[1]
Dosage:	30, 60 mg/kg
Administration:	P.o.; daily for 4 weeks
Result:	Decreased the escape time and the distance, increased TSPQ and TSTZ levels, significantly decreased the expression of pTau levels and improved memory and cognitive function.

REFERENCES

[1]. Jun J, et al. Carbamate JNK3 Inhibitors Show Promise as Effective Treatments for Alzheimer's Disease: In Vivo Studies on Mouse Models. J Med Chem. 2023 Apr 24.

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