JNK3 inhibitor-3

Cat. No.: HY-151928

CAS No.: 2873465-25-7

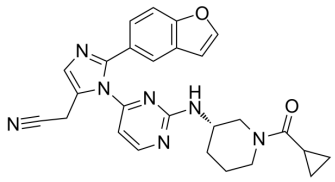
Molecular Formula: $C_{26}H_{25}N_7O_2$

Molecular Weight: 467.52

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-3 (compound 15g) is a selective, BBB permeable and orally active c-Jun N-terminal kinase 3 (JNK3) inhibitor. JNK3 inhibitor-3 has inhibitory activities to JNK1, JNK2 and JNK3 with IC_{50} values of 147.8, 44.0 and 4.1 nM, respectively. JNK3 inhibitor-3 significantly improves the memory in mouse dementia model. JNK3 inhibitor-3 can be used for the research of Alzheimer's disease[1].

IC_{50} & Target

JNK3	JNK2	JNK1
4.1 nM (IC_{50})	44 nM (IC_{50})	147.8 nM (IC_{50})

In Vitro

JNK3 inhibitor-3 (0-10 μM) shows inhibitory activities to JNK1, JNK2 and JNK3 with IC_{50} values of 147.8, 44.0 and 4.1 nM, respectively[1].JNK3 inhibitor-3 (20 μM; 24 and 48 h) demonstrates neuroprotective effects in vitro[1].

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

Cell Viability Assay[1]

Cell Line:	Rat cortical neurons
Concentration:	20 μM
Incubation Time:	24 and 48 hours
Result:	Protected rat cortical neurons against 10 μM $A\beta_{1-42}$ induced neurotoxicity.

In Vivo

JNK3 inhibitor-3 (30 and 60 mg/kg; oral administration, once daily for 2 or 2.2 month) improves the memory of 3xTg mouse dementia model[1].

Pharmacokinetic Properties of JNK3 inhibitor-3 in Rats[1].

	Rats IV 1 mg/kg	Rats PO 3 mg/kg
AUC (hr•ng/mL)	1085.24	2806.77
C_{max} (ng/mL)		1238.85

T_{max} (hr)		0.67
$T_{1/2}$ (hr)	0.36	1.14
BA (%)		86.21

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Animal Model:	Homozygous 3xTg and APPswe/PS1dE9 double-transgenic mice model of Alzheimer's disease[1]
Dosage:	30 and 60 mg/kg
Administration:	Oral administration; once daily for 2 or 2.2 month
Result:	Induced no abnormal symptoms or weight changes, significantly enhanced the spontaneous alteration in APP/PS1 and doses of 30 and 60 mg/kg than that of vehicle group in Y-maze test and showed a significant difference compared to the 3xTg vehicle control in the passive avoidance test.

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.

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