

Product Data Sheet

Product Name: JNK-IN-8

Cat. No.: GC13841

Chemical Properties

Cas. No. 1410880-22-6

Chemical Name 3-[[[E]-4-(dimethylamino)but-2-enoyl]amino]-N-[3-methyl-4-[(4-pyridin-3-yl)pyrimidin-2-yl)amino]phenyl]benzamide

SMILES CC1=C(C=CC(=C1)NC(=O)C2=CC(=CC=C2)NC(=O)C=CCN(C)C)NC3=NC=CC(=N3)C4=CN=CC=C4

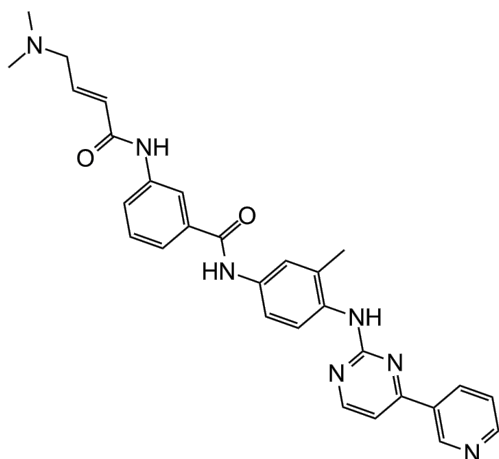
Formula $C_{29}H_{29}N_7O_2$ M.Wt 507.59

Solubility ≥ 25.4 mg/mL in DMSO, ≥ 9.24 mg/mL in EtOH with ultrasonic and warming
Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

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Cell lines HEK293-ILR1、 A375 cells

Preparation Method The cells were incubated with JNK-IN-8 at concentrations of 0.1, 0.3, 1, and 3 μ M for 3 h.

Reaction Conditions 0.1, 0.3, 1, 3 μ M ; 3 h

Applications The superior potency and selectivity of JNK-IN-8 in the HEK293 cells suggested that the compound would likely serve as very useful pharmacological probes of JNK-dependent cellular phenomena.

Animal experiment [2]:

Animal models SD rats

Preparation Method Rats were given an intraperitoneal injection of vehicle (saline 150 δ l and 20% dimethylsulfoxide in PBS) or JNK-IN-8 (20 mg/kg dissolved in 20% dimethylsulfoxide) after MCAO.

Dosage form 20 mg/kg; i.p.

Applications JNK-IN-8-treated rats with MCAO exerted a significant improvement in spatial learning as measured by the improved mNSS, and showed sensorimotor functional recovery as measured by the Foot-fault test.

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References:

- [1] Zhang T, Inesta-Vaquera F, et al, Discovery of potent and selective covalent inhibitors of JNK. *Chemical Biology*. 2012, 19(1):140-154.
- [2] Geng W, Tang H, Dai Q, et al. JNK-IN-8, a c-Jun N-terminal kinase inhibitor, improves functional recovery through suppressing neuroinflammation in ischemic stroke[J]. Cold Spring Harbor Laboratory, 2018.

Background

JNK-IN-8 is the first irreversible JNK inhibitor that acts on JNK1, JNK2, and JNK3 with high specificity, with IC_{50} values of 4.7 nM, 18.7 nM, and 1 nM in the A375 cell line, respectively [1]. JNK-IN-8 forms a covalent bond with the conserved cysteine residue of JNK 1/2/3, causing a conformational change in the activation loop and blocking substrate binding, thereby inhibiting the activity of JNK 1/2/3 [1]. JNK 1, 2, and 3 are part of the mitogen-activated protein kinase (MAPK) family, capable of phosphorylating the Ser 63 and Ser 73 residues of c-Jun, responding to stress stimuli such as cytokines and heat shock, and involved in T cell differentiation and apoptosis processes.

In vitro, JNK-IN-8 inhibits c-Jun phosphorylation in HeLa and A375 cells, with EC_{50} values of 486 nM and 338 nM, respectively [1]. JNK-IN-8 also shows significant selectivity in HEK 293 cells [1]. Additionally, JNK-IN-8 (10 mM) exhibits anti-inflammatory effects, reducing microglial activation and the expression of IL-6, IL-1 β , and TNF- α [2].

In vivo, JNK-IN-8 (20 mg/kg; i.p.) treated rats with middle cerebral artery occlusion show significant improvements in spatial learning and sensorimotor function recovery [2]. Administration of JNK-IN-8 (3 μ g/ μ L) into the lateral ventricles of male KM mice 24 h before brain injury significantly reduces neuronal apoptosis after brain injury [3].

References:

- [1] Zhang T, Inesta-Vaquera F, et al, Discovery of potent and selective covalent inhibitors of JNK. *Chemical Biology*. 2012, 19(1):140-154.
- [2] Geng W, Tang H, Dai Q, et al. JNK-IN-8, a c-Jun N-terminal kinase inhibitor, improves functional

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recovery through suppressing neuroinflammation in ischemic stroke[J].Cold Spring Harbor Laboratory, 2018.

[3] Li D1, Liu N, et al, Protective effect of resveratrol against nigrostriatal pathway injury in striatum via JNK pathway. Brain Res. 2017 Jan 1;1654(Pt A):1-8.

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