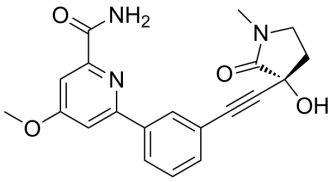
NIK SMI1

Cat. No.:	HY-112433
CAS No.:	1660114-31-7
Molecular Formula:	$C_{20}H_{19}N_3O_4$
Molecular Weight:	365.38
Target:	NF-κB
Pathway:	NF-κB

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (342.11 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7369 mL	13.6844 mL	27.3688 mL
5 mM	0.5474 mL	2.7369 mL	5.4738 mL
10 mM	0.2737 mL	1.3684 mL	2.7369 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (6.84 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.69 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.69 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NIK SMI1 is a potent, selective NF-κB inducing kinase (NIK) inhibitor, which inhibits NIK-catalyzed hydrolysis of ATP to ADP with IC_{50} of 0.23±0.17 nM. NIK SMI1 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target	NIK[1]
In Vitro	NIK SMI1 (Compound 4f) inhibits NIK-catalyzed hydrolysis of ATP to ADP (fluorescence polarization, FP) with an IC_{50} of 0.23±0.17 nM. NIK SMI1 inhibits the expression of NIK SMI1 response elementregulated firefly luciferase reporter gene in HEK293 cells with an IC_{50} of 34±6 nM. Consistent with expectations for a NIK inhibitor, NIK SMI1 is shown to inhibit nuclear translocation of p52 (RelB) (IC_{50}=70 nM). NIK SMI1 inhibits BAFF-induced B cell (mouse) survival in vitro with an IC_{50} of 373±64 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	C57BL/6 mice are treated twice daily for 7 days with orally administered NIK SMI1 or with three injections of recombinant BAFF receptor fusion protein (Br3- mIgG2a) over the course of the 7-day experiment as a positive control. The nonlinearity of exposure relative to dose between 100 and 200 mg/kg is a result of saturation of clearance mechanisms. The pharmacology of NIK SMI1 is examined in SD rat, CD-1 mouse, beagle, and cynomologous monkey with 20, 32, 18, and 7.8 mL/kg per min, respectively. Volume of distribution (Vd, L/kg) is 1.35, 1.58, 0.778, and 1.39, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Human B cells are re-suspended in RPMI with 10% FBS for the proliferation assays and 2.5% FBS for the survival assays. Mouse B cells are plated in Co-star 96-well plates at either 50,000 cells/well for the survival assays or at 150,000 cells/well for the proliferation assays. Compounds (e.g., NIK SMI1) diluted in DMSO (final DMSO assay concentration=0.1%) are added to the cells. The cells are incubated with NIK SMI1 for one hour at 37°C. Stimulus is then added to the plates and survival or proliferation is measured after four days. For the proliferation assays, cells are treated with either Anti-IgM (20 μg/mL) or rhCD40L (10 μg/mL) or anti-mouse CD40 (100 ng/mL). For the BAFF survival assay, cells are treated with human or mouse rBAFF at 10 ng/mL followed by Cell Titer Glo to measure survival on day four[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Age-matched C57BL/6 mice are used. Only female mice are used in these experiments. The single oral doses of NIK SMI1 are 10, 20, 60, 100, and 200 mg/kg. For PO dosing, animals are manually restrained, then dosed via oral gavage using an appropriately sized gavage needle. Animals are monitored for any signs of aspiration or distress-respiratory abnormalities, lethargy, pale extremities, etc. For sample collection, 3 mice per group are bled a total of 8 times via tail prick using a 27 G needle (lateral tail vein). 10 μL of blood is collected at each timepoint and deposited into a pre-filled costar cluster tube containing 40 μL of 1.7 mg/mL EDTA/water, the tube is capped, votexed for 5 seconds, then stored on dry ice. Samples are transferred to a -80°C freezer for storage[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Immunol. 2020 May;21(5):535-545.
- Sci Immunol. 2022 Aug 12;7(74):eabn3800.
- Mol Neurobiol. 2021 Jan 13.
- J Immunol Res. 2020 Jul 31;2020:1859260.
- Research Square Print. 2022 Jun.

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REFERENCES

[1]. Blaquiere N, et al. Scaffold-Hopping Approach To Discover Potent, Selective, and Efficacious Inhibitors of NF-κB Inducing Kinase. J Med Chem. 2018 Aug 9;61(15):6801-6813.

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