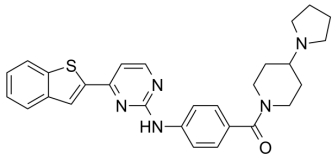
IKK 16

Cat. No.:	HY-13687
CAS No.:	873225-46-8
Molecular Formula:	$C_{28}H_{29}N_5OS$
Molecular Weight:	483.63
Target:	IKK; LRRK2
Pathway:	NF-κB; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 27 mg/mL (55.83 mM)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	2.0677 mL	10.3385 mL	20.6770 mL
5 mM	0.4135 mL	2.0677 mL	4.1354 mL
10 mM	0.2068 mL	1.0338 mL	2.0677 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.17 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.17 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IKK 16 is a selective IκB kinase (IKK) inhibitor for IKK2, IKK complex and IKK1 with IC_{50}s of 40 nM, 70 nM and 200 nM, respectively. IKK16 also inhibits leucine-rich repeat kinase-2 (LRRK2) with an IC_{50} of 50 nM.

IC_{50} & Target	IKK2	IKK1	IKK	LRRK2
	40 nM (IC_{50})	200 nM (IC_{50})	70 nM (IC_{50})	50 nM (IC_{50})

In Vitro	IKK 16 is a potent inhibitor of IKK2 with IC_{50} value of 40 nM[1]. IKK 16, a leucine-rich repeat kinase-2 (LRRK2) kinase inhibitor, exhibits in vitro IC_{50}s of 50 nM. IKK 16 exhibits sub-micromolar IC_{50} concentrations for LRRK2 in vitro, which is lower than what observed for cellular inhibition of Ser935 phosphorylation. IKK 16 (20 μM) can inhibit LRRK2 Ser935 phosphorylation in HEK293 GFP-LRRK2G2019S cells (GS) or A2016T/G2019S (IRM) cells in vitro. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	IKK 16 also demonstrates significant in vivo activity in an acute model of cytokine release. Both routes of administration of IKK 16 (30 mg/kg, sc) or orally (30 mg/kg, p.o) at the indicated dose results in a significant inhibition of 86% (sc) and 75% (p.o.). IKK 16(10 mg/kg, sc) is also active in the thioglycollate-induced peritonitis model in the mouse. The maximal inhibition of neutrophil extravasation in this model is about 50%[1]. Treatment of septic mice with IKK 16 (1 mg/kg body weight i.v.) results in a significantly increased degree of phosphorylation ($P<0.05$) of serine residues on Akt and eNOS in the liver[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	SH-SY5Y cells are transduced with 25% (v/v) BacMam LRRK2-GFP G2019S and plated (20 μL/well, 20,000 cells/well) onto eight 384-well assay plates. Then 25% BacMam LRRK2-GFP G2019S transduced SH-SY5Y cells are incubated with indicated concentrations of indicated compounds (e.g., IKK 16, 0.01, 0.1, 1, 10 and 100 μM) for 90 min prior to the TR-FRET detection with Tb-anti-LRRK2 pSer935 antibody. The % inhibition is calculated[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][3]	Rats and Mice[1] IKK 16 is tested in two animal models. First, its efficacy to inhibit TNFα release into plasma upon LPS-challenge in the rat is determined. IKK 16 is dosed sc (30 mg/kg) or orally (30 mg/kg) 1 h prior to the LPS-challenge. Four hours after the challenge, plasma is collected and the systemic TNFα levels are analyzed using a commercially available ELISA kit. Both routes of administration of IKK 16 at the indicated dose results in a significant inhibition of 86% (sc) and 75% (p.o.). In a second experiment, IKK 16 is also active in the thioglycollate-induced peritonitis model in the mouse. The maximal inhibition of neutrophil extravasation in this model is about 50% at a dose of 10 mg/kg sc. Mice[3] Two-month-old male C57BL/6 mice receive LPS (9 mg/kg body weight) and PepG (3 mg/kg body weight) in 0.9% saline (5 mL/kg body weight) intraperitoneally. Sham mice are not subjected to LPS/PepG, but are otherwise treated the same way. At 1 hour after LPS/PepG co-administration, mice are treated either with IKK 16 (1 mg/kg body weight i.v.) or vehicle (5 mL/kg body weight 10% DMSO i.v.). At 24 hours the experiment is terminated and organ and blood samples are collected for quantification of organ dysfunction and/or injury. Mice are randomly allocated into four different groups: (1) sham+vehicle (n=10); (2) sham+IKK 16 (n=3); (3) LPS/PepG+vehicle (n=9); (4) LPS/PepG+IKK 16 (n=10). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Hepatol. 2021 Aug;75(2):363-376.
- J Immunother Cancer. 2020 Sep;8(2):e000517.
- Theranostics. 2020 Feb 18;10(8):3579-3593.
- J Exp Clin Cancer Res. 2021 Aug 27;40(1):273.
- Cell Death Dis. 2019 Apr 3;10(4):304.

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REFERENCES

[1]. Waelchli R, et al. Design and preparation of 2-benzamido-pyrimidines as inhibitors of IKK. Bioorg Med Chem Lett. Bioorg Med Chem Lett. 2006 Jan 1;16(1):108-12.

[2]. Hermanson SB, et al. Screening for novel LRRK2 inhibitors using a high-throughput TR-FRET cellular assay for LRRK2 Ser935 phosphorylation. PLoS One. 2012;7(8):e43580.

[3]. Coldewey SM, et al. Inhibition of IκB kinase reduces the multiple organ dysfunction caused by sepsis in the mouse. Dis Model Mech. 2013 Jul;6(4):1031-42.

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