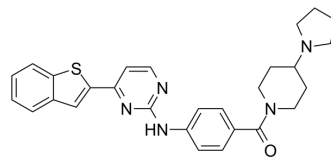


IKK 16

Cat. No.:	HY-13687		
CAS No.:	873225-46-8		
Molecular Formula:	C ₂₈ H ₂₉ N ₅ O ₅		
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)
 H₂O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	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

- 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
- 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
- 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 IC₅₀s of 40 nM, 70 nM and 200 nM, respectively. IKK16 also inhibits leucine-rich repeat kinase-2 (LRRK2) with an IC₅₀ of 50 nM.

IC₅₀ & Target

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	<p>IKK 16 is a potent inhibitor of IKK2 with IC₅₀ value of 40 nM^[1]. IKK 16, a leucine-rich repeat kinase-2 (LRRK2) kinase inhibitor, exhibits in vitro IC₅₀s of 50 nM. IKK 16 exhibits sub-micromolar IC₅₀ 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.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

PROTOCOL

Cell Assay ^[2]	<p>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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^{[1][3]}	<p>Rats and Mice^[1]</p> <p>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.</p> <p>Mice^[3]</p> <p>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).</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

CUSTOMER VALIDATION

- J Hepatol. 2021 Aug;75(2):363-376.
- Nat Commun. 2022 Mar 31;13(1):1700.
- 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.

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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*. 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 I κ B 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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Caution: Product has not been fully validated for medical applications. For research use only.