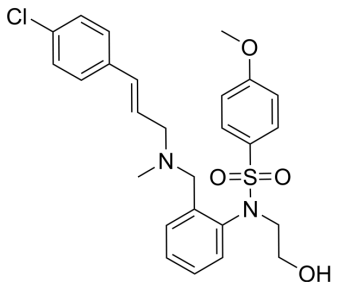
KN-93

Cat. No.:	HY-15465
CAS No.:	139298-40-1
Molecular Formula:	$C_{26}H_{29}ClN_2O_4S$
Molecular Weight:	501.04
Target:	CaMK; Autophagy
Pathway:	Neuronal Signaling; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (99.79 mM; Need ultrasonic)

H_2O : 1 mg/mL (2.00 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9958 mL	9.9792 mL	19.9585 mL
5 mM	0.3992 mL	1.9958 mL	3.9917 mL
10 mM	0.1996 mL	0.9979 mL	1.9958 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.83 mg/mL (1.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KN-93 is a cell-permeable, reversible and competitive inhibitor calmodulin-dependent kinase type II (CaMKII) with a K_i of 370 nM.

IC_{50} & Target

CaMK II

In Vitro

After 2 days of KN-93 treatment, 95% of cells are arrested in G1. G1 arrest is reversible; 1 day after KN-93 release, a peak of cells had progressed into S and G2-M. KN-93 also blocks cell growth stimulated by basic fibroblast growth factor, platelet-derived growth factor-BB, and epidermal growth factor in NIH 3T3 fibroblasts[1]. KN-93 inhibits the H^+, K^+-ATPase activity but strongly dissipates the proton gradient formed in the gastric membrane vesicles and reduces the volume of luminal space[2]. KN-93 (0.5 μM) prevents increased LV developed pressure during action potential prolongation and early afterdepolarizations. Ca^{2+}-independent CaM kinase activity is increased during early afterdepolarizations and this increase

	is prevented by KN-93[3]. KN-93 (10 μM)significantly inhibits the activation of CaMKII/NF-κB signaling induced by elevated glucose, and subsequently decreases the expression of VEGF, iNOS and ICAM-1 in Müller cells[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	KN-93 (1 mg/kg/day, i.p.) inhibits retinal vascular leakage induced by diabetes, and suppresses phosphorylation of CaMKII and NF-κB in diabetic retina[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [4]	Cell viability is assessed by the 3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide (MTT) assay. Briefly, Müller cells are seeded at a density of 10×10^4 cells per well in 96-well plates and cultured until sub-confluence. Next, cells are treated with curcumin for 24 h before incubation with MTT (5 mg/mL) at 37°C in 5% CO_2 atmosphere for 4 h. The culture medium is then removed, and the formazan formed in the reaction is dissolved in 150 μL DMSO. The optical density of the solution is measured at 490 nm using a multifunctional microplate reader. Cell viability in each well is presented as a percentage of the control (vehicle-treated group). MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Male Sprague-Dawley rats (8 weeks of age) weighing 180-200 g are used in this study. Rats are housed in ventilated microisolator cages with free access to water and food. The rats are randomLy assigned to receive either 60 mg/kg STZ intraperitoneally or citrate buffer alone. Rats are categorized as diabetic when blood glucose levels exceeded 16.7 mM at 48 h after STZ treatment. Two weeks after the induction of diabetes, rats are divided randomLy into three subgroups: STZ-diabetic rats (n=12), STZ-treated diabetic rats administered curcumin (n=12), or STZ-diabetic rats administered KN93 (n=12) for a 12-week period. Curcumin is suspended in saline containing 0.5% carboxymethylcellulose at a concentration of 20 mg/mL and administered via oral gavage at a total dose of 100 mg/kg/day. KN93 is administered by intraperitoneal injection at 1 mg/kg/day. Control STZ-treated diabetic rats and non-diabetic controls (n=12) are gavage administered saline containing 0.5% carboxymethylcellulose on a daily basis. Body weights and blood glucose levels are measured every 2 weeks. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2022 Jun 23;185(13):2354-2369.e17.
- Nat Commun. 2022 Jul 22;13(1):4255.
- Redox Biol. October 2021, 102115.
- EMBO Mol Med. 2022 Dec 13;e16373.
- Sci Total Environ. 2020 Feb 10;703:134702.

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REFERENCES

[1]. Tombes RM, et al. G1 cell cycle arrest and apoptosis are induced in NIH 3T3 cells by KN-93, an inhibitor of CaMK (the multifunctional Ca2+/CaM kinase). Cell Growth Differ. 1995 Sep;6(9):1063-70.

[2]. Mamiya N, et al. Inhibition of acid secretion in gastric parietal cells by the Ca2+/calmodulin-dependent protein kinase II inhibitorKN-93. Biochem Biophys Res Commun. 1993 Sep 15;195(2):608-15.

[3]. Anderson ME, et al. KN-93, an inhibitor of multifunctional Ca++/calmodulin-dependent protein kinase, decreases early afterdepolarizations in rabbit heart. J Pharmacol Exp Ther. 1998 Dec;287(3):996-1006.

[4]. Li J, et al. Curcumin Attenuates Retinal Vascular Leakage by Inhibiting Calcium/Calmodulin-Dependent Protein Kinase II Activity in Streptozotocin-Induced Diabetes. Cell Physiol Biochem. 2016;39(3):1196-208.

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