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产品名称：N-[2-[N-(4-氯肉桂)-N-甲基氨基]苯基]-N-(2-羟乙基)-4-甲氧苯磺酰胺磷酸酯盐
产品别名：KN-93

生物活性：

Description	KN-93 is a cell-permeable, reversible and competitive inhibitor calmodulin-dependent kinase type II (CaMKII) with a Ki of 370 nM.
IC_{50} & Target	Ki: 370 nM (CaMK)
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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 50 mg/mL (99.79 mM)** * "≥" means soluble, but saturation unknown.

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 0.83 mg/mL (1.66 mM); Clear solution

此方案可获得 ≥ 0.83 mg/mL (1.66 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 8.3 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 0.83 mg/mL (1.66 mM); Clear solution; Need ultrasonic and warming 此方案可获得 0.83 mg/mL (1.66 mM)的澄清溶液。 以 1 mL 工作液为例，取 100 μL 8.3 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 0.83 mg/mL (1.66 mM); Clear solution 此方案可获得 ≥ 0.83 mg/mL (1.66 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 8.3 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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).
Animal Administration	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.
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.