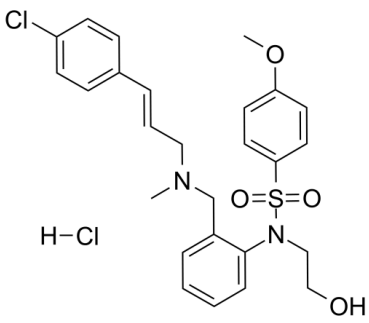
Data Sheet

Product Name:	KN-93 (hydrochloride)
Cat. No.:	CS-1561
CAS No.:	1956426-56-4
Molecular Formula:	C26H30Cl2N2O4S
Molecular Weight:	537.50
Target:	Autophagy; CaMK
Pathway:	Autophagy; Neuronal Signaling
Solubility:	H2O : 0.45 mg/mL (0.84 mM; Need ultrasonic and warming); DMSO : ≥ 31 mg/mL (57.67 mM)



BIOLOGICAL ACTIVITY:

KN-93 hydrochloride is a cell-permeable, reversible and competitive inhibitor calmodulin-dependent kinase type II (**CaMKII**) with a K_i of 370 nM. IC50 & Target: Ki: 370 nM (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].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Cells are grown on 12-mm diameter glass coverslips in DMEM 100% serum and various concentrations of KN-93 or KN-92. After 0, 1, 2, and 3 days of culture in the presence of drug, coverslips are removed from culture, rinsed once in PBS, and then submerged in 100% methanol at -20°C for 3 min. Fixed cells are stored in PBS until staining using the TUNEL assay. Cells are overlaid on 20 μL PBS/1 mg/mL BSA for 30 min, rinsed in PBS, and then overlaid on 20 μL containing 100 mM sodium cacodylate (pH 6.8), 1 mM $CoCl_2$, 0.1 mM DTT, 0.1 mg/mL BSA, 20 μM fluorescein-12-dUTP, and 0.1 unit/μL terminal transferase at 37°C for 60 min. Coverslips are rinsed in PBS twice, mounted on slides, and photographed using an OLYMPUS BX5O epifluorescent microscope using a UPLAN APO 40X oil immersion objective.

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-II (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.

CAIndexNames:

Benzenesulfonamide, N-[2-[[[3-(4-chlorophenyl)-2-propen-1-yl]methylamino]methyl]phenyl]-N-(2-hydroxyethyl)-4-methoxy- hydrochloride

SMILES:

[H]Cl.O=S(C1=CC=C(OC)C=C1)(N(C2=CC=CC=C2CN(C/C=C/C3=CC=C(Cl)C=C3)C)CCO)=O

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