

Product Data Sheet

Product Name: KN-92 phosphate

Cat. No.: GC16981

Chemical Properties

Cas. No. 1135280-28-2

Chemical Name (E)-N-(2-(((3-(4-chlorophenyl)allyl)(methyl)amino)methyl)phenyl)-4-methoxybenzenesulfonamide phosphate

SMILES CN(CC1=CC=CC=C1NS(C2=CC=C(OC)C=C2)(=O)=O)C/C([H])=C([H])/C3=CC=C(Cl)C=C3.OP(O)(O)=O

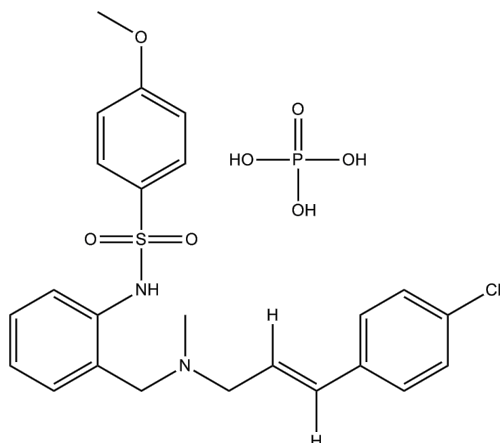
Formula $C_{24}H_{28}ClN_2O_7PS$ M.Wt 554.98

Solubility ≥ 25 mg/mL in DMSO, ≥ 43.1 mg/mL in EtOH with gentle warming Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility, please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

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Cell lines rabbit hypertrophic cardiac myocytes

Preparation method The solubility of this compound in DMSO is >25mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 0.5 µmol/L and 1 µmol/L

Applications KN-92 is the inactive analog of KN-93. Under the conditions of low potassium, low magnesium Tyrode's solution perfusion, and slow frequency electrical stimulation, the incidence of early after-depolarizations (EADs) was 0/12, 11/12, 10/12, and 5/12 in sham group, left ventricular hypertrophy (LVH) group, KN-92 group (0.5 µmol/L), and KN-93 group (0.5 µmol/L), respectively. When the drug concentration was increased to 1 µmol/L in KN-92 group and KN-93 group, the incidence of EADs was 10/12 and 2/12, respectively. When the drug concentration was 0.5 µmol/L in KN-92 and KN-93 groups, the peak $I_{Ca, L}$ at 0 mV was decreased by (9.4±2.8)% and (10.5±3.0)%, respectively. When the drug concentration was increased to 1 µmol/L, the peak $I_{Ca, L}$ values were lowered by (13.4±3.7)% and (40±4.9)%, respectively.

Animal experiment [2]:

Animal models Spontaneously hypertensive rats

Dosage form 1 µmol/L

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Application

In spontaneously hypertensive rats, action potential duration alternans (APD-ALT) was evoked at significantly lower pacing rate, KN-93 (1 $\mu\text{mol/L}$), but not its inactive analog, KN-92 (1 $\mu\text{mol/L}$), completely reversed these changes in APD-ALT. The magnitude of APD-ALT was also significantly greater in SHR than WKY and was completely normalized by KN-93. KN-93 also abolished ventricular fibrillation (VF) induced by rapid pacing in SHR.

Other notes

Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

- [1]. Ke J1, Chen F, Zhang C, et al. Effects of calmodulin-dependent protein kinase II inhibitor, KN-93, on electrophysiological features of rabbit hypertrophic cardiac myocytes. J Huazhong Univ Sci Technolog Med Sci. 2012 Aug;32(4):485-9.
- [2]. Mitsuyama H1, Yokoshiki H2, Watanabe M1, et al. Ca^{2+} /calmodulin-dependent protein kinase II increases the susceptibility to the arrhythmogenic action potential alternans in spontaneously hypertensive rats. Am J Physiol Heart Circ Physiol. 2014 Jul 15;307(2):H199-206.

Background

KN-92 phosphate is an inactive derivative of KN-93. KN-93 is a selective inhibitor of Ca^{2+} /calmodulin-dependent kinase II (CaMKII), competitively blocking CaM binding to the kinase ($K_i = 370 \text{ nM}$). IC_{50} value:Target: KN-92 is intended to be used as a control compound in studies designed to elucidate the antagonist activities of KN-93. KN-93 inhibits histamine-induced aminopyrine uptake in parietal cells ($\text{IC}_{50} = 300 \text{ nM}$). KN-93 has been used to implicate roles for CaMKII in Ca^{2+} -induced Ca^{2+} release in cardiac myocytes, constitutive phosphorylation of 5-lipoxygenase in 3T3 cells, and Ca^{2+} -dependent activation of HIF-1 α in colon cancer cell.

References:

- [1]. Rokhlin OW, Guseva NV, Taghiyev AF et al. KN-93 inhibits androgen receptor activity and

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- induces cell death irrespective of p53 and Akt status in prostate cancer. *Cancer Biol Ther.* 2010 Feb;9(3):224-35.
- [2]. Park SW, et al. CRABP1 protects the heart from isoproterenol-induced acute and chronic remodeling. *J Endocrinol.* 2018 Mar;236(3):151-165.
- [3]. An P, Zhu JY, Yang Y et al. KN-93, a specific inhibitor of CaMKII inhibits human hepatic stellate cell proliferation in vitro. *World J Gastroenterol.* 2007 Mar 7;13(9):1445-8.
- [4]. Gao L, Blair LA, Marshall J. et al. CaMKII-independent effects of KN93 and its inactive analog KN92: reversible inhibition of L-type calcium channels. *Biochem Biophys Res Commun.* 2006 Jul 14;345(4):1606-10.
- [5]. Rezazadeh S, Claydon TW, Fedida D. et al. KN-93 (2-[N-(2-hydroxyethyl)]-N-(4-methoxybenzenesulfonyl)]amino-N-(4-chlorocinnamyl)-N-methylbenzylamine), a calcium/calmodulin-dependent protein kinase II inhibitor, is a direct extracellular blocker of voltage-gated potassium channels. *J Pharmacol Exp Ther.* 2006 Apr;317(1):292-9.
- [6]. Anderson ME, Braun AP, Wu Y 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.
- [7]. Sumi M, Kiuchi K, Ishikawa T et al. The newly synthesized selective Ca²⁺/calmodulin dependent protein kinase II inhibitor KN-93 reduces dopamine contents in PC12h cells. *Biochem Biophys Res Commun.* 1991 Dec 31;181(3):968-75.

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