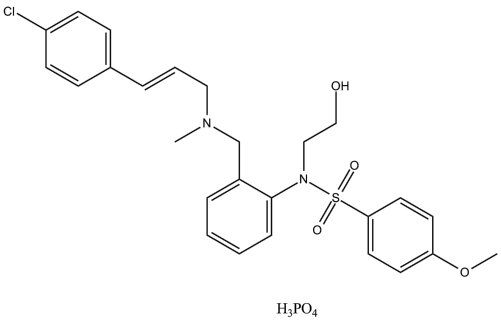
Product Data Sheet

Product Name: KN-93 Phosphate
Cat. No.: GC12804

Chemical Properties

Cas. No.	1913269-12-1		
SMILES	CN(C/C=C/C1=CC=C(Cl)C=C1)CC2=CC=CC=C2N(CCO)S(C3=CC=C(OC)C=C3)(=O)=O.O=P(OO)=O.[HH]		
Formula	$C_{26}H_{32}ClN_2O_8PS$	M.Wt	599.03
Solubility	≥ 29.95mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°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]:

Cell lines	LX-2 cells
Preparation Method	LX-2 cells were incubated with 0, 5, 10, 25, 50μM of KN-93 Phosphate for 24h, and cell viability was then measured using the CCK-8 assay.

Product Data Sheet

Reaction Conditions	0, 5, 10, 25, 50μM; 24h
Applications	After incubation of KN-93 Phosphate at various concentrations for 24h, the number of LX-2 cells reduced dramatically from 81.76% (5μM) to 27.15% (50μM).

Animal experiment [2]:

Animal models	Sprague Dawley rats

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Preparation Method	6-hydroxydopamine (OHDA) injections were used to create a rat model of Parkinson's disease (PD). After 3 weeks of injections, rats exhibiting stable apomorphine-induced rotations (≥0.7 turns/minute) were selected as valid PD rats. Forty of these PD rats were treated with levodopa plus benserazide twice daily for 21 days. Abnormal involuntary movement (AIM) scores were measured on days 1, 7, 14, and 21 of treatment. In addition, one group of PD rats (PD group, n=10) and another group of sham-operated rats (sham group, n=10) were treated with vehicle twice daily for 21 days. On day 22, the 40 levodopa-treated PD rats were randomly divided into four groups: levodopa+KN-93 Phosphate (1μg) group, levodopa+KN-93 Phosphate (2μg) group, levodoap+KN-93 Phosphate (5μg) group, and levodopa+vehicle group. These rats received intrastriatal injections of different doses of KN-93 Phosphate (1μg, 2μg, or 5μg) or vehicle before levodopa treatment. As a control, the sham group and PD group rats received intrastriatal injections of vehicle before vehicle treatment. Apomorphine-induced rotations were measured to assess the antiparkinsonian effect of KN-93 Phosphate on days 1 and 22. AIM scores were measured to assess the antidyskinetic effect of KN-93 Phosphate on days 1, 7, 14, 21, and 22. At the end of the experiment, rats were euthanized with deep anesthesia using 3% phenobarbital. Western blot analysis was used to determine the levels of GluR1 and pGluR1S845. Real-time polymerase chain reaction (PCR) was used to measure the levels of Gad1 and Nurr77.
Dosage form	1, 2, 5μg; 21 days; intrastriatally treated
Applications	2μg and 5μg KN-93 Phosphate treatment lowered AIMs scores in levodopa priming PD rats without affecting the antiparkinsonian effect of levodopa. In agreement with behavioral analysis, KN-93 Phosphate treatment reduced pGluR1S845 levels in PD rats. Moreover, KN-93 Phosphate treatment reduced the expression of Gad1 and Nur77 in PD rats.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

References:
[1] An P, Zhu J Y, Yang Y, et al. KN-93 Phosphate, a specific inhibitor of CaMKII inhibits human hepatic stellate cell proliferation in vitro[J]. World Journal of Gastroenterology: WJG, 2007, 13(9): 1445.
[2]Yang X, Wu N, Song L, et al. Intrastriatal injections of KN-93 Phosphate ameliorates levodopa-induced dyskinesia in a rat model of Parkinson's disease[J]. Neuropsychiatric disease and treatment, 2013: 1213-1220.

Background

KN-93 Phosphate is an effective, cell-membrane permeable, and selective inhibitor of Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) with an IC_{50} value of 0.37μM[1, 2]. KN-93 Phosphate inhibits the rapid component of the delayed rectifier potassium current (IKr) in mammalian cardiomyocytes[3]. KN-93 Phosphate induces nuclear translocation of histone deacetylase 4 (HDAC4), thereby promoting fatty acid oxidation in myocardial infarction[4].

In vitro, treatment of LX-2 human hepatic stellate cells with KN-93 Phosphate (0-50μM) for 24h decreased cell viability and the expression of cell cycle regulatory proteins p53 and p21 in a dose-dependent manner[5]. Treatment of NMDA-induced neuronal cells with KN-93 Phosphate (1μM) significantly reduced cell apoptosis, LDH release, and intracellular calcium concentration[6].

In vivo, 21-day treatment of Parkinson's disease rats with KN-93 Phosphate (2μg, 5μg) via striatal injection significantly alleviated levodopa-induced motor dysfunction, reduced phosphorylation levels of GluR1 in the nucleus accumbens, and decreased the expression levels of glutamate decarboxylase 1 (Gad1) and Nur77 (NR4A1, an orphan receptor of the nuclear receptor superfamily)[7].

References:
[1] Anderson M E, Braun A P, Wu Y, et al. KN-93 Phosphate, an inhibitor of multifunctional Ca++/calmodulin-dependent protein kinase, decreases early afterdepolarizations in rabbit heart[J]. The Journal of pharmacology and experimental therapeutics, 1998, 287(3): 996-1006.
[2] Agulló L, Garcia-Dorado D, Escalona N, et al. Membrane association of nitric oxide-sensitive guanylyl cyclase in cardiomyocytes[J]. Cardiovascular research, 2005, 68(1): 65-74.

Product Data Sheet

[3] Hegyi B, Chen-Izu Y, Jian Z, et al. KN-93 Phosphate inhibits IKr in mammalian cardiomyocytes[J]. Journal of Molecular and Cellular Cardiology, 2015, 89: 173-176.
[4] Zhao J, Li L, Wang X, et al. KN-93 Phosphate promotes HDAC4 nucleus translocation to promote fatty acid oxidation in myocardial infarction[J]. Experimental Cell Research, 2024, 438(2): 114050.
[5] An P, Zhu J Y, Yang Y, et al. KN-93 Phosphate, a specific inhibitor of CaMKII inhibits human hepatic stellate cell proliferation in vitro[J]. World Journal of Gastroenterology: WJG, 2007, 13(9): 1445.
[6] Liu X, Ma C, Xing R, et al. The calmodulin-dependent protein kinase II inhibitor KN-93 Phosphate protects rat cerebral cortical neurons from N-methyl-D-aspartic acid-induced injury☆[J]. Neural Regeneration Research, 2013, 8(2): 111-120.
[7] Yang X, Wu N, Song L, et al. Intrastriatal injections of KN-93 Phosphate ameliorates levodopa-induced dyskinesia in a rat model of Parkinson’s disease[J]. Neuropsychiatric disease and treatment, 2013: 1213-1220.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA