

Product Data Sheet

Product Name: SIS3 HCl

Cat. No.: GC17191

Chemical Properties

Cas. No. 521984-48-5

Chemical Name (E)-1-(6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)-3-(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)prop-2-en-1-one hydrochloride

SMILES CN1C(C2=CC=CC=C2)=C(C3=C1N=CC=C3)/C([H])=C([H])/C(N4CCC5=CC(OC)=C(OC)C=C5C4)=O.Cl

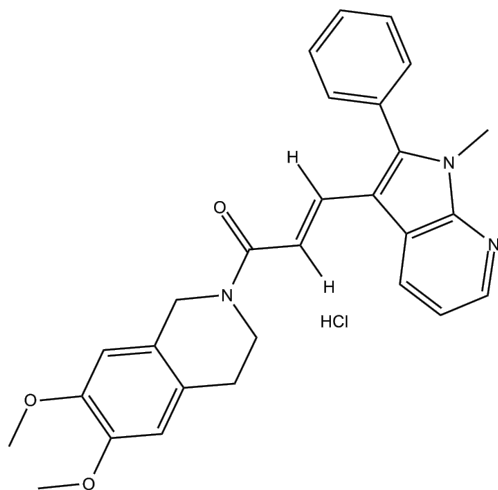
Formula $C_{28}H_{28}ClN_3O_3$ M.Wt 489.99

Solubility ≥ 49 mg/mL in DMSO, ≥ 11 mg/mL in EtOH with ultrasonic and warming 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]:

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell lines HK-2 cells

Preparation Method Cells were incubated with 0.1% DMSO, or 5 μ M SIS3 HCl for 1 h and then incubated with or without 25 μ M CdCl₂ (Cd) for 30 h. The viability of cells was determined by trypan blue exclusion assay.

Reaction
Conditions 5 μ M, 1 h

Applications SIS3 HCl inhibited cadmium-induced HK-2 cell death.

Animal experiment [2]:

Animal models T2DM mouse model

Preparation Method The diagnosed type 2 diabetic mice were randomly divided into three groups, including T2DM + saline group, T2DM + vehicle group, and T2DM + SIS3 HCl treatment group. Fasting blood glucose, oral glucose tolerance, and insulin tolerance data were measured after 45 d of continuous drug administration.

Dosage form 5 mg/kg, 45 days, i.p.

Applications SIS3 HCl significantly reduced body weight, adiposity, fasting blood glucose and also improved insulin sensitivity and oral glucose tolerance in mice.

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References:

[1] Fujiki K, Inamura H, Sugaya T, Matsuoka M. Blockade of ALK4/5 signaling suppresses cadmium- and erastin-induced cell death in renal proximal tubular epithelial cells via distinct signaling mechanisms. *Cell Death Differ.* 2019 Nov;26(11):2371-2385.

[2] Wang D C, Yan T T, Chen B, et al. SIS3, a good candidate for the reverse of type 2 diabetes mellitus in mice[J]. *Fundamental & Clinical Pharmacology*, 2021, 35(2): 389-396.

Background

SIS3 HCl is a Smad3 inhibitor that inhibits the phosphorylation of Smad3 with an IC₅₀ of 3 μ M [1].

SIS3 HCl can dose-dependently eliminate enhanced p3TP-lux luciferase activity, attenuated Smad3 phosphorylation induced by transforming growth factor (TGF-1) and the interaction between Smad3 and Smad4, but SIS3 HCl does not affect Smad2 phosphorylation. SIS3 HCl attenuates the effects of TGF-1 by reducing transcriptional activity and inhibits differentiation of adult myofibroblasts via TGF-1[1]. SIS3 HCl (10 μ M) in ML-12 cells blocked TGF- β -mediated Smad3 phosphorylation, while total Smad2/3 levels remained unchanged[2].

In a study of Tie2-Cre; Loxp-EGFP mice, SIS3 HCl (2.5 mg/kg/day) inhibited Smad3 activation in streptozotocin (STZ)-induced diabetic nephropathy. SIS3 HCl eliminates endothelial mesenchymal transition, reduces renal fibrosis, and slows the progression of kidney disease[3]. SIS3 HCl (5 mg/kg) significantly reduced body weight, adiposity, and fasting blood glucose in high-fat diet-induced type 2 diabetes mellitus (T2DM) model mice, and also improved insulin sensitivity and oral glucose tolerance in mice[4].

References:

[1] Jinnin M et al. Characterization of SIS3, a novel specific inhibitor of Smad3, and its effect on transforming growth factor-beta1-induced extracellular matrix expression. *Mol Pharmacol.* 2006 Feb;69(2):597-607.

[2] Leiting S, Seidl S, Martinez-Palacian A, Muhl L, Kanse SM. Transforming Growth Factor- β (TGF- β) Inhibits the Expression of Factor VII-activating Protease (FSAP) in Hepatocytes. *J Biol Chem.* 2016 Sep 30;291(40):21020-21028.

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- [3] Li J et al. Blockade of endothelial-mesenchymal transition by a Smad3 inhibitor delays the early development of streptozotocin-induced diabetic nephropathy. *Diabetes*.2010 Oct;59(10):2612-24.
- [4] Wang D C, Yan T T, Chen B, et al. SIS3, a good candidate for the reverse of type 2 diabetes mellitus in mice[J]. *Fundamental & Clinical Pharmacology*, 2021, 35(2): 389-396.

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