SB 216763

Cat. No.: HY-12012

CAS No.: 280744-09-4

Molecular Formula: $C_{19}H_{12}Cl_2N_2O_2$

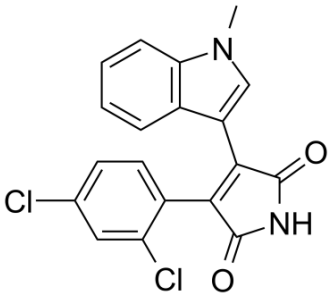
Molecular Weight: 371.22

Target: GSK-3; Autophagy

Pathway: PI3K/Akt/mTOR; Stem Cell/Wnt; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (269.38 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6938 mL	13.4691 mL	26.9382 mL
5 mM	0.5388 mL	2.6938 mL	5.3876 mL
10 mM	0.2694 mL	1.3469 mL	2.6938 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.73 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.73 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SB 216763 is potent, selective and ATP-competitive GSK-3 inhibitor with IC_{50}s of 34.3 nM for both GSK-3α and GSK-3β.

IC_{50} & Target

GSK-3α	GSK-3β
34.3 nM (IC_{50})	34.3 nM (IC_{50})

In Vitro

SB-216763 (10-20 μM) induces β-catenin mediated-transcription in a dose-dependent manner in HEK293 cells. SB-216763

	(10, 15 and 20 μM) can maintain mESCs with a pluripotent-like morphology in long-term culture. SB-216763 (10 μM) can maintain J1 mESCs in a pluripotent state for more than a month[2]. SB-216763 inhibits GSK-3 with IC_{50} of 34 nM[3]. SB-216763 is equally effective at inhibiting human GSK-3α and GSK-3β[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SB216763 (20 mg/kg, i.v.) significantly improves the survival of BLM-treated mice. Mice randomized to receive BLM plus SB216763 shows a noteworthy reduction, compared with BLM-treated mice. SB216763 (20 mg/kg, i.v.) reduces the magnitude of BLM-induced alveolitis[1]. SB 216763 (0.2 mg/kg, i.v.) with either 17β-E_{100} or $Geni_{100}$ reverses the ceiling effect because these agents significantly reduce infarct size when the rabbits' hearts are submitted to 30-min CAO[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	MESCs maintained with LIF or 10 μM SB-216763 for more than a month are resuspended at 40,000 cells/mL in LIF-free mESC medium. EBs are prepared by a hanging drop procedure. Briefly, 20 μL drops containing mESCs are pipetted on the inside of a 10-cm Petri dish lid. The lids are placed onto Petri dishes containing 10 mL of HBSS and the EBs are allowed to form and grow for 4 days in the incubator. After 4 days, 15-20 EBs are transferred to a well containing LIF-free mESC medium in a 24-well plate. The medium is exchanged every two days and autonomously beating cell aggregates are observed and counted. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice are allocated to four groups (n=12/group) as follows: 1) intratracheal saline + vehicle (25% dimethyl sulfoxide, 25% polyethylene glycol, and 50% saline), 2) intratracheal saline + SB216763 (20 mg/kg) dissolved in vehicle, 3) intratracheal BLM (3 U/kg) + vehicle, and 4) intratracheal BLM + SB216763 (20 mg/kg) in vehicle. Another set of experiments to assess cytokine expression by reverse transcription-PCR is conducted in the mice (n=12/group) to receive 1) intratracheal saline + vehicle, 2) intratracheal BLM, and 3) intratracheal BLM + SB216763. To induce pulmonary fibrosis, BLM is intratracheally administered in mice (n=15/group) on day 0. BLM and saline-treated mice are administered with SB216763 dissolved in vehicle or vehicle alone intravenously at day 0 and then intraperitoneally twice a week until day 28. Mice are sacrificed by CO_2 inhalation on days 2, 7, and 28. In the terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) experiments, the cohorts of mice are as follows: saline-treated (n=6), BLM-treated (n=6), and BLM + SB216763-treated (n=6). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Theranostics. 2019 Aug 12;9(20):5769-5783.
- Haematologica. 2020 Mar;105(3):661-673.
- Biochem Pharmacol. 2018 Apr;150:280-292.
- Biomed Pharmacother. 2019 Sep 19;120:109231.
- J Cell Biochem. 2018 Jul;119(7):5934-5943.

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REFERENCES

[1]. Gurrieri, et al. 3-(2,4-dichlorophenyl)-4-(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione (SB216763), a glycogen synthase kinase-3 inhibitor, displays therapeutic properties in a mouse model of pulmonary inflammation and fibrosis. J.Pharmacol.Exp.Ther.2010

[2]. Kirby LA, et al. Glycogen synthase kinase 3 (GSK3) inhibitor, SB-216763, promotes pluripotency in mouse embryonic stem cells.PLoS One. 2012;7(6):e39329. Epub 2012 Jun 26.

[3]. Wang M, et al. The first synthesis of [(11)C]SB-216763, a new potential PET agent for imaging of glycogen synthase kinase-3 (GSK-3).Bioorg Med Chem Lett. 2011 Jan 1;21(1):245-9. Epub 2010 Nov 11.

[4]. The ceiling effect of pharmacological postconditioning with the phytoestrogen genistein is reversed by the GSK3beta inhibitor SB 216763 [3-(2,4-dichlorophenyl)-4(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione] through mitochondrial ATP-dependent potassium channel opening.

[5]. Coghlan MP, et al. Selective small molecule inhibitors of glycogen synthase kinase-3 modulate glycogen metabolism and gene transcription. Chem Biol. 2000 Oct;7(10):793-803.

[6]. Wang W, et al. Inhibition of glycogen synthase kinase 3beta ameliorates triptolide-induced acute cardiac injury by desensitizing mitochondrial permeability transition. Toxicol Appl Pharmacol. 2016 Dec 15;313:195-203.

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