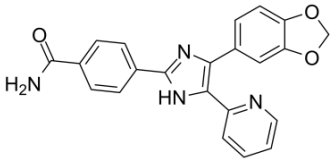
SB-431542

Cat. No.:	HY-10431
CAS No.:	301836-41-9
Molecular Formula:	$C_{22}H_{16}N_4O_3$
Molecular Weight:	384.39
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
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 : ≥ 40 mg/mL (104.06 mM)
Ethanol : 11.17 mg/mL (29.06 mM; Need ultrasonic and warming)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6015 mL	13.0076 mL	26.0152 mL
	5 mM	0.5203 mL	2.6015 mL	5.2030 mL
	10 mM	0.2602 mL	1.3008 mL	2.6015 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 (6.50 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SB-431542 is a potent and selective inhibitor of ALK5/TGF-β type I Receptor with an IC_{50} value of 94 nM[1].

IC_{50} & Target

ALK5
94 nM (IC_{50})

In Vitro

SB-431542 (1 μM) significantly reduces the TGF-β-induced nuclear accumulation of Smad proteins in A498 cells. SB-431542 inhibits TGF-β1-induced collagen Iα1 and PAI-1 mRNA with IC_{50} values of 60 and 50 nM, respectively. In addition, SB-431542 inhibits TGF-β1-induced fibronectin mRNA and protein with IC_{50} values of 62 and 22 nM, respectively[1]. SB-431542 (10 μM) is

	a selective inhibitor of TGF-β signaling but has no effect on BMP signaling in NIH 3T3 cells[2]. TRKI, SB-431542, inhibits TGF-beta-induced transcription, gene expression, apoptosis, and growth suppression. SB-431542 attenuates the tumor-promoting effects of TGF-beta, including TGF-beta-induced EMT, cell motility, migration and invasion, and vascular endothelial growth factor secretion in human cancer cell lines. SB-431542 induces anchorage independent growth of cells that are growth-inhibited by TGF-beta, whereas it reduces colony formation by cells that are growth-promoted by TGF-beta [3]. SB-431542 (0.3 μM) inhibits cell proliferation induced by TGF-β in MG63 cells[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SB-431542 (10 mg/kg, i.p.) decreases lung metastasis but does not significantly alter growth of the primary tumor 4T1 xenograft[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [3]	A total of 100,000 cells from each pool of A549 and HT29 are seeded into each well of 12-well plate. Cells are cultured in media containing 0.2% FBS for 18 hours, and then treated with 5 ng/mL TGF-β1 in the presence of SB-431542 (10 μM) in 0.5 mL of media for 24 hours. One hundred μLs of each supernatant media is used for VEGF assay according to the manufacturer's instruction. For TGF-β1 ELISA, 100,000 cells from each pool of A549, VMRC-LCD, and HT29 are seeded into each well of 12-well plates and serum-starved for 20 hours. Cells are then treated with SB-431542 in 0.5 mL of serum-free RPMI media for 24 hours. One hundred μLs of each supernatant media is activated and used for TGF-β1 assay according to the manufacturer's instruction. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	A498 cells are seeded at 5,000 to 10,000 cells/well in 96-well plates. The cells are serum-deprived for 24 h and then treated with SB-431542 for 48 h to assess the cellular toxicity. Cell viability is determined by incubating cells for 4 h with XTT labeling and electron coupling reagent according to the manufacturer's directions. Live cells with active mitochondria produce an orange-colored product, formazan, which is detected using a plate reader at between A 450 nm and A 500 nm with a reference wavelength greater than 600 nm. The absorbance values correlate with the number of viable cells. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [5]	Ten thousand 4T1 cells are injected subcutaneously into the second mammary fat pad of 6-week-old Balb/c female mice. Tumors are measured twice weekly, and volume is calculated using the following formula: Volume = width^2×length×0.52. Mice are randomly assigned to two treatment groups: control, n = 14 (20% DMSO/80% corn oil); SB-431542-treated, n = 15 (10 mg/kg body weight in 20% DMSO/80% corn oil, administered intraperitoneally three times per week starting one day after tumor cell inoculation. Primary tumors are resected when the volume at day 10 post-injection of 4T1 cells. All mice are monitored daily and euthanized after 4 weeks. The metastases are dissected to snap-freeze for further analysis. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Small. 2020 Jun;16(22):e2001371.
- Biomaterials. 2020 May;240:119849.
- Cancer Res. 2020 Oct.
- Cancer Res. 2019 Sep 1;79(17):4466-4479.
- EMBO Mol Med. 2020 Jan 9;12(1):e10681.

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REFERENCES

[1]. N. J. Laping, et al. Inhibition of Transforming Growth Factor (TGF)-β1-Induced Extracellular Matrix with a Novel Inhibitor of the TGF-β Type I Receptor Kinase Activity: SB-431542.

[2]. Inman GJ, et al. SB-431542 is a potent and specific inhibitor of transforming growth factor-beta superfamily type I receptor-like kinase (ALK) receptors ALK4, ALK5, and ALK7. Mol Pharmacol, 2002, 62(1), 65-74.

[3]. Halder SK, et al. A specific inhibitor of TGF-beta receptor kinase, SB-431542, as a potent antitumor agent for human cancers. Neoplasia, 2005, 7(5), 509-521.

[4]. Matsuyama S, et al. SB-431542 inhibits transforming growth factor-beta-induced proliferation of human osteosarcoma cells. Cancer Res, 2003, 63(22), 7791-7798.

[5]. Sato M, et al. Differential Proteome Analysis Identifies TGF-β-Related Pro-Metastatic Proteins in a 4T1 Murine Breast Cancer Model. PLoS One. 2015 May 18;10(5):e0126483.

[6]. Ma J, et al. Growth differentiation factor 11 improves neurobehavioral recovery and stimulates angiogenesis in rats subjected to cerebral ischemia/reperfusion. Brain Res Bull. 2018 Feb 9;139:38-47

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