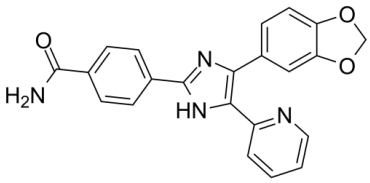
Data Sheet

Product Name:	SB-431542
Cat. No.:	CS-0135
CAS No.:	301836-41-9
Molecular Formula:	C22H16N4O3
Molecular Weight:	384.39
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
Solubility:	DMSO : ≥ 40 mg/mL (104.06 mM); Ethanol : 11.17 mg/mL (29.06 mM; Need ultrasonic and warming)



BIOLOGICAL ACTIVITY:

SB-431542 is a potent and selective inhibitor of **ALK5/TGF-β type I Receptor** with an **IC_{50}** value of 94 nM. IC50 & Target: IC50: 94 nM (ALK5)[2] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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. **Cell Assay:** SB-431542 is dissolved at a concentration of 10 mM in DMSO.[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. **Animal Administration:** SB-431542 is formulated in 20% DMSO/80% corn oil.[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 = $width^2 \times length \times 0.52$. 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.

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. "

CAIndexNames:

Benzamide, 4-[4-(1,3-benzodioxol-5-yl)-5-(2-pyridinyl)-1H-imidazol-2-yl]-

SMILES:

O=C(C1=CC=C(C=C1)C2=NC(C3=CC=C4OCOC4=C3)=C(N2)C5=NC=CC=C5)N

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA