SB-505124 hydrochloride

Cat. No.: HY-13521A

CAS No.: 356559-13-2

Molecular Formula: $C_{20}H_{22}ClN_3O_2$

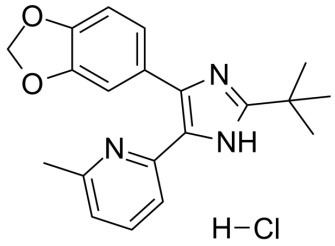
Molecular Weight: 371.86

Target: TGF-β Receptor

Pathway: TGF-beta/Smad

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

Methanol : 125 mg/mL (336.15 mM; Need ultrasonic)

DMSO : 50 mg/mL (134.46 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6892 mL	13.4459 mL	26.8918 mL
5 mM	0.5378 mL	2.6892 mL	5.3784 mL
10 mM	0.2689 mL	1.3446 mL	2.6892 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 (6.72 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.72 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SB-505124 hydrochloride is a selective inhibitor of TGF-β Receptor type I receptor (ALK4, ALK5, ALK7), with IC_{50}s of 129 nM and 47 nM for ALK4, ALK5, respectively, but it does not inhibit ALK1, 2, 3, or 6.

IC_{50} & Target

IC50: 129 nM (ALK4), 47 nM (ALK5)

In Vitro

SB-505124 demonstrates no toxicity to renal epithelial A498 cells at concentrations up to 100 μM for 48 h. 505124 inhibits the closely related ALK4 with an IC_{50} value of 129±11 nM (about 2.5-fold less sensitive than ALK5) but does not inhibit ALK2 at concentrations up to 10 μM. SB-505124 (1 μM) inhibits the TGF-β-induced phosphorylation of Smad2 in all three of these cell lines in a concentration-dependent fashion. SB-505124 (1 or 5 μM) potently inhibits TGF-β-induced activation of JNK/SAP, extracellular signal-regulated kinase 1/2, and p38 despite the different patterns of activation in these cells[1]. SB-505124 (10

	μM) impairs Smad2 phosphorylation and CTGF and α-SMA expression in vitro[2]. SB-505124 susspresses CTGF and α-SMA observed by immunofluorescence. Cell outgrowth from explants dissected from eyes to which SB-505124 is applied during GFS is robust while outgrowth is poor from those treated with MMC[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SB-505124 (5 mg/kg; i.p.) alone has no effect in C57Bl6 mice with A549 xenografts, but administration of SB-505124 with a single dose of Carboplatin (60 mg/kg) results in durable responses without the need for maintenance therapy in five animals [4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57Bl6 mice with A549 xenografts[4]
Dosage:	5 mg/kg
Administration:	I.p.; daily
Result:	Had no effect alone, but administration with a single dose of carboplatin (60 mg/kg) resulted in durable responses without the need for maintenance therapy in five animals.

CUSTOMER VALIDATION

- Nat Metab. 2022 Oct;4(10):1306-1321.
- ACS Nano. 2022 Jan 13.
- Adv Sci (Weinh). 2022 Aug 10;e2201451.
- Exp Mol Med. 2022 Oct 12.
- Bone Res. 2019 Mar 6;7:8.

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REFERENCES

[1]. DaCosta Byfield S, et al. SB-505124 is a selective inhibitor of transforming growth factor-beta type I receptors ALK4, ALK5, and ALK7. Mol Pharmacol. 2004 Mar;65(3):744-52.

[2]. Sutariya V, et al. Thermoreversible gel for delivery of receptor-like kinase 5 inhibitor SB-505124 for glaucoma filtration surgery. Pharm Dev Technol. 2013 Jul-Aug;18(4):957-62.

[3]. Sapitro J, et al. Suppression of transforming growth factor-β effects in rabbit subconjunctival fibroblasts by receptor-like kinase 5 inhibitor. Mol Vis. 2010 Sep 16;16:1880-92.

[4]. Marini KD, et al. Inhibition of activin signaling in lung adenocarcinoma increases the therapeutic index of platinum chemotherapy. Sci Transl Med. 2018 Jul 25;10(451). pii: eaat3504.

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