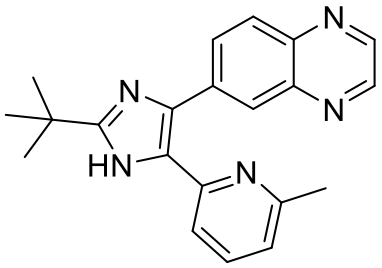
Product data sheet

MedKoo Cat#: 406415 Name: SB525334 CAS#: 356559-20-1 Chemical Formula: $C_{21}H_{21}N_5$ Exact Mass: 343.1797 Molecular Weight: 343.42	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

SB525334 is a potent and selective inhibitor of the transforming growth factor-beta1 (TGF-beta1) receptor, activin receptor-like kinase (ALK5). SB525334 inhibited ALK5 kinase activity with an IC(50) of 14.3 nM and was approximately 4-fold less potent as an inhibitor of ALK4 (IC(50) = 58.5 nM). SB-525334 was inactive as an inhibitor of ALK2, ALK3, and ALK6 (IC(50) > 10,000 nM). In cell-based assays, SB-525334 (1 microM) blocked TGF-beta1-induced phosphorylation and nuclear translocation of Smad2/3 in renal proximal tubule cells and inhibited TGF-beta1-induced increases in plasminogen activator inhibitor-1 (PAI-1) and procollagen alpha1(I) mRNA expression in A498 renal epithelial carcinoma cells.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	30.0343	87.36

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.91 mL	14.56 mL	29.12 mL
5 mM	0.58 mL	2.91 mL	5.82 mL
10 mM	0.29 mL	1.46 mL	2.91 mL
50 mM	0.06 mL	0.29 mL	0.58 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Thomas M, Docx C, Holmes AM, Beach S, Duggan N, England K, Leblanc C, Lebret C, Schindler F, Raza F, Walker C, Crosby A, Davies RJ, Morrell NW, Budd DC. Activin-like kinase 5 (ALK5) mediates abnormal proliferation of vascular smooth muscle cells from patients with familial pulmonary arterial hypertension and is involved in the progression of experimental pulmonary arterial hypertension induced by monocrotaline. Am J Pathol. 2009 Feb;174(2):380-9. doi: 10.2353/ajpath.2009.080565. Epub 2008 Dec 30. PMID: 19116361; PMCID: PMC2630548.

2. Grygielko ET, Martin WM, Tweed C, Thornton P, Harling J, Brooks DP, Laping NJ. Inhibition of gene markers of fibrosis with a novel inhibitor of transforming growth factor-beta type I receptor kinase in puromycin-induced nephritis. J Pharmacol Exp Ther. 2005 Jun;313(3):943-51. doi: 10.1124/jpet.104.082099. Epub 2005 Mar 15. PMID: 15769863.

In vivo study

1. Thomas M, Docx C, Holmes AM, Beach S, Duggan N, England K, Leblanc C, Lebret C, Schindler F, Raza F, Walker C, Crosby A, Davies RJ, Morrell NW, Budd DC. Activin-like kinase 5 (ALK5) mediates abnormal proliferation of vascular smooth muscle cells

from patients with familial pulmonary arterial hypertension and is involved in the progression of experimental pulmonary arterial hypertension induced by monocrotaline. Am J Pathol. 2009 Feb;174(2):380-9. doi: 10.2353/ajpath.2009.080565. Epub 2008 Dec 30. PMID: 19116361; PMCID: PMC2630548.

2. Laping NJ, Everitt JI, Frazier KS, Burgert M, Portis MJ, Cadacio C, Gold LI, Walker CL. Tumor-specific efficacy of transforming growth factor-beta RI inhibition in Eker rats. Clin Cancer Res. 2007 May 15;13(10):3087-99. doi: 10.1158/1078-0432.CCR-06-1811. PMID: 17505012.

7. Bioactivity

Biological target:

SB 525334 is a potent and selective transforming growth factor β1 receptor (ALK5) inhibitor with an IC50 of 14.3 nM.

In vitro activity

The potent and selective ALK5 kinase inhibitor, SB52533413 was used to assess the contribution of ALK5 in mediating the abnormal TGF-β1 responses observed in familial iPAH PASMCs. Significantly, the TGF-β1-mediated proliferation of familial iPAH PASMCs is abolished by pre-incubation of cells with a potent ALK5 kinase inhibitor, SB525334 implying that ALK5 transduces the abnormal pro-proliferative signal after ligand addition to these cells in vitro (Figure 3). Consistent with previously published data,13 SB525334 inhibited TGF-β1-mediated proliferation of familial iPAH PASMCs at an IC50 of 295 nmol/L (data not shown).

Reference: Am J Pathol. 2009 Feb;174(2):380-9. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/19116361/

In vivo activity

A rat MCT model of pulmonary hypertension was used to determine the effects of therapeutic ALK5 inhibition using SB525334 on the development and progression of PAH pathologies in vivo. Previous optimization studies in rats had provided a model, which, after subcutaneous injection of MCT, established hypertensive pathologies by day 17, which became progressively worse, peaking at days 28 to 35 (data not shown). RV pressure rose from 25 to 64 mmHg by day 17, at which point ALK5 was inhibited via oral dosing of SB525334. Vehicle-treated animals continued to worsen, with a mean RV pressure of 92 mmHg attained by day 35. This deterioration was abrogated by treatment with 3 mg/kg of SB525334 (62 mmHg), with a trend toward reversal observed in 30 mg/kg treated animals (53 mmHg) (Figure 6A). The progression of RV hypertrophy measured by the Fulton index (RV/LV + S) was more pronounced beyond day 17. Treatment of animals with SB525334 significantly inhibited RV hypertrophy as the Fulton index ratio was reduced from 0.45 in vehicle-treated animals compared with 0.37 in 30 mg/kg SB525334-treated animals (Figure 6B).

Reference: Am J Pathol. 2009 Feb;174(2):380-9. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/19116361/