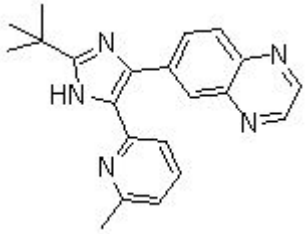
Product Introduction

SB525334

SB525334 is a potent and selective inhibitor of **TGFβ receptor I (ALK5)** with **IC50** of 14.3 nM, is 4-fold less potent to ALK4 than ALK5 and inactive to ALK2, 3, and 6.

Technical Data:

Molecular Weight (MW):	343.42	
Formula:	$C_{21}H_{21}N_5$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 69 mg/mL	
	Water <1mg/mL	
	Ethanol 69 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	356559-20-1	

Biological Activity

SB 525334 shows no inhibition in the enzymes ALK2, 3, and 6, with IC50 values > 10 μM. SB 525334 blocks phosphorylation induced by TGF-β1 and nuclear translocation of Smad2/3 in renal proximal tubule cells. SB 525334 also inhibits the increased mRNA expression levels of plasminogen activator inhibitor-1 (PAI-1) and procollagen α1(I) induced by TGF-β1 in A498 renal epithelial carcinoma cells at 1 μM). [1] SB 525334 (1 μM) attenuates the heightened sensitivity to TGF-β1 exhibited by pulmonary artery smooth muscle cells (PASMCs) from patients with familial forms of idiopathic pulmonary arterial hypertension (PAH). [2]

SB 525334 (10 mg/kg/day) decreases the renal mRNA levels of PAI-1, procollagen α1(I), and procollagen α1(III) in a nephritis-induced renal fibrosis rat model. Furthermore, PAN-induced proteinuria is significantly inhibited by SB 525334 (10 mg/kg/day). [1] SB 525334 may also be efficacious in mesenchymal tumors. SB 525334 (10 mg/kg/day) significantly decreases uterine mesenchymal tumor incidence, multiplicity, and size in Eker rats. [3] SB 525334 significantly reverses pulmonary arterial pressure and inhibits right ventricular hypertrophy in a rat model of PAH. This is revealed by a significant reduction in pulmonary arteriole muscularization induced by monocrotaline (used to induce PAH) after treatment with SB 525334 (3 or 30 mg/kg). [2] In a Bleomycin-induced pulmonary fibrosis mice model, SB 525334 (10 mg/kg or 30 mg/kg) attenuates the histopathological alterations in the lung, and significantly decreased mRNA expression of Type I and III procollagen and fibronectin. SB 525334 also attenuates Smad2/3 nuclear translocation, myofibroblast proliferation, deposition of Type I collagen, and decreases CTGF-expressing cells. [4]

References

[1] Grygielko ET, et al. J Pharmacol Exp Ther, 2005, 313(3), 943-951.

[2] Thomas M, et al. Am J Pathol, 2009, 174(2), 380-389.

[3] Laping NJ, et al. Clin Cancer Res, 2007, 13(10), 3087-3899.

[4] Higashiyama H, et al. Exp Mol Pathol, 2007, 83(1), 39-46.