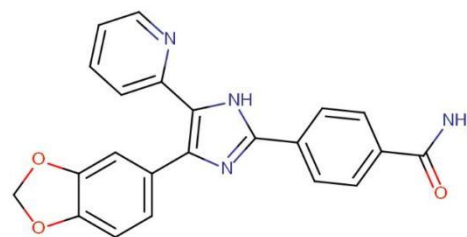


SB431542 (TGF- β /Smad 抑制剂)

货号: RPM0014

◆ 产品信息

中文名称/Chinese Name:	SB431542
别称/Synonyms:	4-[4-(1,3-苯并二唑-5-基)-5-(2-吡啶基)-1H-咪唑-2-基]-苯酰胺水合物
CAS 号/CAS NO.:	301836-41-9
化学式/Formula:	C ₂₂ H ₁₆ N ₄ O ₃
分子量/M.Wt:	384.39
外观/Appearance:	固体
保存条件/Storage:	Powder: -20°C, 3 年 Insolvent: -80°C, 1 年



◆ 溶解信息

溶解度/Solubility:	DMSO: 16.67 mg/mL (43.36 mM)
	Ethanol: 3.8 mg/mL (10 mM)

溶液配制参考/Preparing Stock Solutions:

	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	5.203 mL
10 mM	0.2602 mL	1.3008 mL	2.6015 mL
50 mM	0.052 mL	0.2602 mL	0.5203 mL

◆ 生物活性

产品描述/Description	SB431542 是一种 ALK5/TGF- β type I Receptor 的抑制剂, 具有选择性, 对 ALK4 和 ALK7 也有抑制活性, 但对其他蛋白没有抑制作用。SB431542 可以用于干细胞的诱导分化。
靶点活性/Targets (IC ₅₀)	ALK5: 94 nM, ALK4: 140 nM
体外活性/In vitro	1.用 SB431542 (2-10 μM) 和 TGF-β1 (12.5 ng/mL) 处理人肾细胞 293T、人类结肠癌来源的非致瘤性细胞 FET 和人肺腺癌细胞 A549 1 h, Western Blot 检测靶点蛋白表达水平。TGF-β1 诱导了 Smad2/3 和 Smad4 之间的复合物形成。SB431542 以剂量依赖的方式, 通过阻断 TGF-β诱导的磷酸化和 Smad2/3 的激活, 阻断复合物形成。^[1] 2.用 SB431542 (1-10 μM) 处理人胶质母细胞瘤细胞 D54MG 24 h, Transwell

	检测细胞迁移情况。SB431542 抑制 TGF-βRI 信号传导以浓度依赖的方式阻断 D54MG 细胞的细胞迁移。^[2] 3.用含 SB431542 (10 nM) 和 Noggin (500 ng/mL) 的 KSR 培养基培养人多能干细胞 hESCs 11 天, 免疫荧光检测细胞分化情况。与单独使用 Noggin 或 SB431542 时不到 10%的 PAX6+细胞相比, 用 Noggin 和 SB431542 联合处理显著提高了神经诱导的效率, 使其超过总细胞的 80%。^[3]
体内活性/In vivo	1.将 SB431542 (10 mg/kg in 20% DMSO/80% corn oil) 腹腔注射给携带小鼠乳腺癌肿瘤 4T1 的 Balb/c 小鼠, 每周三次, 持续四周, 检测体内抗肿瘤活性。SB431542 可显著抑制 4T1 乳腺肿瘤的肺转移。^[4] 2.将 SB431542 (10 mg/kg) 腹腔注射给大面积肩袖撕裂的 C57B/6J 小鼠模型, 每天一次, 持续二或六周, 研究肌腱损伤的治疗方法。SB431542 抑制 TGF-β1 信号传导可减少纤维化、脂肪浸润和肌肉重量减轻。SB431542 治疗通过促进纤维/脂肪生成祖细胞 (FAP) 的凋亡, 减少了损伤肌肉中 FAP 的数量。^[5]
激酶实验/Kinase Assay	Kinase assays were performed with 65 nM GSTALK5 and 184 nM GST-Smad3 in 50 mM HEPES, 5 mM MgCl₂, 1 mM CaCl₂, 1 mM dithiothreitol, and 3 M ATP. Reactions were incubated with 0.5 μCi of [33P]γATP for 3 h at 30°C. Phosphorylated protein was captured on P-81 paper, washed with 0.5% phosphoric acid, and counted by liquid scintillation. Alternatively, Smad3 or Smad1 protein was also coated onto FlashPlate Sterile Basic Microplates. Kinase assays were then performed in FlashPlates with same assay conditions using either the kinase domain of ALK5 with Smad3 as a substrate or the kinase domain of ALK6 (BMP receptor) with Smad1 as substrate. Plates were washed three times with phosphate buffer and counted by TopCount ^[2].

◆ 参考文献

- [1] Halder SK, et al. A specific inhibitor of TGF- β receptor kinase, SB-431542, as a potent antitumor agent for human cancers. *Neoplasia*. 2005 May;7(5):509-21.
- [2] Hjelmeland MD, et al. SB-431542, a small molecule transforming growth factor- β -receptor antagonist, inhibits human glioma cell line proliferation and motility. *Mol Cancer Ther*. 2004 Jun;3(6):737-45.
- [3] Chambers SM, et al. Highly efficient neural conversion of human ES and iPS cells by dual inhibition of SMAD signaling. *Nat Biotechnol*. 2009 Mar;27(3):275-80. doi: 10.1038/nbt.1529. Epub 2009 Mar 1. Erratum in: *Nat Biotechnol*. 2009 May;27(5):485.
- [4] 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.
- [5] Davies MR, et al. TGF- β Small Molecule Inhibitor SB431542 Reduces Rotator Cuff Muscle Fibrosis and Fatty Infiltration By Promoting Fibro/Adipogenic Progenitor Apoptosis. *PLoS One*. 2016 May 17;11(5):e0155486.

◆ 注意事项

- 请在收到本产品后立即按照说明书中推荐的条件保存, 使用前进行离心, 使粉末充分沉降至管底。
- 请根据实验目的及本产品的溶解性, 选择相应的溶剂配制高浓度母液后使用, 最佳工作浓度请参考相关文献通过实验摸索优化, 本说明书中的数据来源于公开文献, 仅供参考。
- 本产品仅供科研使用, 不可用于诊断或治疗领域。
- 为了您的安全和健康, 请穿实验服并戴一次性手套操作。