产品名称：CP-673451
产品别名：CP-673451

生物活性：

Description	CP-673451 is a potent and selective inhibitor of PDGFR with IC_{50}s of 10 and 1 nM for PDGFRα and PDGFRβ, respectively.	
IC_{50} & Target [1]	PDGFRα	PDGFRβ
	10 nM (IC_{50})	1 nM (IC_{50})
In Vitro	CP-673451 efficiently suppresses the PDGFR downstream signaling pathway. It inhibits phosphorylation of Akt, GSK-3β, p70S6, and S6 in A549 cells in a concentration-dependent manner. CP-673451 (0.0625-4 μM) significantly reduces the viability of NSCLC cell lines A549 and H1299 in a time- and concentration-dependent manner, with IC50s of 0.49 and 0.61 μM, respectively. CP-673451 (1, 4 μM) induces apoptosis in non-small-cell lung cancer cells. CP-673451 (25, 100, or 400 nM) is effective at inhibiting migration and invasion of NSCLC cells by suppression of lamellipodia formation[1]. CP-673451 and crenolanib show selective lethality toward cells with CA. U2OS cells treated with 1 to 4 μM CP-673451 or crenolanib show a ruffled cell surface as a sign for alterations of the cortical actin cytoskeleton. CP-673451 attenuates PDGF-BB-induced signaling, and significantly enhances the phosphorylation of PDGFR-β downstream effectors, Akt and MEK[2]. CP-673,451 (0.5 μM) regulates cell proliferation through mechanisms involving reduced phosphorylation of GSK-3α and GSK-3β. CP-673,451 impairs rhabdosphere-forming capacity in both RD and RUCH2 cultures[3]. CP-673,451 inhibits PDGFR-β in PAE-β cells with an IC50 value of 6.4 nM. Besides, CP-673,451 incubation in H526 and PAE-β cells results in an IC50 value of 1.1 μM against c-kit[4].	
In Vivo	CP-673451 (20 mg/kg) leads to a medium suppression of tumor growth, while high-dose CP-673451 (40 mg/kg) strongly inhibits tumor growth in mice without significant weitht loss[1]. CP-673,451 (10, 33, and 100 mg/kg, p.o., b.i.d) inhibits the growth of Colo205 tumor in a dose-dependent manner, and similar tumor growth inhibition experiments completes on LS174T, H460, and U87MG xenografts, with no signs of morbidity or weight loss[4].	

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (239.52 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3952 mL	11.9760 mL	23.9521 mL
	5 mM	0.4790 mL	2.3952 mL	4.7904 mL
	10 mM	0.2395 mL	1.1976 mL	2.3952 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现

	用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.75 mg/mL (6.59 mM); Clear solution 此方案可获得 ≥ 2.75 mg/mL (6.59 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.75 mg/mL (6.59 mM); Clear solution 此方案可获得 ≥ 2.75 mg/mL (6.59 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。
References	[1]. Xi Y, et al. CP-673451, a platelet-derived growth-factor receptor inhibitor, suppresses lung cancer cell proliferation and migration. Onco Targets Ther. 2014 Jul 3;7:1215-21. [2]. Konotop G, et al. Pharmacological Inhibition of Centrosome Clustering by Slingshot-Mediated Cofilin Activation and Actin Cortex Destabilization. Cancer Res. 2016 Nov 15;76(22):6690-6700. [3]. Ehnman M, et al. Distinct effects of ligand-induced PDGFRα and PDGFRβ signaling in the human rhabdomyosarcoma tumor cell and stroma cell compartments. Cancer Res, 2013, 73(7), 2139-2149. [4]. Roberts WG, et al. Antiangiogenic and antitumor activity of a selective PDGFR tyrosine kinase inhibitor, CP-673,451. Cancer Res, 2005, 65(3), 957-966.

实验参考：

Cell Assay	Cell proliferation/viability is analyzed using the CyQuant proliferation assay. Pre-starved cells are treated every 24 hours with vehicle (dimethyl sulfoxide) or 0.5 μM CP-673,451 diluted in serum-reduced medium (1.5 % FBS) for 96 hours. The amount of nucleic acid present in lysed cells is normalized to the amount when treatment is initiated. Cell proliferation/viability in response to 300 ng/mL PDGF-CC is likewise analyzed, but cells are then kept in serum-free medium and treated twice during a 48-hour period. [3]
Animal Administration	A subcutaneous A549 xenograft model in nude mice is used to evaluate the anticancer activity of CP-673451. Briefly, A549 cells are injected into the axillary regions of mice (2×10^6 cells/mouse). When the tumor volumes reach 70 mm^3, the mice are randomly assigned to a control group and two CP-673451 groups (n=6 per group): low-dose (20 mg/kg) and high dose (40 mg/kg) groups (vehicle 10% 1-methyl-2-pyrrolidinone and 90% polyethylene glycol 300). These animals are administered intraperitoneally with CP-673451 (20 or 40 mg/kg/day) or with vehicle. During the treatment period, the implanted tumors are measured by caliper once a day in a blind fashion. The animal body weights are also measured at the same time. The tumor volume is calculated. After treatment, the mice are killed, and the tumors are harvested and analyzed. [1]
References	[1]. Xi Y, et al. CP-673451, a platelet-derived growth-factor receptor inhibitor, suppresses lung cancer cell proliferation and migration. Onco Targets Ther. 2014 Jul 3;7:1215-21. [2]. Konotop G, et al. Pharmacological Inhibition of Centrosome Clustering by Slingshot-Mediated Cofilin Activation and Actin Cortex Destabilization. Cancer Res. 2016 Nov 15;76(22):6690-6700. [3]. Ehnman M, et al. Distinct effects of ligand-induced PDGFRα and PDGFRβ signaling in the

	human rhabdomyosarcoma tumor cell and stroma cell compartments. Cancer Res, 2013, 73(7), 2139-2149. [4]. Roberts WG, et al. Antiangiogenic and antitumor activity of a selective PDGFR tyrosine kinase inhibitor, CP-673,451. Cancer Res, 2005, 65(3), 957-966.