产品名称：Ki8751
产品别名：Ki8751

生物活性：

Description	Ki8751 is a potent VEGFR2 inhibitor with an IC50 of 0.9 nM.
IC_{50} & Target	VEGFR2
	0.9 nM (IC_{50})
In Vitro	Ki8751 inhibits VEGFR-2 phosphorylation at an IC50 value of 0.90 nM, and also inhibits the PDGFR family members such as PDGFRR and c-Kit at 67 nM and 40 nM, respectively. However, Ki8751 does not have any inhibitory activity against other kinases such as EGFR, HGFR, InsulinR and others even at 10000 nM. Ki8751 suppresses the growth of the VEGF-stimulated human umbilical vein endothelial cell (HUVEC) on a nanomolar level[1].
In Vivo	Ki8751 shows significant antitumor activity against five human tumor xenografts such as GL07 (glioma), St-4 (stomach carcinoma), LC6 (lung carcinoma), DLD-1 (colon carcinoma) and A375 (melanoma) in nude mice and also shows complete tumor growth inhibition with the LC-6 xenograft in nude rats following oral administration once a day for 14 days at 5 mg/kg without any body weight loss[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 92 mg/mL (195.99 mM)** **H2O : < 0.1 mg/mL (insoluble)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1303 mL	10.6517 mL	21.3033 mL
5 mM	0.4261 mL	2.1303 mL	4.2607 mL
10 mM	0.2130 mL	1.0652 mL	2.1303 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: 2.5 mg/mL (5.33 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.33 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 25.0 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: 2.5 mg/mL (5.33 mM); Suspended solution; Need ultrasonic

	此方案可获得 2.5 mg/mL (5.33 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.33 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.33 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Kubo K, et al. Novel potent orally active selective VEGFR-2 tyrosine kinase inhibitors: synthesis, structure-activity relationships, and antitumor activities of N-phenyl-N'-{4-(4-quinolyloxy)phenyl}ureas. J Med Chem, 2005, 48(5), 1359-1366.

实验参考：

Cell Assay	HUVECs are placed at a density of 4000 cells/200 μL/well on collagene type I precoated 96-well plates in M199 medium with 5% fetal bovine serum (FBS). After 24 h, the cells are incubated for 1 h in the presence or absence of Ki8751; then the cells are stimulated by rhVEGF (20 ng/mL). The cultures are incubated at 37 °C for 72 h, then pulsed with 1 μCi/well [3H]thymidine and reincubated for 14 h. Cells are assayed for the incorporation of tritium using a beta counter[1].
Animal Administration	Mice: The effects of Ki8751 on tumor growth is tested against various tumors, human stomach carcinoma (St-4), human lung carcinoma (LC-6), human colon carcinoma (DLD-1) and human melanoma (A375), using human tumor xenografts in nude mice. Ki8751 is administered orally to mice in the experimental groups once a day for 9 consecutive days at 5 mg/kg, and the vehicle is administered to control animals. Tumor volumes are monitored twice weekly[1].
Kinase Assay	VEGFR-2 kinase assay is described below; GST-fusion proteins of KDR (Flk-1: cytoplasmic domain) are produced in the baculo-virus expression system. GST-KDR is premixed with a serial dilution of Ki8751 in the kinase buffer. The kinase reaction is initiated by the addition of 2 μM ATP in a solution of MnCl2. After 20 min incubation at room temperature, the reaction is stopped with an addition of EDTA. Phosphorylation levels of GST-KDR are detected by immunoblotting with anti-phosphotyrosine monoclonal antibodies (PY20) and detected by ECL fluorography[1].
References	[1]. Kubo K, et al. Novel potent orally active selective VEGFR-2 tyrosine kinase inhibitors: synthesis, structure-activity relationships, and antitumor activities of N-phenyl-N'-{4-(4-quinolyloxy)phenyl}ureas. J Med Chem, 2005, 48(5), 1359-1366.