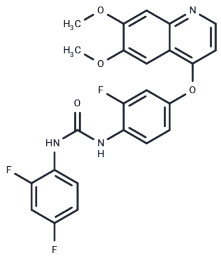
Data Sheet (Cat.No.T2446)

TargetMol

KI8751

Chemical Properties



CAS No. : 228559-41-9

Formula: C24H18F3N3O4

Molecular Weight: 469.41

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	KI8751 is a potent and selective inhibitor of VEGFR2 with IC50 of 0.9 nM.
Targets(IC50)	EGFR,FGFR,c-Kit,PDGFR,VEGFR
In vitro	In human umbilical vein endothelial cells (HUVECs), Ki8751 (1 nM-100 nM) effectively reduced VEGF-stimulated cell proliferation and vascular permeability. In metastatic colorectal cancer (CRC) cells MIP, RKO, SW620 and SW480, Ki8751 (10 nM) increased cellular senescence, but not in HCT116.Ki8751 potently and selectively inhibited VEGFR-2 with an IC50 of 0.9 nM.Ki8751 also inhibited PDGFRα, c-Kit and FGFR-2 with higher IC50. Ki8751 also inhibits PDGFRα, c-Kit and FGFR-2, with higher IC50 values of 40 nM-170 nM.
In vivo	In human umbilical vein endothelial cells (HUVECs), Ki8751 (1 nM-100 nM) effectively reduced VEGF-stimulated cell proliferation and vascular permeability. In metastatic colorectal cancer (CRC) cells MIP, RKO, SW620 and SW480, Ki8751 (10 nM) increased cellular senescence, but not in HCT116.Ki8751 potently and selectively inhibited VEGFR-2 with an IC50 of 0.9 nM.Ki8751 also inhibited PDGFRα, c-Kit and FGFR-2 with higher IC50. Ki8751 also inhibits PDGFRα, c-Kit and FGFR-2, with higher IC50 values of 40 nM-170 nM.
Kinase Assay	Cellular Kinase Assays: NIH3T3 cells prepared by transfection of human KDR. The cells are cultured in a collagen type I coated 96-well plate in an amount of 1.5 × 104 per well. The medium is then replaced by a DMEM medium containing 0.1% FCS. Ki8751 diluted in DMSO is added to each well and cultured. rhVEGF is added to a final concentration of 100 ng/mL, and the stimulation of cells is carried out at 37 °C. The cells are washed with PBS (pH 7.4), 50 μL of a solubilization buffer (20 mM HEPES (pH 7.4), 150 mM NaCl, 0.2% Triton X-100, 10% glycerol, 5 mM Na3VO4, 5 mM disodium ethylenediamine tetraacetate, and 2 mM Na4P2O7) is then added and a cell extract is prepared. Separately, PBS (50 μL, pH 7.4) containing 5 μg/mL of antiphosphotyrosine antibody (PY20) is added to a microplate for ELISA. After washing of the plate, 300 μL of a blocking solution is added. The cell extract is transferred to the plate. An anti-VEGFR2 antibody and a peroxidase-labeled anti-rabbit Ig antibody are added. Next, a chromophoric substrate for peroxidase is added, and the absorbance at 450 nm is measured with microplate reader. The VEGFR2 phosphorylation activity for each well is determined by presuming the absorbance with the addition of VEGF and without the addition of the test sample to be 100% VEGFR2 phosphorylation activity and VEGF to be 0% VEGFR2 phosphorylation activity. The concentration of the inhibition (%) of VEGFR2 Phosphorylation is determined for each case, and IC50 value is calculated.

Cell Research	To evaluate the inhibition of VEGF-Stimulated HUVEC proliferation by Ki8751, HUVECs are plated at a density of 4000 cells/200 μL/well in a type I collagen pre-coated 96-well plates. After 24 hours, the cells are incubated for 1 hour with Ki8751 and then stimulated with 20 ng/mL rhVEGF. The cultures are incubated at 37 °C for 72 hours, then pulsed with 1 μCi/well [3H]thymidine and re-incubated for 14 hours. Cells are assayed for the incorporation of tritium using a beta counter. (Only for Reference)

Solubility Information

Solubility	DMSO: 14 mg/mL (29.82 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1303 mL	10.6517 mL	21.3033 mL
5 mM	0.4261 mL	2.1303 mL	4.2607 mL
10 mM	0.213 mL	1.0652 mL	2.1303 mL
50 mM	0.0426 mL	0.213 mL	0.4261 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Kubo K, et al. J Med Chem, 2005, 48(5), 1359-1366.
Tamura D, et al. Cancer Sci, 2010, 101(6), 1403-1408.
Hasan MR, et al. Int J Cancer, 2011, 129(9), 2115-2123.