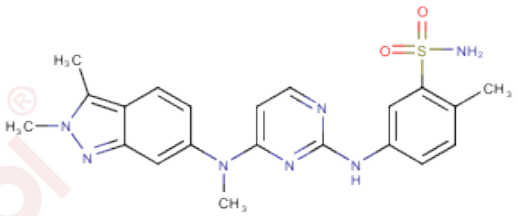
Data Sheet (Cat.No.T0097L)

TargetMol®
A DRUG SCREENING EXPERT

Pazopanib

Chemical Properties



CAS No. : 444731-52-6

Formula: C21H23N7O2S

Molecular Weight: 437.52

Appearance: no data available

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

Biological Description

Description	Pazopanib (GW786034), a small molecule inhibitor, inhibits multiple protein tyrosine kinases with potential antineoplastic activity. Pazopanib selectively inhibits VEGFR-1, -2 and -3, c-kit and PDGF-R, which may result in inhibition of angiogenesis in tumors in which these receptors are upregulated.
Targets(IC50)	VEGFR,FGFR,PDGFR,c-Kit,Autophagy
In vitro	Mice demonstrated good tolerance to Pazopanib treatment without any noticeable weight differences across all groups. When compared to those treated with low doses (vehicle or 10 mg/kg Pazopanib), mice in the high-dose groups (30 mg/kg or 100 mg/kg Pazopanib) exhibited a significant reduction in tumor burden.
In vivo	In all synovial sarcoma cell lines, including SYO-1 and HS-SY-II, Pazopanib exhibited dose-dependent inhibitory effects on growth. At a concentration of 1μg/ml, Pazopanib suppressed the proliferation of SYO-1 and HS-SY-II cells, achieving complete inhibition at 5μg/ml. Pazopanib effectively inhibited VEGFR2 phosphorylation (IC50: 8 nM) in VEGF-induced HUVEC cells. The growth of synovial sarcoma cells was hindered by Pazopanib due to the induction of G1 phase arrest. Unlike cells treated with the control vector, Pazopanib treatment resulted in the suppression of phosphorylation of Akt, GSK-3β, JNKs, p70 S6 kinase, and mTOR in SYO-1 cells. When Pazopanib concentration was increased between 20 mg/ml and 22.5 mg/ml, a consequent reduction in RPE cell viability was observed.
Kinase Assay	VEGFR enzyme assays for VEGGR1, VEGFR2, and VEGFR3 are run in homogeneous time-resolved fluorescence (HTRF) format in 384-well microtiter plates using a purified, baculovirus-expressed glutathione-S-transferase (GST) fusion protein encoding the catalytic c-terminus of human VEGFR receptor kinases 1, 2, or 3. Reactions are initiated by the addition of 10 μL of activated VEGFR2 kinase solution [final concentration, 1 nM enzyme in 0.1 M 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), pH 7.5, containing 0.1 mg/mL bovine serum albumin (BSA), 300 μM dithiothreitol (DTT)] to 10 μL substrate solution [final concentration, 360 nM peptide, (biotin-aminohexyl-EEEEYFELVAKKKK-NH2), 75 μM ATP, 10 μM MgCl2], and 1 μL of titrated compound in DMSO. Plates are incubated at room temperature for 60 min, and then the reaction is quenched by the addition of 20 μL of 100 mM ethylene diamine tetraacetic acid (EDTA). After quenching, 20 μL HTRF reagents (final concentration, 15 nM Streptavidin-linked allophycocyanin, 1 nM Europium-labeled antiphosphotyrosine antibody diluted in 0.1 mg/mL BSA, 0.1 M HEPES, pH 7.5) is added and the plates incubated for a minimum of

	10 min. The fluorescence at 665 nM is measured with a Wallac Victor plate reader using a time delay of 50 μs[1].
Cell Research	Pazopanib is prepared in DMSO and then diluted to final concentration in medium[1]. The effect of Pazopanib on cell proliferation is measured using 5-bromo-2-deoxyuridine (BrdU) incorporation method using commercially available kits. HUVEC is seeded in medium containing 5% fetal bovine serum (FBS) in type 1 collagen coated 96-well plates and incubated overnight at 37°C, 5% CO2. The medium is aspirated from the cells, and various concentrations of Pazopanib in serum-free medium are added to each well. After 30 min, either VEGF (10 ng/mL) or bFGF (0.3 ng/mL) is added to the wells. Cells are incubated for an additional 72 h and BrdU (10 μM) is added during the last 18 to 24 h of incubation. At the end of incubation, BrdU incorporation in cells is measured by ELISA. Data are fitted with a curve described by the equation, y=Vmax(1?(x/(K+x))), where K is equal to the IC50[1].

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 81 mg/mL (185.1 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2856 mL	11.428 mL	22.8561 mL
5 mM	0.4571 mL	2.2856 mL	4.5712 mL
10 mM	0.2286 mL	1.1428 mL	2.2856 mL
50 mM	0.0457 mL	0.2286 mL	0.4571 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

Harris PA, et al. J Med Chem. 2008, 51(15), 4632-4640.
Hosaka S, et al. J Orthop Res. 2012.

Tel:781-999-4286 E_mail:info@targetmol.com Address:36 Washington Street,Wellesley Hills,MA 02481