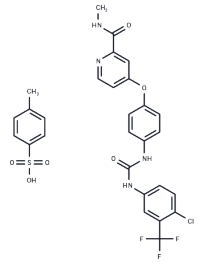
Data Sheet (Cat.No.T0093)

TargetMol

Sorafenib tosylate

Chemical Properties



CAS No. : 475207-59-1

Formula: C21H16ClF3N4O3·C7H8O3S

Molecular Weight: 637.03

Appearance: no data available

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

Biological Description

Description	Sorafenib tosylate (Bay 43-9006) is a potent multikinase inhibitor (IC50s: 6/20/22 nM for Raf-1/VEGFR-3/B-Raf).
Targets(IC50)	Apoptosis,Raf,FLT,Ferroptosis,Autophagy,c-Kit,PDGFR,VEGFR
In vitro	Besides Raf-1, Sorafenib also inhibits VEGFR-3 (IC50: 20 nM), BRAF wt (IC50: 22 nM), B-RAF V599E (IC50: 38 nM), VEGFR-2 (IC50: 90 nM), PDGFR-β (IC50: 57 nM), c-KIT (IC50: 68 nM), and Flt3 (IC50: 58 nM) in biochemical assays [1]. Sorafenib-induced phosphorylation of c-Met, p70S6K and 4EBP1 is significantly reduced when 10-0505 cells are co-treated with anti-human anti-HGF antibody, suggesting that treatment with Sorafenib leads to increased HGF secretion and activation of c-Met and mTOR targets [2].
In vivo	Sorafenib Tosylate, administered orally at doses of 10, 30, 50, and 100 mg/kg, dose-dependently inhibits the growth of 06-0606 and 10-0505 xenograft tumors, with significant efficacy (P<0.01). Particularly, in mice, Sorafenib at 50/100 mg/kg reduces the mass of 06-0606 tumors to about 13% and 5% of untreated controls, respectively. A 50 mg dose significantly curtails tumor expansion in the 5-1318, 26-1004, and 10-0505 lines (P<0.01). With this dose, the T/C ratio—an indicator of treatment effectiveness comparing the median weights of Sorafenib-treated and control tumors—significantly declines in these xenograft models, showcasing Sorafenib's potent anti-tumor activity. Furthermore, Sorafenib improves survival rates and markedly reduces the liver index (a measure of liver enlargement) in a model of liver damage induced by Diethylnitrosamine (DENA), demonstrating enhanced survival and liver condition in treated groups compared to both DENA-exposed and normal controls.
Kinase Assay	Recombinant baculoviruses expressing Raf-1 (residues 305–648) and B-Raf (residues 409–765) are purified as fusion proteins. Full-length human MEK-1 is generated by PCR and purified as a fusion protein from Escherichia coli lysates. Sorafenib tosylate is added to a mixture of Raf-1 (80 ng), or B-Raf (80 ng) with MEK-1 (1 μg) in assay buffer [20 mM Tris (pH 8.2), 100 mM NaCl, 5 mM MgCl2, and 0.15% β-mercaptoethanol] at a final concentration of 1% DMSO. The Raf kinase assay (final volume of 50 μL) is initiated by adding 25 μL of 10 μM γ[33P]ATP (400 Ci/mol) and incubated at 32 °C for 25 minutes. Phosphorylated MEK-1 is harvested by filtration onto a phosphocellulose mat, and 1% phosphoric acid is used to wash away unbound radioactivity. After drying by microwave heating, a β-plate counter is used to quantify filter-bound radioactivity. Human VEGFR2 (KDR) kinase domain is expressed and purified from Sf9 lysates. Time-resolved

	fluorescence energy transfer assays for VEGFR2 are performed in 96-well opaque plates in the time-resolved fluorescence energy transfer format. Final reaction conditions are as follows: 1 to 10 μM ATP, 25 nM poly GT-biotin, 2 nM Europium-labeled phospho (p)-Tyr antibody (PY20), 10 nM APC, 1 to 7 nM cytoplasmic kinase domain in final concentrations of 1% DMSO, 50 mM HEPES (pH 7.5), 10 mM MgCl2, 0.1 mM EDTA, 0.015% Brij-35, 0.1 mg/mL BSA, and 0.1% β-mercaptoethanol. Reaction volumes are 100 μL and are initiated by the addition of enzyme. Plates are read at both 615 and 665 nM on a Perkin-Elmer VictorV Multilabel counter at ~1.5 to 2.0 hours after reaction initiation. Signal is calculated as a ratio: (665 nm/615 nM) × 10,000 for each well. For IC50 generation, Sorafenib tosylate is added before the enzyme initiation. A 50-fold stock plate is made with Sorafenib tosylate serially diluted 1:3 in a 50% DMSO/50% distilled water solution. Final Sorafenib tosylate concentrations range from 10 μM to 4.56 nM in 1% DMSO.
Cell Research	Tumor cell lines were plated at 2 × 105 cells per well in 12-well tissue culture plates in DMEM growth media (10% heat-inactivated FCS) overnight. Cells were washed once with serum-free media and incubated in DMEM supplemented with 0.1% fatty acid-free BSA containing various concentrations of BAY 43-9006 in 0.1% DMSO for 120 minutes to measure changes in basal pMEK 1/2, pERK 1/2, or pPKB. Cells were washed with cold PBS (PBS containing 0.1 mmol/L vanadate) and lysed in a 1% (v/v) Triton X-100 solution containing protease inhibitors. Lysates were clarified by centrifugation, subjected to SDS-PAGE, transferred to nitrocellulose membranes, blocked in TBS-BSA, and probed with anti-pMEK 1/2 (Ser217/Ser221; 1:1000), anti-MEK 1/2, anti-pERK 1/2 (Thr202/Tyr204; 1:1000), anti-ERK 1/2, anti-pPKB (Ser473; 1:1000), or anti-PKB primary antibodies. Blots were developed with horseradish peroxidase (HRP)-conjugated secondary antibodies and developed with Amersham ECL reagent on Amersham Hyperfilm [1].
Animal Research	Female NCr-nu/nu mice (Taconic Farms, Germantown, NY) were used for all studies. Three to five million cells were injected s.c. into the right flank of each mouse. DLD-1 tumors were established and maintained as a serial in vivo passage of s.c. fragments (3 × 3 mm) implanted in the flank using a 12-gauge trocar. A new generation of the passage was initiated every three weeks, and studies were conducted between generations 3 and 12 of this line. Treatment was initiated when tumors in all mice in each experiment ranged in size from 75 to 144 mg for antitumor efficacy studies and from 100 to 250 mg for studies of microvessel density and ERK phosphorylation. All treatment was administered orally once daily for the duration indicated in each experiment.

Solubility Information

Solubility	DMSO: 200 mg/mL (313.96 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (7.85 mM),Solution. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.5698 mL	7.8489 mL	15.6978 mL
5 mM	0.314 mL	1.5698 mL	3.1396 mL
10 mM	0.157 mL	0.7849 mL	1.5698 mL
50 mM	0.0314 mL	0.157 mL	0.314 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

Wei JC, et al. Sorafenib inhibits proliferation and invasion of human hepatocellular carcinoma cells via up-regulation of p53 and suppressing FoxM1. Acta Pharmacol Sin. 2015 Feb;36(2):241-51.
Gao X, Jiang P, Wei X, et al.Novel fusion protein PK5-RL-Gal-3C inhibits hepatocellular carcinoma via anti-angiogenesis and cytotoxicity.BMC cancer.2023, 23(1): 1-16.
Zhang Y, et al. Sorafenib inhibited cell growth through the MEK/ERK signaling pathway in acute promyelocytic leukemia cells. Oncol Lett. 2018 Apr;15(4):5620-5626.
Tesori V, et al. The multikinase inhibitor Sorafenib enhances glycolysis and synergizes with glycolysis blockade for cancer cell killing. Sci Rep. 2015 Mar 17;5:9149.
Wilhelm SM, et al. BAY 43-9006 exhibits broad spectrum oral antitumor activity and targets the RAF/MEK/ERK pathway and receptor tyrosine kinases involved in tumor progression and angiogenesis. Cancer Res. 2004 Oct 1; 64(19):7099-109.