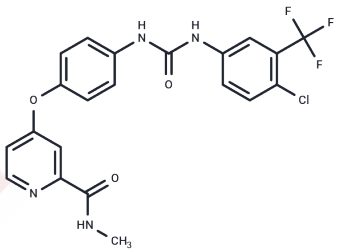
Data Sheet (Cat.No.T0093L)

TargetMol

Sorafenib

Chemical Properties



CAS No. : 284461-73-0

Formula: C21H16ClF3N4O3

Molecular Weight: 464.82

Appearance: no data available

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

Biological Description

Description	Sorafenib (Bay 43-9006) is a multikinase inhibitor that targets Raf-1, B-Raf, VEGFR2, VEGFR3, VEGFR4, PDGFRβ, FLT3, c-Kit, and others (IC50=6/22/90/15/20/20/57/58 nM) with oral activity. It exhibits antitumor properties and can induce autophagy, apoptosis, and agonistic iron death.
Targets(IC50)	Apoptosis,Raf,FLT,Ferroptosis,Autophagy,c-Kit,PDGFR,VEGFR
In vitro	**METHODS**: Human hepatocellular carcinoma cells HepG2 and HuH-7 were treated with Sorafenib (2-20 μmol/L) for 48 h, and cell growth inhibition was detected using MTT method. **RESULTS**: Sorafenib dose-dependently inhibited the growth of HepG2 and HuH-7 cells with IC50 of approximately 6 μmol/L.[1] **METHODS**: Human acute promyelocytic leukemia cells NB4 were treated with Sorafenib (1.5-12 μM) for 24-48 h. Apoptosis was detected using Flow Cytometry. **RESULTS**: Sorafenib dose-dependent apoptosis of NB4 cells, with a significant increase in the proportion of both early and late apoptotic cells. [2] **METHODS**: Rat hepatobiliary cholangiocarcinoma cells LCC-2 were treated with Sorafenib (2.5-5 μM) for 12 h. Mitochondrial membrane potential was measured using JC-1 dye. **RESULTS**: Sorafenib depolarized the isolated mitochondria. [3]
In vivo	**METHODS**: To assay antitumor activity in vivo, Sorafenib (7.5-60 mg/kg) was orally administered once daily for two to four days to NCr-nu/nu mice harboring human tumors MDA-MB-231, Colo-205, HT-29, DLD-1, NCI-H460, and A549. **RESULTS**: Sorafenib showed broad oral antitumor efficacy in various human tumor xenograft models. [4] **METHODS**: To assay antitumor activity in vivo, Sorafenib (30 mg/kg/five times per week) and everolimus (10 mg/kg/three times per week) were administered by gavage to PTEN-mutant mice bearing CRPC, a tumor of desmoplasia-resistant prostate cancer, once a day for four weeks. **RESULTS**: Sorafenib administration increased the expression of androgen receptor p-GSK3β and p-ERK1/2 in CRPC, and the combination of Sorafenib and everolimus overcame treatment escape in CRPC tumors treated with Sorafenib alone. [5]
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	H2O: < 1 mg/mL (insoluble or slightly soluble), 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5.9 mg/mL (12.69 mM),Suspension. DMF: 3.33 mg/mL (7.16 mM),Sonication is recommended. DMSO: 55 mg/mL (118.33 mM),Sonication is recommended.

Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1514 mL	10.7569 mL	21.5137 mL
5 mM	0.4303 mL	2.1514 mL	4.3027 mL
10 mM	0.2151 mL	1.0757 mL	2.1514 mL
50 mM	0.043 mL	0.2151 mL	0.4303 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 FoxMActa Pharmacol Sin. 2015 Feb;36(2):241-51.
Wang C, Huang M, Lin Y, et al.ENO2-derived phosphoenolpyruvate functions as an endogenous inhibitor of HDAC1 and confers resistance to antiangiogenic therapy.Nature Metabolism.2023: 1-22.
Feng J, Lu P, Zhu G, et al. ACSL4 is a predictive biomarker of sorafenib sensitivity in hepatocellular carcinoma. Acta Pharmacologica Sinica. 2021 Jan;42(1):160-170. doi: 10.1038/s41401-020-0439-x. Epub 2020 Jun 15.
Liu Y, Ouyang L, Mao C, et al. PCDHB14 promotes ferroptosis and is a novel tumor suppressor in hepatocellular carcinoma. Oncogene. 2022: 1-14
Xu J, Su Z, Cheng X, et al. High PPT1 expression predicts poor clinical outcome and PPT1 inhibitor DC661 enhances sorafenib sensitivity in hepatocellular carcinoma. Cancer Cell International. 2022, 22(1): 1-20.
Ma A, Biersack B, Goehringer N, et al. Novel Thienyl-Based Tyrosine Kinase Inhibitors for the Treatment of Hepatocellular Carcinoma. Journal of Personalized Medicine. 2022, 12(5): 738
Zhou J, Feng J, Wu Y, et al. Simultaneous treatment with sorafenib and glucose restriction inhibits hepatocellular carcinoma in vitro and in vivo by impairing SIAH1-mediated mitophagy. Experimental & Molecular Medicine. 2022: 1-15.
Bai C, Sun Y, Pan X, et al. Antitumor Effects of Trimethylellagic Acid Isolated From Sanguisorba officinalis L. on Colorectal Cancer via Angiogenesis Inhibition and Apoptosis Induction. Frontiers in Pharmacology. 2020, 10: 1646
Uhrig S, Ellermann J, Walther T, et al. Accurate and efficient detection of gene fusions from RNA sequencing data. Genome Research. 2021, 31(3): 448-460
Xu S, Liu Y, Ding Y, et al. The zinc finger transcription factor, KLF2, protects against COVID-19 associated endothelial dysfunction. Signal Transduction and Targeted Therapy. 2021, 6(1): 1-9.
Feng J, Lu P, Zhu G, et al. ACSL4 is a predictive biomarker of sorafenib sensitivity in hepatocellular carcinoma. Acta Pharmacologica Sinica. 2021 Jan;42(1):160-170. doi: 10.1038/s41401-020-0439-x. Epub 2020 Jun 15.
Fang T, Lv H, Lv G, et al. Tumor-derived exosomal miR-1247-3p induces cancer-associated fibroblast activation to foster lung metastasis of liver cancer. Nature Communications. 2018, 9(1): 1-13
Sun L, Wan A H, Yan S, et al.A multidimensional platform of patient-derived tumors identifies drug susceptibilities for clinical lenvatinib resistance.Acta Pharmaceutica Sinica B.2023
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.
Liu Q, Wang J, Sun H, et al.Targeting RORγ inhibits the growth and metastasis of hepatocellular carcinoma. Molecular Therapy.2024
Dong Y, Luo J, Pei M, et al.Biomimetic Hydrogel-Mediated Mechano-Immunometabolic Therapy for Inhibition of ccRCC Recurrence After Surgery.Advanced Science.2024: 2308734.
Breitenecker K, Hedrich V, Pupp F, et al.Synergism of the receptor tyrosine kinase Axl with ErbB receptors mediates resistance to regorafenib in hepatocellular carcinoma.Frontiers in Oncology.2023, 13: 1238883.
Viperino A, Höpfner M, Edel N, et al.Identification of a New Pentafluorosulfanyl-Substituted Chalcone with Activity Against Hepatoma and Human Parasites.Pharmaceuticals.2025, 18(1): 50.
An effective two-stage NMBzA-induced rat esophageal tumor model revealing that the FAT-Hippo-YAP1 axis drives the progression of ESCC
Wang X, Ji Y, Qi J, et al.Mitochondrial carrier 1 (MTCH1) governs ferroptosis by triggering the FoxO1-GPX4 axis-mediated retrograde signaling in cervical cancer cells.Cell Death & Disease.2023, 14(8): 1-13.
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.
Shan X, Jiang R, Gou D, et al.Identification of a diketopiperazine-based O-GlcNAc transferase inhibitor sensitizing hepatocellular carcinoma to CDK9 inhibition.The FEBS Journal.2023
Yamamoto Y, et al. Evaluation of in vivo responses of sorafenib therapy in a preclinical mouse model of PTEN-deficient of prostate cancer. J Transl Med. 2015 May 8;13:150.
Liu M, Shi C, Song Q, et al.Sorafenib induces ferroptosis by promoting TRIM54-mediated FSP1 ubiquitination and

degradation in hepatocellular carcinoma.Hepatology Communications.2023, 7(10).
Ni H, Ruan G, Sun C, et al. Tanshinone IIA inhibits gastric cancer cell stemness through inducing ferroptosis. Environmental Toxicology. 2021
Li Z, Dai H, Huang X, et al. Artesunate synergizes with sorafenib to induce ferroptosis in hepatocellular carcinoma [J]. Acta Pharmacologica Sinica. 2020: 1-10.
Uhrig S, Ellermann J, Walther T, et al. Accurate and efficient detection of gene fusions from RNA sequencing data[J]. Genome Research. 2021
Wang H, Cui Y, Gong H, et al. Suppression of AGTR1 Induces Cellular Senescence in Hepatocellular Carcinoma Through Inactivating ERK Signaling. Frontiers in Bioengineering and Biotechnology. 2022, 10.
Li Z, Dai H, Huang X, et al. Artesunate synergizes with sorafenib to induce ferroptosis in hepatocellular carcinoma. Acta Pharmacologica Sinica. 2020: 1-10
Fang, Tian, et al. Tumor-derived exosomal miR-1247-3p induces cancer-associated fibroblast activation to foster lung metastasis of liver cancer. Nature communications. 2018 Jan 15;9(1):191.
Zhang H, Xu H, Tang Q, et al. The selective serotonin reuptake inhibitors enhance the cytotoxicity of sorafenib in hepatocellular carcinoma cells. Anti-Cancer Drugs. 2021, 32(8): 793-801.