

Product Data Sheet

Product Name: Sorafenib

Cat. No.: GC17369

Chemical Properties

Cas. No. 284461-73-0

Chemical Name 4-[4-[[4-chloro-3-(trifluoromethyl)phenyl]carbamoylamino]phenoxy]-N-methylpyridine-2-carboxamide

SMILES CNC(=O)C1=NC=CC(=C1)OC2=CC=C(C=C2)NC(=O)NC3=CC(=C(C=C3)Cl)C(F)(F)F

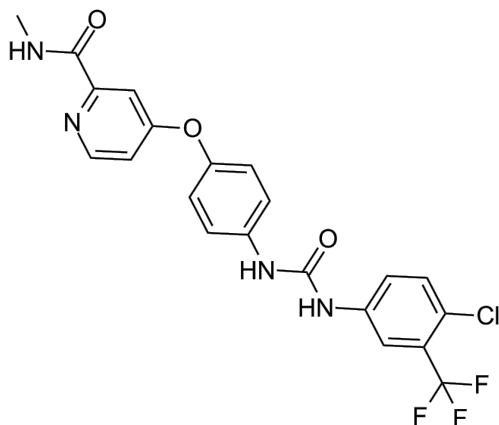
Formula $C_{21}H_{16}ClF_3N_4O_3$ M.Wt 464.82

Solubility $\geq 23.25\text{mg/mL}$ in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

***In vitro* Kinase Assays with Recombinant Raf-1, BRAF, V599E BRAF, MEK-1, and ERK1 [1]:**

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Preparation method	Test compound inhibition against various RAF kinase isoforms, sorafenib was added to a mixture of Raf-1 (80 ng), wt BRAF, or V599E BRAF (80 ng) with MEK-1 (1 µg) in assay buffer [20 mmol/L Tris (pH 8.2), 100 mmol/L NaCl, 5 mmol/L MgCl₂, and 0.15% β-mercaptoethanol] at a final concentration of 1% DMSO. The RAF kinase assay (final volume of 50 µL) was initiated by adding 25 µL of 10 µmol/L γ-[³³P]ATP (400 Ci/mol) and incubated at 32°C for 25 minutes. Phosphorylated MEK-1 was harvested by filtration onto a phosphocellulose mat, and 1% phosphoric acid was used to wash away unbound radioactivity. After drying by microwave heating, a β-plate counter was used to quantify filter-bound radioactivity.
Applications	Sorafenib inhibited Raf-1 with <i>IC</i>₅₀ of 6nM; Sorafenib inhibited B-Raf activity of wild type and V599E mutant with <i>IC</i>₅₀ of 22 nM and 38 nM, respectively; Sorafenib has no activity against ERK-1, MEK-1.
Cell experiment [2]:	
Cell lines	HSC-T6 cells
Preparation method	Cells were seeded into 96-well plates. When the cell density reached 70%, different concentrations of sorafenib were added, and equal amounts of DMSO without drug were exposed to the control group for 24 h.
Reaction Conditions	5-40µM; 24 h

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Applications	HSC-T6 cell viability was dose-dependently inhibited by sorafenib at concentrations ranging from 5 to 40 μ M.
Animal experiment [2]:	
Animal models	Male C57BL/6 mice (6-8 weeks)
Preparation method	Mice were randomly divided into five groups (n=6 per group) including the vehicle group, CCl ₄ -treated group, CCl ₄ + sorafenib (2.5, 5, 10 mg/kg)-treated groups. The groups treated with CCl ₄ , CCl ₄ + sorafenib were subjected intraperitoneal injections of olive oil with 10% CCl ₄ for 8 weeks to induce liver fibrosis. The vehicle group was subjected intraperitoneal injections of the same dose of olive oil. After 4 weeks, each mouse in the groups treated with CCl ₄ + sorafenib was orally administered sorafenib daily. The vehicle group and the CCl ₄ -treated group were orally administered the same dose of saline daily.
Dosage form	2.5, 5, 10 mg/kg; i.p; twice a week for 8 weeks
Applications	Sorafenib attenuated liver injury and ECM accumulation in CCl ₄ -induced fibrotic livers.

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[1]. Wilhelm SM, Carter C, 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. doi: 10.1158/0008-5472.CAN-04-1443. PMID: 15466206.

[2]. Yuan S, Wei C, et.al. Sorafenib attenuates liver fibrosis by triggering hepatic stellate cell ferroptosis via HIF-1 α /SLC7A11 pathway. Cell Prolif. 2022 Jan;55(1):e13158. doi: 10.1111/cpr.13158. Epub 2021 Nov 22. PMID: 34811833; PMCID: PMC8780895.

Background

Sorafenib acts as a multi-kinase inhibitor, targeting Raf-1 and B-Raf with IC_{50} values of 6 nM and 22 nM, respectively. Additionally, Sorafenib demonstrates inhibitory effects on VEGFR-2, VEGFR-3, PDGFR- β , Flt-3, and c-KIT, displaying corresponding IC_{50} values of 90 nM, 20 nM, 57 nM, 59 nM, and 68 nM. Beyond these kinase activities, Sorafenib is capable of inducing autophagy and apoptosis while triggering ferroptosis activation, resulting in its notable antitumor efficacy [1-3].

Sorafenib(5-40 μ M; 24 h) had a dose-dependent inhibitory effect on HSC-T6 cells viability [4]. Sorafenib(25mM;0-42h) alters the lipid composition in Huh7.5 cells[5].

Sorafenib(2.5, 5, 10 mg/kg; i.p; twice a week for 8 weeks) attenuated liver injury and extracellular matrix (ECM) accumulation in CCl₄ -induced fibrotic livers, accompanied by reduction of SLC7A11 and GPX4 proteins[4]. Treatment with erastin and sorafenib(10 mg/kg; i.p; once every other day) alleviated liver fibrosis in mice by inducing hepatic stellate cells(HSCs) ferroptosis in mice[6].The synergism of sorafenib and T cells is mediated via reduced ATF4 expression, causing activation of the IRF7-IL-15 axis in leukemia cells and thereby leading to metabolic reprogramming of leukemia-reactive T cells in humans[7].

References:

[1]. Abdelgalil AA, Alkahtani HM, et.al.Sorafenib. Profiles Drug Subst Excip Relat Methodol. 2019;44:239-266. doi: 10.1016/bs.podrm.2018.11.003. Epub 2019 Jan 18. PMID: 31029219.

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[3]. Xia S, Pan Y, et.al.The microenvironmental and metabolic aspects of sorafenib resistance in hepatocellular carcinoma. EBioMedicine. 2020 Jan;51:102610. doi: 10.1016/j.ebiom.2019.102610. Epub 2020 Jan 6. PMID: 31918403; PMCID: PMC7000339.

[4]. Yuan S, Wei C, et.al. Sorafenib attenuates liver fibrosis by triggering hepatic stellate cell ferroptosis via HIF-1 α /SLC7A11 pathway. Cell Prolif. 2022 Jan;55(1):e13158. doi: 10.1111/cpr.13158. Epub 2021 Nov 22. PMID: 34811833; PMCID: PMC8780895.

[5]. Liu G, Kuang S, et.al.Sorafenib kills liver cancer cells by disrupting SCD1-mediated synthesis of monounsaturated fatty acids via the ATP-AMPK-mTOR-SREBP1 signaling pathway. FASEB J. 2019 Sep;33(9):10089-10103. doi: 10.1096/fj.201802619RR. Epub 2019 Jun 14. PMID: 31199678.

[6]. Zhang Z, Guo M, et.al. RNA-binding protein ZFP36/TTP protects against ferroptosis by regulating autophagy signaling pathway in hepatic stellate cells. Autophagy. 2020 Aug;16(8):1482-1505. doi: 10.1080/15548627.2019.1687985. Epub 2019 Nov 11. PMID: 31679460; PMCID: PMC7469536.

[7]. Mathew NR, Baumgartner F, et.al. Sorafenib promotes graft-versus-leukemia activity in mice and humans through IL-15 production in FLT3-ITD-mutant leukemia cells. Nat Med. 2018 Mar;24(3):282-291. doi: 10.1038/nm.4484. Epub 2018 Feb 12. Erratum in: Nat Med. 2018 Apr 10;24(4):526. PMID: 29431743; PMCID: PMC6029618.

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