SZABO SCANDIC

Part of Europa Biosite

Produktinformation

- Forschungsprodukte & Biochemikalien
- Zellkultur & Verbrauchsmaterial
- Diagnostik & molekulare Diagnostik
- Laborgeräte & Service

Weitere Information auf den folgenden Seiten!
See the following pages for more information!

Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

SZABO-SCANDIC HandelsgmbH

Quellenstraße 110, A-1100 Wien

T. +43(0)1 489 3961-0

F. +43(0)1 489 3961-7

mail@szabo-scandic.com

www.szabo-scandic.com

linkedin.com/company/szaboscandic

Sorafenib

Cat. No.: HY-10201

CAS No.: 284461-73-0

Molecular Formula: $C_{21}H_{16}ClF_3N_4O_3$

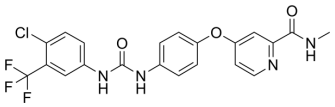
Molecular Weight: 464.83

Target: Raf; VEGFR; FLT3; Autophagy; Apoptosis; Ferroptosis

Pathway: MAPK/ERK Pathway; Protein Tyrosine Kinase/RTK; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 45 mg/mL (96.81 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1513 mL	10.7566 mL	21.5132 mL
	5 mM	0.4303 mL	2.1513 mL	4.3026 mL
	10 mM	0.2151 mL	1.0757 mL	2.1513 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 2% DMSO >> 40% PEG300 >> 5% Tween-80 >> 53% saline
   Solubility: 4 mg/mL (8.61 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.08 mg/mL (4.47 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.47 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sorafenib (Bay 43-9006) is a potent and orally active Raf inhibitor with IC_{50}s of 6 nM and 20 nM for Raf-1 and B-Raf, respectively. Sorafenib is a multikinase inhibitor with IC_{50}s of 90 nM, 15 nM, 20 nM, 57 nM and 58 nM for VEGFR2, VEGFR3, PDGFRβ, FLT3 and c-Kit, respectively. Sorafenib induces autophagy and apoptosis. Sorafenib has anti-tumor activity. Sorafenib is a ferroptosis activator[1].

IC_{50} & Target				
	VEGFR3 20 nM (IC_{50})	Braf 22 nM (IC_{50})	Raf-1 6 nM (IC_{50})	VEGFR2 90 nM (IC_{50})
	PDGFRβ 57 nM (IC_{50})	$Braf^{V599E}$ 38 nM (IC_{50})	c-Kit 68 nM (IC_{50})	Flt3 58 nM (IC_{50})

In Vitro

Sorafenib (BAY 43-9006) also inhibits $BRAF^{wt}$ (IC_{50}=22 nM), $BRAF^{V599E}$ (IC_{50}=38 nM), VEGFR-2 (IC_{50}=90 nM), VEGFR-3 (IC_{50}=20 nM), PDGFR-β (IC_{50}=57 nM), c-KIT (IC_{50}=68 nM), and Flt3 (IC_{50}=58 nM) in biochemical assays. In MDA-MB-231 breast cancer cells, Sorafenib completely blocks activation of the MAPK pathway. Cells are preincubated with Sorafenib (0.01 to 3 μM), and dose-dependent inhibition of basal MEK 1/2 and ERK 1/2 phosphorylation (IC_{50}, 40 and 100 nM, respectively)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Sorafenib demonstrates broad oral antitumor efficacy in panel of human tumor xenograft models. Sorafenib is given orally at 7.5 to 60 mg/kg. There is no lethality and no increase in weight loss in any treated group relative to the corresponding control group. Daily oral administration of Sorafenib (30 to 60 mg/kg) produces complete tumor stasis during treatment in five of the six models[1]. The survival rate is 73.3 % in Diethyl nitrosamine (DENA) group and 83.3 % in Sorafenib group compared to 100 % in the normal control group. DENA group shows a significant increase in liver index (1.51-fold increase, $p<0.05$) compared to normal control group, while treatment with Sorafenib shows significant decrease ($p<0.05$) in liver index when compared to DENA group. The liver index in Sorafenib group significantly decreases to lower than its value in the normal control[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

To test compound inhibition against various RAF kinase isoforms, Sorafenib is 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 mM Tris (pH 8.2), 100 mM NaCl, 5 mM $MgCl_2$, 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-[^{33}P]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[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

The MDA-MB-231 human mammary adenocarcinoma cell lines are plated at 2×10^5 cells per well in 12-well tissue culture plates in DMEM growth media (10% heat-inactivated FCS) overnight. Cells are 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 (0.01, 0.03 , 0.1, 0.3, 1, 3 μM) in 0.1% DMSO for 120 minutes to measure changes in basal pMEK 1/2, pERK 1/2, or pPKB. Cells are washed with cold PBS (PBS containing 0.1 mM vanadate) and lysed in a 1% (v/v) Triton X-100 solution containing protease inhibitors. Lysates are clarified by centrifugation, subjected to SDS-PAGE, transferred to nitrocellulose membranes, blocked in TBS-BSA, and probed with anti-pMEK 1/2 (Ser^{217}/Ser^{221}; 1:1000), anti-MEK 1/2, anti-pERK 1/2 (Thr^{202}/Tyr^{204}; 1:1000), anti-ERK 1/2, anti-pPKB (Ser^{473}; 1:1000), or anti-PKB primary antibodies. Blots are developed with horseradish peroxidase (HRP)-conjugated secondary antibodies and developed with Amersham ECL reagent on Amersham Hyperfilm[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [1][2]

Mice[1]

Female NCr-nu/nu mice are used. Mice bearing 75 to 150 mg tumors are treated orally with Sorafenib (7.5 to 60 mg/kg), administered daily for 9 days. In each model, Sorafenib produces dose-dependent tumor growth inhibition with no evidence of toxicity, as measured by increased weight loss relative to control animals or drug-related lethality. In parallel to the antitumor efficacy studies, additional groups of four mice bearing 100 to 200 mg tumors are treated orally with vehicle or Sorafenib (30 to 60 mg/kg), administered daily for 5 days, which is the shortest treatment duration producing complete tumor stasis in the treated groups.

Rats[2]

In the study, 100- to 120-g male albino rats are utilized. After acclimatization period, rats are weighed and randomly divided

into three groups: Group 1 (normal control group; n=10) is given the vehicle daily for 8 weeks. Group 2 (DENA group; n=15) receive i.p. single dose of 200 mg/kg DENA. Group 3 (Sorafenib group; n=12) is given Sorafenib orally at a dose of 10 mg/kg daily for 2 weeks, 6 weeks after DENA i.p. injection. At the end of the experiment (8 weeks), rats are weighed, anesthetized by ether, and killed, and their livers are dissected. Fresh liver is washed twice with ice-cold saline, dried on clean paper towel, and weighed. Liver index is calculated as liver weight (g)/final body weight (g)×100. The liver is divided into five portions: one portion is preserved in 10 % formalin for histopathological examination and the other portions are immediately frozen in liquid nitrogen and stored at −80°C.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2023 Sep 14;8(1):348.
- Cell Discov. 2022 May 3;8(1):40.
- Cell Metab. 2021 Sep 8;S1550-4131(21)00375-2.
- Cancer Discov. 2019 Dec;9(12):1686-1695.
- ACS Nano. 2023 Nov 15.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. 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.

[2]. El-Ashmawy NE, et al. Sorafenib effect on liver neoplastic changes in rats: more than a kinase inhibitor. Clin Exp Med. 2016 Apr 16.

[3]. Jin W, et al. Long non-coding RNA TUC338 is functionally involved in sorafenib-sensitized hepatocarcinoma cells by targeting RASAL1. Oncol Rep. 2017 Jan;37(1):273-280.

[4]. Li M, et al. Activation of an AKT/FOXM1/STMN1 pathway drives resistance to tyrosine kinase inhibitors in lung cancer. Br J Cancer. 2017 Aug 29.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA