Sunitinib Malate

Cat. No.: HY-10255

CAS No.: 341031-54-7

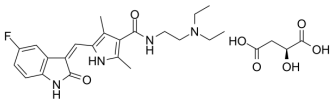
Molecular Formula: $C_{26}H_{33}FN_4O_7$

Molecular Weight: 532.56

Target: PDGFR; VEGFR; IRE1; Mitophagy; Autophagy; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Cell Cycle/DNA Damage; Autophagy; Apoptosis

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 15 mg/mL (28.17 mM)
H_2O : 12.5 mg/mL (23.47 mM; ultrasonic and adjust pH to 3 with HCl)
H_2O : 3.33 mg/mL (6.25 mM; ultrasonic and warming and heat to 60°C)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8777 mL	9.3886 mL	18.7772 mL
5 mM	0.3755 mL	1.8777 mL	3.7554 mL
10 mM	0.1878 mL	0.9389 mL	1.8777 mL

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

In Vivo

1. Add each solvent one by one: 100 mM citrate buffer
   Solubility: 10 mg/mL (18.78 mM); Suspended solution; Need ultrasonic and adjust pH to 5 with HCl
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sunitinib Malate (SU 11248 Malate) is a multi-targeted receptor tyrosine kinase inhibitor with IC_{50}s of 80 nM and 2 nM for VEGFR2 and PDGFRβ, respectively[1]. Sunitinib Malate, an ATP-competitive inhibitor, effectively inhibits autophosphorylation of Ire1α by inhibiting autophosphorylation and consequent RNase activation[2].

IC_{50} & Target	VEGFR2 80 nM (IC_{50})	PDGFRβ 2 nM (IC_{50})

In Vitro

Sunitinib Malate is also a good inhibitor of KIT and FLT-3[1]. In RS4;11 cells (FLT3-WT), treatment with Sunitinib (SU11248) inhibits FLT3-WT phosphorylation in a dose-dependent manner with IC_{50} of approximately 250 nM. In MV4;11 cells that express FLT3-ITD, Sunitinib inhibits FLT3-ITD phosphorylation in a dose-dependent manner with an IC_{50} of 50 nM following a 2-hour treatment[3].In biochemical assays, Sunitinib (SU11248) exhibits competitive inhibition (with regard to ATP) against Flk-1 and PDGFRβ with K_i values of 9 nM and 8 nM, respectively. Sunitinib is also a competitive, albeit less potent, inhibitor of FGFR1 tyrosine kinase activity, with a K_i value of 0.83 μM. In addition to these three structurally related split kinase domain RTKs, the activity of Sunitinib has also been evaluated against a broad panel of additional tyrosine and serine/threonine kinases. In these biochemical assays, the IC_{50} values for Sunitinib are generally at least 10-fold higher than those for Flk-1 and PDGFR (e.g., IC_{50}values of: >10 μM for EGFR and Cdk2; 4 μM for Met; 2.4 μM for IGFR-1; 0.8 μM for Abl; and 0.6 μM for Src) [4].

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

In Vivo

Sunitinib Malate has very good oral bioavailability, is highly efficacious in a number of preclinical tumor models, and is well tolerated at efficacious doses[1]. Sunitinib (80 mg/kg/day) inhibits the growth of established SF763T and Colo205 tumor xenografts in athymic mice. Sunitinib (SU11248) treatment effectively inhibits the growth of established tumor xenografts[4].

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

PROTOCOL

Kinase Assay [2]

Biochemical assays to determine the activity of Sunitinib against different protein kinases are performed. K_i values for SU11248 against Flk-1, PDGFRβ, and FGFR1 are determined using glutathione S-transferase-fusion proteins containing the complete cytoplasmic domain of the RTK. Cellular assays to directly determine the ability of SU11248 to inhibit ligand-dependent RTK phosphorylation or cell proliferation and mitogenic responses are performed using serum-starved cells stimulated with 40 ng/mL $VEGF_{165}$ (Flk-1/KDR), 0.5 μg/mL basic FGF (FGFR), or 50 ng/mL PDGF-AA (PDGFRα) or PDGF-BB (PDGFRβ)[2].

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

Cell Assay [3]

RS4;11 and MV4;11 cell lines are starved overnight in medium containing 0.1% FBS prior to addition of SU11248 (1 nM, 5 nM, 10 nM, 25 nM, 75 nM, 100 nM, 250 nM, 500 nM) and FL (50 ng/mL; FLT3-WT cells only). Proliferation is measured after 48 hours of culture using the Alamar Blue assay in triplicate for each condition, as described by the manufacturer. Trypan blue cell viability assays are performed in parallel and yielded similar results[3].

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

Animal Administration [2][4]

Mice[2]

Female nu/nu mice (8-12 weeks old, 25 g) are used. Briefly, $3\text{-}5\times10^6$ tumor cells are implanted s.c. into the hind flank region of mice on day 0. Daily treatment of tumor-bearing mice with oral administration of SU11248 as a carboxymethyl cellulose suspension or as a citrate buffered (pH 3.5) solution is initiated once the tumors reached the indicated average size. Tumor growth is evaluated based on twice-weekly measurement of tumor volume. Typically, studies are terminated when tumors in vehicle-treated animals reach an average size of 1000 mm^3 or when the tumors are judged to adversely effect the well being of the animals.

Rats[4]

Forty female Sprague-Dawley rats (200-230 g) are used. Each group consists of 5-10 animals fed ad libitum. 1×10^4 Walker 256 cells are injected into the left abdominal mammary fat pad, under gas anesthesia (2% isoflurane). Rats are weighed daily and given Sunitinib malate (30 mg/kg) and/or Fingolimod (5 mg/kg) in olive oil by gavage. The tumors are measured with calipers. The animals are anesthetized and killed by an intracardiac injection of ketamine (50 mg/mL) before tumor ulceration. Rats are dissected to detect pulmonary, liver, kidney, or intestinal metastasis.

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

CUSTOMER VALIDATION

- Cell Metab. 2021 Sep 8;S1550-4131(21)00375-2.
- Nat Biomed Eng. 2018 Aug;2(8):578-588.
- Blood. 2019 Oct 17;134(16):1323-1336.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Theranostics. 2021 Mar 12;11(11):5387-5403.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Sun L, et al. Discovery of 5-[5-fluoro-2-oxo-1,2- dihydroindol-(3Z)-ylidenemethyl]-2,4- dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide, a novel tyrosine kinase inhibitor targeting vascular endothelial and platelet-derived growth factor r

[2]. Ali MM, et al. Structure of the Ire1 autophosphorylation complex and implications for the unfolded protein response. EMBO J. 2011 Mar 2;30(5):894-905.

[3]. O'Farrell AM, et al. SU11248 is a novel FLT3 tyrosine kinase inhibitor with potent activity in vitro and in vivo. Blood. 2003 May 1;101(9):3597-605.

[4]. Mendel DB, et al. In vivo antitumor activity of SU11248, a novel tyrosine kinase inhibitor targeting vascular endothelial growth factor and platelet-derived growth factor receptors: determination of a pharmacokinetic/pharmacodynamic relationship. Clin Can

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