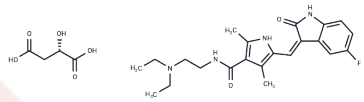
Data Sheet (Cat.No.T0374)

TargetMol

Sunitinib Malate

Chemical Properties



CAS No. : 341031-54-7

Formula: C26H33FN4O7

Molecular Weight: 532.56

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Sunitinib Malate (Sunitinib) is an indolinone-based tyrosine kinase inhibitor. It blocks the tyrosine kinase activities of VEGFR2, PDGFRβ (IC50: 80/2 nM), and c-kit.
Targets(IC50)	Apoptosis,Mitophagy,FLT,Autophagy,c-Kit,IRE1,PDGFR,VEGFR
In vitro	Sunitinib is also a good inhibitor of KIT and FLT-3 [1]. In biochemical assays, Sunitinib exhibits competitive inhibition (with regard to ATP) against Flk-1 and PDGFRβ with Ki values of 9 nM and 8 nM, respectively. Sunitinib is also a competitive, albeit less potent, an inhibitor of FGFR1 tyrosine kinase activity, with a Ki value of 0.83 μM. In these biochemical assays, the IC50 values for Sunitinib are generally at least 10-fold higher than those for Flk-1 and PDGFR (e.g., IC50s: >10 μM for EGFR and Cdk2; 4 μM for Met; 2.4 μM for IGFR-1; 0.8 μM for Abl; 0.6 μM for Src) [2]. In RS4;11 cells (FLT3-WT), treatment with Sunitinib inhibits FLT3-WT phosphorylation in a dose-dependent manner with IC50 of approximately 250 nM. In MV4;11 cells that express FLT3-ITD, Sunitinib inhibits FLT3-ITD phosphorylation in a dose-dependent manner with an IC50 of 50 nM following a 2-hour treatment [3].
In vivo	Sunitinib (80 mg/kg/day) inhibits the growth of established SF763T and Colo205 tumor xenografts in athymic mice. Sunitinib treatment effectively inhibits the growth of established tumor xenografts[2]. Sunitinib malate is an inhibitor of VEGFR, PDGFR, FGFR, and is used in the treatment of advanced renal cell carcinoma and gastrointestinal stromal tumors. Sunitinib malate-treated rats display much lower levels of tumor growth than untreated rats, and their tumors have much smaller necrotic areas and lower vascular density [4]
Kinase Assay	Ki values for Sunitinib 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 Sunitinib to inhibit ligand-dependent RTK phosphorylation or cell proliferation and mitogenic responses are performed using serum-starved cells stimulated with 40 ng/mL VEGF165 (Flk-1/KDR), 0.5 μg/mL basic FGF (FGFR), or 50 ng/mL PDGF-AA (PDGFRα) or PDGF-BB (PDGFRβ) [2].
Cell Research	RS4;11 and MV4;11 cell lines are starved overnight in medium containing 0.1% FBS prior to addition of Sunitinib (1-500 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].

Animal Research	Female nu/nu mice (8-12 weeks old, 25 g) are used. Briefly, 3-5×106 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 citrate buffered (pH 3.5) solution is initiated once the tumors reached the indicated average size. Tumor growth is evaluated based on the twice-weekly measurement of tumor volume. Typically, studies are terminated when tumors in vehicle-treated animals reach an average size of 1000 mm3 or when the tumors are judged to adversely affect the well being of the animals [2].

Solubility Information

Solubility	H2O: 10 mg/mL (18.78 mM),Sonication is recommended. DMSO: 15.47 mg/mL (29.05 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (1.88 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0376 mL	0.1878 mL	0.3755 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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 receptor tyrosine kinase. J Med Chem. 2003 Mar 27;46(7):1116-9.
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 Cancer Res. 2003 Jan;9(1):327-37.
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.
Mousseau Y, et al. Fingolimod potentiates the effects of sunitinib malate in a rat breast cancer model. Breast Cancer Res Treat. 2012 Jul;134(1):31-40.

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