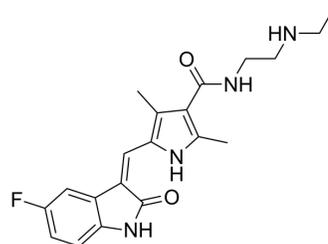


N-Desethyl Sunitinib

Cat. No.:	HY-10873		
CAS No.:	356068-97-8		
Molecular Formula:	C ₂₀ H ₂₃ FN ₄ O ₂		
Molecular Weight:	370.42		
Target:	Drug Metabolite		
Pathway:	Metabolic Enzyme/Protease		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 6.25 mg/mL (16.87 mM; ultrasonic and warming and heat to 60°C)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.6996 mL	13.4982 mL	26.9964 mL
	5 mM	0.5399 mL	2.6996 mL	5.3993 mL
	10 mM	0.2700 mL	1.3498 mL	2.6996 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (6.75 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 0.62 mg/mL (1.67 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: 0.62 mg/mL (1.67 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

N-Desethyl Sunitinib (SU-12662) is a metabolite of sunitinib. Sunitinib is a potent, ATP-competitive VEGFR, PDGFRβ and KIT inhibitor with K_i values of 2, 9, 17, 8 and 4 nM for VEGFR -1, -2, -3, PDGFRβ and KIT, respectively^[1].

In Vitro

Sunitinib also potently inhibits Kit and FLT-3^[1]. Sunitinib is a potent ATP-competitive inhibitor of VEGFR2 (Flk1) and PDGFRβ with K_i of 9 nM and 8 nM, respectively, displaying >10-fold higher selectivity for VEGFR2 and PDGFR than FGFR-1, EGFR, Cdk2, Met, IGF-1, Abl, and src. In serum-starved NIH-3T3 cells expressing VEGFR2 or PDGFRβ, Sunitinib inhibits VEGF-dependent VEGFR2 phosphorylation and PDGF-dependent PDGFRβ phosphorylation with IC₅₀ of 10 nM and 10 nM, respectively.

Sunitinib inhibits VEGF-induced proliferation of serum-starved HUVECs with IC_{50} of 40 nM, and inhibits PDGF-induced proliferation of NIH-3T3 cells overexpressing PDGFR β or PDGFR α with IC_{50} of 39 nM and 69 nM, respectively^[2]. Sunitinib inhibits phosphorylation of wild-type FLT3, FLT3-ITD, and FLT3-Asp835 with IC_{50} of 250 nM, 50 nM, and 30 nM, respectively. Sunitinib inhibits the proliferation of MV4;11 and OC1-AML5 cells with IC_{50} of 8 nM and 14 nM, respectively, and induces apoptosis in a dose-dependent manner^[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Sunitinib (20-80 mg/kg/day) exhibits broad and potent dose-dependent anti-tumor activity against a variety of tumor xenograft models including HT-29, A431, Colo205, H-460, SF763T, C6, A375, or MDA-MB-435, consistent with the substantial and selective inhibition of VEGFR2 or PDGFR phosphorylation and signaling in vivo. Sunitinib (80 mg/kg/day) for 21 days leads to complete tumor regression in six of eight mice, without tumor re-growing during a 110-day observation period after the end of treatment. Second round of treatment with Sunitinib remains efficacious against tumors that are not fully regressed during the first round of treatment. Sunitinib treatment results in significant decrease in tumor MVD, with approx 40% reduction in SF763T glioma tumors. SU11248 treatment results in a complete inhibition of additional tumor growth of luciferase-expressing PC-3M xenografts, despite no reduction in tumor size^[2]. Sunitinib treatment (20 mg/kg/day) dramatically suppresses the growth subcutaneous MV4;11 (FLT3-ITD) xenografts and prolongs survival in the FLT3-ITD bone marrow engraftment model^[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay ^[1]

IC_{50} values for Sunitinib against VEGFR2 (Flk-1) and PDGFR β are determined using glutathione S-transferase fusion proteins containing the complete cytoplasmic domain of the RTK. Biochemical tyrosine kinase assays to quantitate the trans-phosphorylation activity of VEGFR2 (Flk-1) and PDGFR β are performed in 96-well microtiter plates precoated (20 μ g/well in PBS; incubated overnight at 4°C) with the peptide substrate poly-Glu,Tyr (4:1). Excess protein binding sites are blocked with the addition of 1-5% (w/v) BSA in PBS. Purified GST-fusion proteins are produced in baculovirus-infected insect cells. GST-VEGFR2 and GST-PDGFR β are then added to the microtiter wells in 2 \times concentration kinase dilution buffer consisting of 100 mM HEPES, 50 mM NaCl, 40 μ M NaVO₄, and 0.02% (w/v) BSA. The final enzyme concentration for GST-VEGFR2 or GST-PDGFR β is 50 ng/mL. Twenty-five μ L of diluted sunitinib are subsequently added to each reaction well to produce a range of inhibitor concentrations appropriate for each enzyme. The kinase reaction is initiated by the addition of different concentrations of ATP in a solution of MnCl₂ so that the final ATP concentrations spanned the K_m for the enzyme, and the final concentration of MnCl₂ is 10 mM. The plates are incubated for 5-15 minutes at room temperature before stopping the reaction with the addition of EDTA. The plates are then washed three times with TBST. Rabbit polyclonal antiphosphotyrosine antisera are added to the wells at a 1:10,000 dilution in TBST containing 0.5% (w/v) BSA, 0.025% (w/v) nonfat dry milk, and 100 μ M NaVO₄ and incubated for 1 hour at 37°C. The plates are then washed three times with TBST, followed by the addition of goat antirabbit antisera conjugated with horseradish peroxidase (1:10,000 dilution in TBST). The plates are incubated for 1 hour at 37°C and then washed three times with TBST. The amount of phosphotyrosine in each well is quantitated after the addition of 2,2'-azino-di-[3-ethylbenzthiazoline sulfonate] as substrate.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay ^[3]

Cells are starved overnight in medium containing 0.1% FBS prior to addition of Sunitinib and FL (50 ng/mL; FLT3-WT cells only). Proliferation is measured after 48 hours of culture using the Alamar Blue assay or trypan blue cell viability assays. Apoptosis is measured 24 hours after Sunitinib addition by Western blotting to detect cleavage of poly (ADP-ribose) polymerase (PARP) or levels of caspase-3.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Acta Pharmacol Sin. 2016 Jul;37(7):930-40.

- Biol Pharm Bull. 2021;44(10):1565-1570.
- Biomed Chromatogr.2015 May;29(5):679-88.
- SSRN. 23 Sep 2021.

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]. 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
- [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. Epub 2003 Jan 16.
-

Caution: Product has not been fully validated for medical applications. For research use only.

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