# Product Data Sheet

Product Name: N-Desethyl Sunitinib
Cat. No.: GC36710

## Chemical Properties

| | | | |
|---|---|---|---|
| Cas. No. | 356068-97-8 | | |
| SMILES | O=C1NC2=CC=C(F)C=C2/C1=C/C3=C(C)C(C(NCCNCC)=O)=C(C)N3 | | |
| Formula | $C_{20}H_{23}FN_4O_2$ | M.Wt | 370.42 |
| Solubility | DMSO: 50 mg/mL (134.98 mM) | Storage | Store at -20°C |
| General tips | For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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 | N-Desethyl Sunitinib | | |

## Protocol

IC50 values for Sunitinib against VEGFR2 (Flk-1) and PDGFRβ 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 PDGFRβ are performed in 96-well microtiter plates precoated (20 μg/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-PDGFRβ are then added to the microtiter wells in 2× concentration kinase dilution buffer consisting of 100 mM HEPES, 50 mM NaCl, 40 μM NaVO4, and 0.02% (w/v) BSA.


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**Kinase experiment:**

The final enzyme concentration for GST-VEGFR2 or GST-PDGFRβ is 50 ng/mL. Twenty-five μL 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 $MnCl_2$ so that the final ATP concentrations spanned the Km for the enzyme, and the final concentration of $MnCl_2$ 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 μM $NaVO_4$ 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.


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**Cell experiment:**

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.


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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.

## Background

N-desethyl Sunitinib is an active metabolite of sunitinib , a small molecule, multi-targeted receptor tyrosine kinase inhibitor.[1,2] N-desethyl Sunitinib is formed when sunitinib undergoes N-de-ethylation by the cytochrome P450 (CYP) isomer CYP3A4.[2] N-desethyl Sunitinib is pharmacologically active having similar inhibitory activity to sunitinib.


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1.O'Farrell, A.M., Abrams, T.J., Yuen, H.A., et al.SU11248 is a novel FLT3 tyrosine kinase inhibitor with potent activity in vitro and in vivoBlood101(9)3597-3605(2003) 2.Yu, H., Steeghs, N., Kloth, J.S.L., et al.Integrated semi-physiological pharmacokinetic model for both sunitinib and its active metabolite SU12662Br. J. Clin. Pharmacol.79(5)809-819(2015)


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