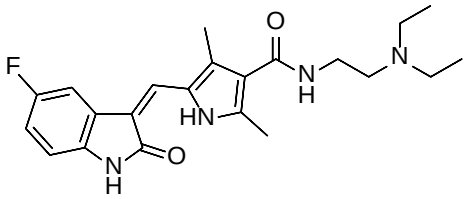
Product data sheet

MedKoo Cat#: 100791 Name: Sunitinib free base CAS#: 557795-19-4 (free base) Chemical Formula: $C_{22}H_{27}FN_4O_2$ Exact Mass: 398.2118 Molecular Weight: 398.48	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Sunitinib free base is an oral, small-molecule, multi-targeted receptor tyrosine kinase (RTK) inhibitor. Sunitinib malate salt was approved by the FDA for the treatment of renal cell carcinoma (RCC) and imatinib-resistant gastrointestinal stromal tumor (GIST) on January 26, 2006. Sunitinib inhibits cellular signaling by targeting multiple receptor tyrosine kinases (RTKs). The simultaneous inhibition of these targets therefore reduces tumor vascularization and triggers cancer cell apoptosis and thus results in tumor shrinkage. Sunitinib also inhibits CD117 (c-KIT), the receptor tyrosine kinase that (when improperly activated by mutation) drives the majority of gastrointestinal stromal cell tumors.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under “QC And Documents” section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	25.0	62.74
Ethanol	8.0	20.08

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.51 mL	12.55 mL	25.10 mL
5 mM	0.50 mL	2.51 mL	5.02 mL
10 mM	0.25 mL	1.25 mL	2.51 mL
50 mM	0.05 mL	0.25 mL	0.50 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of “Calculator”

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Li J, Abudula M, Fan X, Wang F, Chen Y, Liu L. Sunitinib induces primary ectopic endometrial cell apoptosis through up-regulation of STAT1 in vitro. J Clin Lab Anal. 2020 Nov;34(11):e23482. doi: 10.1002/jcla.23482. Epub 2020 Aug 5. PMID: 32761670; PMCID: PMC7676178.

2. Mendel DB, Laird AD, Xin X, Louie SG, Christensen JG, Li G, Schreck RE, Abrams TJ, Ngai TJ, Lee LB, Murray LJ, Carver J, Chan E, Moss KG, Haznedar JO, Sukbuntherng J, Blake RA, Sun L, Tang C, Miller T, Shirazian S, McMahon G, Cherrington JM. 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. PMID: 12538485.

In vivo study

1. Mendel DB, Laird AD, Xin X, Louie SG, Christensen JG, Li G, Schreck RE, Abrams TJ, Ngai TJ, Lee LB, Murray LJ, Carver J, Chan E, Moss KG, Haznedar JO, Sukbuntherng J, Blake RA, Sun L, Tang C, Miller T, Shirazian S, McMahon G, Cherrington JM. 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. PMID: 12538485.
2. Paech F, Abegg VF, Duthaler U, Terracciano L, Bouitbir J, Krähenbühl S. Sunitinib induces hepatocyte mitochondrial damage and apoptosis in mice. Toxicology. 2018 Nov 1;409:13-23. doi: 10.1016/j.tox.2018.07.009. Epub 2018 Jul 18. PMID: 30031043.

7. Bioactivity

Biological target: Sunitinib (SU 11248) is a tyrosine kinase inhibitor with IC50s of 80 nM and 2 nM for VEGFR2 and PDGFRβ, respectively.

In vitro activity

In order to determine the impact of sunitinib on ectopic endometrial cells, ectopic and normal endometrial cells were treated with sunitinib at appointed concentrations of 0, 1, 2, 4, 8, and 16 uM for 48 hours. The MTT assay revealed that the half maximal inhibitory concentration (IC50) of normal endometrial cells to sunitinib (IC50 = 7.9 μM) was significantly higher, when compared to ectopic endometrial cells (IC50 = 3.32 μM), suggesting that sunitinib has no effect on the normal endometrium within the therapeutic concentration range, since it is on the ectopic endometrium in vitro (Figure 2A). Then, it was measured that sunitinib reduced the cell apoptosis by nuclear-fluorescence staining. These results show that the number of apoptotic cells in the ectopic endometrial group (100x) increased with the increase in sunitinib concentration (Figure 2B). Furthermore, in order to confirm the results above, the cell apoptosis was determined by flow cytometry. The cell apoptosis rate (FITC + plus FITC+/PI+) in ectopic endometrial cells was 51.9%±8.3% and 78.8% ± 3.2% at a sunitinib concentration of 4 μM and 8 μM, respectively, and both were significantly higher than that in normal endometrial cells, with 0.2% ± 1.2% (vs ectopic endometrial cells, $P < .0001$, $t = 26.89$) and 68.1% ± 2.1% (vs ectopic endometrial cells, $P = .025$, $t = 3.49$), respectively (Figure 2C). These results demonstrate that sunitinib can affect the cell proliferation and apoptosis of ectopic endometrial cells in a dose-dependent manner.

Reference: J Clin Lab Anal. 2020 Nov;34(11):e23482. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7676178/

In vivo activity

Mice were treated orally with sunitinib (7.5 mg/kg/day) for 2 weeks. Sunitinib did not affect body weight, but increased plasma ALT activity 6-fold. Protein and mRNA expression of several subunits of mitochondrial enzyme complexes were decreased in mitochondria from sunitinib-treated mice. Protein expression of PGC-1α, citrate synthase activity and mtDNA copy number were all decreased in livers of sunitinib-treated mice, indicating impaired mitochondrial proliferation. Caspase 3 activation and TUNEL-positive hepatocytes were increased in livers of sunitinib-treated mice, indicating hepatocyte apoptosis. In conclusion, sunitinib caused concentration-dependent toxicity in isolated mitochondria at concentrations reached in livers in vivo and inhibited hepatic mitochondrial proliferation. Daily mitochondrial insults and impaired mitochondrial proliferation most likely explain hepatocellular injury observed in mice treated with sunitinib.

Reference: Toxicology. 2018 Nov 1;409:13-23.
https://www.sciencedirect.com/science/article/abs/pii/S0300483X18301574?via%3Dihub