Sunitinib

Cat. No.: HY-10255A
CAS No.: 557795-19-4
Molecular Formula: C₂₂H₂₇FN₄O₂
Molecular Weight: 398.47
Target: VEGFR; PDGFR; IRE1; Mitophagy; Autophagy; Apoptosis
Pathway: Protein Tyrosine Kinase/RTK; Cell Cycle/DNA Damage; Autophagy; Apoptosis
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: 25 mg/mL (62.74 mM; Need ultrasonic and warming)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.5096 mL</td>
<td>12.5480 mL</td>
<td>25.0960 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5019 mL</td>
<td>2.5096 mL</td>
<td>5.0192 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2510 mL</td>
<td>1.2548 mL</td>
<td>2.5096 mL</td>
</tr>
</tbody>
</table>

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.11 mg/mL (2.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.11 mg/mL (2.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Sunitinib (SU 11248) is a multi-targeted receptor tyrosine kinase inhibitor with IC₅₀s of 80 nM and 2 nM for VEGFR2 and PDGFRβ, respectively[1]. Sunitinib, an ATP-competitive inhibitor, effectively inhibits autophosphorylation of Ire1α by inhibiting autophosphorylation and consequent RNase activation[2].

IC₅₀ & Target

<table>
<thead>
<tr>
<th>Target</th>
<th>IC₅₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEGFR2</td>
<td>80 nM (IC₅₀)</td>
</tr>
<tr>
<td>PDGFRβ</td>
<td>2 nM (IC₅₀)</td>
</tr>
</tbody>
</table>

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 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
In biochemical assays, Sunitinib (SU11248) 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, inhibitor of FGFR1 tyrosine kinase activity, with a Ki 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 IC50 values for Sunitinib are generally at least 10-fold higher than those for Flk-1 and PDGFR (e.g., IC50 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).

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

Cell Assay [3]

RS4;11 and MV4;11 cell lines are starved overnight in medium containing 0.1% FBS prior to addition of Sunitinib (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 grams) 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 Sunitinib 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 mm³ or when the tumors are judged to adversely effect the well being of the animals.

Rats[4]

Adult male Wistar rats (325-349 g) are used. To validate the ability of the time-lapse imaging method to evaluate the anti-angiogenic effects for a given drug treatment, two drug studies are conducted. In the first study, mesenteric windows are harvested from adult male Wistar rats and cultured for 3 days according to the two experimental groups: 1) 10% serum (n=8 tissues from 4 rats), and 2) 10% serum+Sunitinib (5 μM; n=8 tissues from 4 rats).

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

REFERENCES

- EMBO J. 2021 Apr 28;e106771.

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