Sorafenib

Cat. No.: HY-10201
CAS No.: 284461-73-0
Molecular Formula: C₂₁H₁₆ClF₃N₄O₃
Molecular Weight: 464.83
Target: Raf; VEGFR; FLT3; Ferroptosis; Apoptosis; Autophagy
Pathway: MAPK/ERK Pathway; Protein Tyrosine Kinase/RTK; Apoptosis; Autophagy
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: ≥ 45 mg/mL (96.81 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass</th>
<th>Preparing Stock Solutions</th>
<th>Concentration</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mg</td>
<td></td>
<td>1 mM</td>
<td>2.1513 mL</td>
</tr>
<tr>
<td></td>
<td>5 mg</td>
<td></td>
<td>5 mM</td>
<td>0.4303 mL</td>
</tr>
<tr>
<td></td>
<td>10 mg</td>
<td></td>
<td>10 mM</td>
<td>0.2151 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: ≥ 2.5 mg/mL (5.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sorafenib (Bay 43-9006) is a potent, orally active multikinase inhibitor with IC₅₀s of 6 nM, 20 nM, and 22 nM for Raf-1, B-Raf, and VEGFR-3, respectively.

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEGFR3</td>
<td>20 nM (IC₅₀)</td>
</tr>
<tr>
<td>Braf</td>
<td>22 nM (IC₅₀)</td>
</tr>
<tr>
<td>Raf-1</td>
<td>6 nM (IC₅₀)</td>
</tr>
<tr>
<td>VEGFR2</td>
<td>90 nM (IC₅₀)</td>
</tr>
<tr>
<td>Kinase Assay [1]</td>
<td>To test compound inhibition against various RAF kinase isoforms, Sorafenib is added to a mixture of Raf-1 (80 ng), wt BRAF, or V599E BRAF (80 ng) with MEK-1 (1 μg) in assay buffer [20 mM Tris (pH 8.2), 100 mM NaCl, 5 mM MgCl₂, and 0.15% β-mercaptoethanol] at a final concentration of 1% DMSO. The RAF kinase assay (final volume of 50 μL) is initiated by adding 25 μL of 10 μM γ-[³²P]ATP (400 Ci/mol) and incubated at 32°C for 25 minutes. Phosphorylated MEK-1 is harvested by filtration onto a phosphocellulose mat, and 1% phosphoric acid is used to wash away unbound radioactivity. After drying by microwave heating, a β-plate counter is used to quantify filter-bound radioactivity [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</td>
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<td>---</td>
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<tr>
<td>Cell Assay [1]</td>
<td>The MDA-MB-231 human mammary adenocarcinoma cell lines are plated at 2×10⁵ cells per well in 12-well tissue culture plates in DMEM growth media (10% heat-inactivated FCS) overnight. Cells are washed once with serum-free media and incubated in DMEM supplemented with 0.1% fatty acid-free BSA containing various concentrations of BAY 43-9006 (0.01, 0.03, 0.1, 0.3, 1, 3 μM) in 0.1% DMSO for 120 minutes to measure changes in basal pMEK 1/2, pERK 1/2, or pPKB. Cells are washed with cold PBS (PBS containing 0.1 mM vanadate) and lysed in a 1% (v/v) Triton X-100 solution containing protease inhibitors. Lysates are clarified by centrifugation, subjected to SDS-PAGE, transferred to nitrocellulose membranes, blocked in TBS-BSA, and probed with anti-pMEK 1/2 (Ser²¹⁷/Ser²²¹; 1:1000), anti-MEK 1/2, anti-pERK 1/2 (Thr²⁰²/Tyr²⁰⁴; 1:1000), anti-ERK 1/2, anti-pPKB (Ser⁴⁷³; 1:1000), or anti-PKB primary antibodies. Blots are developed with horseradish peroxidase (HRP)-conjugated secondary antibodies and developed with Amersham ECL reagent on Amersham Hyperfilm [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</td>
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<tr>
<td>Animal Administration [1][2]</td>
<td>Mice [1] Female NCI-nu/nu mice are used. Mice bearing 75 to 150 mg tumors are treated orally with Sorafenib (7.5 to 60 mg/kg), administered daily for 9 days. In each model, Sorafenib produces dose-dependent tumor growth inhibition with no evidence of toxicity, as measured by increased weight loss relative to control animals or drug-related lethality. In parallel to the antitumor efficacy studies, additional groups of four mice bearing 100 to 200 mg tumors are treated orally with vehicle or Sorafenib (30 to 60 mg/kg), administered daily for 5 days, which is the shortest treatment duration producing complete tumor stasis in the treated groups. Rats [2] In the study, 100- to 120-g male albino rats are utilized. After acclimatization period, rats are weighed and randomly</td>
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</tbody>
</table>
divided into three groups: Group 1 (normal control group; n=10) is given the vehicle daily for 8 weeks. Group 2 (DENA group; n=15) receive i.p. single dose of 200 mg/kg DENA. Group 3 (Sorafenib group; n=12) is given Sorafenib orally at a dose of 10 mg/kg daily for 2 weeks, 6 weeks after DENA i.p. injection. At the end of the experiment (8 weeks), rats are weighed, anesthetized by ether, and killed, and their livers are dissected. Fresh liver is washed twice with ice-cold saline, dried on clean paper towel, and weighed. Liver index is calculated as liver weight (g)/final body weight (g)×100. The liver is divided into five portions: one portion is preserved in 10 % formalin for histopathological examination and the other portions are immediately frozen in liquid nitrogen and stored at −80°C.

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**REFERENCES**


