BIBF 1120

Cat. No.: HY-50904
CAS No.: 656247-17-5
Molecular Formula: C₃₁H₃₃N₅O₄
Molecular Weight: 539.62
Target: PDGFR; VEGFR; FGFR
Pathway: Protein Tyrosine Kinase/RTK
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 : 20 mg/mL (37.06 mM; Need ultrasonic and warming)
H₂O : < 0.1 mg/mL (insoluble)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>1.8532 mL</td>
<td>9.2658 mL</td>
<td>18.5316 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.3706 mL</td>
<td>1.8532 mL</td>
<td>3.7063 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.1853 mL</td>
<td>0.9266 mL</td>
<td>1.8532 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 >> 90% corn oil
   Solubility: ≥ 2 mg/mL (3.71 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2 mg/mL (3.71 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description
BIBF 1120 is a potent triple angiokinase inhibitor for VEGFR1/2/3, FGFR1/2/3 and PDGFRα/β with IC₅₀s of 34 nM/13 nM/13 nM, 69 nM/37 nM/108 nM and 59 nM/65 nM, respectively.

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>VEGFR1</th>
<th>VEGFR2</th>
<th>VEGFR3</th>
<th>FGFR1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>34 nM (IC₅₀)</td>
<td>13 nM (IC₅₀)</td>
<td>13 nM (IC₅₀)</td>
<td>69 nM (IC₅₀)</td>
</tr>
<tr>
<td>FGFR2</td>
<td>37 nM (IC₅₀)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FGFR3</td>
<td>108 nM (IC₅₀)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDGFRα</td>
<td>59 nM (IC₅₀)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDGFRβ</td>
<td>65 nM (IC₅₀)</td>
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</tbody>
</table>
**In Vitro**

BIBF 1120 binds to the ATP-binding site in the cleft between the amino and carboxy terminal lobes of the kinase domain. BIBF 1120 inhibits proliferation of PDGF-BB stimulated BRPs with EC\(_{50}\) of 79 nM in cell assays. BIBF1120 (100 nM) blocks activation of MAPK after stimulation with 5% serum plus PDGF-BB. BIBF1120 prevents PDGF-BB stimulated proliferation with an EC\(_{50}\) of 69 nM in cultures of human vascular smooth muscle cells (HUASMC)\(^1\).

**In Vivo**

BIBF1120 (25-100 mg/kg daily p.o.) is highly active in all tumor models, including human tumor xenografts growing in nude mice and a syngeneic rat tumor model. This is evident in the magnetic resonance imaging of tumor perfusion after 3 days, reducing vessel density and vessel integrity after 5 days, and profound growth inhibition\(^1\). BIBF1120 is orally available and displays encouraging efficacy in in vivo tumor models while being well tolerated\(^2\).

### PROTOCOL

**Kinase Assay** \(^2\)

Enzyme activity is assayed in the presence or absence of serial dilutions of BIBF1120 performed in 25% DMSO. Each microtiter plate contains internal controls such as blank, maximum reaction, and historical reference compound. All incubations are conducted at room temperature on a rotation shaker. 10 \(\mu\)L of each BIBF1120 dilution is added to 10 \(\mu\)L of diluted kinase (0.8 \(\mu\)g/mL VEGFR2, 10 mM Tris pH 7.5, 2 mM EDTA, and 2 mg/mL BSA) and preincubated for 1 hour. The reaction is started by addition of 30 \(\mu\)L of substrate mix containing 62.4 mM Tris pH 7.5, 2.7 mM DTT, 5.3 mM MnCl\(_2\), 13.3 mM Mg-acetate, 0.42 mM ATP, 0.83 mg/mL Poly-Glu-Tyr(4:1), and 1.7 \(\mu\)g/mL Poly-Glu-Tyr(4:1)-biotin and incubated for 1 hour. The reaction is stopped by addition of 50 \(\mu\)L of 250 mM EDTA, 20 mM HEPES, pH 7.4. 90 \(\mu\)L of the reaction mix is transferred to a streptavidin plate and incubated for 1-2 hours. After three washes with PBS, the EU-labeled antibody, PY20 is added (recommended dilution 1:2000 of 0.5 mg/mL labeled antibody in DELFIA assay buffer). Excessive detection antibody is removed by three ishes of DELFIA washing buffer. Then 10 minutes before measurement on the multilabel reader, each well is incubated with 100 \(\mu\)L of DELFIA enhancement solution.

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

**Animal Administration** \(^1\)

Five-week-old to 6-wk-old athymic NMRI-nu/nu female mice (21-31 g) are used for the assay. After acclimatization, mice are inoculated with 1 to 5\(\times\)10\(^6\) (in 100 \(\mu\)L) FaDu, Caki-1, SKOV-3, H460, HT-29, or PAC-120 cells s.c. into the right flank of the animal. After acclimatization, F344 Fischer rats are injected with 5\(\times\)10\(^5\) (in 100 \(\mu\)L) GS-9L cells s.c. into the right flank of the animal. For pharmacokinetic analysis, blood is isolated at indicated time points from the retroorbital plexus of mice and plasma is analyzed using high performance liquid chromatography-mass spectrometry methodology.

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### CUSTOMER VALIDATION

- J Photochem Photobiol B. 2016 Feb 5;157:70-76.
- Harvard Medical School LINCS LIBRARY

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### REFERENCES
