AT7519

Cat. No.: HY-50940
CAS No.: 844442-38-2
Molecular Formula: C₁₆H₁₇Cl₂N₅O₂
Molecular Weight: 382.24
Target: CDK; Apoptosis
Pathway: Cell Cycle/DNA Damage; 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 : ≥ 50 mg/mL (130.81 mM)
* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>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>2.6162 mL</td>
<td>13.0808 mL</td>
<td>26.1616 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.5232 mL</td>
<td>2.6162 mL</td>
<td>5.2323 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2616 mL</td>
<td>1.3081 mL</td>
<td>2.6162 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 (6.54 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.54 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
AT7519 as a potent inhibitor of CDKs, with IC₅₀s of 210, 47, 100, 13, 170, and <10 nM for CDK1, CDK2, CDK4 to CDK6, and CDK9, respectively.

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>CDK9/Cyclin T</th>
<th>CDK5/p35</th>
<th>cdk2/cyclin A</th>
<th>Cdk4/cyclin D1</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 nM (IC₅₀)</td>
<td>13 nM (IC₅₀)</td>
<td>47 nM (IC₅₀)</td>
<td>100 nM (IC₅₀)</td>
<td></td>
</tr>
</tbody>
</table>
In Vitro

AT7519 (0-4 μM) results in dose-dependent cytotoxicity with IC\textsubscript{50}s ranging from 0.5 to 2 μM in MM cells, and this induced cytotoxicity is associated with GSK-3β activation independent of transcriptional inhibition. AT7519 overcomes proliferative advantage conferred by cytokines and the protective effect of BMSC. AT7519 (0.5 μM) induces apoptosis of MM cells in a time-dependent manner. Moreover, AT7519 (0.5 μM) inhibits phosphorylation of RNA polymerase II CTD and partially inhibits RNA synthesis in MM.1S cells\textsuperscript{[1]}. AT7519 (250 nM) inhibits cell cycle progression in human tumor cell lines. AT7519 also induces apoptosis of human tumor cell lines\textsuperscript{[2]}. AT7519 (100-700 nM) induces apoptosis in leukemia cell lines. AT7519 also inhibits transcription in human tumor cell lines. Furthermore, AT7519 inhibits RNA polymerase II and reduces antiapoptotic protein levels\textsuperscript{[3]}.

AT7519 inhibits tumor growth in a human MM xenograft mouse model\textsuperscript{[1]}. AT7519 (4.6 and 9.1 mg/kg/dose) inhibits the growth of early-stage HCT116 tumor xenografts. AT7519 (10 mg/kg, i.p.) also inhibits the target CDKs in HCT116 tumor-bearing BALB/c nude mice\textsuperscript{[2]}. AT7519 inhibits tumor growth in a human MM xenograft mouse model\textsuperscript{[1]}.

AT7519 (4.6 and 9.1 mg/kg/dose) inhibits the growth of early-stage HCT116 tumor xenografts. AT7519 (10 mg/kg, i.p.) also inhibits the target CDKs in HCT116 tumor-bearing BALB/c nude mice\textsuperscript{[2]}.

AT7519's effects on viability of MM cell lines, primary MM cells, and PBMCs is assessed by measuring 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrasodium bromide (MTT) dye absorbance. DNA synthesis is measured by tritiated thymidine uptake (3H-TdR). MM cells (2-3 × 10\textsuperscript{4} cells/well) are incubated in 96-well culture plates with media and different concentrations of AT7519 and/or recombinant IL-6 (10 ng/mL) or IGF-1 (50 ng/mL) for 24 or 48 h at 37°C and 3H-TdR incorporation is measured.

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

Animal Administration\textsuperscript{[1]}

To evaluate the in vivo anti-MM activity of AT7519, male SCID mice are inoculated subcutaneously with 5×10\textsuperscript{6} MM.1S cells in 100 μL serum-free RPMI 1640 medium. When tumors are measurable, mice are treated intraperitoneally (IP) with vehicle or AT7519 dissolved in saline 0.9%. The first group of 10 mice is treated with 15 mg/kg once a day for five days for 2 weeks, and the second group is treated with 15 mg/kg once a day three times a week for four consecutive weeks. The control group receives the carrier alone at the same schedule. Tumor size is measured every alternate day in 2 dimensions using calipers, and tumor volume is calculated with the formula: \( V = 0.5 \times a \times b^2 \) (\( a = \) long diameter of the tumor, \( b = \) short diameter of the tumor). Animals are sacrificed when the tumor reaches 2 cm\textsuperscript{3} or when the tumor is ulcerated. Survival and tumor growth are evaluated from the first day of treatment until death.

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

REFERENCES

- Harvard Medical School LINCS LIBRARY
- Harvard Medical School LINCS LIBRARY

See more customer validations on www.MedChemExpress.com
