SB-743921

Cat. No.: HY-12069
CAS No.: 940929-33-9
Molecular Formula: C₃₁H₃₄Cl₂N₂O₃
Molecular Weight: 553.52
Target: Kinesin
Pathway: Cell Cycle/DNA Damage; Cytoskeleton
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: ≥ 100 mg/mL (180.66 mM)
* “≥” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>1.8066 mL</td>
<td>9.0331 mL</td>
<td>18.0662 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.3613 mL</td>
<td>1.8066 mL</td>
<td>3.6132 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.1807 mL</td>
<td>0.9033 mL</td>
<td>1.8066 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% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
SB-743921 is a potent inhibitor of the mitotic kinesin KSP (Eg5), with a Kᵢ of 0.1 nM.

IC₅₀ & Target
- Eg5
- 0.1 nM (Ki)
In Vitro

SB-743921 is a potent inhibitor of Eg5, with a $K_i$ of 0.1 nM\(^1\). SB-743921 (1 nM) potently inhibits colony forming cell (CFC) formation of chronic myeloid leukemia (CML) primary cells, but exhibits slight inhibitory activities on the colony-forming ability of normal bone marrow progenitors. SB-743921 (1, 3 nM) induces apoptosis of CML primary CD34 + cells, and shows slight effect on normal CD34 + cells. SB-743921 (2 nM) in combination with imatinib displays additive anti-proliferative effect in KCL22 and CML CD34 + cells. Furthermore, SB-743921 overcomes imatinib resistance in CML cells. SB-743921 (0.5 nM, 1 nM, 3 nM) inhibits MEK/ERK and AKT signaling in CML cells\(^2\).

In Vivo

SB-743921 has good oral bioavailability and pharmacokinetics and induces complete tumor regression in nude mice bearing lung cancer patient xenografts\(^3\).

PROTOCOL

Cell Assay \(^2\)

K562 and KCL22 cells are seeded in six-well plates at a number of $5 \times 10^5$ in 2 mL RPMI-1640 medium supplemented with 10% FBS in a 5% CO\(_2\) atmosphere at 37°C, and are treated with control (2% DMSO), 50 nM imatinib, 2 nM SB-743921 and 50 nM imatinib + 2 nM SB-743921, respectively. Cell number and viability are determined every 24 h. Results are plotted for live cells against time to generate a growth curve\(^2\).

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

Animal Administration \(^3\)

The animal experiments are performed with female NMRI nu/nu mice. Tumor fragments are obtained from xenografts in serial passage in nude mice. Mice are randomized to the various groups, and dosing is started when the required number of mice carries a tumor of 50-250 mm\(^3\) volume, preferably 80-200 mm\(^3\). Vehicle for 1: 10% ethanol, 10% cremophor, 80% D5W (dextrose 5%); vehicle for all other compounds (including SB-743921): 8% DMSO, 2% Tween 80, distilled water (pH 5). All treatments are given intraperitoneally. Vehicle control mice (group 1) are treated with 10 mL/kg vehicle on days 0, 3, 6, 8, 10, 13, 20, 22, 24, 29, 31, 34, 36, 38, 48, 51, 55, 58, 62, 65, and 69\(^3\).

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

REFERENCES

