Cilengitide

Cat. No.: HY-16141
CAS No.: 188968-51-6
Molecular Formula: C₂₇H₄₀N₈O₇
Molecular Weight: 588.66
Target: Integrin; Autophagy
Pathway: Cytoskeleton; 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 : ≥ 44 mg/mL (74.75 mM)
H₂O : ≥ 32 mg/mL (54.36 mM)
* “≥” means soluble, but saturation unknown.

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>1.6988 mL</td>
<td>8.4939 mL</td>
<td>16.9877 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3398 mL</td>
<td>1.6988 mL</td>
<td>3.3975 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1699 mL</td>
<td>0.8494 mL</td>
<td>1.6988 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description
Cilengitide is a potent and selective integrin inhibitor for αᵥβ₃ and αᵥβ₅ receptor, with IC₅₀s of 4 and 79 nM, respectively.

IC₅₀ & Target
IC50: 4 and 79 nM (αᵥβ₃ and αᵥβ₅)[¹]

In Vitro
Cilengitide (EMD 121974) is the αᵥβ₃ and αᵥβ₅ integrin receptor antagonist. In cell adhesion studies assessing the human melanoma M21 or UCLA-P3 human lung carcinoma cell lines, Cilengitide inhibits integrin-mediated binding to vitronectin with IC₅₀s of 0.4 and 0.4 μM[¹]. In vitro treatment of Cilengitide, at a concentration greater than 1 μM, shows concentration- and time-dependent cytotoxic effects. However, lower doses of Cilengitide monotherapy (0.1 and 0.5 μM) does not elicit the effective death of the both U87MG and U251MG cells. Significant cytotoxic effects are observed in the U87MG cells with the addition of 1 μM Cilengitide in combination with Belotecan monotherapy at concentration of 6.25 nM. Higher concentrations of Cilengitide (5 and 25 μM) does not significantly increase cell
death in the U87MG and U251MG compare to a lower concentration of Cilengitide (1 µM)\(^2\).

**In Vivo**

In nude mice bearing M21-L melanoma tumors, Cilengitide dose i.p. at 10, 50, and 250 µg three times per week demonstrated inhibition of tumor growth with a reduction in both tumor volume (55%, 75%, and 89%, respectively) and tumor weight (23%, 38%, and 61%, respectively), when compared to controls\(^2\). In the rat model studied, the systemic pharmacokinetics of i.p. Cilengitide are not affected by ILP with Cilengitide alone or ILP with Cilengitide plus Melphalan, TNF or both. Systemic Cilengitide levels reach around 20 µg/mL (approximately 35 µM) within 10 min of i.p. administration and continued to rise to approximately 40 µg/mL (approximately 70 µM) in the first hour. Thereafter Cilengitide levels in serum dropped with an elimination half-life of 2.1 hr\(^3\).

**PROTOCOL**

**Cell Assay** \(^2\)

The cytotoxicity of the two drugs, Belotecan and Cilengitide, is measured by the Cell Counting Kit-8 (CCK-8). U87MG and U251MG cells are seeded in 96 well plates at a density of 4×10\(^3\) cells per well to allow for adhesion overnight. After this, the cells are treated with Cilengitide at a concentration of 0, 0.1, 0.5, 1, 5 and 25 µM and Belotecan at a concentration of 0, 6.25, 12.5, 25, 50 and 100 nM. All possible combinations of concentrations are used to assess the combined therapeutic effect of Cilengitide and Belotecan. After 3 days, 10 µL of the CCK-8 solution is added to each well of the plate, and the plate is incubated for 3 hr in the incubator (37°C; 5% CO\(_2\)). The optical density (OD) of the sample plate is measured at 450 nm in a microplate reader. The viability of tumor cells is assessed by calculating the OD ratio of the specific OD in each sample to that of the control. Each experiment is conducted in quadruplicate. The values are averaged and normalized against the controls to generate dose-response curves\(^2\).

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

**Animal Administration** \(^2\)\(^3\)

**Mice**\(^2\)

Male Balb/c-nu mice, at 8 weeks of age, are randomly assigned to four groups: control (n=10), Cilengitide (n=10), Belotecan (n=10) and combination (n=10). Cilengitide is administered intraperitoneally at a dose of 20 mg/kg daily and the Belotecan at a dose of 10 mg/kg every 4 days. The optimal dose is calculated. The control group of animals is injected with saline only. A single dose of the drugs comprised a 3-sec infusion in a volume of 3 mL/kg. The drug treatments began 7 days after the implantation of tumor cells for 16 days. Half of the animals are sacrificed 1 month after the implantation of the tumor cells for tumor volume analysis and the rest of the animals are observed for another 2 months to analyze survival. The death of the animals is defined as a weight reduction of over 25% of the initial weight or an unexpected sudden death beforehand.

**Rats**\(^3\)

Male inbred Brown Norway rats (250 to 300 g) are injected i.p. with 50 mg/kg Cilengitide or saline 2 hr before and 3 hr after Isolated limb perfusion. The Rats are used to investigate the effects of perfusing various combinations of melphalan, TNF and cilengitide with or without the additional i.p. administration of cilengitide before and after the ILP procedure itself. The i.p. administration pre- and post-ILP is intended to optimally saturate available αVβ\(_3\) and αVβ\(_5\) integrins. Saline is used as a control in both the i.p. and perfusion settings.

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**CUSTOMER VALIDATION**

REFERENCES


Caution: Product has not been fully validated for medical applications. For research use only.

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