CX-5461

Cat. No.: HY-13323
CAS No.: 1138549-36-6
Molecular Formula: C₂₇H₂₇N₇O₂S
Molecular Weight: 513.61
Target: DNA/RNA Synthesis
Pathway: Cell Cycle/DNA Damage
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: 2 mg/mL (3.89 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Solvent Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
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</thead>
<tbody>
<tr>
<td>Preparing Stock Solutions</td>
<td></td>
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</tr>
<tr>
<td>1 mM</td>
<td>1.9470 mL</td>
<td>9.7350 mL</td>
<td>19.4700 mL</td>
</tr>
<tr>
<td>5 mM</td>
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<td>---</td>
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<tr>
<td>10 mM</td>
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</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description CX-5461 is a potent and oral rRNA synthesis inhibitor. It inhibits RNA polymerase I-driven transcription of rRNA with IC₅₀ values of 142, 113, and 54 nM in HCT-116, A375, and MIA PaCa-2 cells, respectively[^1].

IC₅₀ & Target IC₅₀: 54 nM (rRNA synthesis, MIA PaCa-2 cells), 113 nM (rRNA synthesis, A375 cells), 142 nM (rRNA synthesis, HCT-116 cells[^1]).

In Vitro CX-5461 is a potent and orally bioavailable inhibitor of Pol I-mediated rRNA synthesis, with IC₅₀ of 142 nM in HCT-116, 113 nM in A375, and 54 nM in MIA PaCa-2 cells, and shows little or no effect on Pol II (IC₅₀ ≥ 25 μM). CX-5461 has modest inhibition on DNA replication and protein translation. CX-5461 also exhibits broad antiproliferative activity against a panel of human cancer cell lines, with a mean EC₅₀ of 147 nM, but has minimal effect on viability of nontransformed human cells, with EC₅₀ values of appr 5000 nM. EC₅₀ of CX-5461 for HCT-116, A375, and MIA PaCa-2 cell lines are 167, 58, and 74 nM, respectively. CX-5461 induces autophagy and senescence in solid tumor cancer cells, rather than apoptosis, through a p53-independent process[^1]. Eμ-Myc lymphoma cells from tumor-bearing mice are exquisitely sensitive to CX-5461 with an IC₅₀ of 27.3 nM ± 8.1 nM for Pol I transcription after 1 hr and IC₅₀ of 5.4 nM ± 2.1 nM for cell death after 16 hr. CX-5461 activates p53 via the nucleolar stress response in Eμ-MycLymphoma Cells[^2].

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

CX-5461 displays antitumor activity against human solid tumors in murine xenograft models. CX-5461 (50 mg/kg, p.o.) shows significant MIA PaCa-2 growth inhibition with TGI equal to 69% on day 31 and 79% TGI on day 32\(^1\). CX-5461 (50 mg/kg, p.o.) inhibits the Eμ-Myc tumor cells with 84% repression in Pol I transcription at 1 hr posttreatment in C57BL/6 mice. CX-5461 also induces a rapid reduction in tumor burden in the lymph nodes and a concomitant reduction of spleen size to within the normal range\(^2\).

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PROTOCOL

Cell Assay\(^1\)

Cells are plated on 96-well plates and treated the next day with dose response of CX-5461 for 96 hours. Cell viability is determined using Alamar Blue and CyQUANT assays\(^1\).

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Animal Administration\(^1\)

Mice\(^1\)

Animal experiments are performed with 5- to 6-week-old female athymic (NCr nu/nu fisol) mice of Balb/c. Mice are inoculated with athymic (NCr nu/nu fisol) mice in 100 μL of cell suspension subcutaneously in the right flank. Tumor measurements are performed by caliper analysis, and tumor volume is calculated using the formula \( (l \times w^2)/2 \), where \( w \) = width and \( l \) = length in mm of the tumor. established tumors (appr 110-120 mm\(^3\)) are randomized into vehicle (50 mM NaH\(_2\)PO\(_4\), pH 4.5), NSC 613327, or CX-5461 treatment groups. Tumor growth inhibition (TGI) is determined on the last day of study according to the formula: TGI (%)\(^3\)=\(100-[(V_f^D-V_i^D)/(V_f^V-V_i^V)] \times 100\), where \( V_i^V \) is the initial mean tumor volume in vehicle-treated group, \( V_f^V \) is the final mean tumor volume in vehicle-treated group, \( V_i^D \) is the initial mean tumor volume in drug-treated group, and \( V_f^D \) is the final mean tumor volume in drug-treated group.

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CUSTOMER VALIDATION


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REFERENCES


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