Tenovin-1

Cat. No.: HY-13423
CAS No.: 380315-80-0
Molecular Formula: C₂₀H₂₃N₃O₂S
Molecular Weight: 369.48
Target: MDM-2/p53; Dihydroorotate Dehydrogenase; Sirtuin; Autophagy
Pathway: Apoptosis; Metabolic Enzyme/Protease; Cell Cycle/DNA Damage; Epigenetics; 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

<table>
<thead>
<tr>
<th>DMSO : 33.33 mg/mL (90.21 mM; Need ultrasonic)</th>
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</thead>
<tbody>
<tr>
<td><strong>Preparation of Stock Solutions</strong></td>
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<tr>
<td><strong>Concentration</strong></td>
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<tr>
<td>1 mM</td>
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<tr>
<td>5 mM</td>
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<tr>
<td>10 mM</td>
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</tbody>
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In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution

BIOLICAL ACTIVITY

Description
Tenovin-1, a p53 activator, protects p53 from MDM2-mediated degradation. Tenovin-1 acts through inhibition of the protein-deacetylating activities of SirT1 and SirT2. Tenovin-1 is also a dihydroorotate dehydrogenase (DHODH) inhibitor[1][2].

IC₅₀ & Target
<table>
<thead>
<tr>
<th>MDM-2/p53</th>
<th>DHODH</th>
<th>Sirtuin</th>
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</table>

In Vitro
Tenovin-1 protects p53 from mdm2-mediated degradation with little effect on p53 synthesis. Tenovin-1 targets a factor(s) upstream of p53 that not only modulates p53 function but also other cellular pathways. Tenovin-1 (10 μM) inhibits SirT2 deacetylase activity[1]. Tenovin-1 (1-10 μM) induces a bell-shaped concentration-dependent cell death in SK-N-MC cells. Tenovin-1 alters
the gene and protein expression of Bcl-2 family members. However, Tenovin-1 has a more powerful effect both on mRNA and protein expression levels at a lower concentration than does the higher concentration. Furthermore, Tenovin-1-induced cytotoxic effects depend on caspases in p53 wild-type WE-68 cells, but not in p53 null SK-N-MC cells. AIF plays a major role in tenovin-1-induced cell death in p53 null SK-N-MC cells, but not in p53 wild-type WE-68 cells. Reactive oxygen species are also involved in tenovin-1-mediated cell death in SK-N-MC cells. In addition, Tenovin-1 causes DNA damage in SK-N-MC cells. Tenovin-1 (5 μM) increases the nuclear size in glioblastoma cells and rat primary astrocytes. Tenovin-1 induces cellular senescence, which does not appear to be related to cell death. Tenovin-1 (10 μM) reduces proliferation and anchorage independent growth of NSCLC cells. Tenovin-1 also inhibits cell growth of H358 lung cancer cells.

In Vivo

Tenovin-1 (92 mg/kg, i.p.) reduces growth of tumors in SCID mice derived from BL2 cells or ARN8 cells.

PROTOCOL

Cell Assay

Cell viability is measured by thiazolyl blue tetrazolium bromide (MTT) assay. Cells are seeded in 96-well plates. When indicated they are treated with 10 μM Tenovin-1 (tunv-1) or are transfected with siRNAs. After the specified period of time, MTT solution (0.5 mg/mL) is added. The formazan crystals are dissolved in an extraction buffer (50% dimethylformamide and 20% SDS, pH 4.7). The absorbance (540/690 nm) is measured in a SunRise plate reader. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration

ARN8 melanoma or BL2 Burkitt’s lymphoma cells are injected into the flank of SCID mice and allowed to develop until tumors become palpable. Tenovin-1 (in 70% cyclodextrin) is administered daily (14 days) by intraperitoneal injection at 92.5 mg/kg and tumor growth is measured over a period of 18 days. Control animals are treated with 70% cyclodextrin. In the BL2 experiment, n = 12 for each treatment. In the ARN8 experiment, n = 14 for the control group and n = 16 for the tenovin-1 treated group. Growth measurements are averaged between groups and plotted.

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REFERENCES


