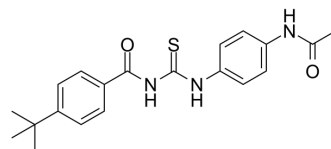


## Tenovin-1

<b>Cat. No.:</b>	HY-13423												
<b>CAS No.:</b>	380315-80-0												
<b>Molecular Formula:</b>	C <sub>20</sub> H <sub>23</sub> N <sub>3</sub> O <sub>2</sub> S												
<b>Molecular Weight:</b>	369.48												
<b>Target:</b>	MDM-2/p53; Dihydroorotate Dehydrogenase; Sirtuin; Autophagy												
<b>Pathway:</b>	Apoptosis; Metabolic Enzyme/Protease; Cell Cycle/DNA Damage; Epigenetics; Autophagy												
<b>Storage:</b>	<table border="0"> <tr> <td>Powder</td> <td>-20°C</td> <td>3 years</td> </tr> <tr> <td></td> <td>4°C</td> <td>2 years</td> </tr> <tr> <td>In solvent</td> <td>-80°C</td> <td>6 months</td> </tr> <tr> <td></td> <td>-20°C</td> <td>1 month</td> </tr> </table>	Powder	-20°C	3 years		4°C	2 years	In solvent	-80°C	6 months		-20°C	1 month
Powder	-20°C	3 years											
	4°C	2 years											
In solvent	-80°C	6 months											
	-20°C	1 month											



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 100 mg/mL (270.65 mM; Need ultrasonic)				
		Solvent Concentration	Mass		
	<b>Preparing Stock Solutions</b>		1 mg	5 mg	10 mg
		1 mM	2.7065 mL	13.5325 mL	27.0651 mL
		5 mM	0.5413 mL	2.7065 mL	5.4130 mL
	10 mM	0.2707 mL	1.3533 mL	2.7065 mL	
Please refer to the solubility information to select the appropriate solvent.					
<b>In Vivo</b>	<ol style="list-style-type: none"> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% corn oil Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution</li> </ol>				

### BIOLOGICAL ACTIVITY

<b>Description</b>	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 <sup>[1][2]</sup> .		
<b>IC<sub>50</sub> &amp; Target</b>	MDM-2/p53	DHODH	Sirtuin
<b>In Vitro</b>	<p>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<sup>[1]</sup>.</p> <p>Tenovin-1 (1-10 μM) induces a bell-shaped concentration-dependent cell death in SK-N-MC cells. Tenovin-1 alters the gene</p>		

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<sup>[3]</sup>. Tenovin-1 (5  $\mu$ M) 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<sup>[4]</sup>.

Tenovin-1 (10  $\mu$ M) reduces proliferation and anchorage independent growth of NSCLC cells. Tenovin-1 also inhibits cell growth of H358 lung cancer cells<sup>[5]</sup>.

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

#### In Vivo

Tenovin-1 (92 mg/kg, i.p.) reduces growth of tumors in SCID mice derived from BL2 cells or ARN8 cells<sup>[5]</sup>.

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## PROTOCOL

#### Cell Assay <sup>[4]</sup>

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  $\mu$ M Tenovin-1 (tnv-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<sup>[4]</sup>.

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

#### Animal Administration <sup>[5]</sup>

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<sup>[5]</sup>.

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

## CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- Eur J Pharmacol. 2020 Jun 5;876:173056.

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## REFERENCES

- [1]. Lain S, et al. Discovery, in vivo activity, and mechanism of action of a small-molecule p53 activator. *Cancer Cell*. 2008;13(5):454-463.
- [2]. Ladds MJGW, et al. Exploitation of DHODH and p53 activation as therapeutic targets - a case study in polypharmacology [published online ahead of print, 2020 Sep 8]. *J Biol Chem*. 2020;jbc.RA119.012056.
- [3]. Marx C, et al. The sirtuin 1/2 inhibitor tenovin-1 induces a nonlinear apoptosis-inducing factor-dependent cell death in a p53 null Ewing's sarcoma cell line. *Invest New Drugs*. 2017 Nov 18.
- [4]. Grbesa I, et al. Expression of sirtuin 1 and 2 is associated with poor prognosis in non-small cell lung cancer patients. *PLoS One*. 2015 Apr 27;10(4):e0124670.
- [5]. Yoon KB, et al. Induction of Nuclear Enlargement and Senescence by Sirtuin Inhibitors in Glioblastoma Cells. *Immune Netw*. 2016 Jun;16(3):183-8.

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

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