Tenovin-1

Cat. No.: HY-13423

CAS No.: 380315-80-0

Molecular Formula: $C_{20}H_{23}N_3O_2S$

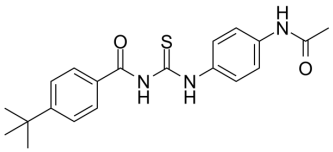
Molecular Weight: 369.48

Target: Sirtuin; MDM-2/p53; Autophagy; Dihydroorotate Dehydrogenase

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis; Autophagy; Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (270.65 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	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.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution

BIOLOGICAL 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].

IC_{50} & Target			
	MDM-2/p53	DHODH	Sirtuin

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[3]. Tenovin-1 (5 μM) increases the nuclear size in glioblastoma cells and rat primary astrocytes. Tenovin-1 induces cellular senescence, wich does not appear to be related to cell death[4]. Tenovin-1 (10 μM) reduces proliferation and anchorage independent growth of NSCLC cells. Tenovin-1 also inhibits cell growth of H358 lung cancer cells[5]. 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[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [4]	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 (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[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [5]	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[5]. 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.
- Acta Pharmacol Sin. 2021 Apr 13.
- 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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