Tenovin-6 Hydrochloride

Cat. No.: HY-15510B

CAS No.: 1011301-29-3

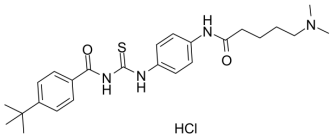
Molecular Formula: $C_{25}H_{35}ClN_4O_2S$

Molecular Weight: 491.09

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

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

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 49 mg/mL (99.78 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0363 mL	10.1814 mL	20.3629 mL
	5 mM	0.4073 mL	2.0363 mL	4.0726 mL
	10 mM	0.2036 mL	1.0181 mL	2.0363 mL

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

BIOLOGICAL ACTIVITY

Description

Tenovin-6 Hydrochloride, an analog of Tenovin-1 (HY-13423), is an activator of p53 transcriptional activity. Tenovin-6 Hydrochloride inhibits the protein deacetylase activities of purified human SIRT1, SIRT2, and SIRT3 with IC_{50}s of 21 μM, 10 μM, and 67 μM, respectively. Tenovin-6 Hydrochloride also inhibits dihydroorotate dehydrogenase (DHODH)[1][2].

IC_{50} & Target

SIRT2	SIRT1	SIRT3	HDAC8
10 μM (IC_{50})	21 μM (IC_{50})	67 μM (IC_{50})	

MDM-2/p53

In Vitro

Tenovin-6 Hydrochloride inhibits the growth of S. cerevisiae cultures with an IC50 of 30 μM and is more toxic to yeast than the less water-soluble tenovin-1. Tenovin-6 Hydrochloride rapidly increases the levels of endogenous K382-Ac p53 in MCF-7 cells[1].

Tenovin-6 Hydrochloride (0 to 15 μM) dose dependently increases the level of LC3-II in diverse cell types, and the increase is ATG5/7 dependent. Tenovin-6 Hydrochloride treatment also increases the number and intensity of autophagic vesicles with or without the presence of Torin 1, and prevents Torin 1-induced SQSTM1/p62 degradation. Tenovin-6 Hydrochloride affects

	the acidification of autolysosomes and impairs the hydrolytic activity of lysosomes but does not affect the fusion between autophagosomes and lysosomes. That Tenovin-6 Hydrochloride inhibits autophagy does not correlate with p53 activation and SIRT1/2 inhibition by knockdown or knockout cannot mimic the effect of Tenovin-6 Hydrochloride on LC3B accumulation[3]. Tenovin-6 Hydrochloride (0, 1, 2.5, 5 or 10 μM) potently inhibits cell proliferation in a dose- and time-dependent manner in all OCI-Ly1, DHL-10, U2932, RIVA, HBL1 and OCI-Ly10 cell lines. Tenovin-6 Hydrochloride consistently increases LC3B-II level in DLBCL cell lines by inhibiting the classical autophagy pathway, without activating p53, and the increase is independent of SIRT1/2/3 and p53. Tenovin-6 Hydrochloride induces apoptosis through the extrinsic cell-death pathway[4]. Tenovin-6 Hydrochloride suppresses the growth of UM cells with IC50 of 12.8 μM, 11.0 μM, 14.58 μM and 9.62 μM for 92.1, Mel 270, Omm 1 and Omm 2.3 cells, respectively[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tenovin-6 Hydrochloride (50 mg/kg, i.p.) inhibits the growth of tumor in mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Assays are carried out using purified components in the Fluor de Lys Fluorescent Assay Systems. Relevant FdL substrates are used at 7 μM and NAD^+ at 1 mM. Tenovins are solubilized in DMSO with the final DSMO concentration in the reaction being less than 0.25%. For SirT1 and HDAC8, one unit of enzyme is used per reaction, and for SirT2 and SirT3, five units is used per reaction. Reactions are carried out at 37°C for 1 hr. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [4]	The MTS assay is used to evaluate cell viability. UM cells are seeded into each well of 96-well plates (5,000 cells/well) and treated the next day with control or Tenovin-6 in an increasing concentrations from 0 to 20 μM for 68 h, and then MTS is added at 20 μL/well to be read at a wave length of 490 nm, the IC_{50} is determined by curve fitting of the sigmoidal dose-response curve. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Female SCID mice are injected subcutaneously with 1×10^6 ARN8 cells suspended in matrigel. Tumors are allowed to reach a size of approximately 10 mm^3. Tenovin-6 is administered daily at 50 mg/kg by intraperitoneal injection. Control animals are treated with vehicle solution containing cyclodextrin 20% (w/v) and DMSO 10% (v/v). Tumor diameters are measured using calipers, and volumes are calculated using the equation $V=\pi4/3[(d1 + d2)/4]^3$. Median values of tumor size are calculated for each time point as well as the corresponding 95% confidence intervals. Comparison of control and drug-treated tumor size distributions are made by Mann-Whitney U-test. An alpha-level of 0.05 is considered appropriate for determination of statistical significance. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Acta Pharmacol Sin. 2021 Apr 13.
- Lipids Health Dis. 2021 Apr 26;20(1):40.
- J Nutr. 2020 Jul 1;150(7):1731-1737.
- Exp Cell Res. 2020 Mar 1;388(1):111810.

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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 May;13(5):454-63.

[2]. Yuan H, et al. Tenovin-6 impairs autophagy by inhibiting autophagic flux. Cell Death Dis. 2017 Feb 9;8(2):e2608.

[3]. Yuan H, et al. Tenovin-6 inhibits proliferation and survival of diffuse large B-cell lymphoma cells by blocking autophagy. Oncotarget. 2017 Feb 28;8(9):14912-14924.

[4]. Dai W, et al. Class III-specific HDAC inhibitor Tenovin-6 induces apoptosis, suppresses migration and eliminates cancer stem cells in uveal melanoma. Sci Rep. 2016 Mar 4;6:22622.

[5]. 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.

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