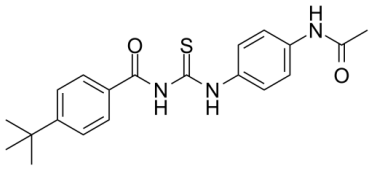
Data Sheet

Product Name:	Tenovin-1
Cat. No.:	CS-1512
CAS No.:	380315-80-0
Molecular Formula:	C20H23N3O2S
Molecular Weight:	369.48
Target:	Autophagy; MDM-2/p53; Sirtuin
Pathway:	Apoptosis; Autophagy; Cell Cycle/DNA Damage; Epigenetics
Solubility:	DMSO : 33.33 mg/mL (90.21 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Tenovin-1 is an inhibitor of **sirtuin 1** and **sirtuin 2**, an activator of **p53** and may have potential in the management of cancer. IC50 & Target: Sirtuin, MDM-2/p53[1] **In Vitro:** 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[1]. 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[2]. 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[3]. Tenovin-1 (10 μM) reduces proliferation and anchorage independent growth of NSCLC cells. Tenovin-1 also inhibits cell growth of H358 lung cancer cells[4]. **In Vivo:** Tenovin-1 (92 mg/kg, i.p.) reduces growth of tumors in SCID mice derived from BL2 cells or ARN8 cells[5].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Tenovin-1 is dissolved in DMSO.[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]. **Animal Administration:** Tenovin-1 is formulated in 70% cyclodextrin.[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].

References:

[1]. 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.

[2]. Yoon KB, et al. Induction of Nuclear Enlargement and Senescence by Sirtuin Inhibitors in Glioblastoma Cells. Immune Netw. 2016 Jun;16(3):183-8.

[3]. 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.

[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]. 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.

CAIndexNames:

Benzamide, N-[[[4-(acetylamino)phenyl]amino]thioxomethyl]-4-(1,1-dimethylethyl)-

SMILES:

O=C(NC(NC1=CC=C(NC(C)=O)C=C1)=S)C2=CC=C(C(C)(C)C)C=C2

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