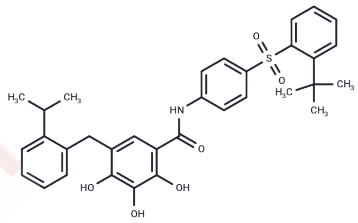
Data Sheet (Cat.No.T6281)

TargetMol

TW-37

Chemical Properties



CAS No. : 877877-35-5

Formula: C33H35NO6S

Molecular Weight: 573.7

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	TW-37 is an nonpeptide inhibitor to recombinant Bcl-2, Bcl-xL and Mcl-1 (Ki: 0.29/1.11/0.26 μM).
Targets(IC50)	Bcl-2 Family
In vitro	TW-37 targets the BH3-binding groove in Bcl-2 where proapoptotic Bcl-2 proteins bind, and shows higher affinity and selectivity for Bcl-2 and Mcl-1 over Bcl-xL with Ki values of 0.29 μM, 0.26 μM and 1.11 μM, respectively. [1] In vitro, TW-37 shows significant anti-proliferative and pro-apoptotic effect in a de novo chemo-resistant WSU-DLCL2 lymphoma cell line and primary cells obtained from a lymphoma patient without effects on normal peripheral blood lymphocytes. [1] TW-37 exhibits the inhibitory effect on both cell growth and cell death in endothelial cell with IC50 of approximately 1.8 μM without effect on the fibroblasts exposed to the same concentration range as the endothelial cells. In addition, TW37 also shows the anti-proliferation effects in MCF-7, LNCaP, and SLK tumor cell lines with the same or lower concentration range than those required to inhibit endothelial cell growth. [2]
In vivo	TW-37 shows a maximum tolerated dose (MTD) of 40 mg/kg for three i.v. injections in severe combined immunodeficient (SCID) mice when given alone, and enhances tumor inhibitory effect of cyclophosphamide-doxorubicin-vincristine-prednisone (CHOP) regimen. [1] TW-37, administrated by i.v. produces the antiangiogenic effect by decreasing the density of functional human microvessels in the severe combined immunodeficient mouse model of human angiogenesis. [2] The combination of TW-37 and MEK inhibitors synergistically block melanoma cell growth in mice by a significant reduction in tumor volume and tumor mass. [3]
Kinase Assay	Fluorescence polarization-based binding assay for recombinant Bcl-2, Bcl-XL, and Mcl-1 protein : For this assay, the 21-residue BH3 peptide QEDIIRNIARHLAQVGDSMDR derived from Bid labeled with 6-carboxyfluorescein succinimidyl ester (FAM-Bid) and recombinant proteins derived from human Bcl-2,Bcl-X L,and Mcl-1 are employed. It is determined that FAM-Bid has a Ki of 11 nM to Bcl-2 protein,25 nM to Bcl-XL protein,and 5.7 nM to Mcl-1 protein. The competitive binding assay for Bcl-XL is same as that for Bcl-2 with the following exceptions: 30 nM Bcl-XL protein and 2.5 nM FAM-Bid peptide in the following assay buffer [50 mM Tris-Bis (pH 7.4) and 0.01% bovine gamma-globulin].
Cell Research	The sulforhodamine B (SRB) cytotoxicity assay is used as described. Briefly, optimal cell density for cytotoxicity assay is determined by growth curve analysis. HDMECs are

	seeded in a 96-well plate and allowed to adhere overnight. Drug or control is diluted in EGM2-MV and layered onto cells, which are allowed to incubate for times as indicated in the figures. Alternatively, HDMECs are coincubated with TW37 and 0 to 100 ng/mL recombinant human VEGF (rhVEGF)165 or 0 to 100 ng/mL recombinant human CXCL8. Cells are fixed on the plates by addition of cold trichloroacetic acid (10% final concentration) and incubation for 1 hour at 4 °C. Cellular protein is stained by addition of 0.4% SRB in 1% acetic acid and incubation at room temperature for 30 minutes. Unbound SRB is removed by washing with 1% acetic acid and the plates are air dried. Bound SRB is resolubilized in 10 mM unbuffered Tris-base and absorbance is determined on a microplate reader at 560 nm. Test results are normalized against initial plating density and drug-free controls. Data are obtained from triplicate wells per condition and are representative of at least three independent experiments(Only for Reference)

Solubility Information

Solubility	DMSO: 57.4 mg/mL (100.05 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7431 mL	8.7154 mL	17.4307 mL
5 mM	0.3486 mL	1.7431 mL	3.4861 mL
10 mM	0.1743 mL	0.8715 mL	1.7431 mL
50 mM	0.0349 mL	0.1743 mL	0.3486 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Mohammad RM, et al. Clin Cancer Res, 2007, 13(7), 2226-2235.
Zeitlin BD, et al. Cancer Res, 2006, 66(17), 8698-8706.
Verhaegen M, et al. Cancer Res. 2006, 66(23), 11348-11359.