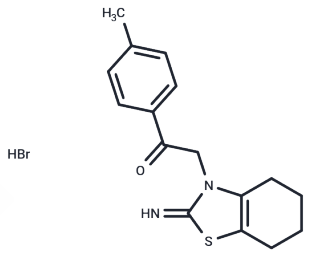
Data Sheet (Cat.No.T2707)

TargetMol

Pifithrin-α hydrobromide

Chemical Properties



CAS No. : 63208-82-2

Formula: C16H18N2OS·HBr

Molecular Weight: 367.3

Appearance: no data available

Storage: keep away from moisture,store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Pifithrin-α hydrobromide (Pifithrin-α hydrobromide) is a p53 inhibitor, inhibiting p53-dependent transactivation of p53-responsive genes.
Targets(IC50)	Ferroptosis,Aryl Hydrocarbon Receptor,p53
In vitro	At a concentration of 10 μM, Pifithrin-α inhibits apoptosis in C8 cells induced by Dox, Etoposide, Taxol, and Cytosine arabinoside. It also reduces activation of the heat shock transcription factor and enhances cell sensitivity to heat, lowers glucocorticoid receptor activation in HeLa cells, and protects murine thymocytes from apoptosis induced by Dexamethasone. Concentrations between 100–200 nM of Pifithrin-α completely block the increase in p53 DNA binding levels and the p53-responsive gene Bax in hippocampal cells induced by Camptothecin, while 200 nM safeguards cultured hippocampal neurons from death caused by DNA damage agents. Furthermore, 200 μM Pifithrin-α stabilizes mitochondrial function, inhibits caspase activation, and shields hippocampal neurons from death induced by glutamate and β-amyloid peptide. Pifithrin-α prevents the p53-dependent growth inhibition in human diploid fibroblasts following DNA damage, though it does not affect fibroblasts lacking p53. It can regulate the nuclear import and export of p53, or both, and decrease nuclear p53 stability. Pifithrin-α inhibits signals from heat shock and glucocorticoid receptors without affecting NF-κB signaling.
In vivo	Intraperitoneal injection of 3.6 μg/kg Pifithrin-α in mice significantly inhibited Dex-induced thymic atrophy. Compared to the control group, Pifithrin-α (2 mg/kg) notably decreased the extent of motor dysfunction in rats with transient cerebral artery occlusion. Administration of Pifithrin-α (2 mg/kg i.p.) 30 minutes before treatment of cerebral artery occlusion in mice reduced ischemic brain damage and shielded hippocampal neurons from excitotoxicity damage. In C57BL and Balb/c mice, intraperitoneal injection of 2.2 mg/kg Pifithrin-α completely protected the mice against the lethal effects of 60% mortality gamma-ray irradiation. Pifithrin-α was observed to substantially lower cellular apoptosis in rats, evidenced by Tunel and caspase 3 staining. When administered within one hour after a stroke, animals treated with Pifithrin-α exhibited fewer motor dysfunctions and smaller infarcts. After 7 days of treatment with Pifithrin-α, rats showed significantly reduced scores of motor dysfunction compared to the placebo control group.

Kinase Assay	The ligand binding competition assays are performed. Cytosolic cell extracts from Hepa-1 cells are generated by the resuspension of the cell pellets in HEDG buffer [25 mM Hepes, 1 mM EDTA, 1 mM dithiothreitol, and 10% (v/v) glycerol, pH 7.5] containing 0.4 mM leupeptin, 4 mg/mL aprotinin, and 0.3 mM phenylmethylsulfonyl fluoride, homogenization, and centrifugation at 100,000 g for 45 min. Aliquots of the supernatant (120 μg) are incubated at room temperature for 2 h with the indicated concentrations of Pifithrin-α in the presence of 3 nM [3H]TCDD in HEDG buffer. After incubation on ice with hydroxyapatite for 30 min, HEDG buffer with 0.5% Tween 80 is added. The samples are centrifuged, washed twice, resuspended in 0.2 mL of scintillation fluid, and subjected to scintillation counting. Nonspecific binding is determined using a 150-fold molar excess of TCDF and subtracted from the total binding to obtain the specific binding. The specific binding is reported relative to [3H]TCDD alone[2].
Cell Research	At the end of cell treatments, the number of attached cells is estimated by staining with 0.25% crystal violet in 50% methanol, followed by elution of the dye with 1% SDS. Optical density (530 nm) reflecting the number of stained cells is determined with a Bio-Tek EL311 microplate reader. Cell viability in suspension of short term culture of primary thymocytes is determined by their staining with 0.1% of methyl blue and microscopic counting of blue (dead) cells.(Only for Reference)

Solubility Information

Solubility	DMSO: 36.7 mg/mL (99.92 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.7226 mL	13.6129 mL	27.2257 mL
5 mM	0.5445 mL	2.7226 mL	5.4451 mL
10 mM	0.2723 mL	1.3613 mL	2.7226 mL
50 mM	0.0545 mL	0.2723 mL	0.5445 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

Komarov PG, et al. Science, 1999, 285(5434), 1733-1737.
Chen L, Zhang L, Jin G, et al.Synergy of 5-aminolevulinate supplement and CX3CR1 suppression promotes liver regeneration via elevated IGF-1 signaling.Cell Reports.2023, 42(8).
Jiang W, Wang X, Su S, et al. Identifying the shared genes and KEGG pathways of Resolvin D1-targeted network and osteoarthritis using bioinformatics. Bioengineered. 2022, 13(4): 9839-9854
Zhou Y, Yang L, Xiong L, et al. KIF11 is upregulated in colorectal cancer and silencing of it impairs tumor growth and sensitizes colorectal cancer cells to oxaliplatin via p53/GSK3β signaling. Journal of Cancer. 2021, 12(12): 3741.
Lu L, Li K, Mao Y H, et al. Gold-chrysophanol nanoparticles suppress human prostate cancer progression through inactivating AKT expression and inducing apoptosis and ROS generation in vitro and in vivo. International Journal of Oncology. 2017 Oct;51(4):1089-1103
Wu X, Wang L, Li Z. Identification of 3-Phenylquinoline Derivative PQ1 as an Antagonist of p53 Transcriptional Activity. ACS Omega. 2022
Su Q, Wang J, Ren J, et al.Parkin deficiency promotes liver cancer metastasis by TMEFF1 transcription activation via TGF-β/Smad2/3 pathway.Acta Pharmacologica Sinica.2024: 1-10.
Lin X, Lin T, Wang X, et al.Sesamol serves as a p53 stabilizer to relieve rheumatoid arthritis progression and inhibits the growth of synovial organoids.Phytomedicine.2023: 155109.
Culmsee C, et al. J Neurochem, 2001, 77(1), 220-228.
Komarova EA, et al. J Biol Chem, 2003, 278(18), 15465-15468.
Wu Y, Zhou T, Qian D, et al.Z-Guggulsterone Induces Cell Cycle Arrest and Apoptosis by Targeting the p53/CCNB1/PLK1 Pathway in Triple-Negative Breast Cancer.ACS Omega.2023
Murphy PJ, et al. J Biol Chem, 2004, 279(29), 320195-3201201.
Hussain M, Lu Y, Tariq M, et al. A small-molecule Skp1 inhibitor elicits cell death by p53-dependent mechanism. Iscience. 2022, 25(7): 104591.
Leker RR, et al. Exp Neurol, 2004, 187(2), 478-486.
Yang R, Yang H, Wei J, et al. Mechanisms Underlying the Effects of Lianhua Qingwen on Sepsis-Induced Acute Lung Injury: A Network Pharmacology Approach. Frontiers in Pharmacology. 2021: 2839.
Wu X, Han C, Wang L, et al. Iron increases the susceptibility of colorectal cancer cells to compound Kushen Injection via the decrease of TOP2A and p53. Pharmacological Research-Modern Chinese Medicine. 2022, 2: 100058.
Yu W, et al. Cyclosporine A Suppressed Glucose Oxidase Induced P53 Mitochondrial Translocation and Hepatic Cell Apoptosis through Blocking Mitochondrial Permeability Transition. Int J Biol Sci. 2016 Jan 1;12(2):198-209.
Kuang SQ, et al. FOXE3 mutations predispose to thoracic aortic aneurysms and dissections. J Clin Invest. 2016 Mar 1;126(3):948-61.
Luo Y, Gao X, Zou L, et al. Bavachin Induces Ferroptosis through the STAT3/P53/SLC7A11 Axis in Osteosarcoma Cells. Oxidative Medicine and Cellular Longevity. 2021
Guo Y, Li Q, Zhao G, et al. Loss of TRIM31 promotes breast cancer progression through regulating K48-and K63-linked ubiquitination of p53. Cell Death & Disease. 2021, 12(10): 1-13.
Lu L, Li K, Mao Y H, et al. Gold-chrysophanol nanoparticles suppress human prostate cancer progression through inactivating AKT expression and inducing apoptosis and ROS generation in vitro and in vivo[J]. International journal of oncology. 2017 Oct;51(4):1089-1103.
Zhou Y, Yang L, Xiong L, et al. KIF11 is upregulated in colorectal cancer and silencing of it impairs tumor growth and sensitizes colorectal cancer cells to oxaliplatin via p53/GSK3β signaling[J]. Journal of Cancer. 2021, 12(12): 3741.
Shang Y, Zhang S, Cheng Y, et al. Tetrabromobisphenol a exacerbates the overall radioactive hazard to zebrafish (Danio rerio). Environmental Pollution. 2022: 120424.