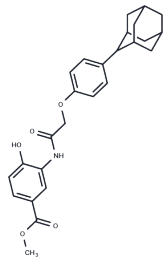
Data Sheet (Cat.No.T3494)

TargetMol

LW6

Chemical Properties



CAS No. : 934593-90-5

Formula: C26H29NO5

Molecular Weight: 435.51

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	LW6 (HIF-1α inhibitor) is a novel HIF-1 inhibitor.
Targets(IC50)	Apoptosis,HIF/HIF Prolyl-Hydroxylase,HIF,Dehydrogenase
In vitro	LW6 decreases the expression of HIF-1α protein without affecting HIF-1β expression. LW6 affects the stability of the HIF-1α protein. LW6 promotes the degradation of wild type HIF-1α while not of a DM-HIF-1α with modifications of P402A and P564A, at hydroxylation sites in the oxygen-dependent degradation domain. LW6 induces the expression of von Hippel-Lindau (VHL), which interacts with prolyl-hydroxylated HIF-1α for proteasomal degradation. The knockdown of VHL does not abolish HIF-1α protein accumulation in the presence of LW6 which indicates that LW6 degraded HIF-1α via regulation of VHL expression[2]. In MDCKII-BCRP cells overexpressing BCRP, LW6 enhances significantly the cellular accumulation of mitoxantrone, a BCRP substrate. LW6 also down-regulates BCRP expression at concentrations of 0.1-10 μM[3]. LW6 inhibits the expression of HIF 1α induced by hypoxia in A549 cells at 20 mM, independently of the von Hippel Lindau protein. LW6 induces hypoxia selective apoptosis together with a reduction in the mitochondrial membrane potential[4].
In vivo	LW6 exhibits potent anti-tumor activity in vivo, leading to reduced HIF-1α expression as observed through immunohistochemical staining of frozen tissues in mice with xenografts derived from human colon cancer HCT116 cells[2].
Cell Research	Inhibition of HIF-1a is assayed by a reporter assay using dualluciferase reporter assay system. HCT116 cells in 75-90% confluence are transiently co-transfected with pGL3-HRE-luciferase plasmid containing six copies of HREs from human VEGF genes and pRLSV40 encoding firefly renilla luciferase and incubated for 24 h. Cells are treated with LW6 or 17-AAG for 16 h before report assay. Luciferase activity is integrated over a 10 second period and measured using a luminometer[2].

Solubility Information

Solubility	DMSO: 50 mg/mL (114.81 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

In vivo Formulation	10% DMSO+90% Corn Oil: 2.5 mg/mL (5.74 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2962 mL	11.4808 mL	22.9616 mL
5 mM	0.4592 mL	2.2962 mL	4.5923 mL
10 mM	0.2296 mL	1.1481 mL	2.2962 mL
50 mM	0.0459 mL	0.2296 mL	0.4592 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Naik R , Won M , Ban H S , et al. Synthesis and Structure–Activity Relationship Study of Chemical Probes as Hypoxia Induced Factor-1α/Malate Dehydrogenase 2 Inhibitors[J]. Journal of Medicinal Chemistry, 2014, 57(22):9522-9538.
Zhu B, Wu Y, Huang S, et al. Uncoupling of macrophage inflammation from self-renewal modulates host recovery from respiratory viral infection. Immunity. 2021, 54(6): 1200-1218. e9.
Lee K, et al. LW6, a novel HIF-1 inhibitor, promotes proteasomal degradation of HIF-1alpha via upregulation of VHL in a colon cancer cell line. Biochem Pharmacol. 2010 Oct 1;80(7):982-9.
Song JG, et al. Discovery of LW6 as a new potent inhibitor of breast cancer resistance protein.
Sato M, et al. LW6, a hypoxia-inducible factor 1 inhibitor, selectively induces apoptosis in hypoxic cells through depolarization of mitochondria in A549 human lung cancer cells. Mol Med Rep. 2015 Sep;12(3):3462-8.
Zhu B, Wu Y, Huang S, et al. Uncoupling of macrophage inflammation from self-renewal modulates host recovery from respiratory viral infection[J]. Immunity. 2021