LW6

Cat. No.: HY-13671

CAS No.: 934593-90-5

Molecular Formula: $C_{26}H_{29}NO_5$

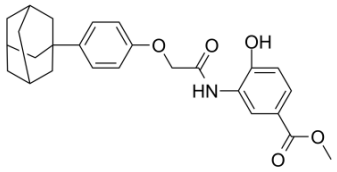
Molecular Weight: 435.51

Target: HIF/HIF Prolyl-Hydroxylase; Apoptosis

Pathway: Metabolic Enzyme/Protease; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (57.40 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.74 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.74 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LW6 (HIF-1α inhibitor) is a novel HIF-1 inhibitor with an IC_{50} of 4.4 μM. LW6 decreases HIF-1α protein expression without affecting HIF-1β expression.

IC_{50} & Target

IC50: 4.4 μM (HIF-1)[1]

In Vitro

LW6 affects the stability of the HIF-1α protein. LW6 promotes the degradation of wild type HIF-1α, but 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. In the presence of LW6, knockdown of VHL does not abolish HIF-1α protein accumulation, indicating 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 μM, independently of the von Hippel Lindau protein. LW6 induces hypoxia selective apoptosis together with a reduction in the mitochondrial membrane potential[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In mice carrying xenografts of human colon cancer HCT116 cells, LW6 demonstrates strong anti-tumor efficacy in vivo and causes a decrease in HIF-1α expression in frozen-tissue immunohistochemical staining[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice: The mice receive the following treatments using a dosing vehicle solution, containing 10% dimethylacetamide, 10% Cremophor EL and 80% of sodium carbonate buffer (pH 10), by intraperitoneal (i.p.) injection: group1(control group; six mice), vehicle solution; group2 (six mice), LW6 at a dose of 10 and 20mg/kg (QD); and group 3 (six mice), topotecan at a dose of 2mg/kg, (Q2D), which is the dose and dosing schedule that showed more than 60% inhibition of growth of HCT116 tumors. The treatments are continued for 13 days[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Front Physiol. 2020 Jun 30;11:669.
- J Appl Genet. 2019 Oct.

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REFERENCES

[1]. Naik R, et al. Synthesis and structure-activity relationship study of chemical probes as hypoxia induced factor-1α/malate dehydrogenase 2 inhibitors. J Med Chem. 2014 Nov 26;57(22):9522-38.

[2]. 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.

[3]. Song JG, et al. Discovery of LW6 as a new potent inhibitor of breast cancer resistance protein.

[4]. 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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