# LW6

**Cat. No.:** HY-13671

**CAS No.:** 934593-90-5

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

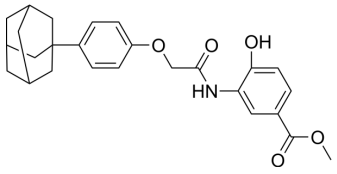
**Molecular Weight:** 435.51

**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)
DMF : 17.24 mg/mL (39.59 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% 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

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|---|---|
| | 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].<br>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].<br>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].<br>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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- Cell Metab. 2023 Jun 14;S1550-4131(23)00209-7.
- Cell Death Dis. 2021 May 14;12(5):490.
- Oncogene. 2022 Nov 18.
- iScience. 2021 May 7;24(6):102521.
- Int J Mol Sci. 2023 Jun 16, 24(12), 10236.

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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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