

Product Data Sheet

Product Name: LW6 (HIF-1 α inhibitor)

Cat. No.: GC32724

Chemical Properties

Cas. No. 934593-90-5

SMILES O=C(OC)C1=CC=C(O)C(NC(COC2=CC=C(C3(C4)CC5CC4CC(C5)C3)C=C2)=O)=C1

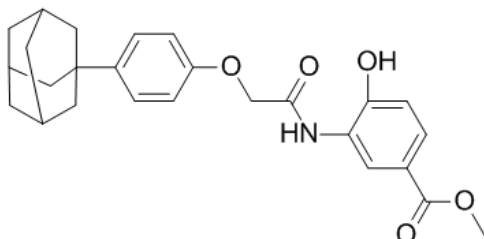
Formula $C_{26}H_{29}NO_5$ M.Wt 435.51

Solubility DMSO : ≥ 33 mg/mL (75.77 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines MDCKII-BCRP cells (overexpressing BCRP)

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

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Preparation Method Cells were seeded into a 96-well plate. At 3 days post-seeding, cells were incubated with mitoxantrone (5 μ M) with/without inhibitor LW6 over the concentration range of 0.01-25 μ M. After incubation for 30 min, the drug solution was removed and the cells were washed twice with ice-cold PBS.

Reaction Conditions 0.01-25 μ M; 30 min

Applications LW6 enhanced significantly the cellular accumulation of mitoxantrone (BCRP substrate).

Animal experiment [2]:

Animal models Male ICR mice

Preparation Method Mice were given a single intravenous (i.v.; 5 mg/kg) or oral dose (p.o.; 5 mg/kg) of LW6.

Dosage form 5 mg/kg; i.v./p.o;

Applications LW6 exhibited a small volume of distribution (0.5 ± 0.1 L/kg), and a short terminal half-life (0.6 ± 0.1 h). LW6 was slowly degraded in mouse liver microsomes ($t_{1/2} > 1$ h) and serum ($t_{1/2} > 6$ h). About 54% or 44.8% of LW6 was available systemically as APA in the mouse after a single intravenous or oral administration, respectively.

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References:

- [1]. Song JG, Lee YS, et.al. Discovery of LW6 as a new potent inhibitor of breast cancer resistance protein. *Cancer Chemother Pharmacol.* 2016 Oct;78(4):735-44. doi: 10.1007/s00280-016-3127-2. Epub 2016 Aug 12. PMID: 27520631.
- [2]. Lee JY, Lee K, et.al. Pharmacokinetic Characterization of LW6, a Novel Hypoxia-Inducible Factor-1 α (HIF-1 α) Inhibitor in Mice. *Molecules.* 2021 Apr 12;26(8):2226. doi: 10.3390/molecules26082226. PMID: 33921487; PMCID: PMC8070284.

Background

LW6 is a hypoxia-inducing factor 1 (HIF) inhibitor, which effectively inhibits HIF-1 α accumulation by degrading HIF-1 α , but does not affect HIF-1A mRNA level during hypoxia. LW6 inhibits the expression of HIF and MDH2, with IC50 values of 4.4 and 6.3 μ M, respectively [1-2].

LW6 (0.01-25 μ M ; 30 min) enhanced significantly the cellular accumulation of mitoxantrone (BCRP substrate) in MDCKII-BCRP cells (overexpressed BCRP) [3]. LW6 inhibited hypoxia-induced HIF1 α expression at 20 mM in A549 cells, and at this concentration, LW6 induced hypoxia-selective apoptosis and decreased mitochondrial membrane potential [4]. LW6 (40-160 μ M) inhibited proliferation and induced cell death in a dose-dependent manner in 6606PDA and MIA PaCa-2 cells [5]. LW6 (80 μ M) significantly inhibited migration, besides, LW6 reduced cell proliferation and induced cell death in a dose dependent manner [6]. LW6 (30 μ M; 72 h) stimulates T cells to decrease HIF-1 α levels [7]. LW6 inhibited T-cell clonal expansion in two-way mixed lymphocyte reaction (MLR) [8].

LW6 (5 mg/kg; i.v/p.o) exhibited a small volume of distribution and a short terminal half-life. LW6 was slowly degraded in mouse liver microsomes and serum. About 54% or 44.8% of LW6 was available systemically as APA in the mouse after a single intravenous or oral administration, respectively [1].

References:

- [1]. Lee K, Lee JH, et.al. (Aryloxyacetyl amino) benzoic acid analogues: A new class of hypoxia-inducible factor-1 inhibitors. *J Med Chem.* 2007 Apr 5;50(7):1675-84. doi: 10.1021/jm0610292. Epub 2007 Mar 1. PMID: 17328532.
- [2]. Naik R, Won M, et.al. Synthesis and structure-activity relationship study of chemical probes as

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- hypoxia induced factor-1 α /malate dehydrogenase 2 inhibitors. J Med Chem. 2014 Nov 26;57(22):9522-38. doi: 10.1021/jm501241g. Epub 2014 Nov 12. PMID: 25356789.
- [3]. Song JG, Lee YS, et,al. Discovery of LW6 as a new potent inhibitor of breast cancer resistance protein. Cancer Chemother Pharmacol. 2016 Oct;78(4):735-44. doi: 10.1007/s00280-016-3127-2. Epub 2016 Aug 12. PMID: 27520631.
- [4]. Sato M, Hirose K, 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):3462-3468. doi: 10.3892/mmr.2015.3862. Epub 2015 May 27. PMID: 26017562; PMCID: PMC4526100.
- [5]. Zhang X, Kumstel S, et,al. LW6 enhances chemosensitivity to gemcitabine and inhibits autophagic flux in pancreatic cancer. J Adv Res. 2019 Apr 24;20:9-21. doi: 10.1016/j.jare.2019.04.006. PMID: 31193017; PMCID: PMC6514270.
- [6]. Zhang X, Liu P, et,al.Metformin and LW6 impairs pancreatic cancer cells and reduces nuclear localization of YAP1. J Cancer. 2020 Jan 1;11(2):479-487. doi: 10.7150/jca.33029. PMID: 31897243; PMCID: PMC6930432.
- [7]. Eleftheriadis T, Pissas G, et,al. Malate dehydrogenase-2 inhibitor LW6 promotes metabolic adaptations and reduces proliferation and apoptosis in activated human T-cells. Exp Ther Med. 2015 Nov;10(5):1959-1966. doi: 10.3892/etm.2015.2763. Epub 2015 Sep 22. PMID: 26640580; PMCID: PMC4665222.
- [8]. Eleftheriadis T, Pissas G, et,al.Comparison of the effect of the aerobic glycolysis inhibitor dichloroacetate and of the Krebs cycle inhibitor LW6 on cellular and humoral alloimmunity. Biomed Rep. 2017 Nov;7(5):439-444. doi: 10.3892/br.2017.980. Epub 2017 Sep 11. PMID: 29181155; PMCID: PMC5700391.

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