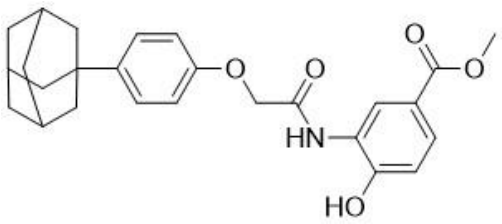
Product data sheet

MedKoo Cat#: 401535 Name: CAY10585 CAS#: 934593-90-5 Chemical Formula: $C_{26}H_{29}NO_5$ Exact Mass: 435.20457 Molecular Weight: 435.51216	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

CAY10585, also known as LW6, was first identified and reported by a group scientists from Korea. LW8 was found to inhibit the accumulation of HIF-1alpha. LW6 decreased HIF-1alpha protein expression without affecting HIF-1beta expression. It was further found that LW8 promoted the degradation of wild type HIF-1alpha, but not of a DM-HIF-1alpha with modifications of P402A and P564A, at hydroxylation sites in the oxygen-dependent degradation domain (ODDD). LW6 did not affect the activity of prolyl hydroxylase (PHD), but induced the expression of von Hippel-Lindau (VHL), which interacts with prolyl-hydroxylated HIF-1alpha for proteasomal degradation. In the presence of LW8, knockdown of VHL did not abolish HIF-1alpha protein accumulation, indicating that LW8 degraded HIF-1alpha via regulation of VHL expression. In mice carrying xenografts of human colon cancer HCT116 cells, LW8 demonstrated strong anti-tumor efficacy in vivo and caused a decrease in HIF-1alpha expression in frozen-tissue immunohistochemical staining. These data suggest that LW8 may be valuable in the development of a HIF-1alpha inhibitor for cancer treatment. (source: Biochem Pharmacol. 2010 Oct 1;80(7):982-9.)

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under “QC And Documents” section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	17.5	40.18
DMF	25.6	58.8

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.30	11.48	22.96
5 mM	0.46	2.30	4.59
10 mM	0.23	1.15	2.30
50 mM	0.05	0.23	0.46

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of “Calculator”

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Zhang X, Kumstel S, Jiang K, Meng S, Gong P, Vollmar B, Zechner D. 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.

2. Sato M, Hirose K, Kashiwakura I, Aoki M, Kawaguchi H, Hatayama Y, Akimoto H, Narita Y, Takai Y. 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.

Product data sheet

In vivo study

1. Lee K, Kang JE, Park SK, Jin Y, Chung KS, Kim HM, Lee K, Kang MR, Lee MK, Song KB, Yang EG, Lee JJ, Won M. 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. doi: 10.1016/j.bcp.2010.06.018. Epub 2010 Jun 23. PMID: 20599784.
2. Lee JY, Lee K, Lee K, Kang JS, Kim MJ, Yoo DG, Kim JA, Shin EJ, Oh SJ. Pharmacokinetic Characterization of LW6, a Novel Hypoxia-Inducible Factor-1α (HIF-1α) Inhibitor in Mice. Molecules. 2021 Apr 12;26(8):2226. doi: 10.3390/molecules26082226. PMID: 33921487; PMCID: PMC8070284.

7. Bioactivity

Biological target:

LW6 (HIF-1α inhibitor) is a novel HIF-1 inhibitor with an IC50 of 4.4 μM.

In vitro activity

To clarify, if hypoxia is necessary to investigate the anti-cancer effects of LW6, 6606PDA and MIA PaCa-2 cells were cultured under normoxic and hypoxic conditions. Surprisingly, the inhibition of cell proliferation by LW6 was not influenced by the oxygen supply (Fig. 1). Thus, the following experiments were performed under normoxic conditions. To investigate the anti-cancer effects of LW6, the proliferation and cell death of 6606PDA and MIA PaCa-2 cells were analyzed. In both cell lines, LW6 inhibited proliferation (Fig. 2A and 2B) and induced cell death (Fig. 2C and D) in a dose-dependent manner. In 6606PDA and MIA PaCa-2 cells, the application of 80 μM and 160 μM LW6 significantly inhibited cell proliferation compared to Sham-treated or 40 μM LW6-treated cells, respectively (Fig. 2A and B). In 6606PDA cells, these concentrations of LW6 also significantly increased cell death (Fig. 2C). In addition, LW6 had more efficient cytotoxic effects on MIA PaCa-2 cells than on 6606PDA cells. A dose of 80 μM LW6 killed almost 84% of the MIA PaCa-2 cells within 48 h (Fig. 2D). In order to evaluate, if and how LW6 influences the autophagic flux, the accumulation of LC3II and p62 was analyzed. It was observed that 80 μM LW6 induced the accumulation of LC3II in a time-dependent manner in 6606PDA cells as well as MIA PaCa-2 cells, with the strongest induction at 12 h (Fig. 7A and B). Moreover, LW6 also induced the accumulation of LC3II in a dose-dependent manner in both cell lines (Fig. 7C and D). Similar to LC3II, p62 also accumulated after treating the cells with LW6 (Fig. 7E and F). LW6 inhibited the accumulation of LC3II and p62 in a similar manner to CQ, a traditional inhibitor of autophagic flux after 6 h (Fig. 8A) as well as 12 h (Fig. 8B). In addition, CQ in combination with LW6 failed to increase the accumulation of LC3II and p62, when compared to cells treated by LW6 monotherapy (Fig. 8). These data demonstrate that 80 μM LW6 completely blocks autophagic flux leading to increased accumulation of LC3II and p62.

J Adv Res. 2019 Nov; 20: 9–21. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6514270/

In vivo activity

The objective of this study was to investigate the pharmacokinetics and metabolism of LW6 in male ICR mice to support its preclinical development as an antitumor agent. After i.v. administration of LW6 at a dose of 5 mg/kg, the plasma concentration declined rapidly in an apparent polyexponential fashion. The plasma level of LW6 was below the quantitation limit beyond 4 h (Figure 1A). An apparent terminal phase was defined in the plasma concentration-time curve of LW6 between 1 to 4 h post-administration with a t1/2 of 0.6 ± 0.1 h (Figure 1 and Table 1); the volume of distribution at steady state (Vss) was 0.5 ± 0.1 L/kg, close to the total body water volume (0.7 L/kg), indicating that LW6 was distributed outside the vasculature. The systemic clearance (CL) of LW6 was 1.7 ± 0.1 L/hr/kg (Table 1), lower than the hepatic blood flow of the mouse (Table 1). LW6 (1 μM) was incubated with pooled mouse liver microsomes (0.5 mg/mL) in the absence or presence of NADPH (1 mM) to determine its conversion to APA. LW6 was degraded slowly in the absence or presence of NADPH, with 63% or 65% remaining after 60 min microsomal incubations, respectively (Figure 3A). LW6 was converted slowly to APA (t1/2 > 60 min) in a quantitative manner in liver microsomes (Figure 3A). APA, following its formation, gradually disappeared from the microsomal incubation media only in the presence of NAPDH (Figure 3A). To determine whether APA was metabolized by cytochrome P450 (CYP450), APA (1 μM) also was incubated with pooled male mouse liver microsomes (0.5 mg/mL) in the absence or presence of NADPH (1 mM). As shown in Figure 4, APA was progressively decreased when incubated with mouse liver microsomes in the presence of NADPH. These results suggested that LW6 was metabolized to APA, which was further metabolized by CYP450. In the case of mouse serum, LW6 was also converted slowly to APA (Figure 3B). These results suggested that LW6 as an anticancer drug is highly likely to work as its active metabolite APA in the body.

Molecules. 2021 Apr; 26(8): 2226. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8070284/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.