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产品名称：
4-Hydroxy-3-[[2-(4-tricyclo[3.3.1.13,7]dec-1-ylphenoxy)acetyl]amino]-benzoic Acid Methyl Ester
产品别名：LW6； HIF-1α inhibitor; LW8

生物活性：

Description	LW6 (HIF-1α inhibitor) is a novel HIF-1 inhibitor with an IC50 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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 33 mg/mL (75.77 mM)** * "≥" means soluble, but saturation unknown.

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

	Solubility: 2.5 mg/mL (5.74 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.74 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.74 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.74 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.74 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.74 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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].
Animal Administration	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].
	[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

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