L-165041

Cat. No.: HY-20019

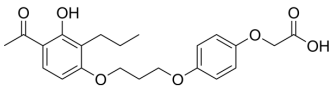
CAS No.: 79558-09-1

Molecular Formula: $C_{22}H_{26}O_7$

Molecular Weight: 402.44

Target: PPAR

Pathway: Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor



Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year

SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (124.24 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4848 mL	12.4242 mL	24.8484 mL
	5 mM	0.4970 mL	2.4848 mL	4.9697 mL
	10 mM	0.2485 mL	1.2424 mL	2.4848 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 (6.21 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

L-165041 is a cell permeable PPARδ agonist, with K_is of 6 nM and appr 730 nM for PPARδ and PPARγ, respectively, and induces adipocyte differentiation in NIH-PPARδ cells.

IC_{50} & Target

PPARδ	PPARγ
6 nM (Ki)	730 nM (Ki)

In Vitro

L-165041 is a PPARδ agonist, with K_is of 6 nM and appr 730 nM for PPARδ and PPARγ, respectively[1]. L-165041 (1 or 5 μM) inhibits VEGF-induced endothelial cells (ECs) proliferation and migration. L-165041 negatively affects cell cycle progression in VEGF-activated human umbilical vein ECs (HUVECs). L-165041 (10 μM)inhibits PPARδ-independent, VEGF-induced

	angiogenesis[2]. PPARδ ligand L-165041 inhibits PDGF-induced rVSMC proliferation and migration. With 1 h of L-165041 pretreatment, PDGF-induced cellular migration is inhibited. L-165041 (10 μM) significantly suppresses S phase transition induced by PDGF[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	L-165041 (5 mg/kg/day, i.p.) significantly lowers the formation of lipid droplets in mice. L-165041 markedly reduces the level of both the hepatic cholesterol and triglycerides in mice. L-165041 increases mRNA expression levels of PPARδ compared to the vehicle group. Lipoprotein lipase (LPL) expression in L-165041-treated mice is significantly higher than that in the vehicle group[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Human umbilical vein ECs (HUVECs) are cultured in EGM-2. Subconfluent HUVECs are made quiescent by serum starvation [EBM-2 containing 0.1% fetal bovine serum (FBS)] for 4 h. The cells are pretreated with the PPARδ ligand L-165041 or GW501516 for 6 h followed by VEGF (10 ng/mL) induction[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	$LDLR^{-/-}$ mice are divided into vehicle (0.1 N NaOH) and L-165041 (5 mg/kg/day) group (9 animals in each group). $LDLR^{-/-}$ mice receive either NaOH or L-165041 via daily intraperitoneal injection (i.p.) for 16 weeks with the Western diet. Body weight is measured once a week and the blood samples for a serum parameter analysis are collected using an eye-bleeding method every 4 weeks. At the end of the experiment, $LDLR^{-/-}$ mice are fasted for 24 h before sacrificed and the liver samples are either fixed in formalin or frozen at −70°C for further analysis. All animals are housed in polycarbonate cages in a room with a 12-h light/12-h dark cycle, and maintained at a constant temperature of 22°C[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Berger J, et al. Novel peroxisome proliferator-activated receptor (PPAR) gamma and PPARdelta ligands produce distinct biological effects. J Biol Chem. 1999 Mar 5;274(10):6718-25.

[2]. Park, Jin-Hee., et al. The PPARδ ligand L-165041 inhibits vegf-induced angiogenesis, but the antiangiogenic effect is not related to PPARδ. Journal of Cellular Biochemistry (2012), 113(6), 1947-1954.

[3]. Lim, Hyun-Joung., et al. PPARδ ligand L-165041 ameliorates Western diet-induced hepatic lipid accumulation and inflammation in LDLR-/- mice. European Journal of Pharmacology (2009), 622(1-3), 45-51.

[4]. Lim, Hyun-Joung., et al. PPARδ agonist L-165041 inhibits rat vascular smooth muscle cell proliferation and migration via inhibition of cell cycle. Atherosclerosis (Amsterdam, Netherlands) (2009), 202(2), 446-454.

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