

Product Data Sheet

Product Name: L-165041

Cat. No.: GC16125

Chemical Properties

Cas. No. 79558-09-1

Chemical Name 2-[4-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]phenoxy]acetic acid

SMILES CCCC1=C(C=CC(=C1O)C(=O)C)OCCCOCC2=CC=C(C=C2)OCC(=O)O

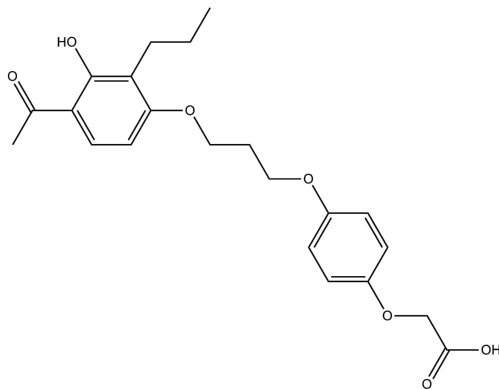
Formula $C_{22}H_{26}O_7$ M.Wt 402.44

Solubility ≥ 40.2 mg/mL in DMSO 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: 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 PPAR δ ligand L-165041 or GW501516 for 6 h followed by VEGF (10 ng/mL) induction[2].

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

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Animal experiment: 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].

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 PPAR δ ligand L-165041 inhibits vegf-induced angiogenesis, but the antiangiogenic effect is not related to PPAR δ . Journal of Cellular Biochemistry (2012), 113(6), 1947-1954.
- [3]. Lim, Hyun-Joung., et al. PPAR δ 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. PPAR δ 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.

Background

Ki: 6 nM for PPAR γ

Peroxisome proliferator-activated receptor (PPAR γ) is known to be expressed ubiquitously and involved in lipid and glucose metabolism. Studies have demonstrated that PPAR γ is expressed in endothelial cells and plays a potential role in endothelial proliferation and survival. L-165041 is reported as a selective and potent PPAR γ ligand.

In vitro: L-165041, which is a selective and potent PPAR δ ligand, displayed in this specified

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transactivation system, apart from its highly efficacious PPAR δ agonist activity, partial and full agonism at, respectively, PPAR γ 2 and PPAR α subtypes [1].

In vivo: L-165041 could drastically reduce lipid accumulation in the mouse liver, decreasing total hepatic triglyceride and cholesterol content compared to the vehicle group. Gene analysis demonstrated that L-165041 lowered hepatic expression of PPAR γ , apolipoprotein B, IL-1 β , and interleukin-6. In contrast, L-165041 increased hepatic expressions of PPAR δ , lipoprotein lipase, and ATP-binding cassette transporter G1 (ABCG1) [2].

Clinical trial: Up to now, L-165041 is still in the preclinical development stage.

Reference:

[1] Wurch T, Junquero D, Delhon A, Pauwels J. Pharmacological analysis of wild-type alpha, gamma and delta subtypes of the human peroxisome proliferator-activated receptor. Naunyn Schmiedeberg Arch Pharmacol. 2002 Feb;365(2):133-40.

[2] Lim HJ, Park JH, Lee S, Choi HE, Lee KS, Park HY. PPARdelta ligand L-165041 ameliorates Western diet-induced hepatic lipid accumulation and inflammation in LDLR $^{-/-}$ mice. Eur J Pharmacol. 2009 Nov 10;622(1-3):45-51.

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