Product Data Sheet

Product Name: Imiglitazar (TAK-559)
Cat. No.: GC32521

Chemical Properties

Cas. No.	250601-04-8		
SMILES	CC(OC(C1=CC=CC=C1)=N2)=C2COC(C=C3)=CC=C3CO/N=C(CCC(O)=O)/C4=CC=CC=C4		
Formula	$C_{28}H_{26}N_2O_5$	M.Wt	470.52
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	Imiglitazar (TAK-559)		

Protocol

Kinase experiment:

Competition binding assays are performed with cell extract containing hPPARδ and 20 nM [3H]L-783483 in the presence of indicated concentrations of TAK-559 (1, 10, 100 μM) or Iloprost. Data are expressed as the percentage of specific binding in the absence of competitor (vehicle (V) (1% DMSO)) [1].

Cell experiment:

COS-1 cells are cotransfected with expression plasmid for full-length hPPARγ1 as a VP16 fusion protein, GAL4-SRC-1 (A) or GAL4-NcoR (B) expression plasmid and (UAS)5-tk-Luciferase reporter plasmid. Cells are cultured in the presence of TAK-559 (0.01, 0.1, 1 μM) or rosiglitazone for 2 days. The cell extracts are assayed for luciferase activity[1].

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References:

[1]. Sakamoto J, et al. A novel oxyiminoalkanoic acid derivative, TAK-559, activates human peroxisome proliferator-activated receptor subtypes. Eur J Pharmacol. 2004 Jul 8;495(1):17-26.
[2]. Seki N, et al. A potent activator of PPARalpha and gamma reduces the vascular cell recruitment and inhibits the intimal thickning in hypercholesterolemic rabbits. Atherosclerosis. 2005 Jan;178(1):1-7.
[3]. Ding SY, et al. A novel peroxisome proliferator--activated receptor alpha/gamma dual agonist ameliorates dyslipidemia and insulin resistance in prediabetic rhesus monkeys. Metabolism. 2007 Oct;56(10):1334-9.

Background

Imiglitazar (TAK559) is a potent and dual human PPARα and PPARγ1 agonist with EC50 values of 67 and 31 nM.

TAK-559 is a partial agonist for hPPARg1 with about 68% of maximal activation obtained with rosiglitazone, a known PPARγ agonist. PPARy is significantly activated at a high concentration (10 μM) of TAK-559. Competition-binding assays using radiolabeled ligand indicates that the transactivation of all hPPAR subtypes by TAK-559 is due to direct binding of TAK-559 to each subtype. TAK-559 also recruit the coactivator SRC-1 to each of hPPARγ1 and hPPARα, and to dissociate the corepressor NCoR from each of hPPARγ1 and hPPARα[1].TNFα- or IL-1β-induced THP-1 cell attachment to cultured endothelial cells is significantly reduced in the presence of 10 μM TAK-559. The secretion of monocyte chemoattractant protein-1 (MCP-1) from endothelial cells is reduced by 36% in the presence of 10 μM TAK-559, accompanied with the decreased mRNA expression in the cells. The proliferation and migration of cultured smooth muscle cells are significantly decreased in the presence of TAK-559[2].

TAK-559 treatment results in significant elevation of circulating high-density lipoprotein (HDL)

cholesterol levels, consisting of an increase in large HDL particles and a decrease in small dense HDL particles. Plasma triglyceride and apolipoprotein B-100 levels decrease, whereas apolipoprotein A-I increasesduring TAK-559 treatment. Hyperinsulinemia and insulin resistance are significantly corrected with the highest dose of 3.0 mg/kg per day in these prediabetic monkeys. In addition, no adverse effects on representative liver function parameters are observed during the study period[3].

[1]. Sakamoto J, et al. A novel oxyiminoalkanoic acid derivative, TAK-559, activates human peroxisome proliferator-activated receptor subtypes. Eur J Pharmacol. 2004 Jul 8;495(1):17-26. [2]. Seki N, et al. A potent activator of PPARalpha and gamma reduces the vascular cell recruitment and inhibits the intimal thickning in hypercholesterolemic rabbits. Atherosclerosis. 2005 Jan;178(1):1-7. [3]. Ding SY, et al. A novel peroxisome proliferator--activated receptor alpha/gamma dual agonist ameliorates dyslipidemia and insulin resistance in prediabetic rhesus monkeys. Metabolism. 2007 Oct;56(10):1334-9.

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