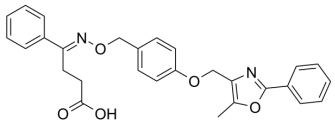
Imiglitazar

Cat. No.:	HY-101649
CAS No.:	250601-04-8
Molecular Formula:	$C_{28}H_{26}N_2O_5$
Molecular Weight:	470.52
Target:	PPAR
Pathway:	Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Imiglitazar (TAK559) is a potent and dual human PPARα and PPARγ1 agonist with EC_{50} values of 67 and 31 nM.
IC_{50} & Target	PPARγ1 31 nM (EC50) PPARα 67 nM (EC50)
In Vitro	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Competition binding assays are performed with cell extract containing hPPARδ and 20 nM [^{3}H]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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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.

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