Imiglitazar

**Cat. No.:** HY-101649  
**CAS No.:** 250601-04-8  
**Molecular Formula:** C₂₈H₂₆N₂O₅  
**Molecular Weight:** 470.52  
**Target:** PPAR  
**Pathway:** Cell Cycle/DNA Damage  
**Storage:** Please store the product under the recommended conditions in the COA.

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**BIOLOGICAL ACTIVITY**

**Description**

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

**IC₅₀ & Target**

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>PPARγ₁</th>
<th>PPARα</th>
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<tr>
<td>31 nM (EC₅₀)</td>
<td>67 nM (EC₅₀)</td>
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**In Vitro**

TAK-559 is a partial agonist for hPPARγ₁ with about 68% of maximal activation obtained with rosiglitazone, a known PPARγ agonist. PPARγ 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].

**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 increases during 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].

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**PROTOCOL**

**Kinase Assay** [1]

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].

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

