Indeglitazar

Cat. No.: HY-14817

CAS No.: 835619-41-5

Molecular Formula: $C_{19}H_{19}NO_6S$

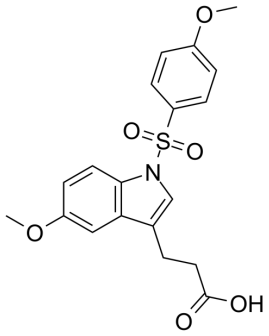
Molecular Weight: 389.42

Target: PPAR

Pathway: Cell Cycle/DNA Damage; 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 : 100 mg/mL (256.79 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5679 mL	12.8396 mL	25.6792 mL
	5 mM	0.5136 mL	2.5679 mL	5.1358 mL
	10 mM	0.2568 mL	1.2840 mL	2.5679 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 (6.42 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.42 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Indeglitazar (PPM 204) is an orally available PPAR pan-agonist for all three PPARα, PPARδ and PPARγ[1].

IC_{50} & Target			
	PPARα	PPARδ	PPARγ

In Vitro

In an assay of preadipocyte differentiation, measuring in part functional insulin sensitization capability of the cells, Indeglitazar shows an EC_{50} of 0.32 μM compared with Rosiglitazone, which shows an EC_{50} of 13 nM, although the maximal response obtained from the 2 compounds is comparable[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	An initial assessment of in vivo activity is carried out using the Zucker rat model of diabetes. The significant lowering of glucose, HbA_{1C}, triglycerides, and total cholesterol are observed after i.v. treatment with 10 mg/kg Indeglitazar once per day for 3 weeks. Notably, the level of Adiponectin (on day 21) is essentially unchanged in treated vs. untreated animals (4.8 mcg/mL vs. 4.9 mcg/mL), thus the observed reductions in glucose and HbA_{1C} are achieved in an adiponectin-independent fashion. These differences in the effects of Indeglitazar in vivo may be a consequence of synergy between the 3 PPAR activities or because of the SPPARM profile of the compound, or a combination of these factors. The oral activity of Indeglitazar is assessed in the ob/ob model of diabetes and insulin resistance. Indeglitazar significantly decreases glucose, insulin, triglycerides, and free fatty acid levels[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The purified PPAR_ LBD protein is diluted to 12 mg/mL and 1mM of Indeglitazar and 2x molar excess of steroid receptor coactivator-1 (SRC-1) peptide are added before crystallization by mixing equal volumes of a protein/compound sample with reservoir solution containing 27% polyethylene glycol (PEG) 4000, 0.1 M 2-(bis-(2-hydroxy-ethyl)-amino)-2-hydroxymethyl-propane-1,3-diol (BisTris) buffer at pH 6.5, 0.2 M ammonium acetate, and 5% glycerol. The crystals are soaked in cryo-protective buffer (30% PEG 4000, 0.1 M BisTris buffer at pH 6.5, 0.2 M ammonium acetate, and 5% glycerol) before flash-freezing in liquid nitrogen for data collection[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats[1] Indeglitazar is administered once daily i.v. as a solution (10% SolutolHS15,10%ethanol,80%saline) to ZDF/GmiCrl-fa/fa rats. Treatment is initiated at age 7-8 weeks, and blood samples are analyzed before the treatment and 21 days after the treatment. Mice[1] Ob/ob mouse study. Indeglitazar (10 mg/kg) or Pioglitazone (30 mg/kg) are orally administered to 9-week-old B6.V-Lepob mice for 14 days. Compounds are suspected in 0.5% methylcellulose and 2% Tween 80 before dosing. On the last day, blood is collected for insulin, triglyceride, free fatty acid, and adiponectin measurements. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Artis DR, et al. Scaffold-based discovery of Indeglitazar, a PPAR pan-active anti-diabetic agent. Proc Natl Acad Sci U S A. 2009 Jan 6;106(1):262-7.

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