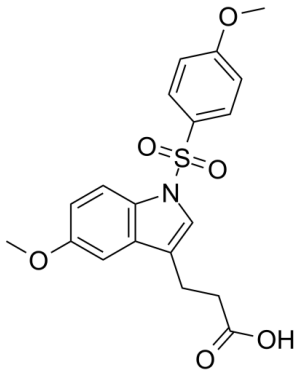
Data Sheet

Product Name:	Indeglitazar
Cat. No.:	CS-6601
CAS No.:	835619-41-5
Molecular Formula:	C19H19NO6S
Molecular Weight:	389.42
Target:	PPAR
Pathway:	Cell Cycle/DNA Damage
Solubility:	DMSO : 33 mg/mL (84.74 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Indeglitazar is an orally available peroxisome proliferator-activated receptor (**PPAR**) pan-agonist for all three PPAR subtypes alpha (α), delta (δ) and gamma (γ). IC50 & Target: PPAR[1] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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].

Animal Administration: Indeglitazar is prepared as a solution (10% Solutol HS15,10% ethanol,80% saline) (Rats)[1].
Indeglitazar is suspected in 0.5% methylcellulose and 2% Tween 80 before dosing (Mouse)[1].[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.

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.

CAIndexNames:

1H-Indole-3-propanoic acid, 5-methoxy-1-[(4-methoxyphenyl)sulfonyl]-

SMILES:

O=C(O)CCC1=CN(S(=O)(C2=CC=C(OC)C=C2)=O)C3=C1C=C(OC)C=C3

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