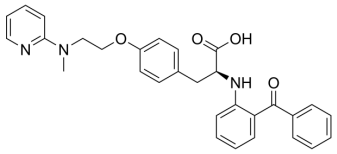
GW1929

Cat. No.:	HY-15655
CAS No.:	196808-24-9
Molecular Formula:	$C_{30}H_{29}N_3O_4$
Molecular Weight:	495.57
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 : ≥ 35 mg/mL (70.63 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0179 mL	10.0894 mL	20.1788 mL
	5 mM	0.4036 mL	2.0179 mL	4.0358 mL
	10 mM	0.2018 mL	1.0089 mL	2.0179 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 (5.04 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.04 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GW 1929 is an orally active peroxisome proliferator-activated receptor-γ (PPARγ) agonist with a pK_i of 8.84 for human PPAR-γ, and pEC_{50}s of 8.56 and 8.27 for human PPAR-γ and murine PPAR-γ, respectively. GW 1929 (hydrochloride) has antidiabetic efficacy and neuroprotective potential[1][2].

IC_{50} & Target

PPAR-γ
8.56 (pEC50, Human PPAR-γ)

In Vitro

GW1929 is a potent PPAR-γ activator, with pK_is of 8.84, < 5.5, and < 6.5 for human PPAR-γ, PPAR-α, and PPAR-δ, and pEC_{50}s of 8.56 and 8.27 for human PPAR-γ and murine PPAR-γ, respectively[1].

	GW1929 (10 μM) inhibits TBBPA-induced caspase-3 increase and TBBPA-stimulated LDH release in neocortical cell cultures[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GW1929 (0.5, 1, 5 mg/kg, p.o.) highly decreases nonfasted plasma glucose levels in Zucker diabetic fatty (ZDF) rats after treatment for 14 days, and possesses antilipolytic efficacy. GW1929 (1, 5 mg/kg, p.o.) increases glucose-stimulated insuline secretion of β-cell in ZDF rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Ligand binding to bacterially expressed ligand binding domain (LBD) of hPPAR-γ is determined by scintillation proximity assay (SPA). The assay measures the ability of putative ligands to displace receptor bound [^{3}H]BRL 49653. Assays are conducted in 96-well plates. Wells contained varying concentrations of GW1929 or troglitazone; streptavidin-modified SPA beads to which biotinylates PPAR-γ LBD is prebound; and 10 nM of the specific radioligand [^{3}H]BRL 49653 in a volume of 100 μL. The amount of nonspecific binding, as assessed by control wells that contained 50 μM of the corresponding unlabeled ligand, is subtracted from each data point. For each compound tested, plots of ligand concentration versus counts/min of radioligand bound are constructed, and apparent K_i values are estimated from a nonlinear least squares fit of the data, assuming simple competitive binding. The results are expressed as pK_i, where $pK_i = -\log_{10}(K_I)$[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	For the experiments, the cells are plated in 96-well plates at a density 2×10^5 cells per cm^2 and cultured in the presence of TBBPA, in a concentrations range from 1 nM to 100 μM TBBPA. TBBPA is dissolved in DMSO, resulting in a final vehicle concentration of 0.1 % (v/v). Control (no vehicle) and DMSO-treated wells are included in the experimental design to determine the effect of DMSO. To study whether PPAR-γ is involved in the neurotoxic effect of TBBPA, cells are co-treated with 10 μM TBBPA and 10 μM GW1929 or GW9662. After 6 or 24 h of culture, 100 μL medium is collected for the LDH analysis, and the cells are collected and frozen at −70°C for the caspase-3 activity measurements[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Animals are housed at 72°F and 50% relative humidity with a 12-h light and dark cycle, and fed Formulab Diet 5008. Age- (60-day) and glucose-matched male Zucker diabetic fatty rats are gavaged twice daily for 14 days with vehicle (0.05 M N-methylglucamine), GW1929 (0.5, 1.0, or 5.0 mg/kg), or troglitazone (as the milled extrudate, in a suspension in methylcellulose, 50, 150, and 500 mg/kg). Another group of animals receives a mixture of Humulin N and Humulin R by subcutaneous injection twice daily. On days 7 and 14 of dosing, nonfasted measurements of glucose, lactate, insuline, total cholesterol, TGs, F FAs, and hematocrit are obtained. On day 14 of dosing, samples for serum drug levels (2-h postdose) and glycosylated hemoglobin measurements are also collected. In addition, once weekly, three animals from each group are placed in metabolic chambers for 48 h for quantitation of 24-h food and water consumption. Body weights are recorded throughout the study. At the conclusion of the study, perfused pancreas experiments are performed on 12 animals (n = 4 per group) that have received either GW1929 (1 and 5 mg/kg) or vehicle, to directly evaluate the effects of treatment on basal and glucose-stimulated insuline secretion. The remaining animals are killed, and their pancreases are processed for immunocytochemistry[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Phytother Res. 2023 Aug 26.
- Ecotoxicol Environ Saf. 2020 Sep 15;201:110801.
- Int Immunopharmacol. 2023 Sep 9;124(Pt A):110840.

- Aging. 2021 May 25;13(11):15240
- J Zhejiang Univ Sci B. 2020 Dec; 21(12): 990–998.

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REFERENCES

[1]. Brown KK, et al. A novel N-aryl tyrosine activator of peroxisome proliferator-activated receptor-gamma reverses the diabetic phenotype of the Zucker diabetic fatty rat. Diabetes. 1999 Jul;48(7):1415-24.

[2]. Wojtowicz AK, et al. PPAR-γ agonist GW1929 but not antagonist GW9662 reduces TBBPA-induced neurotoxicity in primary neocortical cells. Neurotox Res. 2014 Apr;25(3):311-22.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA