GW9662

Cat. No.: HY-16578

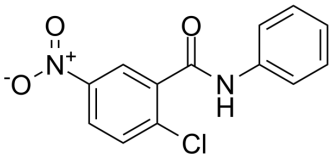
CAS No.: 22978-25-2

Molecular Formula: $C_{13}H_9ClN_2O_3$

Molecular Weight: 276.68

Target: PPAR

Pathway: Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; 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 (361.43 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.6143 mL	18.0714 mL	36.1428 mL
5 mM	0.7229 mL	3.6143 mL	7.2286 mL
10 mM	0.3614 mL	1.8071 mL	3.6143 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 (9.04 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (9.04 mM); Clear solution
3. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: ≥ 0.5 mg/mL (1.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GW9662 is a potent and selective PPARγ antagonist with an IC_{50} of 3.3 nM, showing 10 and 1000-fold selectivity over PPARα and PPARδ, respectively.

IC_{50} & Target	PPARγ	PPARα	PPARδ

	3.3 nM (IC_{50})	32 nM (IC_{50})	2000 nM (IC_{50})

In Vitro

GW9662 inhibits radioligand binding to PPARγ, PPARα, and PPARδ with pIC_{50}s of 8.48±0.27 (IC_{50}=3.3 nM; n=10), 7.49±0.17 (IC_{50}=32 nM; n=9), and 5.69±0.17 (IC_{50}=2000 nM; n=3), respectively. GW9662 has nanomolar IC_{50} versus PPARγ and is 10- and 600-fold less potent in binding experiments using PPARα and PPARδ, respectively. In cell-based reporter assays, GW9662 is a potent and selective antagonist of full-length PPARγ[1]. Co-treatment with both 50 μM BRL 49653 and 10 μM GW9662 results in statistically lower viable cell numbers after 7 days when compared to treatment with either 50 μM BRL 49653 (P=0.001) or 10 μM GW9662 (P=0.01) alone[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Bone marrow (BM) nucleated cell counts in both BADGE- and GW9662(1 mg/kg, i.p.)-treated mice are significantly higher than counts in the aplastic anemia (AA) group[3]. GW9662 (1 mg/kg, i.p.) largely attenuates the renoprotective effects of Lipopolysaccharide (LPS) in the rat[4].

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PROTOCOL

Cell Assay [2]

Cells (MCF7, MDA-MB-231, MDA-MB-468) are plated in 96-well plates at a density of 1×10^3 cells per well in RPMI medium. After overnight incubation to allow for cell attachment, the medium is removed and replaced with fresh medium containing varying concentrations of BRL 49653 (1-100 μM), GW9662 (100 nM-50 μM) or solvent (DMSO) alone. MDA-MB-231 cells are also subjected to combinations of BRL 49653 (10, 50 μM) and GW9662 (1, 10 μM) added simultaneously. The final concentration of DMSO in all cases does not exceed 0.1% and is not found to be cytotoxic in any of the cell lines tested at this concentration. Chemosensitivity is assessed following a continuous 72 h exposure using a standard MTT assay.

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Animal Administration [3][4]

Mice[3]

Inbred C57BL/6 (B6, $H2^{b/b}$), DBA/1J (DBA/1, $H2^{q/q}$), FVB/NJ (FVB, $H2^{q/q}$) mice and congenic C.B10-$H2^{b/b}$/LilMcd (CB10, $H2^{b/b}$) mice are used. BADGE or GW9662, are administrated by daily intraperitoneal injection at 30 mg/kg for BADGE, or at 1 mg/kg for GW9662, from one day prior to the experiment and continued for up to 2 weeks. In the FVB AA model, some mice are injected with CsA (50 mg/kg/day) starting 1 hour after the LN injection, and continued for 5 days as immunosuppression. At the end of the experiments, the mice are euthanized by CO_2 inhalation.

Rats[4]

Sixty-two male Wistar rats weighing 215 to 315 g are used in this study. Animals are randomly allocated into 6 groups as follows: (1) I/R group: control, rats are administered 10% (v/v) DMSO (vehicle for GW9662, 1 mL /kg, IP) 24 and 12 hours prior to renal I/R, and saline (vehicle for LPS, 1 mL /kg, IP) 24 hours prior to renal I/R (N=12); (2) I/R LPS group: rats are administered 10% (v/v) DMSO (vehicle for GW9662, 1 mL /kg, IP) 24 and 12 hours prior to renal I/R, and LPS (1 mg/kg, IP) 24 hours prior to renal I/R (N=11); (3) I/R GW9662 group: rats are administered GW9662 (1 mg/kg, IP) 24 and 12 hours prior to renal I/R, and saline (vehicle for LPS, 1 mL /kg, IP) 24 hours prior to renal I/R (N=9); (4) I/R LPS+GW9662 group: rats are administered GW9662 (1 mg/kg, IP) 24 and 12 hours prior to renal I/R, and LPS (1 mg/kg, IP) 24 hours prior to renal I/R (N=11); (5) Sham group: rats are subjected to the same surgical procedures as above, except for renal I/R. Rats are administered 10% (v/v) DMSO (vehicle for GW9662, 1 mL /kg, IP) and saline (vehicle for LPS, 1 mL /kg, IP) at times equivalent to those described above (N=12); (6) Sham GW9662 group: rats are subjected to the same surgical procedures as above, except for renal I/R. Rats are administered GW9662 (1 mg/kg, IP) and saline (vehicle for LPS, 1 mL /kg, IP) at times equivalent to those described above (N=7).

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CUSTOMER VALIDATION

- Nat Commun. 2022 Apr 13;13(1):1989.

- Brain Behav Immun. 2020 Nov;90:55-69.
- Brain Behav Immun. 2020 Jul;87:568-578.
- Cell Death Differ. 2021 Jun;28(6):1880-1899.
- Cell Death Differ. 2019 Nov;26(11):2253-2267.

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REFERENCES

[1]. Leesnitzer LM, et al. Functional consequences of cysteine modification in the ligand binding sites of peroxisome proliferator activated receptors by GW9662. Biochemistry. 2002 May 28;41(21):6640-50.

[2]. Seargent JM, et al. GW9662, a potent antagonist of PPARgamma, inhibits growth of breast tumor cells and promotes the anticancer effects of the PPARgamma agonist BRL 49653, independently of PPARgamma activation. Br J Pharmacol. 2004 Dec;143(8):933-7.

[3]. Sato K, et al. PPARγ antagonist attenuates mouse immune-mediated bone marrow failure by inhibition of T cell function.Haematologica. 2016 Jan;101(1):57-67.

[4]. Collino M, et al. The selective PPARgamma antagonist GW9662 reverses the protection of LPS in a model of renal ischemia-reperfusion. Kidney Int. 2005 Aug;68(2):529-36.

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