

Product Data Sheet

Product Name: GW9662

Cat. No.: GC13969

Chemical Properties

Cas. No. 22978-25-2

Chemical Name 2-chloro-5-nitro-N-phenylbenzamide

SMILES C1=CC=C(C=C1)NC(=O)C2=C(C=CC(=C2)[N+](=O)[O-])Cl

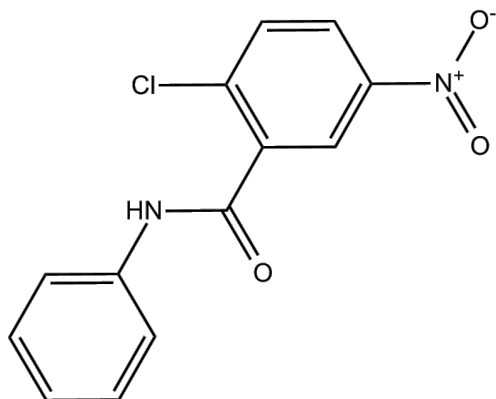
Formula $C_{13}H_9ClN_2O_3$ M.Wt 276.68

Solubility ≥ 13.75 mg/mL in DMSO, ≥ 9.08 mg/mL in EtOH with ultrasonic Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Kinase experiment [1]:

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Preparation method	Human PPARα, PPARγ, and PPARδ ligand binding domains (LBDs) are expressed in <i>E. coli</i> as polyhistidine labeled fusion proteins. In the experimental buffer, the desired receptor (15 nM) was added to the streptavidin modified SPA bead (0.5 mg/mL) pulp to fix the receptor to the SPA bead. The mixture was equilibrated at room temperature for at least 1 hour, then the beads were precipitated at $1 \times 10^3 g$ rotation speed, the supernatant was removed, the beads were gently mixed, the beads were suspended in fresh experimental buffer, the centrifugation/re-suspension procedure was repeated, the resulting acceptor coated bead slurry was used immediately, or stored at 4°C for up to 1 week before use. Competitive binding to PPARα, PPARγ, and PPARδ was determined using [^3H]GW9662 as a radioligand. Unless otherwise indicated, all experimental buffers were 50 mM HEPES (pH 7), 50 mM NaCl, 5 mM CHAPS, 0.1 mg/mL BSA, and 10 mM DTT. In some experiments, 50 mM Tris (pH 8) was used instead of HEPES (pH 7).
Applications	GW9662 is a potent and selective PPAR γ antagonist with an IC_{50} of 3.3 nM.
Cell experiment [2]:	
Cell lines	J774A.1 cells

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Preparation method	Cells were challenged with 50 ng/ml lipopolysaccharide with(or no) 10 μ M GW9662 or vehicle for 18 h. Cell culture supernatant was collected, cells were lysed for RNA separation, or cells were lysed with nitric oxide synthase (NOS) buffer added with protease inhibitors, and NOS activity was measured.
Reaction Conditions	10 μ M GW9662; 18 h
Applications	Treatment with GW9662 significantly attenuated LPS-induced expression of Il1b, interleukin 6 (Il6) and inducible nitric oxide synthase (iNos) as well as NO ₂ -formation.
Animal experiment [3]:	
Animal models	Male Wistar rats
Preparation method	Rats were pretreated with LPS (1 mg/kg, IP, 24 hours prior to ischemia) in the absence (control) or presence of the selective PPAR γ antagonist GW9662 (1 mg/kg, IP, 24 and 12 hours prior to ischemia). Twenty-four hours after injection of LPS, rats were subjected to 60 minutes of bilateral renal ischemia, followed by 6 hours of reperfusion.
Dosage form	1 mg/kg GW9662; IP; 24 and 12 hours prior to ischemia

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Applications	Administration of the selective PPAR γ antagonist GW9662 24 and 12 hours before ischemia/reperfusion (I/R) eliminated the renal protection observed in LPS preconditioning.
References: [1]. Leesnitzer LM, Parks DJ, 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. doi: 10.1021/bi0159581. PMID: 12022867. [2]. Baumann A, Burger K, et.al. GW9662, a peroxisome proliferator-activated receptor gamma antagonist, attenuates the development of non-alcoholic fatty liver disease. Metabolism. 2022 Aug;133:155233. doi: 10.1016/j.metabol.2022.155233. Epub 2022 May 30. PMID: 35654114. [3]. Collino M, Patel NS, et.al. The selective PPAR γ antagonist GW9662 reverses the protection of LPS in a model of renal ischemia-reperfusion. Kidney Int. 2005 Aug;68(2):529-36. doi: 10.1111/j.1523-1755.2005.00430.x. PMID: 16014029.	

Background

GW9662 is a specific inhibitor of peroxisome proliferator activated receptor-gamma (PPAR-gamma) with an IC₅₀ of 3.3 nM, GW9662 acts 10 to 600 times more selectively on PPAR γ in cells than on PPAR α and PPAR δ [1-3].

Treatment with GW9662 significantly attenuated LPS-induced expression of Il1b, interleukin 6 (Il6) and inducible nitric oxide synthase (iNos) as well as NO₂-formation in J774A.1 cells [4]. DMBA-induced mammary alveolar lesions (MAL) were significantly inhibited by PPAR γ antagonist GW9662[5]. GW9662(2.5/5 μ M) prevented disruption of the Colon carcinoma cells cycle induced by resveratrol and consequently abrogated resveratrol-induced apoptosis[6].

GW9662(p.o;3 mg/kg/day ;2 weeks) worsened the brain injury in alcohol-fed reperfusion mice[7]. Pretreatment with LPS significantly attenuated all markers of renal injury and dysfunction caused by I/R. Most notably, GW9662(1 mg/kg GW9662; IP;24 and 12 hours prior to ischemia) abolished the protective effects of LPS[8].

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- [2]. Lea MA, Sura M, et.al. Inhibition of cell proliferation by potential peroxisome proliferator-activated receptor (PPAR) gamma agonists and antagonists. *Anticancer Res*. 2004 Sep-Oct;24(5A):2765-71. PMID: 15517883.
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- [5]. Mehta RG, Peng X, et.al. PPAR γ antagonist GW9662 induces functional estrogen receptor in mouse mammary organ culture: potential translational significance. *Mol Cell Biochem*. 2013 Jan;372(1-2):249-56. doi: 10.1007/s11010-012-1466-9. Epub 2012 Sep 24. PMID: 23001870.
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