GW9662

Cat. No.: HY-16578
CAS No.: 22978-25-2
Molecular Formula: \( \text{C}_{13}\text{H}_9\text{ClN}_2\text{O}_3 \)
Molecular Weight: 276.68
Target: PPAR
Pathway: Cell Cycle/DNA Damage

Storage:
- Powder: -20°C 3 years
- 4°C: 2 years
- In solvent: -80°C 6 months
- -20°C: 1 month

SOLVENT & SOLUBILITY

In Vitro:
- DMSO: ≥ 100 mg/mL (361.43 mM)
- \( \text{H}_2\text{O} \): < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Prepare Stock Solutions:

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>3.6143 mL</td>
<td>18.0714 mL</td>
<td>36.1428 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.7229 mL</td>
<td>3.6143 mL</td>
<td>7.2286 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3614 mL</td>
<td>1.8071 mL</td>
<td>3.6143 mL</td>
</tr>
</tbody>
</table>

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

BIOLOGICAL ACTIVITY

Description:
GW9662 is a potent and selective PPAR\(\gamma\) antagonist with an IC\(50\) of 3.3 nM, showing 10 and 1000-fold selectivity over PPAR\(\alpha\) and PPAR\(\delta\), respectively.

IC\(50\) & Target:
- PPAR\(\gamma\): 3.3 nM (IC\(50\))
- PPAR\(\alpha\): 32 nM (IC\(50\))
- PPAR\(\delta\): 2000 nM (IC\(50\))

In Vitro:
GW9662 inhibits radioligand binding to PPAR\(\gamma\), PPAR\(\alpha\), and PPAR\(\delta\) with pIC\(50\)s of 8.48±0.27 (IC\(50\)=3.3 nM; n=10),
7.49±0.17 (IC\textsubscript{50}=32 nM; n=9), and 5.69±0.17 (IC\textsubscript{50}=2000 nM; n=3), respectively. GW9662 has nanomolar IC\textsubscript{50} versus PPAR\textgamma and is 10- and 600-fold less potent in binding experiments using PPAR\textalpha and PPAR\textdelta, respectively. In cell-based reporter assays, GW9662 is a potent and selective antagonist of full-length PPAR\textgamma\textsuperscript{[1]}. Co-treatment with both 50 \mu M Rosiglitazone and 10 \mu M GW9662 results in statistically lower viable cell numbers after 7 days when compared to treatment with either 50 \mu M rosiglitazone (P=0.001) or 10 \mu M GW9662 (P=0.01) alone\textsuperscript{[2]}.

### 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\textsuperscript{[3]}. GW9662 (1 mg/kg, i.p.) largely attenuates the renoprotective effects of Lipopolysaccharide (LPS) in the rat\textsuperscript{[4]}. |

### PROTOCOL

#### Cell Assay\textsuperscript{[2]}

Cells (MCF7, MDA-MB-231, MDA-MB-468) are plated in 96-well plates at a density of 1×10\textsuperscript{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 Rosiglitazone (1-100 \mu M), GW9662 (100 nM-50 \mu M) or solvent (DMSO) alone. MDA-MB-231 cells are also subjected to combinations of Rosiglitazone (10, 50 \mu M) and GW9662 (1, 10 \mu M) 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.

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

#### Animal Administration\textsuperscript{[3][4]}

**Mice\textsuperscript{[3]}**

Inbred C57BL/6 (B6, H\textsuperscript{2}b/b), DBA/1J (DBA/1, H\textsuperscript{2}q/q), FVB/NJ (FVB, H\textsuperscript{2}q/q) mice and congenic C.B10-H\textsuperscript{2}b/b/LitMcd (CB10, H\textsuperscript{2}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 cyclosporine A (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\textsubscript{2} inhalation.

**Rats\textsuperscript{[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 administrated GW9662 (1 mg/kg, IP) 24 and 12 hours prior to renal I/R, 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 administrated 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

REFERENCES


