# Gemfibrozil

**Cat. No.:** HY-B0258

**CAS No.:** 25812-30-0

**Molecular Formula:** $C_{15}H_{22}O_3$

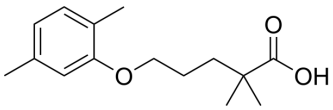
**Molecular Weight:** 250.33

**Target:** PPAR; Cytochrome P450

**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 (399.47 mM; Need ultrasonic)

| Preparing Stock Solutions | Mass / Solvent / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 3.9947 mL | 19.9736 mL | 39.9473 mL |
| | 5 mM | 0.7989 mL | 3.9947 mL | 7.9895 mL |
| | 10 mM | 0.3995 mL | 1.9974 mL | 3.9947 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 (9.99 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (9.99 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (9.99 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Gemfibrozil is an activator of PPAR-α, used as a lipid-lowering agent; Gemfibrozil is also a nonselective inhibitor of several P450 isoforms, with $K_i$ values for CYP2C9, 2C19, 2C8, and 1A2 of 5.8, 24, 69, and 82 μM, respectively.

**$IC_{50}$ & Target**

| | | | |
|---|---|---|---|
| PPAR-α | CYP2C9<br>5.8 μM (Ki) | CYP2C19<br>24 μM (Ki) | CYP2C8<br>69 μM (Ki) |
| CYP1A2 | | | |

| | |
|---|---|
| | 82 μM (Ki) |
| **In Vitro** | Gemfibrozil is an activator of PPAR-α, used as a lipid-lowering drug[1]; also a nonselective inhibitor of several P450 isoforms, with $K_i$ values for CYP2C9, 2C19, 2C8, and 1A2 of 5.8, 24, 69, and 82 μM, respectively[3]. Gemfibrozil (100, 150, 200 μM) inhibits the cytokine-induced NO production in a concentration dependent manner in human U373MG astroglial cells, and such effects are not due to any change of the stability of iNOS mRNA. Gemfibrozil (50, 100, 200 μM) inhibits human iNOS promoter-derived luciferase activity in cytokine-stimulated human U373MG astroglial cells. Furthermore, Gemfibrozil (50, 100, 150, and 200 μM) shows no effects on the viability of the cells[1]. Gemfibrozil considerably inhibits both M-23 and M-1 formation (catalyzed by CYP2C8 and CYP3A4), with $K_i$ ($IC_{50}$) values of 69 μM (95 μM) and 273 μM (>250 μM), respectively, in human liver microsomes. Gemfibrozil (0-250 μM) dose dependently inhibits the formation of M-23 ($IC_{50}$, 68 μM) and M-1 ($IC_{50}$, 78 μM) in recombinant CYP2C8, but shows no appreciable effect on the formation of these metabolites in recombinant CYP3A4[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | Gemfibrozil (62 mg/kg/day, p.o.) treatment initiated 3 days before spinal cord injury (SCI) causes decreased locomotor function, and induces a trend for decreased white matter sparing after injury in mice. Gemfibrozil (62 mg/kg/day, p.o.) decreases macrophage immunoreactivity but increases T cell infiltration into spared tissue[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

| | |
|---|---|
| **Kinase Assay** [3] | Activities of CYP3A4 (testosterone 6β-hydroxylation) and CYP2C8 (paclitaxel 6α-hydroxylation) are determined. The marker substrate concentrations used, 25 μM testosterone and 1 to 5 μM paclitaxel, are comparable with or around the $K_m$ values of the reactions. Gemfibrozil is either coincubated at 37°C for 15 min with the marker substrate and NADPH (1 mM) before the reaction is initiated with human liver microsomes (0.1 mg/mL) or preincubated with human liver microsomes and NADPH for 15 min before adding the marker substrate[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Cell Assay** [1] | Briefly, 400 μL of culture supernatant is allowed to react with 200 μL of Griess reagent and incubated at room temperature for 15 min. The optical density of the assay samples is measured spectrophotometrically at 570 nm. Fresh culture medium serves as the blank in all experiments. Nitrite concentrations are calculated from a standard curve derived from the reaction of $NaNO_2$ in the assay[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [2] | Mice are given vehicle or gemfibrozil beginning 3 days before SCI to ensure drug availability at the time of the injury (n=5-6/group). The drug is delivered orally by dissolving it in ethanol (0.25% w/w of gemfibrozil) and coating food pellets such that each animal receives appr 62 mg/kg/day; chow for control groups is treated with ethanol. Ethanol for each group is allowed to completely evaporate before giving the food to the animals. In addition, animals receive an intraperitoneal injection of vehicle or gemfibrozil (500 μg dissolved in 200 μL PBS) 1 h after the injury, and then continued to receive the drug in their food until the end of the study (28 days post-injury)[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- Chemosphere. 2019 Jun;225:378-387.

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## REFERENCES

[1]. Pahan K, et al. Gemfibrozil, a lipid-lowering drug, inhibits the induction of nitric-oxide synthase in human astrocytes. J Biol Chem. 2002 Nov 29;277(48):45984-91. Epub 2002 Sep 18.

[2]. Almad A, et al. The PPAR alpha agonist gemfibrozil is an ineffective treatment for spinal cord injured mice. Exp Neurol. 2011 Dec;232(2):309-17.

[3]. Wang JS, et al. Gemfibrozil inhibits CYP2C8-mediated cerivastatin metabolism in human liver microsomes. Drug Metab Dispos. 2002 Dec;30(12):1352-6.



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