GW0742

Cat. No.: HY-13928

CAS No.: 317318-84-6

Molecular Formula: $C_{21}H_{17}F_4NO_3S_2$

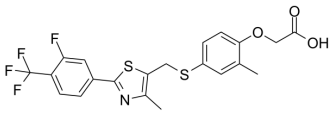
Molecular Weight: 471.49

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 : ≥ 34 mg/mL (72.11 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1209 mL	10.6047 mL	21.2094 mL
5 mM	0.4242 mL	2.1209 mL	4.2419 mL
10 mM	0.2121 mL	1.0605 mL	2.1209 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 (5.30 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GW0742 is a potent PPARβ and PPARδ agonist, with an IC_{50} of 1 nM for human PPARδ in binding assay, and EC_{50}s of 1 nM, 1.1 μM and 2 μM for human PPARδ, PPARα, and PPARγ, respectively.

IC_{50} & Target

PPARδ	PPARα	PPARγ
1 nM (EC50)	1.1 μM (EC50)	2 μM (EC50)

In Vitro

GW0742 is a potent PPARβ and PPARδ agonist, with an IC_{50} of 1 nM for human PPARδ, and EC_{50}s of 1 nM, 1.1 μM and 2 μM for human PPARδ, PPARα, and PPARγ respectively[1]. GW0742 (100 μM) activates human PPARα and mouse PPARβ in MCF-7 cells. GW0742 (100 μM) significantly reduces low-KCl-induced apoptosis of cerebellar granule neurons. GW0742 shows no

	obvious inherent toxicity on cerebellar granule neuronal cells after treatment of 3-100 μM for 24 h, but induces increased cell death at 100 μM after 48 hr of treatment. Moreover, GW0742 (100 μM) increases c-Jun expression in cerebellar granule neuron cultures observed at 6 hr[2]. GW0742 (1 μM) induces PPARδ protein in neonatal rat cardiomyocytes. GW0742 also raises mRNA levels of long-chain acyl-CoA dehydrogenase (LCAD), very long-chain acyl-CoA dehydrogenase (VLCAD), acyl-CoA oxidase 1 (ACOX1), uncoupling protein 3 (UCP3), malonyl-CoA decarboxylase (MCD), and pyruvate dehydrogenase kinase 4 (PDK4) in neonatal rat cardiomyocytes[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GW0742 (0.3 mg/kg, i.p.) reduces intensity masson-trichrome staining, and attenuates the histological signs in bleomycin instillatio (BLEO)-induced lung injury of mice. GW0742 (0.3 mg/kg, i.p.) also causes a reduction of the BLEO-induced loss body weight, and a decrease of myeloperoxidase (MPO) activity. GW0742 shows significant inhibition of TNF-a and IL-1β in instilled-mice. GW0742 prevents bleomycin-induced IkB-a degradation, reduces the levels of NF-kB p65 in the lung, and decreases iNOS and p-ERK expression in BLEO-induced mice[3]. GW0742 (5 mg/kg/day, i.v.) increases PPARδ protein level in the heart of rats. GW0742 also induces the increase in LCAD, VLCAD, and ACOX1 in the heart of rats[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The PPARβ activator GW0742 and the RXR activator 9-cis-retinoic acid are dissolved in DMSO. The final DMSO concentration des not exceed 0.5% v/v, and this concentration is used in control wells. For each culture plate, one row of wells is treated with 500 μM glutamate. These wells serve as a positive control and for normalisation of data. Cell death (toxicity) is assessed by using an assay designed to measure lactate dehydrogenase (LDH) release[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Male CD mice (25-35 g) are housed in a controlled environment and provided with standard rodent chow and water. Mice are randomized into four experimental groups: bleomycin-treated group: mice are subjected to lung injury induced by intratracheal instillation of bleomycin and treated daily via intraperitoneal injection with vehicle of GW0742 (10% dimethylsulfoxide (OMSO, 1 mL/kg), 1 h after BLEO instillation (n = 15). GW0742 group: identical to bleomycin-treated group but mice are treated daily with GW0742 (0.3 mg/kg, 1h after BLEO instillation) via intraperitoneal injection (n = 15). Sham-operated mice + vehicle group: animals are subjected to the identical surgical procedure but receive intratracheal instillation of saline (0.9%) instead of BLEO and are treated daily with the vehicle of GW0742 (10% dimethylsulfoxide (DMSO), 1 mL/kg, i.p.), 1 h after saline instillation (n = 15). Sham-operated mice + GW0742 group: identical to sham + vehicle group but mice are treated daily with GW0742 (0.3 mg/kg, 1 h after saline instillation) via intraperitoneal injection (n = 15)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biol Psychiatry. 2021 Mar 15;89(6):615-626.
- Pharmacol Res. 2020 Mar;153:104679.
- Br J Pharmacol. 2020 May;177(10):2286-2302.
- Eur J Med Chem. 5 February 2022, 114061.
- Eur J Med Chem. 2021 Aug 25;225:113807.

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REFERENCES

[1]. Sznaidman ML, et al. Novel selective small molecule agonists for peroxisome proliferator-activated receptor delta (PPARdelta)--synthesis and biological activity. Bioorg Med Chem Lett. 2003 May 5;13(9):1517-21.

[2]. Smith SA, et al. Effect of the peroxisome proliferator-activated receptor beta activator GW0742 in rat cultured cerebellar granule neurons. J Neurosci Res. 2004 Jul 15;77(2):240-9.

[3]. Galuppo M, et al. GW0742, a high affinity PPAR-β/δ agonist reduces lung inflammation induced by bleomycin instillation in mice. Int J Immunopathol Pharmacol. 2010 Oct-Dec;23(4):1033-46.

[4]. Kuo SC, et al. Activation of receptors δ (PPARδ) by agonist (GW0742) may enhance lipid metabolism in heart both in vivo and in vitro. Horm Metab Res. 2013 Nov;45(12):880-6.

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