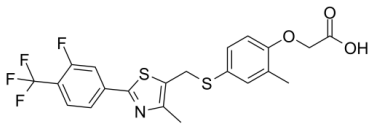
Data Sheet

Product Name:	GW0742
Cat. No.:	CS-5560
CAS No.:	317318-84-6
Molecular Formula:	C21H17F4NO3S2
Molecular Weight:	471.49
Target:	PPAR
Pathway:	Cell Cycle/DNA Damage
Solubility:	DMSO : ≥ 34 mg/mL (72.11 mM)



BIOLOGICAL ACTIVITY:

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. IC50 & Target: IC50: 1 nM (Human PPARδ)[1]
EC50: 1 nM (Human PPARδ), 1.1 μM (Human PPARα), 2 μM (Human PPARγ)[1]
PPARβ[2] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: GW0742 is dissolved in DMSO.[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]. **Animal Administration:** GW0742 is dissolved in 10% DMSO.[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].

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.

CAIndexNames:

Acetic acid, 2-[4-[[[2-[3-fluoro-4-(trifluoromethyl)phenyl]-4-methyl-5-thiazolyl]methyl]thio]-2-methylphenoxy]-

SMILES:

O=C(O)COC1=CC=C(SCC2=C(C)N=C(C3=CC=C(C(F)(F)F)C(F)=C3)S2)C=C1C

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA