GW7647

Cat. No.: HY-13861

CAS No.: 265129-71-3

Molecular Formula: $C_{29}H_{46}N_2O_3S$

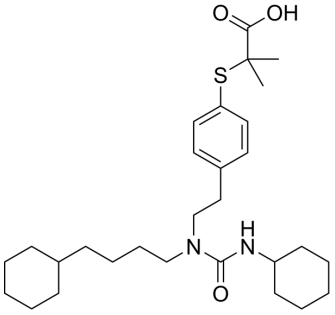
Molecular Weight: 502.75

Target: PPAR

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	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 60 mg/mL (119.34 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9891 mL	9.9453 mL	19.8906 mL
5 mM	0.3978 mL	1.9891 mL	3.9781 mL
10 mM	0.1989 mL	0.9945 mL	1.9891 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 (4.97 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.97 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GW7647 is a potent PPARα agonist, with EC_{50}s of 6 nM, 1.1 μM, and 6.2 μM for human PPARα, PPARγ and PPARδ, respectively.

IC_{50} & Target

PPARα	PPARγ	PPARδ
6 nM (EC50, Human PPARα)	1.1 μM (EC50, Human PPARγ)	6.2 μM (EC50, Human PPARδ)

In Vitro

GW7647 (1 μM) causes a significant increase of PDZK1 protein expression to 129.7 ± 6.5% of vehicle treated control in Caco2BBE cells in the absence and presence of IL-1β. GW7647 also attenuates the IL-1β-mediated decrease in PDZK1

	expression[1]. GW7647 (50 nM) stimulates the PI3K phosphorylation followed by the Akt (Ser473) phosphorylation, which induces NOS1 phosphorylation increased the amounts of NO released in the stripped antral mucosa. GW7647 (50 nM) enhances the initial phase of Ca^{2+}-regulated exocytotic events stimulated by ACh in antral mucous cells, but GW7647 alone does not evoke any exocytotic event. GW7647 plus ACh stimulates the effects of wortmannin (50 nM) and AKT-inh (100 nM) on the exocytotic events in antral mucous cells[2]. GW 7647 (100 nM) reduces the AQP9 protein abundance by 43%, but it shows not significant effect at 10 and 1,000 nM in WIF-B9 hepatocytes. GW 7647 (100 nM) causes a 24% reduction in AQP9 protein abundance in HepG2 cells, however, it does not significantly increase the protein abundance of L-FABP in HepG2 hepatocytes[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	GW7647 (3 mg/kg per day) does not prevent the development of cardiac hypertrophy, but it prevents the decline in left ventricular ejection fraction in vivo[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [4]	Newborn New Zealand White rabbits of either sex (7 days old, 90-200 g) are anesthetized with inhaled isofluorane (2%), and are subjected to an aorto-caval shunt to induce volume-overload cardiac hypertrophy. The presence of a successful fistula is verified at postsurgical days 7 and 13 by color flow doppler that visualizes a physical shunt between the abdominal aorta and the inferior vena cava in both an axial and transverse plane. This is further validated by an enlarged inferior vena cava. After validation, the animals in shunt group are randomly assigned to receive an intraperitoneal injection of vehicle (dimethyl sulfoxide, the solvent of GW7647) or GW7647 (3 mg/kg per day; EC_{50}=6 nM for PPARα) twice a day for 14 days. Animals that undergo surgery to create shunt, but consequently the shunt either not exhibiting or closed, are excluded from the study. Left ventricular ejection fraction (%) and other cardiac parameters are assessed by transthoracic echocardiography at postsurgical days 7 and 13. At 21 days of age (14 days post surgery), all animals are euthanized with Na^+ pentobarbital, and hearts are removed for isolated biventricular working heart perfusions. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Theranostics. 2022 Jan 1;12(2):910-928.
- Pharmacol Res. 2020 Mar;153:104679.
- Cell Chem Biol. 2021 Apr 27;S2451-9456(21)00213-0.
- J Med Chem. 2022 Jan 21.
- Br J Pharmacol. 2020 May;177(10):2286-2302.

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REFERENCES

[1]. Luo M, et al. IL-1β-Induced Downregulation of the Multifunctional PDZ Adaptor PDZK1 Is Attenuated by ERK Inhibition, RXRα, or PPARα Stimulation in Enterocytes. Front Physiol. 2017 Feb 7;8:61.

[2]. Tanaka S, et al. PPARα induced NOS1 phosphorylation via PI3K/Akt in guinea pig antral mucous cells: NO-enhancement in Ca(2+)-regulated exocytosis. Biomed Res. 2016;37(3):167-78.

[3]. Lebeck J, et al. Hepatic AQP9 expression in male rats is reduced in response to PPARα agonist treatment. Am J Physiol Gastrointest Liver Physiol. 2015 Feb

1;308(3):G198-205.

[4]. Lam VH, et al. Activating PPARα prevents post-ischemic contractile dysfunction in hypertrophied neonatal hearts. Circ Res. 2015 Jun 19;117(1):41-51.

[5]. Brown PJ, et al. Identification of a subtype selective human PPARalpha agonist through parallel-array synthesis. Bioorg Med Chem Lett. 2001 May 7;11(9):1225-7.

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