GW6471

Cat. No.: HY-15372

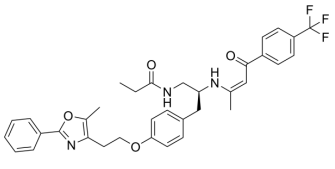
CAS No.: 880635-03-0

Molecular Formula: $C_{35}H_{36}F_3N_3O_4$

Molecular Weight: 619.67

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	2 years
	-20°C	1 year

SOLVENT & SOLUBILITY

In Vitro

DMSO : 83.33 mg/mL (134.47 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6138 mL	8.0688 mL	16.1376 mL
	5 mM	0.3228 mL	1.6138 mL	3.2275 mL
	10 mM	0.1614 mL	0.8069 mL	1.6138 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: ≥ 2.08 mg/mL (3.36 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.36 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GW6471 is a potent PPARα antagonist.

IC_{50} & Target

PPARα

In Vitro

In a cell-based reporter assay, GW6471 completely inhibits GW409544-induced activation of PPARα with an IC_{50} of 0.24 μM[1]. The functional role of PPARα is evaluated on renal cell carcinoma (RCC) cell viability by MTT assay. Both Caki-1 (VHL wild

	type) and 786-O (VHL mutated) cells are incubated separately with a specific PPARα agonist, WY14,643, or a specific PPARα antagonist, GW6471 at concentrations from 12.5 to 100 μM for 72 hours, and cell viability is assessed. While WY14,643 either has no affect on, or slightly increased, cell viability, GW6471 significantly and dose-dependently inhibits cell viability (up to approximately 80%) in both cell lines[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To test the antitumor activity of PPARα antagonism in vivo, a subcutaneous xenograft mouse model is used. Caki-1 cells are implanted subcutaneously in nude (Nu/Nu) mice. After tumor masses reach ⊠5 mm in diameter, GW6471 is administrated intraperitoneally every other day for 4 wk at a dose (20 mg/kg mouse body wt) that is described to be effective in an in vivo dose-response study and confirmed here to be efficacious. There are significant differences in tumor growth between vehicle- and GW6471-treated animals. No toxicity is observed at the doses of GW6471 based on weights of the animals, and laboratory values, including kidney and liver function tests, are not adversely affected. To demonstrate on-target effects of GW6471, c-Myc levels are evaluated in the tumors, which show significant decreases in the GW6471-treated animals[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	786-O and Caki-1 cells are plated in 96 well plates. Both cells are incubated separately with WY14,643 or GW 6471 at concentrations from 12.5 to 100 μM for 72 hours, and after the indicated treatments, the cells are incubated in MTT solution/media mixture. Then, the MTT solution is removed and the blue crystalline precipitate in each well is dissolved in DMSO. Visible absorbance of each well at 540 nm is quantified using a microplate reader[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Male athymic ***Nu/Nu*** mice (8 wk of age, ~25 g body wt) are injected with 1×10^5 Caki-1 cells subcutaneously (3:1 DMEM-Matrigel) in the flank region. Tumor progression is monitored weekly by calipers. When tumor size reaches ~80-100 mm^3, animals are randomly assigned to four groups and treatments are started (day 1). The vehicle group receive DMSO (4% in PBS) intraperitoneally and vegetable oil via oral gavage. The PPARα group is injected intraperitoneally with GW 6471 in the same vehicle (20 mg/kg body wt; murine dose response is reported elsewhere) every other day. The Sunitinib group receive Sunitinib in vegetable oil via oral gavage (40 mg/kg body wt) 5 days/wk. Another group receive GW 6471+Sunitinib. To determine any potential toxicity of the treatment(s), body weights of the animals are measured and signs of adverse reactions are monitored. On day 28, the mice are euthanized and the tumor mass is determined. Tumor growth rate is calculated[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Gut. 2021 Nov;70(11):2183-2195.
- Cell Stem Cell. 2022 Sep 1;29(9):1366-1381.e9.
- Environ Int. 2023 Aug 8;178:108138.
- Pharmacol Res. 2021 Apr 27;169:105640.
- Cell Death Dis. 2022 Nov 23;13(11):987.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Xu HE, et al. Structural basis for antagonist-mediated recruitment of nuclear co-repressors by PPARalpha. Nature. 2002 Feb 14;415(6873):813-7.

[2]. Abu Aboud O, et al. Inhibition of PPARα induces cell cycle arrest and apoptosis, and synergizes with glycolysisinhibition in kidney cancer cells. PLoS One. 2013 Aug 7;8(8):e71115.

[3]. Abu Aboud O, et al. PPARα inhibition modulates multiple reprogrammed metabolic pathways in kidney cancer and attenuates tumor growth. Am J Physiol Cell Physiol. 2015 Jun 1;308(11):C890-8.

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