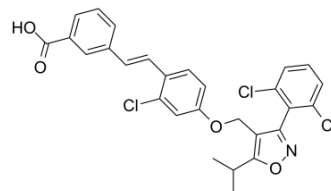


GW 4064

Cat. No.:	HY-50108		
CAS No.:	278779-30-9		
Molecular Formula:	C ₂₈ H ₂₂ Cl ₃ NO ₄		
Molecular Weight:	542.84		
Target:	FXR; Autophagy		
Pathway:	Metabolic Enzyme/Protease; Autophagy		
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 : ≥ 100 mg/mL (184.22 mM)
 H₂O : < 0.1 mg/mL (insoluble)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent		Mass		
	Concentration		1 mg	5 mg	10 mg
	1 mM		1.8422 mL	9.2108 mL	18.4216 mL
	5 mM		0.3684 mL	1.8422 mL	3.6843 mL
	10 mM		0.1842 mL	0.9211 mL	1.8422 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (4.61 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (4.61 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GW 4064 is a potent FXR agonist with an EC₅₀ of 65 nM.

IC₅₀ & Target

EC₅₀: 65 nM (FXR)^[1]

In Vitro

Treatment with different concentrations of GW4064 (1, 2.5, 5, 10 μM) reduces the lipid accumulation in the cells. Concordantly, GW4064 treatment significantly represses oleic acid-induced CD36 protein levels in a dose-dependent manner. Taken together, these data indicate that prevention of hepatic lipid accumulation is likely due to an inhibition of Cd36 expression by long-term GW4064 treatment^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

GW4064 suppresses weight gain in C57BL/6 mice fed with either a high-fat diet (HFD) or high-fat, high-cholesterol diet. GW4064 treatment of mice on HFD significantly represses diet-induced hepatic steatosis as evidenced by lower triglyceride and free fatty acid level in the liver. GW4064 markedly reduces lipid transporter CD36 expression without affecting expression of genes that are directly involved in lipogenesis. GW4064 treatment attenuates hepatic inflammation while having no effect on white adipose tissue^[2]. GW4064 (30 mg/kg) treatment results in substantial, statistically significant reductions in serum activities of ALT, AST, LDH, and ALP in the ANIT-treated rats. Serum bile acid levels are also significantly reduced by GW4064 treatment. Bilirubin levels are decreased in the GW4064-treated rats, but statistical significance is not achieved. Notably, GW4064 is much more effective in decreasing these markers of liver damage than TUDCA, which reduces only LDH levels^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

Mouse liver cells (BNL CL.2) are maintained in a humidified incubator under 5% CO₂ at 37°C in Dulbecco's Modified Eagle's Medium (DMEM). When cells are divided into six-well plates and reach ~90% confluence, sub-confluent cells are washed three times with phosphate buffered saline (PBS) and replaced with serum-free DMEM supplemented with 1% fatty acid-free BSA. Oleic acid (final concentration 500 μM) and GW4064 at various concentrations are added and incubated for 24 h. Cells are then fixed with 4% formaldehyde for Oil Red O staining or harvested for protein and western blot analysis^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^{[2][3]}

Mice^[2]

Fifteen-week-old male C57BL/6 mice are fed a high-fat diet with or without additional 0.2% Cholesterol and received twice weekly injections of GW 4064 (50 mg/kg, intra-peritoneal) or carrier solution (DMSO) solution for 6 weeks. Animals are weighed weekly and their body composition is determined using EchoMRI-100™ from Echo Medical Systems.

Rats^[3]

Animals. Adult male CRL:CD(SD)IGS rats weighing 300-350 g, are used. Twenty-four hours after laparotomy, groups of rats (n=6) receive intraperitoneal injections once daily for 4 days. Bile duct-ligated (BDL) rats are treated with 5 mL/kg corn oil as vehicle, 30 mg/kg GW4064 in corn oil, or 15 mg/kg TUDCA in corn oil. Sham-operated animals received 5 mL/kg corn oil vehicle. Four hours after the final dose, serum and livers are collected for analysis.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Dev Cell. 2019 Feb 25;48(4):460-474.e9.
- J Am Soc Nephrol. 2019 Jun;30(6):962-978.
- Acta Pharm Sin B. 2019 May;9(3):526-536.
- EBioMedicine. 2018 Nov;37:322-333.
- FASEB J. 2019 Feb;33(2):2472-2483.

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REFERENCES

[1]. Akwabi-Ameyaw A, et al. Conformationally constrained farnesoid X receptor (FXR) agonists: Naphthoic acid-based analogs of GW 4064. Bioorg Med Chem Lett, 2008, 18(15), 4339-4343.

[2]. Ma Y, et al. Synthetic FXR agonist GW4064 prevents diet-induced hepatic steatosis and resistance. *Pharm Res.* 2013 May;30(5):1447-57.

[3]. Liu Y, et al. Hepatoprotection by the farnesoid X receptor agonist GW4064 in rat models of intra- and extrahepatic cholestasis. *J Clin Invest.* 2003 Dec;112(11):1678-87.

Caution: Product has not been fully validated for medical applications. For research use only.

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