GW 4064

Cat. No.: HY-50108

CAS No.: 278779-30-9

Molecular Formula: $C_{28}H_{22}Cl_3NO_4$

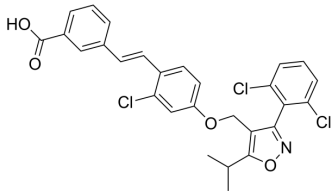
Molecular Weight: 543

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 (184.16 mM; Need ultrasonic)

DMF : 100 mg/mL (184.16 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8416 mL	9.2081 mL	18.4162 mL
5 mM	0.3683 mL	1.8416 mL	3.6832 mL
10 mM	0.1842 mL	0.9208 mL	1.8416 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC/saline water
   Solubility: 5 mg/mL (9.21 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 5 mg/mL (9.21 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMF >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.60 mM); Clear solution
4. Add each solvent one by one: 10% DMF >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.60 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.60 mM); Clear solution
6. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	GW 4064 is a potent FXR agonist with an EC_{50} of 65 nM.
IC_{50} & 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

- Cell Host Microbe. 2024 Jan 11:S1931-3128(23)00510-3.
- Nat Commun. 2023 Mar 9;14(1):1305.
- Acta Pharm Sin B. 2019 May;9(3):526-536.
- J Am Soc Nephrol. 2019 Jun;30(6):962-978.
- Theranostics. 2022 Aug 15;12(14):6130-6142.

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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.

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