产品名称：GW 4064
产品别名：GW 4064

生物活性：

Description	GW 4064 is a potent FXR agonist with an EC50 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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL** (**184.22 mM**) **H_2O : < 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (4.61 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.61 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；

	向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 1.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.61 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.61 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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].
Animal Administration	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-100TM 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.
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.