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产品名称：GW-1100
产品别名：GW-1100

生物活性：

Description	GW-1100 is a selective GPR40 antagonist with a pIC50 of 6.9. GW1100 acts as a GPR40 inverse agonist.
IC_{50} & Target	pIC50: 6.9 (GPR40)[1]
In Vitro	GW-1100 (GW1100) dose dependently inhibits GPR40-mediated Ca^{2+} elevations stimulated by GW9508 and linoleic acid (pIC_{50} values of 5.99±0.03 and 5.99±0.06, respectively). GW-1100 at a concentration of 1 μM produces a significant rightward shift in the concentration-response curve to GW9508 (pEC_{50}=7.17±0.08 in the absence and pEC_{50}=6.79±0.09 in the presence of 1 μM GW-1100; P<0.05; n=3). At concentrations of GW-1100 of 3 μM and higher a significant decrease in the maximal response is observed with a continuing rightward shift in the pEC_{50} response[2]. GW-1100 (GW1100) reduces FFAR1 ligand-induced intracellular calcium in CHO-K1/bFFAR1 cells and neutrophils. CHO-K1/bFFAR1 cells are incubated for 15 min with 10 μM GW1100 or vehicle (0.1% DMSO) and then stimulated with vehicle, oleic acid, linoleic acid or GW9508. GW-1100 significantly reduces the increase in intracellular calcium induced by 300 μM oleic acid ($AUC_{(60\text{-}150\ s)}$, p<0.05), 100 μM linoleic acid ($AUC_{(60\text{-}150\ s)}$, p<0.05) and 10 μM GW9508 ($AUC_{(60\text{-}150\ s)}$, p<0.05)[3].
In Vivo	The intracerebroventricular injection of DHA (50 μg) and GW9508 (1.0 μg), a GPR40-selective agonist, significantly reduces mechanical allodynia and thermal hyperalgesia at day 7, but not at day 1, after CFA injection. These effects are inhibited by intracerebroventricular pretreatment with GW-1100 (10 μg), a GPR40 antagonist[4].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL (96.05 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9209 mL	9.6047 mL	19.2093 mL
5 mM	0.3842 mL	1.9209 mL	3.8419 mL
10 mM	0.1921 mL	0.9605 mL	1.9209 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 →90% corn oil

	Solubility: ≥ 2.5 mg/mL (4.80 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.80 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]. Stoddart LA, et al. Uncovering the pharmacology of the G protein-coupled receptor GPR40: high apparent constitutive activity in guanosine 5'-O-(3-[35S]thio)triphosphate binding studies reflects binding of an endogenous agonist. Mol Pharmacol. 2007 Apr;71([2]. Briscoe CP, et al. Pharmacological regulation of insulin secretion in MIN6 cells through the fatty acid receptor GPR40: identification of agonist and antagonist small molecules. Br J Pharmacol. 2006 Jul;148(5):619-28. [3]. Manosalva C, et al. Cloning, identification and functional characterization of bovine free fatty acid receptor-1 (FFAR1/GPR40) in neutrophils. PLoS One. 2015 Mar 19;10(3):e0119715. [4]. Nakamoto K, et al. Hypothalamic GPR40 signaling activated by free long chain fatty acids suppresses CFA-induced inflammatorychronic pain. PLoS One. 2013 Dec 12;8(12):e81563.

实验参考：

Cell Assay	CHO-K1/bFFAR1 or CHO-K1/pcDNA3.1 cells (2×10^6 cells/2 mL) are loaded with 2.5 μM Fura-2AM fluorescent indicator dye in recording buffer (10 mM HEPES, 140 mM NaCl, 2 mM $CaCl_2$, 21 mM $MgCl_2$, 25 mM KCl, 10 mM glucose, pH 7.4) for 30 min, washed three times with recording buffer, and returned to the incubator for 10 min. Cells are incubated with different concentrations of propionic acid (1, 10 and 30 mM), oleic acid (0-500 μM), linoleic acid (0-200 μM), GW9508 (0-100 μM), ionomycin (2 μM), thapsigargin (2 μM) or vehicle (0.1% DMSO). The fatty acid concentrations used in all experiments are in the range of concentrations of healthy and peripartum cows. In another set of experiments, cells are incubated with either 10 μM GW-1100 for 15 min, 2 μM U73122 for 3 min or vehicle (0.1% DMSO) for 15 min and then stimulated with either 300 μM oleic acid, 100 μM linoleic acid or 10 μM GW9508. Cellular fluorescence (Ca^{2+}) is measured at 509 nm emission with 340/380 nm dual wavelength excitation using a LS55 spectrofluorimeter. Cuvette temperatures are maintained at 37°C with constant stirring[3].
Animal Administration	Mice[4] Male ddY mice (age, 4 weeks) are housed in cages at 23-24°C with a 12-h light-dark cycle (lights from 8 am to 8 pm) and food and waterad libitum. DHA (50 μg/mouse), the selective GPR40-agonist GW9508 (1.0-25 μg/mouse) and the GPR40 antagonist GW1100 (1-10 μg/mouse) are dissolved in 1% DMSO and the solution is diluted with saline before von Frey testing (1% DMSO final concentration). The doses of GW9508 are chosen based upon our previous publication, whereas GW-1100 is selected on the basis of previous reports and our preliminary experiments. Under a non-anesthetized state, DHA and GW9508 are administered via the intracerebroventricular (i.c.v.) route 10 min before CFA injection, and GW1100 is administered via the i.c.v. route 10 min before GW9508 injection. Flavopiridol (5 and 15 nmol/mouse), a cyclin-dependent kinase inhibitor, is administered by i.c.v. injection into the left lateral ventricle of the mice twice a day (at 9:00 and 19:00) after CFA treatment.
	[1]. Stoddart LA, et al. Uncovering the pharmacology of the G protein-coupled receptor GPR40: high

References	apparent constitutive activity in guanosine 5'-O-(3-[35S]thio)triphosphate binding studies reflects binding of an endogenous agonist. Mol Pharmacol. 2007 Apr;71([2]. Briscoe CP, et al. Pharmacological regulation of insulin secretion in MIN6 cells through the fatty acid receptor GPR40: identification of agonist and antagonist small molecules. Br J Pharmacol. 2006 Jul;148(5):619-28. [3]. Manosalva C, et al. Cloning, identification and functional characterization of bovine free fatty acid receptor-1 (FFAR1/GPR40) in neutrophils. PLoS One. 2015 Mar 19;10(3):e0119715. [4]. Nakamoto K, et al. Hypothalamic GPR40 signaling activated by free long chain fatty acids suppresses CFA-induced inflammatorychronic pain. PLoS One. 2013 Dec 12;8(12):e81563.