Product Data Sheet

Product Name: GW-1100
Cat. No.: GC14027

Chemical Properties

Cas. No.	306974-70-9		
Chemical Name	ethyl 4-[5-[(2-ethoxypyrimidin-5-yl)methyl]-2-[(4-fluorophenyl)methylsulfanyl]-4-oxopyrimidin-1-yl]benzoate		
SMILES	CCOC1=NC=C(C=N1)CC2=CN(C(=NC2=O)SCC3=CC=C(C=C3)F)C4=CC=C(C=C4)C(=O)OCC		
Formula	$C_{27}H_{25}FN_4O_4S$	M.Wt	520.59
Solubility	DMF: 5 mg/ml,DMF:PBS (pH 7.2) (1:4): 0.20 mg/ml,DMSO: 2 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	GW-1100		

Protocol

Cell experiment:

CHO-K1/bFFAR1 or CHO-K1/pcDNA3.1 cells (2×106 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 CaCl2, 21 mM MgCl2, 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 (Ca2+) 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].

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Animal experiment:

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.

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

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[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.

Background

GW1100 is a selective GPR40 antagonist. It dose dependently inhibited GPR40-mediated Ca2+ elevations stimulated by GW9508 and linoleic acid with pIC50 values of 5.9970.03 and 5.9970.06, respectively [1].

GW1100 inhibited the Ca2+ elevations stimulated by GW9508 mediated by GPR40, but not those mediated via GPR120 by either GW9508 or linoleic acid, demonstrating that GW1100 was a selective antagonist of the GPR40 receptor. GW1100 reversed the effects of GW9508 on insulin secretion, but only partially attenuated linoleic acid-stimulated insulin secretion [1]. Ishikawa cells were treated with a GPR40 antagonist, GW1100, in conjunction with GW9508. GW1100 had no effect on the stimulation of cell proliferation, suggesting all pro-proliferative effects of GW9508 are mediated through GPR120 [2].

References:
1. Briscoe CP, Peat AJ, McKeown SC 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.

2. http://www.aups.org.au/Proceedings/41/44P

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