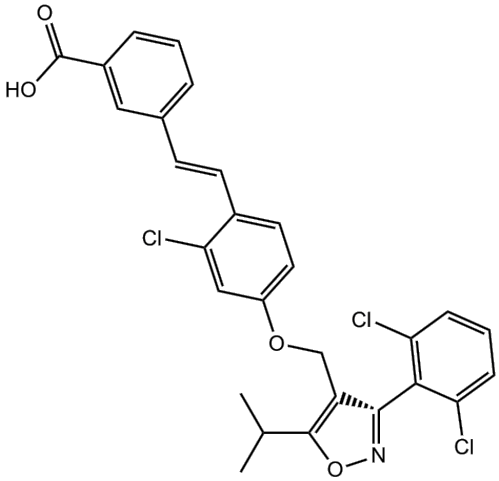
Product Data Sheet

Product Name: GW4064
Cat. No.: GC10975

Chemical Properties

Cas. No.	278779-30-9		
Chemical Name	3-[(E)-2-[2-chloro-4-[[3-(2,6-dichlorophenyl)-5-propan-2-yl-1,2-oxazol-4-yl]methoxy]phenyl]ethenyl]benzoic acid		
SMILES	CC(C)C1=C(C(=NO1)C2=C(C=CC=C2Cl)Cl)COC3=CC(=C(C=C3)C=CC4=CC(=CC=C4)C(=O)O)Cl		
Formula	C28H22Cl3NO4	M.Wt	542.85
Solubility	≥ 24.7mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

Cell lines HEK cells

Product Data Sheet

Preparation Method	HEK cells in chamber slides were treated with 1μM GW4064 or ionomycin (1μM) for 30 minutes, and endogenous NFATc1 was detected by immunocytochemical analysis. The nuclei were stained with 4′,6-diamidino-2-phenylindole (DAPI).
Reaction Conditions	1 μM; 30 minutes
Applications	Consequent to calcineurin activation, nuclear translocation of endogenous NFATc1 was enhanced by GW4064 in a microscopy-based assay.

Animal experiment [2]:

Animal models	4-week-old female BALB/c-nude mice
Preparation Method	HT-29 cells (5×10^6) in logarithmic growth phase were subcutaneously injected into the flanks of nude mice. When the palatable xenograft tumors were established, oxaliplatin (3mg/kg) and GW4064 (15mg/kg) as both single agents and in combination was injected intraperitoneally twice a week for 3 weeks. The tumor width (b) and length (a) were measured using the callipers every 3 days.
Dosage form	15 mg/kg, i.p.
Applications	Compared with using oxaliplatin or GW4064 only, combination of oxaliplatin and GW4064 in HT-29 cell line inhibited the tumor formation more significantly in vivo.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

References:
[1]. Singh N, et al. Synthetic FXR agonist GW4064 is a modulator of multiple G protein-coupled receptors. Mol Endocrinol. 2014 May;28(5):659-73.
[2]. Guo J, et al. GW4064 enhances the chemosensitivity of colorectal cancer to oxaliplatin by inducing pyroptosis. Biochem Biophys Res Commun. 2021 Apr 9;548:60-66.

Background

GW4064, as a synthetic FXR agonist with an EC_{50} of 65nM, is used for the treatment of cholestatic liver diseases, metabolic syndrome and alcoholic liver disease[1].

In vitro, the IC_{50} values of GW4064 on SW620 and HT-29 cells were 7.6μM and 13.8μM, respectively[2]. GW4064 dose dependently enhanced the basal cAMP level with an EC_{50} of 0.241μM, and suppressed forskolin-induced cAMP accumulation with IC_{50} of 0.07μM on HEK cells[3].

In vivo, treatment of short bowel syndrome (SBS) rat model with GW4064 (30mg/kg every other day; 2wk; i.p.). GW4064 rectified bile acid (BA) dysmetabolism to alleviate hepatotoxicity. GW4064 treatment increased the reabsorption of conjugated BAs by inducing *ASBT* expression in the intestine. *FXR*/*FGF15* activation in the presence of GW4064 decreased BA production by repressing the expression of key synthetases, including *CYP7A1*, *CYP8B1*, and *CYP27A1*[4]. GW4064 (20mg/kg; i.p.; twice) treatment alleviated hepatic inflammation in the Lipopolysaccharides(LPS)-induced murine liver injury model as reflected by reduced serum levels of aspartate aminotransferase and pro-inflammatory cytokine mRNA expression, including tumor necrosis factor-α[5].

References:

[1]. Akwabi-Ameyaw, Adwoa, et al. "Conformationally constrained farnesoid X receptor (FXR) agonists: Naphthoic acid-based analogs of GW 4064." *Bioorganic & medicinal chemistry letters* 18.15 (2008): 4339-4343.

[2]. Guo J, et al. GW4064 enhances the chemosensitivity of colorectal cancer to oxaliplatin by

inducing pyroptosis. Biochem Biophys Res Commun. 2021 Apr 9;548:60-66.

[3]. Singh N, et al. Synthetic FXR agonist GW4064 is a modulator of multiple G protein-coupled receptors. Mol Endocrinol. 2014 May;28(5):659-73.

[4]. Cao Y, et al. FXR agonist GW4064 improves liver and intestinal pathology and alters bile acid metabolism in rats undergoing small intestinal resection. Am J Physiol Gastrointest Liver Physiol. 2019 Aug 1;317(2):G108-G115.

[5]. Liu HM, et al. GW4064 attenuates lipopolysaccharide induced hepatic inflammation and apoptosis through inhibition of the Toll like receptor 4 mediated p38 mitogen activated protein kinase signaling pathway in mice. Int J Mol Med. 2018 Mar;41(3):1455-1462.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA