

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

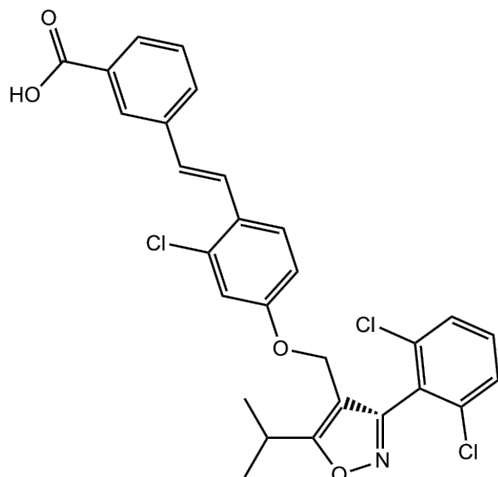
Solubility ≥ 24.7mg/mL in DMSO

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

Caution: Product has not been fully validated for medical applications. For research use only.

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HEK cells in chamber slides were treated with 1 μ M GW4064 or ionomycin (1 μ M) Preparation Method 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 μ M; 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.

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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 EC₅₀ of 65nM, is used for the treatment of cholestatic liver diseases, metabolic syndrome and alcoholic liver disease^[1].

In vitro, the IC₅₀ 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 EC₅₀ of 0.241μM, and suppressed forskolin-induced cAMP accumulation with IC₅₀ 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.
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[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.

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