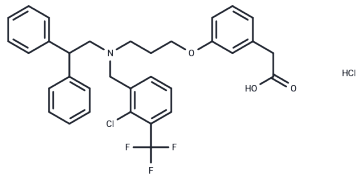
Data Sheet (Cat.No.T6310)

TargetMol®
YOUR TARGET MOLECULES

GW3965 hydrochloride

Chemical Properties



CAS No. : 405911-17-3

Formula: C33H31ClF3NO3·HCl

Molecular Weight: 618.51

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	GW3965 hydrochloride (GW3965 HCl) is an effective and specific LXR agonist for hLXRα/β (EC50: 190/30 nM).
Targets(IC50)	Liver X Receptor
In vitro	GW3965 recruits the steroid receptor coactivator 1 to human LXRα with EC50 of 125 nM in a cell-free ligand-sensing assay. [1] GW3965 shows a potent antagonistic activity against hLXRα and hLXRβ in cell-based assays with EC50 of 190 nM and 30 nM, respectively. Besides, GW3965 also sows excellent selectivity over other nuclear receptors. [1] In human islets, GW3965 (1 μM) reduces expression of selected pro-inflammatory cytokines including IL-8, monocyte chemotactic protein-1 and tissue factor. [4]
In vivo	In mice, GW3965 at a dose of 10 mg/kg upregulates ABCA1 expression 8-fold and raises circulating levels of HDL by 30% with Cmax of 12.7 μg/mL and t1/2 of 2 hours. [1] GW3965 (10 mg/kg) induces expression of ABCA1 and ABCG1 and shows potent antiatherogenic activity in both LDLR?/? and apoE?/? mice. [2] In male sprague-dawley rats, GW3965 reduces Ang II-mediated increases in blood pressure and decreases vascular Ang II receptor gene expression. [3] In Glioblastoma mouse model, GW3965 results in inducible degrader of LDLR-mediated LDLR degradation, increased expression of the ABCA1 cholesterol efflux transporter, and thus potently promotes tumor cell death. [5]
Kinase Assay	Steady-state drug accumulation assay: AuxB1 and CHrB30 cells are grown to confluency in 12-well (24 mm) tissue culture dishes and the steady-state accumulation of [3H]-vinblastine is measured. Accumulation is initiated by the addition of 0.1 μ Ci [3H]-vinblastine and unlabelled vinblastine to a final concentration of 100 nM . The accumulation of [3H]-paclitaxel is measured using 0.1 μ Ci [3H]-paclitaxel and unlabelled drug to a final concentration of 1 μM . Cells are incubated in a reaction volume of 1 mL for 60 min at 37 ℃ under 5% CO2 in order to reach steady-state. The effect of the modulators XR9576 on [3H]-ligand accumulation is investigated in the concentration range 10-9 - 10-6 M. Modulators are added from a DMSO stock giving a final solvent concentration of 0.2 % (v/v). Following cell harvesting, accumulated drug is measured by liquid scintillation counting and normalized for cell protein content. Plots of amount accumulated as a function of modulator concentration are fitted with the general dose-response equation: Y={(a-b)/(1+(X/c)d)}+b Where: Y=response; a=initial response; b=final response; c=EC50 concentration; d=slope value; X=drug

	concentration.
Cell Research	Cells are seeded in 96 wells and are treated after 24 hours with different drugs indicated in each experiment in medium containing 1% FBS or lipoprotein deficient serum. Relative proliferation is determined using Cell Proliferation Assay Kit. Cells are incubated 1.5 hrs after adding tetrazolium salt WST-1 [2-(4-iodophenyl)-3- (4-nitrophenyl)-5-(2, 4-disulfo-phenyl)-2H-tetrazolium, monosodium salt] at 5% CO2, 37oC and the absorbance of the treated and untreated cells are measured using a microplate reader at 420 to 480 nm. Cells seeded in 12 well plates are counted using a hemocytometer, and dead cells are assessed using trypan blue exclusion assays.

Solubility Information

Solubility	DMSO: 61.9 mg/mL (100 mM), Ethanol: 12.4 mg/mL (20 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6168 mL	8.0839 mL	16.1679 mL
5 mM	0.3234 mL	1.6168 mL	3.2336 mL
10 mM	0.1617 mL	0.8084 mL	1.6168 mL
50 mM	0.0323 mL	0.1617 mL	0.3234 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Liu Y, Wang Z, Jin H, et al.Squalene-epoxidase-catalyzed 24 (S), 25-epoxycholesterol synthesis promotes trained-immunity-mediated antitumor activity.Cell Reports.2024, 43(4).