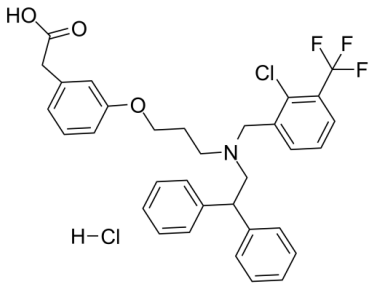
Data Sheet

Product Name:	GW3965 (hydrochloride)
Cat. No.:	CS-0843
CAS No.:	405911-17-3
Molecular Formula:	C33H32Cl2F3NO3
Molecular Weight:	618.51
Target:	LXR
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 125 mg/mL (202.10 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

GW3965 hydrochloride is a potent and selective **liver X receptor (LXR)** agonist with **EC_{50}**s of 190 and 30 nM for hLXRα and hLXRβ , respectively. IC50 & Target: EC50: 190 nM (hLXRα), 30 nM (hLXRβ)[4] **In Vitro:** GW3965 hydrochloride promotes GBM cell death in vitro with enhanced efficacy in EGFRvIII-expressing tumor cells. GW3965 hydrochloride up-regulates expression of the cholesterol transporter gene ABCA1 and the E3 ubiquitin ligase IDOL and reduces LDLR levels[2]. LXR ligands inhibits platelet aggregation and calcium mobilization stimulated by collagen or CRP. GW3965 hydrochloride (1 or 5 μM) displays a minor inhibitory effect on fibrinogen binding and P-selectin exposure, when platelets are stimulated with 1 μg/mL CRP. But using higher concentrations of GW3965 hydrochloride (10 μM) or T0901317 (40 μM), the levels of fibrinogen and P-selectin on the platelet surface are reduced[3]. **In Vivo:** GW3965 hydrochloride induces an increase of neuroactive steroids in the spinal cord, the cerebellum and the cerebral cortex of STZ-rats, but not in the CNS of non-pathological animals. GW3965 hydrochloride treatment induces an increase of dihydroprogesterone in the spinal cord of diabetic animals in association with an increase of myelin basic protein expression[1]. GW3965 hydrochloride (40 mg/kg, p.o.) strongly induces ABCA1 expression and reduces LDLR expression, and this is accompanied by 59% inhibition of tumor growth, and a 25-fold increase in GBM cell apoptosis in vivo[2]. GW3965 hydrochloride (2 mg/kg, i.v.) increases bleeding time and modulated platelet thrombus formation in vivo[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]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% CO_2, 37°C 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. **Animal Administration:** GW3965 is formulated in sesame oil.[1]Diabetes is induced in two-month-old male rats by a single i.p. injection of freshly prepared STZ (65 mg/kg) in 0.09 M citrate buffer, pH 4.8. Control animals are injected with 0.09 mol/L citrate buffer at pH 4.8. Hyperglycemia is confirmed 48 h after streptozotocin injection by measuring tail vein blood glucose levels using a glucometer OneTouch Ultra2. Only animals with mean plasma glucose levels over 300 mg/mL are classified as diabetic. Glycemia is also assessed before treatment with Ro5-4864 or GW3965 hydrochloride and before death. Two months after STZ injection, diabetic animals are treated once a week with Ro5-4864 (3 mg/kg) or GW3965 hydrochloride (50 mg/kg). Thus, they receive four subcutaneous injections in a month. Control diabetic rats receive 200 μL of vehicle (sesame oil). Four-month-old non-diabetic male rats are injected, following the same experimental schedule, with Ro5-4864, GW3965 hydrochloride or vehicle. Rats are killed 24 h after the last treatment.

References:

[1]. Mitro, Nico., et al. LXR and TSPO as new therapeutic targets to increase the levels of neuroactive steroids in the central nervous system of diabetic animals. Neurochemistry International (2012), 60(6), 616-621.

[2]. Guo, Deliang., et al. An LXR Agonist Promotes Glioblastoma Cell Death through Inhibition of an EGFR/AKT/SREBP-1/LDLR-Dependent Pathway. Cancer Discovery (2011), 1(5), 442-456.

[3]. Spyridon, Michael., et al. LXR as a novel antithrombotic target. Blood (2011), 117(21), 5751-5761.

[4]. Collins JL, et al. Identification of a nonsteroidal liver X receptor agonist through parallel array synthesis of tertiary amines. J Med Chem. 2002 May 9;45(10):1963-6.

CAIndexNames:

Benzeneacetic acid, 3-[3-[[[2-chloro-3-(trifluoromethyl)phenyl]methyl](2,2-diphenylethyl)amino]propoxy]-, hydrochloride (1:1)

SMILES:

ClC1=C(C(F)(F)F)C=CC=C1CN(CC(C2=CC=CC=C2)C3=CC=CC=C3)CCCOC4=CC(CC(O)=O)=CC=C4.[H]Cl

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA