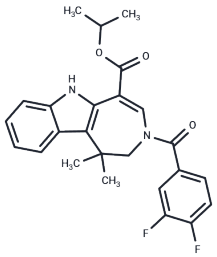
Data Sheet (Cat.No.T6053)

TargetMol

Turofexorate Isopropyl

Chemical Properties



CAS No. : 629664-81-9

Formula: C25H24F2N2O3

Molecular Weight: 438.47

Storage: Keep away from moisture,Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Turofexorate Isopropyl (XL335) is a potent, selective, and orally bioavailable FXR agonist with EC50 of 4 nM
Targets(IC50)	FXR,Autophagy
In vitro	WAY-362450 binds to the ligand-binding domain (LBD) of human FXR. WAY-362450 resides in a predominately hydrophobic pocket with only a few polar atoms making contact with WAY-362450. WAY-362450 promotes transcription of the human BSEP, human SHP, and mouse IBABP genes utilizing reporter constructs with EC50 of 17, 230, and 33 nM, respectively in promoter assays. WAY-362450 at concentration of 1 μM significantly induces mRNAs encoding for BSEP, SHP, and IBABP in human cell cultures to 13-, 2-, and 20-fold, respectively. [1] WAY-362450 at concentration of 1 μM suppresses interleukin-6-induced CRP expression in human Hep3B hepatoma cells, and the inhibitory effect is attenuated when knockdown of FXR by short interfering RNA.
In vivo	WAY-362450 administrated intravenously or orally at does of 3 mg/kg in rats with a protracted half-life of 25 h, modest volume of distribution, and low clearance of 3.3 L/kg. WAY-362450 administered orally at dose of 10 mg/kg in normal C57bl/6 mice for a period of 7 days significantly lowers triglycerides to 62.0 ± 6.4 mg/dL and total cholesterol to 78.1 ± 5.0 mg/dL. WAY-362450 administered orally at dose of 1 and 3 mg/kg daily for 6 weeks in LDLR?/? mice, triglycerides is lowered by 19% and 39%, respectively, total cholesterol is lowered by 23% and 50%, respectively and lesion formation by 18% and 36%, respectively. [1] WAY-362450 intraperitoneally administrated at dose of 30 mg/kg daily for 4 days in wild type C57BL/6 mice attenuates lipopolysaccharide-induced serum amyloid P component and serum amyloid A3 mRNA levels in the liver. [3] WAY-362450 orally administered at dose of 30 mg/kg/day for 4 weeks in adult male C57BL/6 mice reduces in?ammatory cell in?ltration and hepatic ? brosis, the reduction in in?ammatory cell in?ltration correlates with deceased serum levels of keratinocyte derived chemokine (mKC) and MCP 1 and decreased hepatic gene expression of MCP-1 and VCAM-1, and the reduction of hepatic ?brosis by WAY-362450 treatment corresponded to a reduction in hepatic gene expression of ?brosis markers. [3] WAY-362450 administrated orally at dose of 30 mg/kg in LDLR?/? and apoE?/? mice blocks diet-induced hypertriglyceridemia and elevations of non-HDL cholesterol and produced a near complete inhibition of aortic lesion formation, WAY-362450 also induced small heterodimer partner (SHP) expression and repressed cholesterol 7α-

In vivo	hydroxylase (CYP7A1) and sterol 12 α-hydroxylase (CYP8B1) expression. [4]
Kinase Assay	Inhibition of p38α: Inhibition of p38α is determined using recombinant human p38α in a standard filter binding protocol using ATP[γ-33P] and EGFR 21-mer peptide as substrate. Functional inhibition of TNFα in murine peritoneal macrophages is determined using LPS stimulation in the presence of LY2228820. To assess p38α activity in cells more directly, RAW 264.7 cells are treated with LY2228820 and then stimulated with anisomycin. The level of p38α activity is detected using a phosphoMAPKAPK-2 (pMK2) (Thr 334) antibody which reacts with a residue specifically phosphorylated by p38α.
Cell Research	WAY-362450 is prepared in DMSO and stored, and then diluted with appropriate medium (DMSO 0.01%) before use[2]. Mouse AML12 cells are plated at 200,000 cells/well on the 24-well plate in 1 mL of growth medium [DMEM/F12 10% FBS, 1% penicillin and streptomycin, 1% insulin-transferrin-selenium-G supplement (ITS), 0.1% Dexamethasone (40 ng/mL)/well. The cells are treated with increasing concentrations of WAY-362450 (0.001, 0.01, 0.1, 1 and 10 μM) or GW4064 for 24 h. Total RNA is prepared and analyzed by real-time RT-PCR, and short heterodimer partner (SHP) expression is normalized to GAPDH and reported as fold induction vs. vehicle-treated cells. Preplated 24-well plates of human male primary hepatocytes with matrigel overlay are obtained from Cellz Direct. Cells are maintained in serum-free Williams medium E and supplemented with penicillin/streptomycin, dexamethasone, ITS, L-glutamine, and HEPES buffer. They are treated overnight with vehicle (0.01% DMSO) or increasing concentrations of WAY-362450 or GW4064. Total RNA is purified using the Qiagen RNeasy clean kit, and gene expression is quantified by real-time RT-PCR with the Qiagen Quantitech kit using an ABI 7900. The relative amount of mRNA is normalized to 18S ribosomal RNA, and data shown represent an average of two independent experiments[2].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 31 mg/mL (70.7 mM),Sonication is recommended. Ethanol: 2 mg/mL (4.56 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.56 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2807 mL	11.4033 mL	22.8066 mL
5 mM	0.4561 mL	2.2807 mL	4.5613 mL
10 mM	0.2281 mL	1.1403 mL	2.2807 mL
50 mM	0.0456 mL	0.2281 mL	0.4561 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Flatt B, et al. J Med Chem, 2009, 52(4), 904-907.
Zheng W, Lu Y, Tian S, et al. Structural insights into the heterodimeric complex of the nuclear receptors FXR and RXR. Journal of Biological Chemistry. 2018 Aug 10;293(32):12535-12541
Zhang S, et al. J Hepatol, 2009, 51(2), 380-388.
Tschuck J, Theilacker L, Rothenaigner I, et al.Farnesoid X receptor activation by bile acids suppresses lipid peroxidation and ferroptosis.Nature Communications.2023, 14(1): 6908.
Zhang S, et al. Biochem Biophys Res Commun, 2009, 379(2), 476-479.
Hartman HB, et al. J Lipid Res, 2009, 50(6), 1090-1100.
Zheng W, Lu Y, Tian S, et al. Structural insights into the heterodimeric complex of the nuclear receptors FXR and RXR[J]. Journal of Biological Chemistry. 2018 Aug 10;293(32):12535-12541.