XL041

Cat. No.: HY-101973

CAS No.: 1256918-39-4

Molecular Formula: $C_{29}H_{28}Cl_2F_2N_2O_4S$

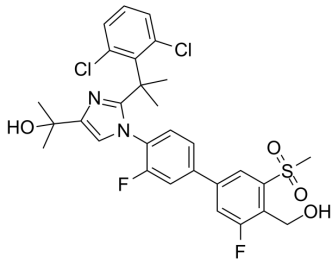
Molecular Weight: 609.51

Target: LXR

Pathway: Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (164.07 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6407 mL	8.2033 mL	16.4066 mL
	5 mM	0.3281 mL	1.6407 mL	3.2813 mL
	10 mM	0.1641 mL	0.8203 mL	1.6407 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.10 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.10 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

XL041 (BMS-852927) is an LXRβ-selective agonist.

IC_{50} & Target

LXRβ[1]

In Vitro

XL041 (BMS-852927) is an LXRβ-selective agonist with 20% LXRα and 88% LXRβ activity compared to a full pan agonist in transactivation assays. XL041 is potent, with an EC_{50}=9 nM and 26% activity in an in vitro human whole-blood endogenous target gene activation assay (WBA). BMS-852927 has similar binding affinity to LXRα and LXRβ (19 and 12 nM, respectively)[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	XL041 (BMS-852927), has a very favorable profile at efficacious doses in cynomolgus monkeys and mice. XL041 pre-treatment of C57BL/6J mice for 7 days results in potent, dose-dependent stimulation of cholesterol efflux in this system, reaching a maximum in the 3 mg/kg/day dose group of 70% above vehicle in the initial efflux rate. Similar results are obtained in LDLR knockout (KO) mice. In a separate study, XL041 inhibits the progression of atherosclerosis in a 12 week study in LDLR KO mice. Importantly, the dose response for inhibition of atherosclerosis (0.1-3 mg/kg/day) is similar to the dose response for macrophage reverse cholesterol transport (RCT) stimulation (0.03-3 mg/kg/day), a major underlying mechanism through which LXR agonists affect the disease[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Peritoneal macrophages are prepared from male C57BL/6 mice that are stimulated with 4% thioglycolate for 4 days. Macrophages are cultured in DMEM supplemented with 20% FBS and 100 U/mL antibiotic-antimycotic. Macrophages are incubated with LXR agonists (eg, XL041) in serum-free DMEM for 20hrs, followed by 5hr treatment of LPS (20 ng/mL). The effect of agonists on IL-23α and Mertk mRNAs is determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] To study effects of LXR agonists on neutrophils, C57BL/6 mice pre-acclimated to oral dosing (n=8/group) are randomly assigned to vehicle; 0.03, 0.1, 1, or 3 mg/kg/day XL041; and 0.3 or 3 mg/kg/day GW3965 and dosed orally for 3 days. Following anesthesia with isoflurane, blood is collected by retro-orbital bleeding and analyzed for neutrophil levels using an Advia hematology instrument employing peroxidase staining. Monkeys[1] All studies are performed in male animals. In a PD study, animals are randomized into six treatment groups (n=3/group) and dosed once daily with vehicle, 10 mg/kg/day T0901317, and 0.1, 0.3, 1, or 3 mg/kg/day XL041 for 14 days. Blood RNA and plasma lipids are determined at baseline and days 1, 4, 7, and 14 of dosing for the pharmacodynamic (PD)study, and on days 1 and 7 for the liver triglyceride (TG) magnetic resonance spectroscopy (MRS) study. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Kirchgessner TG, et al. Beneficial and Adverse Effects of an LXR Agonist on Human Lipid and Lipoprotein Metabolism and Circulating Neutrophils. Cell Metab. 2016 Aug 9;24(2):223-33.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA