LXR-623

Cat. No.: HY-10629

CAS No.: 875787-07-8

Molecular Formula: $C_{21}H_{12}ClF_5N_2$

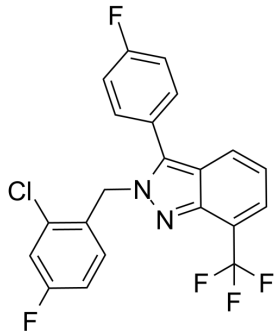
Molecular Weight: 422.78

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 : ≥ 47 mg/mL (111.17 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3653 mL	11.8265 mL	23.6530 mL
	5 mM	0.4731 mL	2.3653 mL	4.7306 mL
	10 mM	0.2365 mL	1.1826 mL	2.3653 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 (5.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LXR-623 is a brain-penetrant partial LXRα and full LXRβ agonist, with IC_{50}s of 24 nM and 179 nM, respectively.

IC_{50} & Target

IC50: 24 nM (LXR-α), 179 nM (LXR-β)[2][3]

In Vitro

LXR-623 potently kills U87EGFRvIII and GBM39 cells in vitro while completely sparing NHAs. LXR-623 also increases ABCA1 protein and decreases LDLR protein levels in all three cell lines. LXR-623 suppresses LDLR expression, increases expression of the ABCA1 efflux transporter, and induces substantial cell death in all of the GBM samples tested. LXR-623 (5 μM) also induces GBM cell death through activation of LXRβ[1]. LXR-623 treatment of human PBMC in vitro significantly increases transcription of ABCA1 and ABCG1[4].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	LXR-623 (400 mg/kg, p.o.) crosses the blood-brain barrier, induces target gene expression, and achieves therapeutic levels in GBM cells in the brain with minimal activity in the periphery. LXR-623 inhibits tumor growth, promotes tumor cell death, and prolongs the survival of mice bearing intracranial patient-derived GBMs[1]. LXR-623 (1.5, 5 mg/kg/day) significantly reduces progression of atherosclerosis in animals compared with the placebo group[2]. WAY-252623 (15 and 50 mg/kg) results in a significant reduction of atherosclerosis in a dose-dependent manner. WAY-252623 (20, 60, and 120 mg/kg/day, p.o.) displays neutral lipid effects in this CETP-expressing Syrian hamster[3]. Moreover, LXR-623 (50 mg/kg) induces gene expression in rodent peripheral blood cells in rat. LXR-623 (0, 15 and 50 mg/kg) dose-dependently upregulates transcription of ABCA1 and ABCG1 in monkey whole blood cells proportional to dose[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Five-week-old female athymic nu/nu mice are used in the experiment. A total of 1×10^5 U87EGFRvIII IRFP720 or GBM39 IRFP720 cells in 5 μL of PBS is intracranially injected into the mouse brain. Tumors are allowed to establish over the course of 7-10 days and engraftment of tumors is quantitatively confirmed via FMT signal intensity. Tumor growth is monitored using an FMT 2500 fluorescence tomography system. For drug treatment studies, vehicle (0.5% methylcellulose, 2% Tween 80 in water) or LXR-623 (400 mg/kg) resuspended in vehicle are administered to mice via oral gavage daily starting at day 7 postinjection. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2019 May 28;10(6):416.
- Cell Death Dis. 2019 Mar 13;10(3):248.
- Life Sci. 2021 Mar 31;119464.
- Nutrients. 2020 Oct 11;12(10):3088.
- Int J Mol Sci. 2023 Mar 21;24(6):5939.

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REFERENCES

[1]. Villa GR, et al. An LXR-Cholesterol Axis Creates a Metabolic Co-Dependency for Brain Cancers. Cancer Cell. 2016 Nov 14;30(5):683-693.

[2]. Giannarelli C, et al. Synergistic effect of liver X receptor activation and simvastatin on plaque regression and stabilization: an magnetic resonance imaging study in a model of advanced atherosclerosis. Eur Heart J. 2012 Jan;33(2):264-73.

[3]. Quinet EM, et al. LXR ligand lowers LDL cholesterol in primates, is lipid neutral in hamster, and reduces atherosclerosis in mouse. J Lipid Res. 2009 Dec;50(12):2358-70.

[4]. DiBlasio-Smith EA, et al. Discovery and implementation of transcriptional biomarkers of synthetic LXR agonists in peripheral blood cells. J Transl Med. 2008 Oct 16;6:59.

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

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