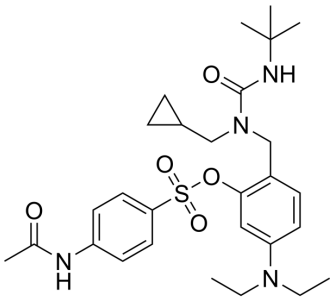
F44-A13

Cat. No.:	HY-163436
CAS No.:	1338190-14-9
Molecular Formula:	$C_{28}H_{40}N_4O_5S$
Molecular Weight:	544.71
Target:	Cytochrome P450; FXR; RAR/RXR; PPAR; ROR
Pathway:	Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor; Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

F44-A13 is an orally active and highly selective farnesoid X receptor (FXR) antagonist with an IC_{50} value of 1.1 μM. F44-A13 can optimize cholesterol metabolism and reduce its activity by inducing CYP7A1 expression. F44-A13 reduces levels of cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C) in mouse models. F44-A13 can be used in the study of metabolic diseases associated with lipid disorders[1].

IC_{50} & Target

PPARα	PPARβ	RXR α	RXRβ
RXRγ	RXR α	RXRβ	RXRγ
RORγ			

In Vitro

F44-A13 demonstrates high selectivity towards various nuclear receptors, including retinoic acid receptor α/β/γ (RARα/β/γ), retinoid X receptor α/β/γ (RXRα/β/γ), pregnane X receptor (PXR), peroxisome proliferators-activated receptors α/β (PPARα/β), thyroid hormone receptor β (THRβ), and retinoic acid receptor-related orphan receptors γ (RORγ)[1].

F44-A13 (50 μM, 24 h) inhibits FXR transcriptional activity in a dose-dependent manner in the presence of 50 μM CDCA (HY-76847) with an IC_{50} value of 3.0 μM. F44-A13 is a low-toxicity, highly selective FXR antagonist[1].

F44-A13 (F44-A13: 3, 10, 30 μM; CDCA: 100 μM; 24 hours) can improve cholesterol metabolism and reduce cholesterol activity by inducing the expression of CYP7A1. F44-A13 can decrease the expression level of Shp and Bsep, and increase the expression level of CYP7A1[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	HepG2 , HEK293A cells
Concentration:	100 μM
Incubation Time:	24h
Result:	Was not cytotoxic to HepG2 and HEK293A cells

RT-PCR[1]

Cell Line:	HepG2 cells

Concentration:	F44-A13: 3, 10, 30 μM; CDCA: 100 μM
Incubation Time:	24h
Result:	Was able to reverse the regulation of FXR downstream target genes Shp, Bsep and Cyp7a1 by CDCA in a dose-dependent manner. Decreased the expression level of Shp and Bsep, and increased the expression level of Cyp7a1.

In Vivo

F44-A13 (20, 40 mg/kg; Oral gavage (p.o.) and Intraperitoneal injection (i.p.); 4 days) effectively reduces the levels of TC, TG and LDL-C in a C57BL/6 mice model[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 mice[1]
Dosage:	20, 40 mg/kg
Administration:	Intraperitoneal injection (i.p.) and Oral gavage (p.o.); 4 days
Result:	Intraperitoneal injection significantly reduced TC levels by more than 28%, and oral administration significantly reduced TC levels in a dose-dependent manner. Reduced TG levels by more than 30% at both 20 and 40 mg/kg orally, while intraperitoneal injection did not significantly reduce TG levels. Oral doses of 20 and 40 mg/kg were effective in reducing LDL-C levels by 12% and 23%, and intraperitoneal injections by 38%.

REFERENCES

[1]. Dou X, et al. Discovery of novel and selective farnesoid X receptor antagonists through structure-based virtual screening, preliminary structure-activity relationship study, and biological evaluation. Eur J Med Chem. 2024;269:116323.

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