FXR agonist 3

Cat. No.: HY-151932

Molecular Formula: $C_{28}H_{28}BrNO_4$

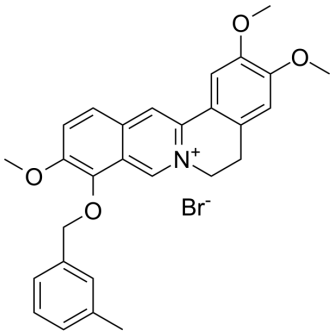
Molecular Weight: 522.43

Target: FXR

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 250 mg/mL (478.53 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9141 mL	9.5707 mL	19.1413 mL
	5 mM	0.3828 mL	1.9141 mL	3.8283 mL
	10 mM	0.1914 mL	0.9571 mL	1.9141 mL

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

BIOLOGICAL ACTIVITY

Description

FXR agonist 3 is an anti-NASH agent, acting by activating FXR. FXR agonist 3 inhibits COL1A1, TGF-β1, α-SMA and TIMP1 expression with anti-fibrogenic activity. FXR agonist 3 significantly reduces liver steatosis and inflammation, improves liver fibrosis level[1].

In Vitro

FXR agonist 3 (compound 3a) (5 μM; 24 h) shows anti-fibrogenic activity, decreases multiple fibrogenic biomarkers level in LX-2 cells in a dose-dependent manner[1].

FXR agonist 3 shows cytotoxic concentration against LX2 cells with an CC_{50} value of 70.36 μM[1].

Metabolic stability of FXR agonist 3 in human, rat and mouse liver microsomes[1]

Species	$T_{1/2}$ (h)	$CL_{Int\ (mic)}$ (μg/min/mg)	$CL_{Int\ (liver)}$ (μg/min/mg)	Remaining Ratio (%) (T=60 min)
Human	53.3	26.0	23.4	44.1

Rat	7.4	187.8	338.0	0.4
Mouse	7.4	187.9	744.1	39.0

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

Western Blot Analysis[1]

Cell Line:	LX-2 cells
Concentration:	0, 2.5, 5, 7.5, and 10 μM
Incubation Time:	24 hours; with or without 2 ng/mL TGF-β1 for another 24 hr
Result:	Decreased COL1A1, TGF-β1, α-SMA, and TIMP1 protein expressions in a dose-dependent manner.

In Vivo

FXR agonist 3 (compound 3a) (200 mg/kg; p.o.; daily for 4 weeks) significantly attenuates the degree of liver fibrosis in choline-deficient, l-amino acid-defined, high-fat diet (CDAHFD)-induced NASH mice model[1].
FXR agonist 3 (200 mg/kg; p.o.; daily for 4 weeks) also exerts liver-protective and anti-fibrosis activities in bile duct ligation (BDL)-induced fibrosis rat model[1].

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

Animal Model:	C57BL/6 N mice fed CDAHFD diet for 16 weeks[1]
Dosage:	200 mg/kg
Administration:	Oral gavage; daily for 4 weeks after CDAHFD-induced
Result:	Decreased expression of IL-1β and IL-6 in livers, indicating the liver-protective effect of 3a in CDAHFD mice may partially through inhibiting inflammasome activation. Lowered the serum levels of biochemical markers of ALT, AST, ALP, LDH, LDL and TBiL significantly, while raised HDL and GLU levels.

Animal Model:	C57BL/6 N mice inuced with BDL[1]
Dosage:	200 mg/kg
Administration:	Oral gavage; daily for 4 weeks after induced
Result:	Protected liver from accumulated bile acid-induced injury. Increased the expression of FXR and decreased the expression of NTCP in BDL rats.

REFERENCES

[1]. Zhang N, et al. Discovery and development of palmatine analogues as anti-NASH agents by activating farnesoid X receptor (FXR). Eur J Med Chem. 2023 Jan 5;245(Pt 1):114886.

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

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