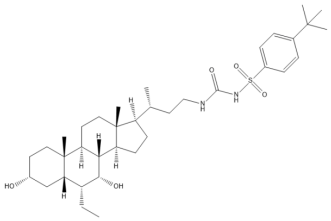
EDP-305

Cat. No.:	HY-134988
CAS No.:	1933507-63-1
Molecular Formula:	$C_{36}H_{58}N_2O_5S$
Molecular Weight:	630.92
Target:	FXR; Phosphatase; Cytochrome P450
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 : ≥ 100 mg/mL (158.50 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5850 mL	7.9249 mL	15.8499 mL
5 mM	0.3170 mL	1.5850 mL	3.1700 mL
10 mM	0.1585 mL	0.7925 mL	1.5850 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 (3.96 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.96 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

EDP-305 is an orally active, potent and selective farnesoid X receptor (FXR) agonist, with EC_{50} values of 34 nM (chimeric FXR in CHO cells) and 8 nM (full-length FXR in HEK cells). EDP-305 shows a potent and consistent antifibrotic effect. EDP-305 can be used for primary biliary cholangitis (PBC) and non-alcoholic steatohepatitis (NASH) research[1][2].

IC_{50} & Target

IC50: 8 ± 3 nM (Full-length FXR in HEK cells), 34 ± 8 nM (Chimeric FXR in CHO cells), >15000 nM (TGR5 in CHO cells)[2]

In Vitro

EDP305 (10 μM, 72 h) directly activates FXR in liver hepatoctyes but not stellate cells[1].
EDP-305 (0-5 μM, 16 h) increases the expression of the FXR target gene, SHP, and downregulates CYP7A1 expression in HepaRG hepatocytes[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	Hepatic stellate cell (HSC) lines, primary HSCs and hepatocytes
Concentration:	10 μM
Incubation Time:	72 h
Result:	Induced mRNA expression of SHP and FGF19 in human hepatocytes, and elicited no induction of downstream targets SHP or FGF15/19 in stellate lines.

RT-PCR[2]

Cell Line:	HepaRG hepatocytes
Concentration:	0.05, 0.1, 0.5, 1, 5, 10, 50, 100, 500, 1000, 5000 nM
Incubation Time:	16 h
Result:	Dose-dependently increased the expression of the FXR target gene, SHP, and downregulated CYP7A1 expression in HepaRG hepatocytes.

In Vivo

EDP305 (0-30 mg/kg, Oral gavage, daily for 2 weeks) reduces serum markers of liver injury, and reduces liver fibrosis in a dose-dependent manner in BDL rats[1].
EDP305 (0-30 mg/kg, Oral gavage, daily for 6 weeks) reduces liver fibrosis in a dose-dependent manner in CDAHFD mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male CD rats (underwent BDL, n=24, n=8 for each group)[1]
Dosage:	0, 10 and 30 mg/kg
Administration:	Oral gavage, daily, started on day 4 after BDL and continued until days 17-18
Result:	Significantly reduced alanine aminotransferase and aspartate aminotransferase. Showed a dose-dependent reduction in CPA. Reduced hydroxyproline levels in whole liver tissue samples. Reduced messenger RNA (mRNA) relative quantification (RQ) for both Col1a1 and actin, alpha 2, smooth muscle, aorta (Acta2).

Animal Model:	Male C57BL/6 mice (n = 24, fed a CDAHFD consisting of 60% kcal fat and 0.1% methionine) [1]
Dosage:	0, 10 and 30 mg/kg
Administration:	Oral gavage, daily, started at the beginning of week 6 on the diet and were continued until week 12
Result:	Reduced serum triglycerides, and significantly reduced hydroxyproline and MR liver signal intensity in a dose-dependent manner. Showed a dose-dependent reduction in mRNA expression of lysyl oxidase genes Lox and Loxl1-4.

REFERENCES

[1]. Erstad DJ, et al. Molecular magnetic resonance imaging accurately measures the antifibrotic effect of EDP-305, a novel farnesoid X receptor agonist. Hepatol Commun. 2018 May 21;2(7):821-835.

[2]. Chau M, et al. Characterization of EDP-305, a Highly Potent and Selective Farnesoid X Receptor Agonist, for the Treatment of Non-alcoholic Steatohepatitis[J]. International Journal of Gastroenterology, 2019(1).

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