Obeticholic acid

Cat. No.: HY-12222

CAS No.: 459789-99-2

Molecular Formula: $C_{26}H_{44}O_4$

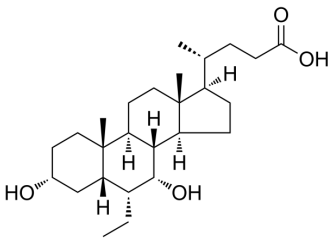
Molecular Weight: 420.63

Target: FXR; Autophagy

Pathway: Metabolic Enzyme/Protease; Autophagy

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 (237.74 mM)

Ethanol : ≥ 50 mg/mL (118.87 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3774 mL	11.8869 mL	23.7739 mL
	5 mM	0.4755 mL	2.3774 mL	4.7548 mL
	10 mM	0.2377 mL	1.1887 mL	2.3774 mL

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

In Vivo

1. Add each solvent one by one: 1% Methylcellulose/saline water
   Solubility: 5 mg/mL (11.89 mM); Suspension solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (11.89 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (11.89 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 4.76 mg/mL (11.32 mM); Clear solution
5. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution
6. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution
7. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution
8. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)

	Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Obeticholic acid (INT-747) is a potent, selective and orally active FXR agonist with an EC_{50} of 99 nM. Obeticholic acid has anticholeretic and anti-inflammation effect. Obeticholic acid also induces autophagy[1][2][3].
IC_{50} & Target	EC50: 99 nM (FXR)
In Vitro	Obeticholic acid (INT-747) increases the expression of FXR-regulated genes in rat hepatocytes[1]. Obeticholic acid (INT-747) reduces expression of liver JNK-1 and JNK-2[2]. Obeticholic acid (INT-747) (256 μg/mL) shows complete inhibition of bacterial growth in all strains tested. Intestinal permeability remains unaffected after INT-747-addition to an IFN-γ-exposed intestinal epithelium of Caco-2 cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Obeticholic acid (INT-747) (10 mg/kg/day) completely reverted cholestasis induced by $E_2$17α. Administration of Obeticholic acid (INT-747) partially prevents the impairment in total bile acid output caused by $E_2$17α by increasing the relative abundance of β-MCA and TCDCA and TDCA[1]. Obeticholic acid (INT-747)7 (10 mg/kg) and HS increases the pulmonary congestion in the animals. INT-747 does not improve renal pathology in the HS-fed animals[2]. Obeticholic acid (INT-747) (5 mg/kg) significantly increases survival in BDL rats. Obeticholic acid (INT-747)-treated BDL rats exhibits a significant selective ileal increase in expression of pore-closing claudin-1. Ileal expression of ZO-1 is significantly up-regulated in INT-747-treated BDL rats[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Initially, all animals (at 6-weeks age) are placed on a standard rodent diet for a week. Baseline blood and urine samples are collected and basal blood pressure (BP) is measured prior to grouping the animals. Subsequently, the animals are randomized into low (LS; n=9) or high salt (HS) diet groups. Hypertension is induced in the HS group by daily high-salt diet feeding and the group is subdivided to receive one of two doses of INT-747: low dose (10 mg/kg/day; n=15) or high dose (30 mg/kg/day; n=15) in 1% methylcellulose; or vehicle (1% methylcellulose in distilled water; n=15) orally everyday for 6 weeks. In parallel, the LS group also receive 1% methylcellulose. BP is measured weekly for the duration of the study as described below. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Host Microbe. 2018 Sep 12;24(3):353-363.e5.
- Cell Stem Cell. 2022 Sep 1;29(9):1366-1381.e9.
- Acta Pharm Sin B. 27 August 2022.
- Biomaterials. 2022 Sep 28;290:121817.
- Biomaterials. 2021, 121006.

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REFERENCES

[1]. Fiorucci S, et al. Protective effects of 6-ethyl chenodeoxycholic acid, a farnesoid X receptor ligand, in estrogen-induced cholestasis. J Pharmacol Exp Ther. 2005 May;313(2):604-12.

[2]. Ghebremariam YT, et al. FXR agonist INT-747 upregulates DDAH expression and enhances sensitivity in high-salt fed Dahl rats. PLoS One. 2013 Apr 4;8(4):e60653.

[3]. Verbeke L, et al. The FXR Agonist Obeticholic Acid Prevents Gut Barrier Dysfunction and Bacterial Translocation in Cholestatic Rats. Am J Pathol. 2015 Feb;185(2):409-19.

[4]. Pellicciari R, et al. 6alpha-ethyl-chenodeoxycholic acid (6-ECDCA), a potent and selective FXR agonist endowed with anticholestatic activity. J Med Chem. 2002 Aug 15;45(17):3569-72.

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