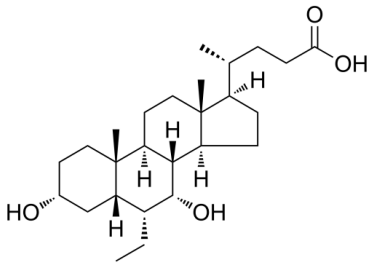
Data Sheet

Product Name:	Obeticholic acid
Cat. No.:	CS-3813
CAS No.:	459789-99-2
Molecular Formula:	$C_{26}H_{44}O_4$
Molecular Weight:	420.63
Target:	Autophagy; FXR
Pathway:	Autophagy; Metabolic Enzyme/Protease
Solubility:	Ethanol : ≥ 50 mg/mL;DMSO : ≥ 100 mg/mL



BIOLOGICAL ACTIVITY:

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]. IC50 & 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]. ***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].

PROTOCOL (Extracted from published papers and Only for reference)

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.

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.

CAIndexNames:

Cholan-24-oic acid, 6-ethyl-3,7-dihydroxy-, (3α,5β,6α,7α)-

SMILES:

C[C@@]([C@]1([H])[C@@H](CC)[C@H]2O)(CC[C@@H](O)C1)[C@]3([H])[C@]2([H])[C@@](CC[C@]4([H])[C@H](C)CCC(O)=O)([H])[C@]4(C)CC3

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