

Product Data Sheet

Product Name: Obeticholic Acid

Cat. No.: GC14158

Chemical Properties

Cas. No. 459789-99-2

Chemical Name (4R)-4-[(3R,5S,6R,7R,8S,9S,10S,13R,14S,17R)-6-ethyl-3,7-dihydroxy-10,13-dimethyl-2,3,4,5,6,7,8,9,11,12,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl]pentanoic acid

SMILES CCC1C2CC(CCC2(C3CCC4(C(C3C1O)CCC4C(C)CCC(=O)O)C)C)O

Formula C₂₆H₄₄O₄ M.Wt 420.63

Solubility ≥ 21.5mg/mL in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

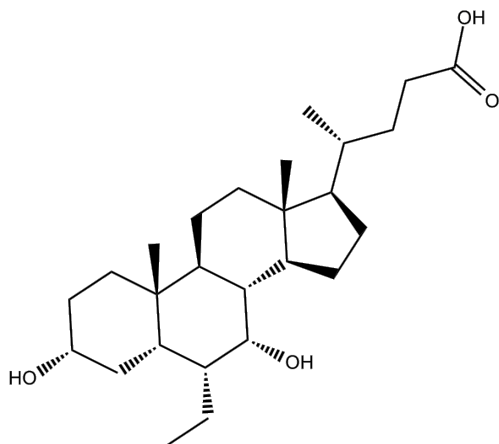
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:

Cell lines HepG2, Huh7, and SNU-449 cells

1.2 to 1.8×10^3 cells per well were seeded in 96-well plates and cultured overnight. Then, the cells were treated with 0.01-100 μ M of Obeticholic Acid, or DMSO. After 72h, MTT reagent was added to the cells in each well followed by incubation for 2h, and the absorbance was determined using a microplate reader. The effect of treatments on cell viability was presented as the percentage of the absorbance at 570nm from treated cells versus that from untreated control cells.

Preparation Method

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Reaction
Conditions 0.01-100μM; 72h

Applications Obeticholic Acid reduced the proliferation rates of HepG2, Huh7, and SNU-449 cells with IC₅₀ values of 1.067μM, 1.038μM, and 0.706μM, respectively.

Animal experiment [2]:

Animal models MC4R-KO mice

Preparation Method 8-week-old MC4R-KO mice were fed Western diet(WD) for 20 weeks, and control WT mice were fed Standard diet(SD) for the same period. MC4R-KO mice fed WD for 6 weeks received a single intraperitoneal injection of CCl₄ diluted 1:20 in olive oil at a dose of 0.2ml/kg. After the onset of non-alcoholic steatohepatitis(NASH) symptoms, MC4R-KO mice were gavaged once daily with 10mg/kg Obeticholic Acid or vehicle (0.5% carboxymethyl cellulose) for 4 or 8 weeks. At the end of the experiment, mice were sacrificed under intraperitoneal pentobarbital anesthesia.

Dosage form 10mg/kg; p.o.

Applications Obeticholic Acid treatment significantly inhibited the number of hepatic crown-like structure(hCLS) and reduced the fibrotic area and mRNA expression of fibrogenic genes. Long-term treatment with Obeticholic Acid had no effect on body weight and adipose tissue weight in MC4R-KO mice.

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References:

[1]Attia Y M, Tawfiq R A, Ali A A, et al. The FXR agonist, obeticholic acid, suppresses HCC proliferation & metastasis: role of IL-6/STAT3 signalling pathway[J]. Scientific reports, 2017, 7(1): 12502.

[2]Goto T, Itoh M, Suganami T, et al. Obeticholic acid protects against hepatocyte death and liver fibrosis in a murine model of nonalcoholic steatohepatitis[J]. Scientific reports, 2018, 8(1): 8157.

Background

Obeticholic Acid (INT-747; 6-ECDCA; 6-Ethylchenodeoxycholic acid) is a potent, selective and orally active farnesoid X receptor(FXR) agonist with an EC_{50} of 99nM^[1]. FXR is a ligand-dependent transcription factor belonging to the nuclear hormone receptor superfamily that plays an important role in bile acid, lipid metabolism, carbohydrate homeostasis and inflammatory response^[2]. Obeticholic Acid is a semisynthetic hydrophobic bile acid analog used to treat primary biliary cholangitis(PBC) and non-alcoholic steatohepatitis(NASH)^[3].

In vitro, treatment of HepG2, Huh7 and SNU-449 cells with Obeticholic Acid (0.01-100 μ M) for 72h significantly inhibited cell proliferation with IC_{50} values of 1.067 μ M, 1.038 μ M and 0.706 μ M, respectively, and also inhibited cell migration and invasion^[4]. Treatment of primary cultures of human intrahepatic cholangiocarcinoma(iCCA) with Obeticholic Acid (0-2.5 μ M) for 3-10 days significantly inhibited the proliferation of mucinous and mixed iCCA cells and upregulated FXR gene expression^[5].

In vivo, oral treatment of mice with NASH with Obeticholic Acid (10mg/kg) for 4 or 8 weeks significantly inhibited the number of hepatic coronary structures(hCLS), reduced the area of fibrosis and the mRNA expression of fibrotic genes, and long-term treatment had no effect on the body weight and adipose tissue weight of mice^[6]. Oral treatment of rats with ascites cirrhosis with Obeticholic Acid (5mg/kg) for 2 weeks significantly reduced intestinal bacterial translocation, reduced intestinal immune cell infiltration, and normalized the expression of inflammatory cytokines^[7].

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- [1] Pellicciari R, Fiorucci S, Camaioni E, et al. 6 α -ethyl-chenodeoxycholic acid (6-ECDCA), a potent and selective FXR agonist endowed with anticholestatic activity[J]. Journal of medicinal chemistry, 2002, 45(17): 3569-3572.
- [2] Shaik F B, Prasad D V R, Narala V R. Role of farnesoid X receptor in inflammation and resolution[J]. Inflammation Research, 2015, 64: 9-20.
- [3] Chapman R W, Lynch K D. Obeticholic acid—a new therapy in PBC and NASH[J]. British medical bulletin, 2020, 133(1): 95-104.
- [4] Attia Y M, Tawfiq R A, Ali A A, et al. The FXR agonist, obeticholic acid, suppresses HCC proliferation & metastasis: role of IL-6/STAT3 signalling pathway[J]. Scientific reports, 2017, 7(1): 12502.
- [5] Di Matteo S, Nevi L, Costantini D, et al. The FXR agonist obeticholic acid inhibits the cancerogenic potential of human cholangiocarcinoma[J]. PLoS One, 2019, 14(1): e0210077.
- [6] Goto T, Itoh M, Suganami T, et al. Obeticholic acid protects against hepatocyte death and liver fibrosis in a murine model of nonalcoholic steatohepatitis[J]. Scientific reports, 2018, 8(1): 8157.
- [7] Úbeda M, Lario M, Muñoz L, et al. Obeticholic acid reduces bacterial translocation and inhibits intestinal inflammation in cirrhotic rats[J]. Journal of hepatology, 2016, 64(5): 1049-1057.

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