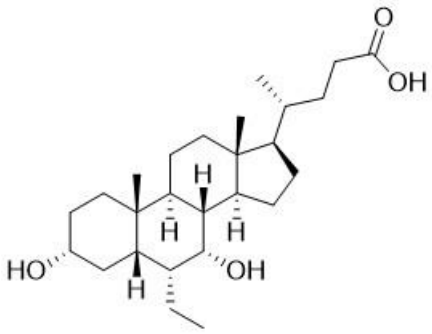
Product data sheet

MedKoo Cat#: 522440 Name: Obeticholic Acid CAS#: 459789-99-2 Chemical Formula: $C_{26}H_{44}O_4$ Exact Mass: 420.32396 Molecular Weight: 420.63	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Obeticholic Acid (INT747; 6-ECDCA) is a novel derivative of cholic acid which acts as a potent and selective FXR agonist displaying anticholeretic activity in an in vivo rat model of cholestasis. It inhibits vascular smooth muscle cell inflammation and migration as well as promotes adipocyte differentiation and regulates adipose cell function in vivo.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	100.00	237.7

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.38 mL	11.89 mL	23.77 mL
5 mM	0.48 mL	2.38 mL	4.75 mL
10 mM	0.24 mL	1.19 mL	2.38 mL
50 mM	0.05 mL	0.24 mL	0.48 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Di Matteo S, Nevi L, Costantini D, Overi D, Carpino G, Safarikia S, Giulitti F, Napoletano C, Manzi E, De Rose AM, Melandro F, Bragazzi M, Berloco PB, Giuliante F, Grazi G, Giorgi A, Cardinale V, Adorini L, Gaudio E, Alvaro D. The FXR agonist obeticholic acid inhibits the cancerogenic potential of human cholangiocarcinoma. PLoS One. 2019 Jan 24;14(1):e0210077. doi: 10.1371/journal.pone.0210077. PMID: 30677052; PMCID: PMC6345424.
2. Anfuso B, Tiribelli C, Adorini L, Rosso N. Obeticholic acid and INT-767 modulate collagen deposition in a NASH in vitro model. Sci Rep. 2020 Feb 3;10(1):1699. doi: 10.1038/s41598-020-58562-x. PMID: 32015483; PMCID: PMC6997404.

In vivo study

1.Wu L, Han Y, Zheng Z, Zhu S, Chen J, Yao Y, Yue S, Teufel A, Weng H, Li L, Wang B. Obeticholic Acid Inhibits Anxiety via Alleviating Gut Microbiota-Mediated Microglia Accumulation in the Brain of High-Fat High-Sugar Diet Mice. Nutrients. 2021 Mar 15;13(3):940. doi: 10.3390/nu13030940. PMID: 33803974; PMCID: PMC7999854.
2. de Haan LR, Verheij J, van Golen RF, Horneffer-van der Sluis V, Lewis MR, Beuers UHW, van Gulik TM, Olde Damink SWM, Schaap FG, Heger M, Olthof PB. Unaltered Liver Regeneration in Post-Cholestatic Rats Treated with the FXR Agonist Obeticholic Acid. Biomolecules. 2021 Feb 10;11(2):260. doi: 10.3390/biom11020260. PMID: 33578971; PMCID: PMC7916678.

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7. Bioactivity

Biological target:

Obeticholic acid (INT-747) is an active FXR agonist with an EC50 of 99 nM (FXR).

In vitro activity

The aim of this study was to evaluate, in primary cultures of human intrahepatic CCA (iCCA), the effects of the FXR agonist obeticholic acid (OCA), a semisynthetic bile acid derivative, on their cancerogenic potential. Primary human iCCA cell cultures were prepared from surgical specimens of mucinous or mixed iCCA subtypes. Increasing concentrations (0–2.5 μM) of OCA were added to culture media and, after 3–10 days, effects on proliferation (MTS assay, cell population doubling time), apoptosis (annexin V-FITC/propidium iodide), cell migration and invasion (wound healing response and Matrigel invasion assay), and cancerogenic potential (spheroid formation, clonogenic assay, colony formation capacity) were evaluated. FXR gene expression was downregulated (RT-qPCR) in iCCA cells vs normal human biliary tree stem cells ($p < 0.05$) and in mucinous iCCA vs mixed iCCA cells ($p < 0.05$) but was upregulated by addition of OCA. OCA significantly ($p < 0.05$) inhibited proliferation of both mucinous and mixed iCCA cells, starting at a concentration as low as 0.05 μM. Also, CDCA (but not UDCA) inhibited cell proliferation, although to a much lower extent than OCA, consistent with its different affinity for FXR. OCA significantly induced apoptosis of both iCCA subtypes and decreased their in vitro cancerogenic potential, as evaluated by impairment of colony and spheroid formation capacity and delayed wound healing and Matrigel invasion. In conclusion, FXR is down-regulated in iCCA cells, and its activation by OCA results in anti-cancerogenic effects against mucinous and mixed iCCA cells, in vitro. The effects of OCA predominated in mixed iCCA cells, consistent with the lower aggressiveness and the higher FXR expression in this CCA subtype. These results, showing the FXR-mediated capacity of OCA to inhibit cholangiocarcinogenesis, represent the basis for testing OCA in clinical trials of CCA patients.

PLoS One. 2019; 14(1): e0210077. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6345424/

In vivo activity

This study assessed the serum biochemical parameters and behavioral performance by open field and Morris water maze tests in HFHS diet-induced MDs mice after obeticholic acid (OCA) intervention for nine and 18 weeks. 32 mice were fed with HFHS diet (fat 60% kcal, carbohydrate 20% kcal, protein 20% kcal (Research Diets, New Brunswick, NJ, USA) and carbohydrates (18.9 g/L sucrose and 23.1 g/L fructose) in drinking water) for nine weeks to induce MDs and 12 mice were fed with normal chow. Then HFHS diet mice were divided into three groups (n = 10–12 per group): MO; mice were daily oral gavage with OCA (Selleck, USA) (2 mg/mL in carboxymethyl cellulose (CMC-Na), 5 mL/kg) ; (2) MA, mice were daily oral gavage with antibiotics cocktail containing1.86 mg ampicillin, 1.86 mg neomycin sulfate, 1.2 mg metronidazole and 0.96 mg vancomycin (Sigma-Aldrich, St. Louis, MO, USA) in 300 μL double distilled water ; M, mice were oral gavage with an equal volume of CMC-Na. Meanwhile, normal chow mice were oral gavage with an equal volume of CMC-Na as the control group (C).The GTT results showed that supplementation with OCA decreased the elevated fasting glucose in HFHS diet mice. These results supported that gut dysbiosis contributed to MDs in HFHS diet mice, which could be improved by OCA supplementation. Our findings highly suggested that the inhibiting effect of OCA on the anxiety-related bacteria may be transmitted from the gut to the brain via the “gut microbiota–brain” axis. Thus, our findings of OCA in improving the ‘leaky gut’ and reducing the LPS-producing bacteria in HFHS-diet MDs mice could partially explain how orally OCA supplementation reduced neuroinflammation in the hippocampus via the ”gut–brain” axis.

Nutrients. 2021 Mar; 13(3): 940. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7999854/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.