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: \( \geq 100 \text{ mg/mL (237.74 mM)} \)
Ethanol: \( \geq 50 \text{ mg/mL (118.87 mM)} \)
* "\( \geq \)" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Concentration</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.3774 mL</td>
<td></td>
<td>11.8869 mL</td>
<td>23.7739 mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td></td>
<td>0.4755 mL</td>
<td>2.3774 mL</td>
<td>4.7548 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td></td>
<td>0.2377 mL</td>
<td>1.1887 mL</td>
<td>2.3774 mL</td>
</tr>
</tbody>
</table>

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: \( \geq 4.76 \text{ mg/mL (11.32 mM)} \); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-\( \beta \)-CD in saline)
   Solubility: \( \geq 5 \text{ mg/mL (11.89 mM)} \); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: \( \geq 5 \text{ mg/mL (11.89 mM)} \); Clear solution
4. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: \( \geq 2.5 \text{ mg/mL (5.94 mM)} \); Clear solution
5. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-\( \beta \)-CD in saline)
   Solubility: \( \geq 2.5 \text{ mg/mL (5.94 mM)} \); Clear solution
6. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: \( \geq 2.5 \text{ mg/mL (5.94 mM)} \); Clear solution
BIOLOGICAL ACTIVITY

Description
Obeticholic acid (INT-747) is a potent, selective and orally active FXR agonist with an EC50 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 E217α. Administration of Obeticholic acid (INT-747) partially prevents the impairment in total bile acid output caused by E217α by increasing the relative abundance of β-MCA and TCDCA and TDCA[1]. Obeticholic acid (INT-747) (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

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 above.

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.
- Cells. 2019 Nov.

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REFERENCES
