产品名称：INT-747
产品别名：奥贝胆酸；Obeticholic acid

生物活性：

Description	Obeticholic acid (INT-747) is a potent, orally active and selective farnesoid X receptor (FXR) agonist with an EC_{50} of 99 nM.
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].
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].
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

Solvent / Mass / 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO →40% PEG300 →5% Tween-80→45% saline

Solubility: ≥ 4.76 mg/mL (11.32 mM); Clear solution

此方案可获得 ≥ 4.76 mg/mL (11.32 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 47.600002 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合

	均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% (20% SBE-β-CD in saline) Solubility: ≥ 5 mg/mL (11.89 mM); Clear solution 此方案可获得 ≥ 5 mg/mL (11.89 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 50.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO→90% corn oil Solubility: ≥ 5 mg/mL (11.89 mM); Clear solution 此方案可获得 ≥ 5 mg/mL (11.89 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 50.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 4.请依序添加每种溶剂： 10% EtOH →40% PEG300 → 5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.94 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 5.请依序添加每种溶剂： 10% EtOH → 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.94 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 6.请依序添加每种溶剂： 10% EtOH → 90% corn oil Solubility: ≥ 2.5 mg/mL (5.94 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.94 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Animal Administration	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. [2]
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.