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产品名称：INT-777
产品别名：S-EMCA

生物活性：

Description	INT-777 is a potent TGR5 agonist with an EC50 of 0.82 μM.
IC_{50} & Target	EC50: 0.82 μM (TGR5)[1]
In Vitro	INT-777 is a novel potent and selective TGR5 agonist with remarkable in vivo activity[1]. INT-777 (3 μM) increases ATP production in the human enteroendocrine cell line NCI-H716 in a cAMP-dependent manner[2]. INT-777 (10 μM) lowers Isc and increases TEER when added on the serosal side of seromuscular stripped distal colon segments. INT-777 effect on basal secretion is reduced in neuron-free and TTX-treated mucosal-submucosal preparations[3].
In Vivo	INT-777 (1 μM/min/kg, p.o.) has a potent choleretic effect, prevents carboxyl CoA activation and subsequent conjugation, thereby favoring its cholehepatic shunt pathway with a ductular absorption and a potent choleretic effect in HF-fed TGR5-Tg male mice[1]. INT-777 (30 mg/kg/day, p.o.) increases energy expenditure and reduces hepatic steatosis and obesity upon high fat feeding in TGR5-Tg mice[2].

Solvent&Solubility

In Vitro:

Ethanol : ≥ 50 mg/mL (110.95 mM)

DMSO : ≥ 31 mg/mL (68.79 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2190 mL	11.0951 mL	22.1902 mL
	5 mM	0.4438 mL	2.2190 mL	4.4380 mL
	10 mM	0.2219 mL	1.1095 mL	2.2190 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: ≥ 2.5 mg/mL (5.55 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.55 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。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

	Solubility: ≥ 2.5 mg/mL (5.55 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.55 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.55 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.55 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]. Pellicciari R, et al. Discovery of 6alpha-ethyl-23(S)-methylcholic acid (S-EMCA, INT-777) as a potent and selective agonist for the TGR5 receptor, a novel target for diabesity. J Med Chem. 2009 Dec 24;52(24):7958-61. [2]. Thomas C, et al. TGR5-mediated bile acid sensing controls glucose homeostasis. Cell Metab. 2009 Sep;10(3):167-77. [3]. Duboc H, et al.Reduction of epithelial secretion in male rat distal colonic mucosa by bile acid receptor TGR5 agonist, INT-777: role of submucosal neurons. Neurogastroenterol Motil. 2016 Jun 3. doi: 10.1111/nmo. [4]. Baiqiang Li, et al. INT-777, a bile acid receptor agonist, extenuates pancreatic acinar cells necrosis in a mouse model of acute pancreatitis. Biochem Biophys Res Commun. 2018 Sep 3;503(1):38-44.

实验参考：

Cell Assay	The experiments are carried out in STC-1 or NCI-H716 cells treated with vehicle (DMSO) or INT-777. INT-777 is assessed for its agonistic activity on TGR5. cAMP production is performed. Cytochrome C oxidase activity is evaluated by following the oxidation of fully reduced cytochrome C at 550 nm. ATP/ADP ratio and GLP-1 release is measured according to the manufacturer's instruction. Primary brown adipocytes are prepared and ileal explants are prepared. [2]
Animal Administration	Age-matched male mice are used for all experiments. Genetically engineered mouse models (GEMMs), i.e. TGR5-Tg and TGR5-/- mice are generated. Diet-induced obesity (DIO) in the GEMMs or C57BL/6J mice is induced by feeding 8-week-old mice with a HF-diet (60%Cal/fat, D12492) for at least 8 weeks, as mentioned in the text and figure legends. In the dietary intervention experiments, INT-777 is mixed with diet at the dose sufficient to reach an in vivo dose of 30mg/kg/d. Mouse phenotyping experiments are performed according to EMPRESS protocols and aimed to assess food and water intake, body composition, energy expenditure, glucose and lipid homeostasis, and plasma biochemistry. [2]
References	[1]. Pellicciari R, et al. Discovery of 6alpha-ethyl-23(S)-methylcholic acid (S-EMCA, INT-777) as a potent and selective agonist for the TGR5 receptor, a novel target for diabesity. J Med Chem. 2009 Dec 24;52(24):7958-61. [2]. Thomas C, et al. TGR5-mediated bile acid sensing controls glucose homeostasis. Cell Metab. 2009 Sep;10(3):167-77.

	[3]. Duboc H, et al.Reduction of epithelial secretion in male rat distal colonic mucosa by bile acid receptor TGR5 agonist, INT-777: role of submucosal neurons. Neurogastroenterol Motil. 2016 Jun 3. doi: 10.1111/nmo. [4]. Baiqiang Li, et al. INT-777, a bile acid receptor agonist, extenuates pancreatic acinar cells necrosis in a mouse model of acute pancreatitis. Biochem Biophys Res Commun. 2018 Sep 3;503(1):38-44.