INT-777

Cat. No.: HY-15677  
CAS No.: 1199796-29-6  
Molecular Formula: C_{27}H_{46}O_{5}  
Molecular Weight: 450.65  
Target: GPCR19  
Pathway: GPCR/G Protein  
Storage: Powder: -20°C 3 years, 4°C 2 years; In solvent: -80°C 6 months, -20°C 1 month

Solvent & Solubility

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Mass</th>
<th>Preparing Stock Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 31 mg/mL (68.79 mM)</td>
<td>*&quot;≥&quot; means soluble, but saturation unknown.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMSO</td>
<td>1 mM</td>
<td>2.2190 mL</td>
<td>11.0951 mL</td>
<td>22.1902 mL</td>
</tr>
<tr>
<td>DMSO</td>
<td>5 mM</td>
<td>0.4438 mL</td>
<td>2.2190 mL</td>
<td>4.4380 mL</td>
</tr>
<tr>
<td>DMSO</td>
<td>10 mM</td>
<td>0.2219 mL</td>
<td>1.1095 mL</td>
<td>2.2190 mL</td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

In Vivo  
1. INT-777 is dissolved in 0.5% of carboxyl methyl cellulose sodium (CMC-Na) to prepare a suspension[^4].

BIOLOGICAL ACTIVITY

**Description**  
INT-777 is a potent TGR5 agonist with an EC_{50} 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, and improves insulin sensitivity, in TGR5-Tg mice[2].

### PROTOCOL

#### Cell Assay [2]

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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Animal Administration [2]

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. 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.

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### REFERENCES


