INT-777 is a potent TGR5 agonist with EC50 of 0.82 μM.

**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** (Extracted from published papers and Only for reference)

**Cell Assay:** INT-777 is dissolved in DMSO[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.

**Animal Administration:** INT-777 is mixed with diet[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.

**References:**


Caution: Product has not been fully validated for medical applications. For research use only.

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