HWL-088

Cat. No.: HY-130120

CAS No.: 2378617-96-8

Molecular Formula: $C_{22}H_{19}FO_4$

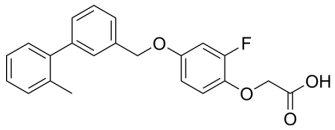
Molecular Weight: 366.38

Target: Free Fatty Acid Receptor; PPAR

Pathway: GPCR/G Protein; Cell Cycle/DNA Damage; Vitamin D Related/Nuclear Receptor

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 : 250 mg/mL (682.35 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7294 mL	13.6470 mL	27.2941 mL
	5 mM	0.5459 mL	2.7294 mL	5.4588 mL
	10 mM	0.2729 mL	1.3647 mL	2.7294 mL

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: 2.08 mg/mL (5.68 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.68 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

HWL-088 is a highly potent and orally active free fatty acid receptor 1 (FFA1/GPR40) agonist (EC_{50} of 18.9 nM) with moderate PPARδ activity (EC_{50} of 570.9 nM) . HWL-088 improves glucose and lipid metabolism, and has anti-diabetic effects[1][2].

IC_{50} & Target

FFAR1/GPR40	PPARδ
18.9 nM (EC50)	570.9 nM (EC50)

In Vitro

HWL-088 (0.3 μM and 3μM) significantly increases insulin secretion fromMIN6 cells at 25 mM but not at 2 mM glucose. HWL-

088 reveals a dose-dependent insulinotropic effect in the presence of 25-mM glucose[2].

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

In Vivo

HWL-088 (40 mg/kg; oral gavage; daily; for 30 days; ob/ob mice) treatment improves β-cell function by up-regulation of pancreas duodenum homeobox-1, reduces fat accumulation in adipose tissue and alleviated fatty liver in ob/ob mice. The effect of HWL-088 involves a reduction in hepatic lipogenesis and oxidative stress, increased lipoprotein lipolysis, glucose uptake, mitochondrial function and fatty acid β-oxidation[2].

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

Animal Model:	Male ob/ob mice[2]
Dosage:	40 mg/kg
Administration:	Oral gavage; daily; for 30 days
Result:	Improved β-cell function by up-regulation of pancreas duodenum homeobox-1, reduced fat accumulation in adipose tissue and alleviated fatty liver in ob/ob mice.

REFERENCES

[1]. Li Z, et al. Discovery of HWL-088: A highly potent FFA1/GPR40 agonist bearing a phenoxyacetic acid scaffold. Bioorg Chem. 2019 Nov;92:103209.

[2]. Yueming Chen, et al. HWL-088, a new potent free fatty acid receptor 1 (FFAR1) agonist, improves glucolipid metabolism and acts additively with metformin in ob/ob diabetic mice. Br J Pharmacol. 2020 May;177(10):2286-2302.

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