Cotadutide acetate

Cat. No.: HY-P2231A

Molecular Formula: $C_{169}H_{256}N_{42}O_{57}$

Molecular Weight: 3788.14

Sequence: 1'-{palmtoyl-Glu}; His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Lys-Ser-Glu-Tyr-Leu-Asp-Ser-Glu-Arg-Ala-Arg-Asp-Phe-Val-Ala-Trp-Leu-Glu-Ala-Gly-Gly (Amide bridge: Glu1'-Lys10)

1'-{palmtoyl-Glu}; HSQGTFTSDKSEYLDSERARDFVAWLEAGG (Amide bridge: Glu1'-Lys10) (acetate salt)

Sequence Shortening: 1'-{palmtoyl-Glu}; HSQGTFTSDKSEYLDSERARDFVAWLEAGG (Amide bridge: Glu1'-Lys10)

Target: GCGR

Pathway: GPCR/G Protein

Storage: Sealed storage, away from moisture

Powder -80°C 2 years

-20°C 1 year

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)

SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (3.30 mM; Need ultrasonic)

H_2O : 2 mg/mL (0.53 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	0.2640 mL	1.3199 mL	2.6398 mL
5 mM	---	---	---
10 mM	---	---	---

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: 1.25 mg/mL (0.33 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1.25 mg/mL (0.33 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (0.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cotadutide (MEDI0382) acetate is a potent dual agonist of glucagon-like peptide-1 (GLP-1) and GCGR with EC_{50} values of 6.9 pM and 10.2 pM, respectively. Cotadutide acetate exhibits ability to facilitate both weight loss and glycaemic control, and alleviate fibrosis. Cotadutide acetate can be used in the research of obesity and type 2 diabetes (T2D)[1][2][3].

IC_{50} & Target	EC50: 6.9 pM (GLP-1); 10.2 pM (GCGR)[1]
In Vitro	Cotadutide acetate stimulates a concentration-dependent increase in cAMP accumulation in rat (INS-1 832/3) and human (EndoC-βH1) β-cell lines (EC_{50}: 226 pM and 1051 pM, respectively), as well as rat, mouse and human hepatocytes (EC_{50}: 462 pM, 840 pM, 1447 pM, respectively)[1]. Cotadutide (100 pM-1 μM) acetate potentiates glucose-stimulated insulin secretion in the rat (INS-1 832/3) pancreatic β□cell line and increases glucose output in rat hepatocytes[1]. Cotadutide (100 nM, 2 h) acetate induces mitochondrial turnover and enhances mitochondrial function in mouse primary hepatocytes[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Cotadutide (10 nmol/kg, s.c., once) acetate suppresses food intake in DIO mice relative to vehicle□treated controls[1]. Cotadutide (10 or 30 nmol/kg, s.c., once daily for 14-16 weeks) acetate reduces body weight in DIO mice[1]. Cotadutide (30 nmol/kg, s.c., once a day for 6 weeks) acetate reduces hepatic fibrosis and inflammation in in ob/ob AMLN NASH mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	DIO mice[1]
Dosage:	10 nmol/kg
Administration:	Subcutaneous injection (s.c.)
Result:	Showed a redction of food intake in mice after an acute administration.

Animal Model:	Diet-induced obesity (DIO) mice[1]
Dosage:	10 or 30 nmol/kg
Administration:	Subcutaneous injection
Result:	Reduced body weight and food intake, and improved glucose tolerance in DIO mice.

REFERENCES

[1]. Resolution of NASH and hepatic fibrosis by the GLP-1R/GcgR dual-agonist Cotadutide via modulating mitochondrial function and lipogenesis. Nat Metab. 2020 May;2(5):413-431.

[2]. Henderson SJ,et al. Robust anti-obesity and metabolic effects of a dual GLP-1/glucagon receptor peptide agonist in rodents and non-human primates.Diabetes Obes Metab. 2016 Dec;18(12):1176-1190.

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