Product Data Sheet

Product Name: (D-Ala2)-GIP (human)
Cat. No.: GA20063

Chemical Properties

Cas. No.	444073-04-5		
Formula	$C_{226}H_{338}N_{60}O_{66}S$	M.Wt	4983.53
Solubility	DMSO : 50 mg/mL (10.03 mM; Need ultrasonic)	Storage	Store at -20°C

General tips: For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.

Shipping Condition: Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure

Tyr-{d-Ala}-Glu-Gly-Thr-Phe-Ile-Ser-Asp-
Tyr-Ser-Ile-Ala-Met-Asp-Lys-Ile-His-Gln-
Gln-Asp-Phe-Val-Asn-Trp-Leu-Leu-Ala-
Gln-Lys-Gly-Lys-Lys-Asn-Asp-Trp-Lys-
His-Asn-Ile-Thr-Gln

Protocol

Cell experiment [1]:

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Cell lines	3T3-L1 pre-adipocytes (mouse embryonic fibroblast cell line)
Preparation Method	3T3-L1 pre-adipocytes were maintained in Dulbecco's minimal essential medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and antibiotics (100U/mL penicillin and 100μg/mL streptomycin) at 37°C, 5% CO_2. Differentiation was induced post-confluence using a cocktail (1μg/mL insulin, 1μM dexamethasone, 0.5mM isobutyl-1-methylxanthine) with or without 1μM (D-Ala2)-GIP. The differentiation medium was replenished every two days.
Reaction Conditions	1μM; 12-day differentiation period
Applications	(D-Ala2)-GIP significantly enhanced adipocyte differentiation and lipid accumulation, as evidenced by increased Oil-red O staining. (D-Ala2)-GIP upregulated key adipogenic genes (Lpl, Fasn, Atgl) and lipolytic genes (Hsl), and stimulated glycerol release in mature adipocytes.

Animal experiment [2]:

Animal models	High-fat-fed (HFF) Swiss NIH mice (diet-induced obesity model)
Preparation Method	Obese-prediabetic mice received daily intraperitoneal injections of (D-Ala2)-GIP (25nmol/kg) for 42 consecutive days. Body weight and non-fasting blood glucose were monitored regularly. An intraperitoneal glucose tolerance test (18mmol/kg) was performed on day 43 after an 18-hour fast.
Dosage form	25nmol/kg; i.p.

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Applications	(D-Ala2)-GIP significantly reduced non-fasting blood glucose levels and improved glucose tolerance during the glucose challenge. (D-Ala2)-GIP enhanced bone strength by increasing ultimate load and work-to-fracture without altering trabecular or cortical bone microarchitecture. (D-Ala2)-GIP improved bone composition by increasing collagen maturity (enzymatic cross-linking) and mineral-to-matrix ratio while reducing heterogeneity in mineral crystallite size.

References:

[1] English A, Craig SL, Flatt PR, et al. Individual and combined effects of GIP and xenin on differentiation, glucose uptake and lipolysis in 3T3-L1 adipocytes. Biol Chem. 2020 Oct 25;401(11):1293-1303.
[2] Vyavahare SS, Mieczkowska A, Flatt PR, et al. GIP analogues augment bone strength by modulating bone composition in diet-induced obesity in mice. Peptides. 2020 Mar;125:170207.

Background

(D-Ala2)-GIP (human) is an analog of glucose-dependent insulinotropic polypeptide that activates the GIP receptor (EC_{50}=630pM) and is commonly used in research on type 2 diabetes treatment [1]. (D-Ala2)-GIP is resistant to degradation by dipeptidyl peptidase-4, thereby prolonging (D-Ala2)-GIP in vivo half-life and enhancing its insulin-secreting activity[2]. (D-Ala2)-GIP can modulate cellular energy metabolism, fat storage, and β-cell function[3]. (D-Ala2)-GIP also has the potential to ameliorate obesity-related insulin resistance and protect β-cells[4].

In vitro, pretreatment of mouse primary cardiomyocytes with (D-Ala2)-GIP (300nM) for 1 hour, followed by stimulation with 30mM high glucose for 24 hours, significantly suppressed NADPH oxidase-driven superoxide generation and reduced mRNA expression levels of the cardiac hypertrophy marker β-Mhc and the key fibrotic factor Tgf-β2[5]. Pretreatment of 3T3-L1 preadipocytes with (D-Ala2)-GIP (1μM) for 96 hours significantly promoted adipocyte differentiation and lipid accumulation, while upregulating gene expression of lipoprotein lipase (Lpl) and fatty acid synthase (Fasn)[6].

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In vivo, daily intraperitoneal injection of (D-Ala2)-GIP (25nmol/kg) for 42 days in high-fat diet-induced obese, prediabetic Swiss NIH mice significantly reduced non-fasting blood glucose levels and improved glucose tolerance[7]. Daily intraperitoneal injection of (D-Ala2)-GIP (25nmol/kg) for 8 weeks in APPswe/PS1 Alzheimer's disease model mice significantly improved spatial memory and synaptic plasticity, increased synaptic density in the hippocampus, reduced amyloid plaque load and neuroinflammation, and enhanced neural progenitor cell proliferation in the dentate gyrus[8].

References:

[1] Hinke SA, Gelling RW, Pederson RA, et al. Dipeptidyl peptidase IV-resistant [D-Ala(2)]glucose-dependent insulinotropic polypeptide (GIP) improves glucose tolerance in normal and obese diabetic rats. Diabetes. 2002 Mar;51(3):652-61.
[2] Gault VA, Porter DW, Irwin N, Patel S, et al. Comparison of sub-chronic metabolic effects of stable forms of naturally occurring GIP(1-30) and GIP(1-42) in high-fat fed mice. J Endocrinol. 2011 Mar;208(3):265-71.
[3] Mansur SA, Mieczkowska A, Bouvard B, et al. Stable Incretin Mimetics Counter Rapid Deterioration of Bone Quality in Type 1 Diabetes Mellitus. J Cell Physiol. 2015 Dec;230(12):3009-18.
[4] Porter DW, Irwin N, Flatt PR, et al. Prolonged GIP receptor activation improves cognitive function, hippocampal synaptic plasticity and glucose homeostasis in high-fat fed mice. Eur J Pharmacol. 2011 Jan 15;650(2-3):688-93.
[5] Hiromura M, Mori Y, Terasaki M, et al. Glucose-dependent insulinotropic polypeptide inhibits cardiac hypertrophy and fibrosis in diabetic mice via suppression of TGF-β2. Diab Vasc Dis Res. 2021 Mar-Apr;18(2):1479164121999034.
[6] English A, Craig SL, Flatt PR, et al. Individual and combined effects of GIP and xenin on differentiation, glucose uptake and lipolysis in 3T3-L1 adipocytes. Biol Chem. 2020 Oct 25;401(11):1293-1303.
[7] Vyavahare SS, Mieczkowska A, Flatt PR, et al. GIP analogues augment bone strength by modulating bone composition in diet-induced obesity in mice. Peptides. 2020 Mar;125:170207.
[8] Hölscher C. The incretin hormones glucagonlike peptide 1 and glucose-dependent insulinotropic polypeptide are neuroprotective in mouse models of Alzheimer's disease. Alzheimers Dement. 2014 Feb;10(1 Suppl):S47-54.

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