Product Data Sheet

Product Name: Taspoglutide (ITM077)
Cat. No.: GC31360

Chemical Properties

Cas. No.	275371-94-3		
SMILES	[H-{Aib}-EGTFTSDVSSYLEGQAAKEFIAWLVK-{Aib}-R-NH2]		
Formula	$C_{152}H_{232}N_{40}O_{45}$	M.Wt	3339.71
Solubility	DMSO : ≥ 28 mg/mL (8.38 mM)	Storage	Store at -20°C,Sealed storage, away from moisture and light
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	Taspoglutide (ITM077)		

Protocol

Cell experiment [1]:

Cell lines	MIN6B1 cells
Preparation Method	MIN6B1 cells were cultured for 24h in MIN6 medium (DMEM-based) pH 7.0. The medium was then replaced by serum-free and low glucose (5mmol/l) MIN6 medium pH 7.0 containing 0, 0.1, 1, 10 or 100nM Taspoglutide.
Reaction Conditions	0, 0.1, 1, 10 or 100nM; 48h.0, 0.1, 1, 10 or 100nM; 48h.
Applications	Taspoglutide stimulated the proliferation of dispersed islet cell.

Animal experiment [2]:

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Animal models	Four-week-old male ApoE^{-}/$^{-}$ mice
Preparation Method	Four-week-old male ApoE^{-}/$^{-}$ mice were started on a high-fat (45% kcal) diet. Modest hyperglycemia was induced using STZ (an initial dose of 75mg/kg followed by a second dose of 125mg/kg 10d later), and mice with glucose levels from 15-25mM were then randomized to different groups and treated for 12 weeks with a once-monthly s.c. 0.4mg Taspoglutide microtablet suspension, a s.c. placebo microtablet, or metformin (400mg/kg·d) continuously provided in the drinking water plus a s.c placebo microtablet.
Dosage form	0.4mg; s.c.; once-monthly for 12 weeks.
Applications	Taspoglutide significantly decreased food intake and body weight.

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References:
[1]. Uhles, S., et al. "Taspoglutide, a novel human once-weekly GLP-1 analogue, protects pancreatic β-cells in vitro and preserves islet structure and function in the Zucker diabetic fatty rat in vivo." Diabetes, Obesity and Metabolism 13.4 (2011): 326-336.
[2]. Panjwani, Naim, et al. "GLP-1 receptor activation indirectly reduces hepatic lipid accumulation but does not attenuate development of atherosclerosis in diabetic male ApoE¯/¯ mice." Endocrinology 154.1 (2013): 127-139.

Background

Taspoglutide (ITM077) is a novel analog of human glucagon-like peptide-1 [hGLP-1(7-36)NH_2] in clinical development for the treatment of type 2 diabetes. Taspoglutide inhibits VEGFR2 in CHO cells with an IC_{50} value of 4.6±0.6nM[1,2]. Taspoglutide is a structural derivative of hGLP-1 with α-aminoisobutyric acid (Aib) substitutions replacing Ala^8 and Gly^{35}[1].

In vitro, Taspoglutide (0.001-100nM) stimulates insulin secretion in a glucose-dependent manner, enhancing secretion at high glucose (16.7mM) even at very low concentrations (0.001nM) in INS-1E rat insulinoma cells[1].

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In vivo, Taspoglutide (0.4mg; s.c.; once-monthly for 12 weeks) significantly decreased food intake and body weight in hyperglycemic ApoE^{-}/$^{-}$ mice[3]. Taspoglutide (0.4mg; s.c.; once-monthly for 12 weeks) treatment significantly increased levels of mRNA transcripts for the transcription factor liver X receptor (*Lxr*) as well as multiple LXR target genes, *Abca1*, *Abcg5*, *Abcg1*, *and Abcg8*, involved in cholesterol shuttling and clearance. Taspoglutide (0.4mg; s.c.; once-monthly for 12wk) also increased mRNA levels for hepatic lipase (*Hl*), a key enzyme in the regulation of triglyceride storage and clearance, as well as *Cpt1a*, a ratelimiting mitochondrial fatty acid carrier regulating the rate of free fatty acid β-oxidation in hyperglycemic ApoE^{-}/$^{-}$ mice[3]. Taspoglutide Treatment (1mg; s.c.; once) significantly reduced proliferating pancreatic β-cells per islet cross-section in ZDF rats[4].

References:
[1]. Sebokova, Elena, et al. "Taspoglutide, an analog of human glucagon-like peptide-1 with enhanced stability and in vivo potency." Endocrinology 151.6 (2010): 2474-2482.
[2]. Rosenstock, Julio, et al. "The fate of taspoglutide, a weekly GLP-1 receptor agonist, versus twice-daily exenatide for type 2 diabetes: the T-emerge 2 trial." Diabetes care 36.3 (2013): 498-504.
[3]. Panjwani, Naim, et al. "GLP-1 receptor activation indirectly reduces hepatic lipid accumulation but does not attenuate development of atherosclerosis in diabetic male ApoE^{-}/$^{-}$ mice." Endocrinology 154.1 (2013): 127-139.
[4]. Uhles, S., et al. "Taspoglutide, a novel human once-weekly GLP-1 analogue, protects pancreatic β-cells in vitro and preserves islet structure and function in the Zucker diabetic fatty rat in vivo." Diabetes, Obesity and Metabolism 13.4 (2011): 326-336.

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