Fasiglifam

Cat. No.: HY-10480

CAS No.: 1000413-72-8

Molecular Formula: $C_{29}H_{32}O_7S$

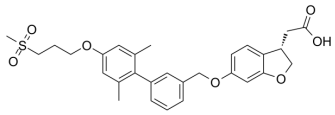
Molecular Weight: 524.63

Target: Free Fatty Acid Receptor

Pathway: GPCR/G Protein

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 128 mg/mL (243.98 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9061 mL	9.5305 mL	19.0611 mL
5 mM	0.3812 mL	1.9061 mL	3.8122 mL
10 mM	0.1906 mL	0.9531 mL	1.9061 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: ≥ 2.5 mg/mL (4.77 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.77 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.77 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Fasiglifam (TAK-875) is a potent, selective and orally bioavailable GPR40 agonist with EC_{50} of 72 nM.

IC_{50} & Target

EC50: 72 nM (GPR40)

In Vitro	Fasiglifam (TAK-875) (0.01-10 μM) produces a concentration-dependent increase in intracellular IP production in CHO-hGPR40, with EC_{50} of 0.072 μM. Fasiglifam (TAK-875) (0.1-10 μM) dose-dependently augments intracellular IP production in CHO cells[1]. Fasiglifam (TAK-875) (3-30 μM) concentration-dependently augments $[Ca^{2+}]_i$. In the presence of 10 mM glucose, TAK-875 (0.001-10 μM) dose-dependently stimulats insulin secretion from INS-1 833/15 cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Fasiglifam (TAK-875) (10 mg/kg, p.o.) increases plasma insulin levels in ZDF rats. Fasiglifam (TAK-875) (30 mg/kg, p.o.) improves fasting hyperglycemia without affecting fasting normoglycemia. Fasiglifam (TAK-875) at 30 mg/kg, which is a 3- to 10-fold higher dose compared with the dose that improved glucose tolerance in diabetic rats, does not alter fasting glucose levels in SD rats with normal glucose homeostasis. Likewise, Fasiglifam (TAK-875) does not significantly alter insulin secretion in SD rats with normal fasting glucose levels [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	INS-1 832/13 cells are suspended in RPMI medium and seeded in a 96-well plate at a density of 2×10^4 cells/well; 1% BSA and 0.1% DMSO alone (control), palmitic acid (10, 100, and 1000 μM), oleic acid (10, 100, and 1000 μM), or Fasiglifam (TAK-875: 1, 10, and 100 μM) is added to the plate. After 72-h culture, medium is discarded, and cells are preincubated for 2 h with KRBH containing 1 mM glucose and 0.2% BSA at 37°C. After discarding of the preincubation buffer, KRBH containing 1 or 20 mM glucose and 0.2% BSA is added, and the plate is further incubated for 2 h. The insulin concentration in the supernatant is measured as described above. To measure intracellular insulin content, INS-1 832/13 cells are exposed to 1% BSA and 0.1% DMSO alone (control), palmitic acid (1000 μM), oleic acid (1000 μM), or Fasiglifam (TAK-875) (100 μM) with 1% BSA and 0.1% DMSO. After incubation, cells are washed once with phosphate-buffered saline, and acid-ethanol solution is added to each well, followed by sonication on ice. Intracellular insulin is extracted by overnight incubation at −30°C, followed by separation of supernatant by centrifugation at 12,000 rpm×5 min at 4°C. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	At 18 weeks of age, the N-STZ-1.5 rats are fasted overnight and orally given vehicle (0.5% methylcellulose) or Fasiglifam (TAK-8751, 3, and 10 mg/kg). Sixty minutes later, all animals receive an oral glucose load (1 g/kg). Blood samples are collected from the tail vein before drug administration, before glucose load (time 0), and 10, 30, 60, and 120 min after the glucose load. Plasma glucose and insulin levels are measured with an AutoAnalyzer 7080 and radioimmunoassay, respectively. To see the effects of Fasiglifam (TAK-875) on fasting normoglycemia and hyperglycemia, SD rats (8 weeks old) or ZDF and ZL rats (12 weeks old) are fasted overnight and orally given vehicle (0.5% methylcellulose), Fasiglifam (TAK-875) (10 or 30 mg/kg), nateglinide (50 mg/kg), or glibenclamide (10 mg/kg). Blood samples are collected from the tail vein before drug administration (time 0) and 0.5, 1, 2, and 3 h (SD rats) and 0.5, 1, 2, 4, and 6 h (ZDF and ZL rats) after drug administration, and plasma glucose and insulin levels are measured as described above. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Allergy Clin Immunol. 2018 Aug;142(2):470-484.e12.
- Proc Natl Acad Sci U S A. 2023 May 30;120(22):e2219569120.
- Biomed Pharmacother. 2023 May.
- Eur J Med Chem. 5 February 2022, 114061.
- Biochem Pharmacol. 2023 Dec 2:115957.

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REFERENCES

[1]. Tsujihata Y,et al. TAK-875, an orally available G protein-coupled receptor 40/free fatty acid receptor 1 agonist, enhances glucose-dependent insulin secretion and improves both postprandial and fasting hyperglycemia in type 2 diabetic rats.J Pharmacol Exp

[2]. Yoshiyuki Tsujihata, et al. TAK-875, an Orally Available GPR40/FFA1 Agonist Enhances Glucose-Dependent Insulin Secretion and Improves Both Postprandial and Fasting Hyperglycemia in Type 2 Diabetic Rats. JPET July 13, 2011

[3]. Nagatake T, et al. 17,18-EpETE-GPR40 axis ameliorates contact hypersensitivity by inhibiting neutrophil mobility in mice and cynomolgus macaques. J Allergy Clin Immunol. 2017 Dec 26. pii: S0091-6749(17)32949-4.

[4]. Urano Y, et al. Comparative hepatic transcriptome analyses revealed possible pathogenic mechanisms of fasiglifam (TAK-875)-induced acute liver injury in mice. Chem Biol Interact. 2018 Sep 20;296:185-197.

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