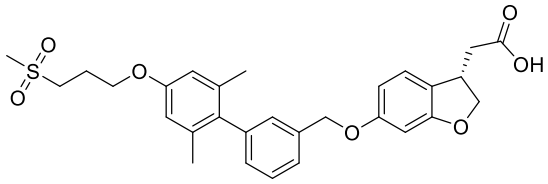
Product data sheet

MedKoo Cat#: 504110 Name: Fasiglifam CAS#: 1000413-72-8 Chemical Formula: $C_{29}H_{32}O_7S$ Exact Mass: 524.18687 Molecular Weight: 524.63	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Fasiglifam, also known as TAK-875, is a potent, selective, and orally bioavailable GPR40 agonist, with a pharmacokinetic profile enabling long-acting drug efficacy. TAK-875 showed potent plasma glucose-lowering action and insulinotropic action during an oral glucose tolerance test in female Wistar fatty rats with impaired glucose tolerance. TAK-875 is currently in clinical trials for the treatment of type 2 diabetes mellitus.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	128	243.98

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.91 mL	9.53 mL	19.06 mL
5 mM	0.38 mL	1.91 mL	3.81 mL
10 mM	0.19 mL	0.95 mL	1.91 mL
50 mM	0.04 mL	0.19 mL	0.38 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Tsujihata Y, Ito R, Suzuki M, Harada A, Negoro N, Yasuma T, Momose Y, Takeuchi K. 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 Ther. 2011 Oct;339(1):228-37. doi: 10.1124/jpet.111.183772. Epub 2011 Jul 13. PMID: 21752941.

2. Negoro N, Sasaki S, Mikami S, Ito M, Suzuki M, Tsujihata Y, Ito R, Harada A, Takeuchi K, Suzuki N, Miyazaki J, Santou T, Odani T, Kanzaki N, Funami M, Tanaka T, Kogame A, Matsunaga S, Yasuma T, Momose Y. Discovery of TAK-875: A Potent, Selective, and Orally Bioavailable GPR40 Agonist. ACS Med Chem Lett. 2010 Jun 18;1(6):290-4. doi: 10.1021/ml1000855. PMID: 24900210; PMCID: PMC4007909.

In vivo study

1. Tsujihata Y, Ito R, Suzuki M, Harada A, Negoro N, Yasuma T, Momose Y, Takeuchi K. 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 Ther. 2011 Oct;339(1):228-37. doi: 10.1124/jpet.111.183772. Epub 2011 Jul 13. PMID: 21752941.

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2. Negoro N, Sasaki S, Mikami S, Ito M, Suzuki M, Tsujihata Y, Ito R, Harada A, Takeuchi K, Suzuki N, Miyazaki J, Santou T, Odani T, Kanzaki N, Funami M, Tanaka T, Kogame A, Matsunaga S, Yasuma T, Momose Y. Discovery of TAK-875: A Potent, Selective, and Orally Bioavailable GPR40 Agonist. ACS Med Chem Lett. 2010 Jun 18;1(6):290-4. doi: 10.1021/ml1000855. PMID: 24900210; PMCID: PMC4007909.

7. Bioactivity

Biological target:

Fasiglifam (TAK-875) is a selective GPR40 agonist with EC50 of 14 nM in human GPR40 expressing CHO cell line, 400-fold more potent than oleic acid.

In vitro activity

Insulinoma cell lines and primary rat islets were used to assess the effects of TAK-875 in vitro. In rat insulinoma INS-1 833/15 cells, TAK-875 increased intracellular inositol monophosphate and calcium concentration, consistent with activation of the Gqα signaling pathway. The insulinotropic action of TAK-875 (10 μM) in INS-1 833/15 and primary rat islets was glucose-dependent. Prolonged exposure of cytokine-sensitive INS-1 832/13 to TAK-875 for 72 h at pharmacologically active concentrations did not alter glucose-stimulated insulin secretion, insulin content, or caspase 3/7 activity, whereas prolonged exposure to palmitic or oleic acid impaired β cell function and survival.

Reference: J Pharmacol Exp Ther. 2011 Oct;339(1):228-37.
https://jpet.aspetjournals.org/cgi/pmidlookup?view=long&pmid=21752941

In vivo activity

The in vivo effects of TAK-875 on postprandial hyperglycemia, fasting hyperglycemia, and normoglycemia were examined in type 2 diabetic and normal rats. In an oral glucose tolerance test in type 2 diabetic N-STZ-1.5 rats, TAK-875 (1-10 mg/kg p.o.) showed a clear improvement in glucose tolerance and augmented insulin secretion. In addition, TAK-875 (10 mg/kg, p.o.) significantly augmented plasma insulin levels and reduced fasting hyperglycemia in male Zucker diabetic fatty rats, whereas in fasted normal Sprague-Dawley rats, TAK-875 neither enhanced insulin secretion nor caused hypoglycemia even at 30 mg/kg. TAK-875 enhances glucose-dependent insulin secretion and improves both postprandial and fasting hyperglycemia with a low risk of hypoglycemia and no evidence of β cell toxicity.

Reference: J Pharmacol Exp Ther. 2011 Oct;339(1):228-37.
https://jpet.aspetjournals.org/cgi/pmidlookup?view=long&pmid=21752941