Sitagliptin

Cat. No.: HY-13749

CAS No.: 486460-32-6

Molecular Formula: $C_{16}H_{15}F_6N_5O$

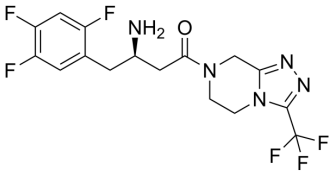
Molecular Weight: 407.31

Target: Dipeptidyl Peptidase; Autophagy

Pathway: Metabolic Enzyme/Protease; Autophagy

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 : ≥ 100 mg/mL (245.51 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4551 mL	12.2757 mL	24.5513 mL
	5 mM	0.4910 mL	2.4551 mL	4.9103 mL
	10 mM	0.2455 mL	1.2276 mL	2.4551 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 (6.14 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.14 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (6.14 mM); Clear solution; Need heat to 60°C
4. Add each solvent one by one: 2% DMSO >> 40% PEG300 >> 5% Tween-80 >> 53% saline
   Solubility: ≥ 2 mg/mL (4.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sitagliptin (MK-0431) is a potent and orally active inhibitor of DPP4 with an IC_{50} of 19 nM in Caco-2 cell extracts[1].

IC_{50} & Target

DPP-4

In Vitro	Sitagliptin phosphate exhibits a potent inhibitory effect on DPP-4 with IC_{50} of 19 nM from Caco-2 cell extracts[1]. Sitagliptin reduces in vitro migration of isolated splenic CD4 T-cells through a pathway involving cAMP/PKA/Rac1 activation[2] . Stagliptin exerts a novel, direct action in order to stimulate GLP-1 secretion by the intestinal L cell through a DPP-4-independent, protein kinase A- and MEK-ERK1/2-dependent pathway. It reduces the effect of autoimmunity on graft survival [3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In vivo, the ED_{50} value of sitagliptin phosphate for inhibition of plasma DPP-4 activity is calculated to be 2.3 mg/kg 7 hour postdose and 30 mg/kg 24 hour postdose in freely fed Han-Wistar rats[1]. The streptozotocin-induced type 1 diabetes mouse model exhibits elevated DPP-4 levels in the plasma that can be substantially inhibited in mice on an Sitagliptin phosphate diet. This is achieved by a positive effect on the regulation of hyperglycemia, potentially through prolongation of islet graft survival[4]. The plasma clearance and volume of distribution of Sitagliptin phosphate are higher in rats (40-48 mL/min/kg, 7-9 L/kg) than in dogs (9 mL/min/kg, 3 L/kg); and its half-life is shorter in rats,2 hours compared with 4 hours in dogs[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	CD4T-cells are plated on membrane inserts in serum-free RPMI 1640, and cell migration is assayed using Transwell chambers (Corning), in the presence or absence of purified porcine kidney DPP-4 (32.1 units/mg; 100 mU/mL final concentration) and DPP-4 inhibitor (100 μM). After 1 hour, cells on the upper surface are removed mechanically, and cells that have migrated into the lower compartment are counted. The extent of migration is expressed relative to the control sample. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Overnight fasted C57BL/6J mice are challenged 45 min after compound administration with an oral glucose load (2 g/kg). Blood samples for glucose measurement are obtained by tail bleed predose and at serial time points after the glucose load. To evaluate the duration of the effect on glucose tolerance, vehicle or DPP-4 inhibitors are administered 16 h before the glucose challenge. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2021 Oct 11;12(10):928.
- Biomed Pharmacother. 2023 Mar 24;162:114555.
- Biochem Pharmacol. 2023 Oct 5:115846.
- iScience. 2023 Feb.
- J Biol Chem. 2018 Dec 7;293(49):18864-18878.

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REFERENCES

[1]. Thomas, L., et al. (R)-8-(3-amino-piperidin-1-yl)-7-but-2-ynyl-3-methyl-1-(4-methyl-quinazolin-2-ylmethyl)-3,7-dihydro-purine-2,6-dione (BI 1356), a novel xanthine-based dipeptidyl peptidase 4 inhibitor, has a superior potency and longer duration of action compared with other dipeptidyl peptidase-4 inhibitors. J Pharmacol Exp Ther. 2008 Apr;325(1):175-82.

[2]. Kim, S.J., et al., Dipeptidyl peptidase IV inhibition with MK0431 improves islet graft survival in diabetic NOD mice partially via T-cell modulation. Diabetes, 2009. 58(3): p. 641-51.

[3]. Sangle, G.V., et al., Novel biological action of the dipeptidylpeptidase-IV inhibitor, sitagliptin, as a GLP-1 secretagogue. Endocrinology, 2012. 153(2): p. 564-73.

[4]. Kim, S.J., et al., Inhibition of dipeptidyl peptidase IV with sitagliptin (MK0431) prolongs islet graft survival in streptozotocin-induced diabetic mice. Diabetes, 2008. 57(5): p. 1331-9.

[5]. Beconi, M.G., et al. Disposition of the dipeptidyl peptidase 4 inhibitor sitagliptin in rats and dogs. Drug Metab Dispos, 2007. 35(4): p. 525-32.

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