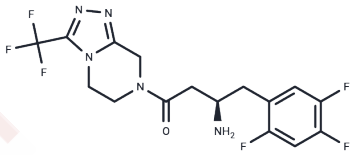
Data Sheet (Cat.No.T0242)

TargetMol

Sitagliptin

Chemical Properties



CAS No. : 486460-32-6

Formula: C16H15F6N5O

Molecular Weight: 407.31

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Sitagliptin (MK0431), a new oral hypoglycemic (anti-diabetic drug), is a new dipeptidyl peptidase-4 (DPP-4) inhibitor. This enzyme-inhibiting drug is used either alone or in combination with metformin or thiazolidinedione for treatment of type 2 diabetes mellitus. The drug can competitively inhibit a protein/enzyme and DPP-4, that leads to an incremental amount of active incretins (GLP-1 and GIP), the diminished amount of release of glucagon and increased release of insulin.
Targets(IC50)	Proteasome,DPP-4,Autophagy
In vitro	Sitagliptin phosphate demonstrates a potent inhibitory effect on dipeptidyl peptidase-4 (DPP-4), achieving an IC50 of 19 nM in Caco-2 cell extracts[1]. It also inhibits in vitro migration of isolated splenic CD4 T-cells through cAMP/PKA/Rac1 pathway activation[2]. Furthermore, sitagliptin directly enhances GLP-1 secretion from intestinal L cells via a pathway that is independent of DPP-4, but relies on protein kinase A and MEK-ERK1/2 activation. Additionally, it mitigates the impact of autoimmunity on graft survival[3].
In vivo	In vivo studies demonstrate that the ED50 (effective dose for 50% of the population) of sitagliptin phosphate, which inhibits DPP-4 activity in plasma, is estimated to be 2.3 mg/kg seven hours post-administration and 30 mg/kg twenty-four hours post-administration in freely fed Han-Wistar rats[1]. In the streptozotocin-induced type 1 diabetes mouse model, characterized by elevated plasma DPP-4 levels, sitagliptin phosphate supplementation notably reduces these levels, effectively regulating hyperglycemia and potentially enhancing islet graft longevity[4]. Moreover, pharmacokinetic profiles reveal that both plasma clearance and the volume of distribution for sitagliptin phosphate are significantly higher in rats (40-48 mL/min/kg, 7-9 L/kg) compared to dogs (9 mL/min/kg, 3 L/kg), with a half-life of 2 hours in rats versus 4 hours in dogs[5].
Kinase Assay	DPP-4 is extracted from confluent Caco-2 cells. After 5 minutes of incubation at room temperature with lysis buffer (10 mM Tris-HCl, 150 mM NaCl, 0.04 U/mL aprotinin, 0.5% Nonidet P40, pH 8.0), cells are centrifuged at 35,000 g at 4°C for 30 minutes, and the supernatant is stored at -80°C. Assays are performed by mixing 20 µL of appropriate compound dilutions with 50 µL of the substrate for the DPP-4 enzyme, H-Ala-Pro-7-amido-4-trifluoromethylcoumarin (final concentration in the assay, 100 µM) and 30 µL of the Caco-2 cell extract (diluted 1000-fold with 100 mM Tris-HCl, 100 mM NaCl, pH 7.8). Plates are incubated at room temperature for 1 hour, and fluorescence is measured at excitation/emission wavelengths of 405/535 nm using a SpectraMax GeminiXS.

Kinase Assay	Dissociation kinetics of inhibitors from the DPP-4 enzyme is determined after a 1-hour preincubation of Caco-2 cell extracts with high inhibitor concentrations (30 nM for BI 1356, 3 μM for vildagliptin). The enzymatic reaction is started by adding the substrate H-Ala-Pro-7-amido-4-trifluoromethylcoumarin after a 3000-fold dilution of the preincubation mixture with assay buffer. Under these conditions, the difference in DPP-4 activity at a certain time point in the presence or absence of an inhibitor reflects the amount of this inhibitor still bound to the DPP-4 enzyme. Maximal reaction rates (fluorescence units/seconds ×1000) at 10-minute intervals are calculated using the SoftMax software of the SpectraMax and corrected for the rate of an uninhibited reaction [(vcontrol-vinhibitor)/vcontrol].
Cell Research	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.

Solubility Information

Solubility	DMSO: 170 mg/mL (417.37 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble) (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.91 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4551 mL	12.2757 mL	24.5513 mL
5 mM	0.491 mL	2.4551 mL	4.9103 mL
10 mM	0.2455 mL	1.2276 mL	2.4551 mL
50 mM	0.0491 mL	0.2455 mL	0.491 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Thomas, L., et al. (R)-8-(3-amino-piperidin-1-yl)-7-but-2-ynyl-3-methyl-1-(4-methyl-quinazolin-2-ylm ethyl)-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 acti

Zhan Z T, Liu L, Cheng M Z, et al. The Effects of 6 Common Antidiabetic Drugs on Anti-PD1 Immune Checkpoint Inhibitor in Tumor Treatment. Journal of Immunology Research. 2022

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.

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

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.

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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