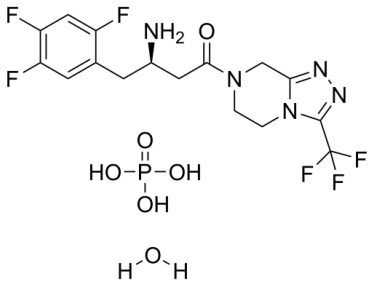
Data Sheet

Product Name:	Sitagliptin (phosphate monohydrate)
Cat. No.:	CS-3683
CAS No.:	654671-77-9
Molecular Formula:	$C_{16}H_{20}F_6N_5O_6P$
Molecular Weight:	523.32
Target:	Autophagy; Dipeptidyl Peptidase
Pathway:	Autophagy; Metabolic Enzyme/Protease
Solubility:	H2O : ≥ 33 mg/mL (63.06 mM)



BIOLOGICAL ACTIVITY:

Sitagliptin phosphate monohydrate (MK-0431 phosphate monohydrate) is a potent inhibitor of **DPP4** with an **IC_{50}** of 19 nM in Caco-2 cell extracts[1]. IC50 & Target: IC50: 19 nM (DPP4, in Caco-2 cell extracts) ***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]. A recent study demonstrates that sitagliptin 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 therefore reduces the effect of autoimmunity on graft survival[3]. ***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].

PROTOCOL (Extracted from published papers and Only for reference)

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. **Animal Administration:** Sitagliptin is formulated in 0.5% aqueous hyroxyethylcellulose.[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.

References:

[1]. 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

[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.

CAIndexNames:

1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate, hydrate (1:1:1)

SMILES:

[H]O[H].O=C(N1CC2=NN=C(C(F)(F)F)N2CC1)C[C@H](N)CC3=CC(F)=C(F)C=C3F.O=P(O)(O)O

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