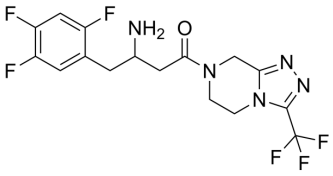
(Rac)-Sitagliptin

Cat. No.:	HY-13749D
CAS No.:	823817-56-7
Molecular Formula:	$C_{16}H_{15}F_6N_5O$
Molecular Weight:	407.31
Target:	Autophagy; Dipeptidyl Peptidase
Pathway:	Autophagy; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	(Rac)-Sitagliptin is an isoform of Sitagliptin (HY-13749), which is a potent and orally active inhibitor of DPP4 with an IC_{50} of 19 nM in Caco-2 cell extracts[1].
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.

REFERENCES

[1]. 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.

[2]. 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.

[3]. 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.

[4]. 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.

[5]. 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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA