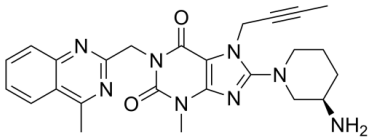
Data Sheet

Product Name:	Linagliptin
Cat. No.:	CS-0637
CAS No.:	668270-12-0
Molecular Formula:	$C_{25}H_{28}N_8O_2$
Molecular Weight:	472.54
Target:	Autophagy; Dipeptidyl Peptidase; Ferroptosis
Pathway:	Apoptosis; Autophagy; Metabolic Enzyme/Protease
Solubility:	DMSO : 25 mg/mL (ultrasonic;warming;heat to 80°C)



BIOLOGICAL ACTIVITY:

Linagliptin is a highly potent, selective **DPP-4** inhibitor with **IC_{50}** of 1 nM. IC50 & Target: IC50: 1 nM (DPP-4) ***In Vitro:*** Linagliptin inhibits DPP-4 activity in vitro in several independent experiments with IC_{50} values of 0.4, 0.5, 0.9, and 1.1 nM (mean IC_{50}, approximately 1 nM). Linagliptin inhibits FAP with an IC_{50} of 89 nM (approximately 90-fold selectivity versus DPP-4)[2]. ***In Vivo:*** In male Wistar rats, Beagle dogs, and Rhesus monkeys, xanthine linagliptin proves to be a highly efficacious, long-lasting, and potent DPP-4 inhibitor providing >70% inhibition for >7 h for all three species after oral administration of 1 mg/kg. Single oral administration of linagliptin to db/db mice 45 min prior to an oral glucose tolerance test reduced plasma glucose excursion in a dose-dependent manner from 0.1 mg/kg (15% inhibition) to 1 mg/kg (66% inhibition)[1]. Linagliptin (3 and 10 mg/kg) dose-dependently inhibits the DPP-4 enzyme in plasma within 30 min of administration. Linagliptin (1 mg/kg, p.o.) significantly reduces glucose excursion by approximately 50%[2]. Oral administration of the DPP-4 inhibitor linagliptin (3 mg/kg, p.o.) strongly reduces DPP-4 activity, stabilizes active GLP-1 in chronic wounds, and improves healing in ob/ob mice. At day 10 postwounding, linagliptin-treated ob/ob mice show largely epithelialized wounds characterized by the absence of neutrophils[3].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [3]EDTA plasma (20 μL) is diluted with 30 μL of DPP-4 assay buffer (100 mM Tris and 100 mM NaCl, adjusted to pH 7.8 with HCl) and mixed with 50 μL of H-Ala-Pro-7-amido-4-trifluoromethylcoumarin. The 200 mM stock solution in dimethylformamide is diluted 1:1000 with water to yield a final concentration of 100 μM. The plate is incubated at room temperature for 10 min, and fluorescence in the wells is determined by using a Victor 1420 Multilabel Counter at an excitation wavelength of 405 nm and an emission wavelength of 535 nm. For the detection of DPP-4 activity in wound lysates, 100 μg of protein from the respective wound lysates are used instead of 20 μL of plasma. Active GLP-1 is also detected from 100 μg of respective wound tissue samples and analyzed by using the Mouse/Rat Total Active GLP-1 Assay Kit. **Cell Assay:** [3]A total of 4.0×10^7 keratinocytes per well are seeded into 24-well plates. After reaching 50% confluence, cells are starved for 24 h with DMEM. Proliferation of cells is assessed by using 1 μCi/mL of [^{3}H]methyl-thymidine in DMEM in the presence of 10% fetal bovine serum and increasing concentrations of linagliptin (3, 30, 300, or 600 nM) for 24 h. Cells are then washed twice with phosphate-buffered saline and incubated in 5% trichloroacetic acid at 4°C for 30 min, and the DNA is solubilized in 0.5mol/LNaOH for 30 min at 37°C. Finally, [^{3}H]thymidine incorporation is determined. **Animal Administration:** Linagliptin is formulated in 1% methylcellulose.[3]Each experimental group (vehicle or linagliptin treatment) consists of 10 individual ob/ob mice (n=10). Animals are treated orally once a day (8:00 AM) by gastrogavage using vehicle (1% methylcellulose) or linagliptin (3 mg/kg body weight in 1% methylcellulose) beginning 2 days (day−2) before wounding. After wounding, animals are subsequently treated once a day throughout the 10-day healing period.

References:

[1]. Eckhardt M, et al. 8-(3-(R)-aminopiperidin-1-yl)-7-but-2-ynyl-3-methyl-1-(4-methyl-quinazolin-2-ylmethyl)-3,7-dihydropurine-2,6-dione (BI 1356), a highly potent, selective, long-acting, and orally bioavailable DPP-4 inhibitor for the treatment of type 2 d

[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

[3]. Schurmann C, et al. The dipeptidyl peptidase-4 inhibitor linagliptin attenuates inflammation and accelerates epithelialization in wounds of diabetic ob/ob mice. J Pharmacol Exp Ther. 2012 Jul;342(1):71-80.

[4]. Huan Y, et al. The dual DPP4 inhibitor and GPR119 agonist HBK001 regulates glycemic control and beta cell function ex and in vivo. Sci Rep. 2017 Jun 28;7(1):4351.

CAIndexNames:

1H-Purine-2,6-dione, 8-[(3R)-3-amino-1-piperidinyl]-7-(2-butyn-1-yl)-3,7-dihydro-3-methyl-1-[(4-methyl-2-quinazolinyl)methyl]-

SMILES:

O=C1N(C2=C(C(N1CC3=NC(C)=C4C=CC=CC4=N3)=O)N(CC#CC)C(N5CCC[C@@H](N)C5)=N2)C

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