Anagliptin

Cat. No.: HY-14877

CAS No.: 739366-20-2

Molecular Formula: $C_{19}H_{25}N_7O_2$

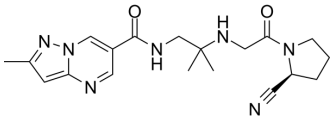
Molecular Weight: 383.45

Target: Dipeptidyl Peptidase

Pathway: Metabolic Enzyme/Protease

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 (260.79 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6079 mL	13.0395 mL	26.0790 mL
5 mM	0.5216 mL	2.6079 mL	5.2158 mL
10 mM	0.2608 mL	1.3040 mL	2.6079 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 (6.52 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.52 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Anagliptin (SK-0403) is a highly selective, potent, orally active inhibitor of dipeptidyl peptidase 4 (DPP-4), with an IC_{50} of 3.8 nM, and less selective at DPP-8 and DDP-9 with IC_{50}s of 68 nM and 60 nM, respectively[1].

IC_{50} & Target

DPP-4	DPP-9	DPP-8
3.8 nM (IC_{50})	60 nM (IC_{50})	68 nM (IC_{50})

In Vitro

Anagliptin (SK-0403) (0-100 μM; 24 h) attenuates s-DPP-4-induced smooth muscle cells proliferation[2].
Anagliptin (100 μM; 10 min) reduces TNF-α production in cultured monocytes[2].
Anagliptin (0.001-10 μM; 24 h) significantly suppresses sterol regulatory element‐binding protein activity in HepG2 cells (21% decrease)[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	Rat smooth muscle cells (SMC)
Concentration:	1, 10 and 100 μM
Incubation Time:	24 h
Result:	Attenuated s-DPP-4-induced SMC proliferation in a dose-dependent manner. Inhibited LPS-induced ERK phosphorylation and markedly suppressed LPS-induced nuclear translocation of NF-κBp65.

Western Blot Analysis[2]

Cell Line:	Rat smooth muscle cells (SMC)
Concentration:	100 μM
Incubation Time:	10 min
Result:	Blocked the early- but not the late-phase ERK phosphorylation induced by s-DPP-4.

In Vivo

Anagliptin (SK-0403) (0.3%; in diet; 16 weeks) reduces atherosclerotic lesion and does not increase the number of circulating EPCs in apoliporotein E (apoE)-deficient mice[2].
Anagliptin (0.3%; in diet; 4 weeks) exhibits a lipid‐lowering effect in a hyperlipidemic mice model[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male apoliporotein E (apoE)-deficient mice[2]
Dosage:	0.3%
Administration:	In diet, 16 weeks
Result:	Reduced DPP-4 activity in the plasma as expected and did not affect food consumption or body weight gain. Significantly reduced total cholesterol level, especially VLDL and LDL-C without affecting triglyceride level. Also decreased the α-SMA-positive area within the individual plaque.

Animal Model:	Male low‐density lipoprotein receptor‐deficient mice (B6.129S7‐Ldlr^{tm1Her}/J)[3]
Dosage:	0.3%
Administration:	In diet, 4 weeks
Result:	Significantly decreased the plasma total cholesterol (14% reduction) and triglyceride levels (27% reduction). Significantly decreased low‐density lipoprotein cholesterol and very low ‐density lipoprotein cholesterol. Sterol regulatory element‐binding protein‐2 messenger ribonucleic acid expression level was significantly decreased at night.

Animal Model:	Male Sprague–Dawley rats and Beagle dogs[1]
Dosage:	0.2, 0.5, 1 and 10 mg/kg
Administration:	Oral or intravenous administration (Pharmacokinetic Studies)

Result:

Selected PK parameters of Anagliptin hydrochloride in rats and dogs[1]

Compound	Species	CL_{tot} (l/h/kg)	V_{dss} (l/h/kg)	C_{max}[c] (ng/ml)	T_{max}[c] (h)	$T_{1/2}$ (h)	AUC (ng/h/ml)	BA (%)
Anagliptin hydrochloride[a]	Rat	2.00 (iv)	0.68 (iv)	309 (62) (po)	0.8 (2.3) (po)	1.9 (po)	1160 (po)	23 (po)
	Dog	0.65 (iv)	0.83 (iv)	261 (po)	1.5 (po)	1.0 (po)	824 (po)	100 (po)

[a]Anagliptin hydrochloride dose in rats, 1 mg/kg, iv (n = 3); 10 mg/kg, po (n = 3). 4a dose in dogs, 0.2 mg/kg, iv (n = 3); 0.5 mg/kg, po (n = 2).[c]Values in parentheses were obtained at a dose of 3 mg/kg (n = 3).

CUSTOMER VALIDATION

- Biochem Pharmacol. 2018 Oct;156:312-321.
- Mol Med Rep. 2017 Dec;16(6):8003-8010.
- Exp Ther Med. February 15, 2022.

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REFERENCES

[1]. Kato N, et al. Discovery and pharmacological characterization of N-[2-({2-[(2S)-2-cyanopyrrolidin-1-yl]-2-oxoethyl}amino)-2-methylpropyl]-2-methylpyrazolo[1,5-a]pyrimidine-6-carboxamide hydrochloride (anagliptin hydrochloride salt) as a potent and selective DPP-IV inhibitor. Bioorg Med Chem. 2011 Dec 1;19(23):7221-7.

[2]. Ervinna N, et al. Anagliptin, a DPP-4 inhibitor, suppresses proliferation of vascular smooth muscles and monocyte inflammatory reaction and attenuates atherosclerosis in male apo E-deficient mice. Endocrinology. 2013 Mar;154(3):1260-70.

[3]. Yano W, et al. Mechanism of lipid-lowering action of the dipeptidyl peptidase-4 inhibitor, anagliptin, in low-density lipoprotein receptor-deficient mice. J Diabetes Investig. 2017 Mar;8(2):155-160.

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