Cofrogliptin

Cat. No.: HY-147257

CAS No.: 1844874-26-5

Molecular Formula: $C_{18}H_{19}F_5N_4O_3S$

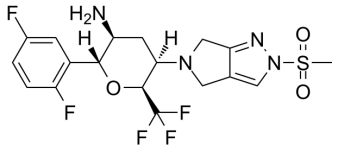
Molecular Weight: 466.43

Target: Dipeptidyl Peptidase

Pathway: Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (214.39 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1439 mL	10.7197 mL	21.4394 mL
5 mM	0.4288 mL	2.1439 mL	4.2879 mL
10 mM	0.2144 mL	1.0720 mL	2.1439 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: ≥ 1.25 mg/mL (2.68 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.68 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cofrogliptin (HSK7653) (compound 2), a tetrahydropyran derivative, is a potent oral dipeptidyl aminopeptidase 4 (DPP-4) inhibitor with Long-acting antidiabetic efficacy. Cofrogliptin (compound 2) has a great potential for type 2 diabetes mellitus (T2DM) [1].

IC_{50} & Target

DPP-4

In Vitro

Cofrogliptin (HSK7653) (compound 2) has the DPP-4 inhibitory activity with an IC_{50} value of 4.18 nM[2].

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

In Vivo

Cofrogliptin (HSK7653) (compound 2) (IV: 0.5 mg/kg; PO: 2 mg/kg) exhibits extremely long half-lives and low rate of reduction of drug concentration after orally administration.
Cofrogliptin (compound 2) (Single, orally, 3 mg/kg, 10 mg/kg, 30 mg/kg) increases of half-lives, has high oral exposure, low i.v. clearance and hepatic microsomal clearance after intravenous dosing.
Cofrogliptin (compound 2) (Single, orally, 10 mg/kg) exhibits longe inhibition time of DPP-4 and decreases HbA1c levelat the doses of 3 and 10 mg/kg in ob/ob mice. Cofrogliptin (compound 2) (Single, orally, 10 mg/kg) also has a great potential of biweekly regimen for T2DM as indicated in rhesus monkeys[2].

Pharmacokinetic Parameters in ICR mice[2]

	IV(dose: 0.5 mg/kg)			PO(dose: 2 mg/kg)			
	CI(mL/min/kg)	V_{dss}(L/kg)	$t_{1/2}$(h)	C_{max}(ng/mL)	$t_{1/2}$(h)	AUC_{0-t} (ng•h/mL)	F%
Omarigliptin	7.39±2.1	1.65±0.27	3.05±0.6	798±122	4.65±1.4	4095±552	95.0±29
Cofrogliptin (compound 2)	2.57±0.09	3.30±0.33	25.6±9.6	352±20	29.9±3.2	7898±873	62.2±6.9

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

Animal Model:	ob/ob mice[2]
Dosage:	3 mg/kg, 10 mg/kg, 30 mg/kg
Administration:	Single, orally, 3 mg/kg, 10 mg/kg, 30 mg/kg
Result:	Exhibited strong inhibition capability of plasma DPP-4 in a dose dependent manner.

Animal Model:	rhesus monkeys[2]
Dosage:	10 mg/kg
Administration:	Single, orally, 10 mg/kg
Result:	Possessed the capability of plasma DPP-4 inhibition over 80% for at least 12 days. Remained the plasma DPP-4 inhibition rates of 76.16% and 43.41%, respectively at the end of second week and third week after administration.

REFERENCES

[1]. International Nonproprietary Names for Pharmaceutical Substances (INN)

[2]. Chen Zhang, et al. Design, Synthesis, and Evaluation of a Series of Novel Super Long-Acting DPP-4 Inhibitors for the Treatment of Type 2 Diabetes. J Med Chem. 2020 Jul 9;63(13):7108-7126.

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

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