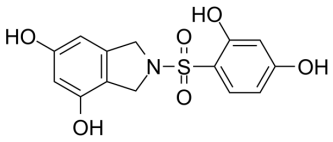
PS10

Cat. No.:	HY-121744
CAS No.:	1564265-82-2
Molecular Formula:	$C_{14}H_{13}NO_6S$
Molecular Weight:	323.32
Target:	PDHK
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 : 62.5 mg/mL (193.31 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0929 mL	15.4646 mL	30.9291 mL
	5 mM	0.6186 mL	3.0929 mL	6.1858 mL
	10 mM	0.3093 mL	1.5465 mL	3.0929 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: ≥ 6.25 mg/mL (19.33 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 6.25 mg/mL (19.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PS10 is a novel, potent and ATP-competitive pan-PDK inhibitor, inhibits all PDK isoforms with IC_{50} of 0.8 μM, 0.76 μM, 2.1 μM and 21.3 μM for PDK2, PDK4, PDK1, and PDK3, respectively. PS10 shows high affinity for PDK2 (K_d= 239 nM) than for Hsp90 (K_d= 47 μM)[1]. PS10 improves glucose tolerance, stimulates myocardial carbohydrate oxidation in diet-induced obesity. PS10 has the potential for the investigation of diabetic cardiomyopathy[2].PDK: pyruvate dehydrogenase kinase

IC_{50} & Target

IC50: 0.8 μM (PDK2); 0.76 μM (PDK4); 2.1 μM (PDK3); 21.3 μM (PDK1)[1]

In Vitro

PS10 shows a higher affinity of PS10 for PDK2 (K_d= 239 nM) than for Hsp90 (K_d= 47,000 nM)[1].
PS10 is less potent than cycloheximide in HeLa cells, it shows an IC_{50} value of 284 μM for the growth inhibition and PS10 has low toxicity in cells[1].

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

In Vivo

PS10 (Intraperitoneal injection; 70 mg/kg; single dose) treatment lead to 11- and 23-fold higher PDC activity in heart and liver, respectively. Meanwhile, there results in a 1.4-fold enhancement of PDC activity in kidneys compared with vehicle-group[1].

PS10 (Intraperitoneal injection; 70 mg/kg; 3 days) treatment results that thePDC activity profiles and the phospho-E1α subunit level is similar to the single-dose. Notably, the three-day treatment attenuates the enhancement of PDK activity in heart[1].

PS10 (intraperitoneal injection; 70 mg/kg; 4 weeks) is treated in mice and subjected to a glucose tolerance test. when challenged with 1.5 g/kg glucose, the plasma glucose level in the vehicle-treated control is at 200 mg/dl at 0 min, peaks at 482 mg/dl at 30 min, and reduces to 210 mg/dl at 120 min. In PS10-treated DIO mice, the glucose level at 168 mg/dl at 0 min is lower than that in vehicle-treated animals, reachs 312 mg/dl at 30 min, and returns to 163 mg/dl at 120 min[1].

PS10 (intraperitoneal injection; 70 mg/kg) and DCA both stimulates flux through PDC as measured by the appearance of hyperpolarized [^{13}C]bicarbonate. It shows similar glucose tolerance response to glucose challenge restores PDC activity in the DIO mouse hearts[2].

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

Animal Model:	C57BL/6J male mice at 6 to 8 weeks old[2]
Dosage:	70 mg/kg/day
Administration:	Intraperitoneal injection
Result:	Improved glucose tolerance in the intact animal.

REFERENCES

[1]. Structure-guided development of specific pyruvate dehydrogenase kinase inhibitors targeting the ATP-binding pocket.J Biol Chem. 2014 Feb 14;289(7):4432-43.

[2]. Wu CY, et al. A novel inhibitor of pyruvate dehydrogenase kinase stimulates myocardial carbohydrate oxidation in diet-induced obesity.J Biol Chem. 2018 Jun 22;293(25):9604-9613.

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