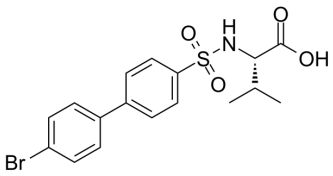
PD-166793

Cat. No.:	HY-107428
CAS No.:	199850-67-4
Molecular Formula:	$C_{17}H_{18}BrNO_4S$
Molecular Weight:	412.3
Target:	MMP
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 (242.54 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4254 mL	12.1271 mL	24.2542 mL
	5 mM	0.4851 mL	2.4254 mL	4.8508 mL
	10 mM	0.2425 mL	1.2127 mL	2.4254 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 (6.06 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.06 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.06 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PD-166793 is a potent, selective, orally active and wide broad spectrum inhibitor of MMP, exhibiting nanomolar potency against MMP-2, MMP-3 and MMP-13 (IC_{50}=4, 7, and 8 nM, respectively) and micromolar potency vs MMP-1, -7 and -9 (IC_{50}=6.0, 7.2, and 7.9 μM, respectively). PD-166793 can attenuate left ventricular remodeling and dysfunction in a rat model of progressive heart failure[1][2][3].

IC_{50} & Target				
	MMP-2	MMP-3	MMP-13	MMP-1
	4 nM (IC_{50})	7 nM (IC_{50})	8 nM (IC_{50})	6.0 μM (IC_{50})

	MMP-7 7.2 μM (IC_{50})	MMP-9 7.9 μM (IC_{50})
In Vitro	PD-166793 (0.1 μM) leads to a 20% inhibition of AMP deaminase (AMPD) activity in rat heart homogenates[2]. PD-166793 (100 μM; 36 h) significantly reduces MMP□9 activity in normal human cardiac fibroblasts[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
In Vivo	PD-166793 (1 mg/kg/d; daily gavage for 10 weeks) largely prevents the adverse remodeling characteristically seen in the aortocaval (AV) fistula model[3]. PD-166793 (5 mg/kg; oral gavage) exhibits superior pharmacokinetics ($t_{1/2}$=43.6 h, C_{max}=42.4 μg/mL, $AUC_{0-\infty}$=2822 μg•h/mL) in rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.	

Animal Model:	Male Sprague-Dawley rats (6 weeks) were induced chronic biventricular volume overload [3]
Dosage:	1 mg/kg
Administration:	Daily gavage beginning 2 weeks before surgery and continued until 8 weeks after surgery
Result:	Prevented ventricular dilatation and attenuated the hypertrophy typically induced by chronic volume overload.

REFERENCES

[1]. O'Brien PM, et, al. Structure-activity relationships and pharmacokinetic analysis for a series of potent, systemically available biphenylsulfonamide matrix metalloproteinase inhibitors. J Med Chem. 2000 Jan 27;43(2):156-66.

[2]. Kaludercic N, et, al. Inhibiting metalloproteases with PD 166793 in heart failure: impact on cardiac remodeling and beyond. Cardiovasc Ther. Spring 2008;26(1):24-37.

[3]. Chancey AL, et, al. Effects of matrix metalloproteinase inhibition on ventricular remodeling due to volume overload. Circulation. 2002 Apr 23;105(16):1983-8.

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