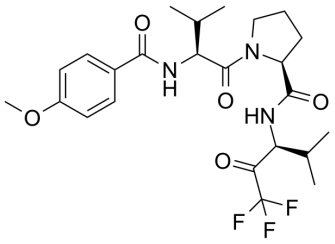
ZD-0892

Cat. No.:	HY-19254
CAS No.:	171964-73-1
Molecular Formula:	$C_{24}H_{32}F_3N_3O_5$
Molecular Weight:	499.52
Target:	Elastase
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 : 250 mg/mL (500.48 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0019 mL	10.0096 mL	20.0192 mL
5 mM	0.4004 mL	2.0019 mL	4.0038 mL
10 mM	0.2002 mL	1.0010 mL	2.0019 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: ≥ 2.08 mg/mL (4.16 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.16 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.16 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ZD-0892 is a selective and potent inhibitor of a neutrophil elastase with K_is of 6.7 and 200 nM for human neutrophil elastase and porcine pancreatic elastase, respectively.

IC_{50} & Target

Ki: 6.7 nM (Human neutrophil elastase), 200 nM (Human neutrophil elastase)[1]

In Vivo

ZD0892 administration to DBA/2 mice infected with the EMC virus results in reduced myocardial elastolytic activity and coronary microvascular perfusion injury. ZD0892 decreases the pathologic severity of the myocardial lesions associated with

murine viral myocarditis[1]. ZD-0892 can reverse advanced pulmonary vascular disease produced in rats[2].

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

PROTOCOL

Animal Administration [1][2]

Rats[2]

Adult male Sprague-Dawley rats (250-300 g in body weight) are induced pulmonary hypertension. In addition to a group of untreated rats, the experimental groups include rats that receive twice-daily gavage tube feedings of ZD0892, at a dose of 240 mg/kg per day or vehicle (5% polyethylene glycol or dimethyl sulfoxide). Rats are examined after 7 days of treatment.

Mice[1]

DBA/2 male mice 8 weeks old is used. ZD0892 is given in a dose of 60 mg/kg or 120 mg/kg[1].

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

REFERENCES

[1]. Lee JK, et al. A serine elastase inhibitor reduces inflammation and fibrosis and preserves cardiac function after experimentally-induced murine myocarditis. Nat Med. 1998 Dec;4(12):1383-91.

[2]. Cowan KN, et al. Complete reversal of fatal pulmonary hypertension in rats by a serine elastase inhibitor. Nat Med. 2000 Jun;6(6):698-702.

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