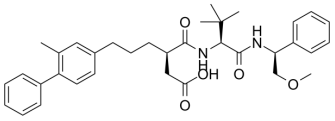
UK-370106

Cat. No.:	HY-107639
CAS No.:	230961-21-4
Molecular Formula:	$C_{35}H_{44}N_2O_5$
Molecular Weight:	572.73
Target:	MMP
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 200 mg/mL (349.20 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7460 mL	8.7301 mL	17.4602 mL
	5 mM	0.3492 mL	1.7460 mL	3.4920 mL
	10 mM	0.1746 mL	0.8730 mL	1.7460 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: ≥ 5 mg/mL (8.73 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (8.73 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (8.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UK-370106 is a potent and highly selective MMP-3 (IC_{50} of 23 nM) and MMP-12 (IC_{50} of 42 nM) inhibitor with >1200-fold higher potency than MMP-1, MMP-2, MMP-9, and MMP-14, and about 100-fold than MMP-13 and MMP-8. UK-370106 potently inhibits cleavage of [^{3}H]-fibronectin by MMP-3 (IC_{50} of 320 nM) and has little effect on keratinocyte migration in vitro[1][2].

IC_{50} & Target

MMP-3 23 nM (IC_{50})	MMP-12 42 nM (IC_{50})	MMP-8 1.75 μM (IC_{50})	MMP-13 2.3 μM (IC_{50})
MMP-7 5.8 μM (IC_{50})	MMP-9 30.4 μM (IC_{50})	MMP-2 34.2 μM (IC_{50})	MMP-14 66.9 μM (IC_{50})

In Vitro	The potency of UK-370106 (compound 7) for the inhibition of MMP-13 is 2.3 μM, some 100-fold less potent than its inhibition of MMP-3. UK-370106 is found to be inactive (IC_{50} > 100 μM) vs zinc metalloproteases PCP and TACE and possesses the following inhibitory potencies vs MMP-2 (IC_{50} of 34.2 μM), MMP-7 (IC_{50} of 5.8 μM), MMP-8 (IC_{50} of 1.75 μM), MMP-9 (IC_{50} of 30.4 μM) and MMP-14 (IC_{50} of 66.9 μM)[1]. UK-370106 potently inhibits cleavage of [^{3}H]-fibronectin by MMP-3 (IC_{50} of 320 nM) but does not inhibit cleavage of [^{3}H]-gelatin by either MMP-2 or -9 up to the highest concentration tested (100 μM)[1]. UK-370106 is not cytotoxic to, nor affected proliferation of, fibroblasts, keratinocytes, or endothelial cells at 50-100 μM in vitro[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Following iv (rat; 2 mg/kg) or topical administration to dermal wounds (rabbit), UK-370106 (compound 7) is cleared rapidly ($t_{1/2}$ = 23 min) from plasma, but slowly ($t_{1/2}$ approximately 3 days) from dermal tissue. In a model of chronic dermal ulcers, topical administration of UK-370106 for 6 days substantially inhibits MMP-3 ex vivo[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Fray MJ, et al. A potent, selective inhibitor of matrix metalloproteinase-3 for the topical treatment of chronic dermal ulcers. J Med Chem. 2003 Jul 31;46(16):3514-25.

[2]. Whitlock GA, et al. A novel series of highly selective inhibitors of MMP-3. Bioorg Med Chem Lett. 2007 Dec 15;17(24):6750-3. Epub 2007 Oct 17.

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