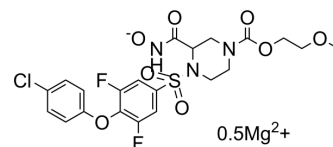


XL-784

Cat. No.:	HY-19485
CAS No.:	1224964-36-6
Molecular Formula:	C ₂₁ H ₂₁ ClF ₂ N ₃ O ₈ S ⁻
Molecular Weight:	548.92
Target:	MMP
Pathway:	Metabolic Enzyme/Protease
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro	DMSO : ≥ 110 mg/mL (200.39 mM) * "≥" means soluble, but saturation unknown.																									
	<table border="1"> <thead> <tr> <th rowspan="2">Solvent</th> <th rowspan="2">Mass</th> <th colspan="3">Concentration</th> </tr> <tr> <th>1 mg</th> <th>5 mg</th> <th>10 mg</th> </tr> </thead> <tbody> <tr> <td rowspan="4">Preparing Stock Solutions</td> <td>1 mM</td> <td>1.8218 mL</td> <td>9.1088 mL</td> <td>18.2176 mL</td> </tr> <tr> <td>5 mM</td> <td>0.3644 mL</td> <td>1.8218 mL</td> <td>3.6435 mL</td> </tr> <tr> <td>10 mM</td> <td>0.1822 mL</td> <td>0.9109 mL</td> <td>1.8218 mL</td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table>	Solvent	Mass	Concentration			1 mg	5 mg	10 mg	Preparing Stock Solutions	1 mM	1.8218 mL	9.1088 mL	18.2176 mL	5 mM	0.3644 mL	1.8218 mL	3.6435 mL	10 mM	0.1822 mL	0.9109 mL	1.8218 mL				
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Please refer to the solubility information to select the appropriate solvent.																										
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.75 mg/mL (5.01 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.75 mg/mL (5.01 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.75 mg/mL (5.01 mM); Clear solution 																									

BIOLOGICAL ACTIVITY

Description	XL-784 is a selective matrix metalloproteinases (MMP) inhibitor, with IC ₅₀ s of ~1900, 0.81, 120, 10.8, 18, 0.56 nM for MMP-1, MMP-2, MMP-3, MMP-8, MMP-9, MMP-13 respectively.			
IC ₅₀ & Target	MMP-2 0.81 nM (IC ₅₀)	MMP13 0.56 nM (IC ₅₀)	MMP-8 10.8 nM (IC ₅₀)	MMP-9 18 nM (IC ₅₀)
	MMP-3 120 nM (IC ₅₀)	MMP-1 1900 nM (IC ₅₀)		

In Vitro	<p>XL-784 is a highly potent, low-molecular-weight (1,122 g/mol) inhibitor of MMPs that has very limited aqueous solubility (20 µg/mL). XL-784 potently inhibits MMP-2, MMP-13, and ADAM10 [TNF-α-converting enzyme (TACE)] activity in vitro, with IC₅₀ values in the range of 1-2 nM. XL-784 also inhibits MMP-9 (IC₅₀ ~20 nM) activity and ADAM17 (IC₅₀ ~70 nM) also known as TACE. However, it exhibits low potency for inhibition of MMP-1 (IC₅₀ ~2,000 nM)^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>All mice tolerate the treatments similarly. Control mice all developed aneurysms with a mean %ΔAD of 158.5%±4.3%. Treatment with all doses of XL-784 and doxycycline are effective in inhibiting aortic dilatation. There is a clear dose-response relationship between XL-784 and reductions in aortic dilatation at harvest (50 mg/kg 140.4%±3.2%; 125 mg/kg 129.3%±5.1%; 250 mg/kg 119.2%±3.5%; all Ps<0.01 compared to control). This continues with the higher doses (375 mg/kg 88.6%±4.4%; 500 mg/kg 76.0%±3.5%). The highest 2 doses of XL-784 tested are more effective than doxycycline (112.2%±2.0%, P<0.05) in inhibiting maximal dilatation of the aorta after elastase perfusion^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

PROTOCOL

Animal Administration ^[2]

Mice^[2]

A total of 89 mice undergo aortic perfusion. Beginning the day of perfusion, animals are treated with the study drug (e.g., XL-784), a negative control, or doxycycline. 76 animals survive to sacrifice and are included in the analysis. Animals treated with the experimental agent, XL-784, receive gavage daily with the agent diluted in 0.1 mL of Cremophor, a nonionic castor oil-based solubilizer and emulsifying agent. Three doses of the drug are used, 50 (n=17), 125 (n=17), and 250 mg/kg per d (n=18) administered as a single daily dose. The fifth group of mice do not receive a gavage treatment but are treated with doxycycline (n=19) in their drinking water at a concentration 100 mg/kg per d of the animals. In the second treatment protocol, a total of 50 animals underwent aortic perfusion and 47 animals survive for analysis at 14 days. The 5 treatment groups are XL-784 at 250, 375, or 500 mg/kg, Cremaphor diluent alone, or doxycycline 100 mg/kg. Animals are assigned in groups of 3 to a treatment group rotating randomly through each treatment group until there are 9 animals in each group except for the 500 mg/kg per d group which totaled to 14 animals^[2].

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

CUSTOMER VALIDATION

- Thromb Res. 2023 Apr 26;226:69-81.

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REFERENCES

- [1]. Williams JM, et al. Evaluation of metalloprotease inhibitors on hypertension and diabetic nephropathy. Am J Physiol Renal Physiol. 2011 Apr;300(4):F983-98.
- [2]. Ennis T, et al. Effect of novel limited-spectrum MMP inhibitor XL784 in abdominal aortic aneurysms. J Cardiovasc Pharmacol Ther. 2012 Dec;17(4):417-26.

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

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