TM5275 sodium

Cat. No.: HY-100447

CAS No.: 1103926-82-4

Molecular Formula: $C_{28}H_{27}ClN_3NaO_5$

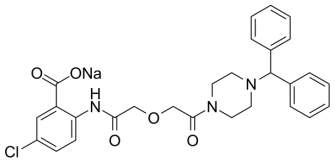
Molecular Weight: 543.97

Target: PAI-1

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 : 62.5 mg/mL (114.90 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8383 mL	9.1917 mL	18.3834 mL
	5 mM	0.3677 mL	1.8383 mL	3.6767 mL
	10 mM	0.1838 mL	0.9192 mL	1.8383 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 (4.60 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.60 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TM5275 sodium is a plasminogen activator inhibitor (PAI-1) with an IC_{50} of 6.95 μM.

IC_{50} & Target

IC50: 6.95 μM (PAI-1)[1]

In Vitro

Docking studies shows that TM5275 binds to strand 4 of the A β-sheet (s4A) position of PAI-1. TM5275 is a selective PAI-1 and (up to 100 μM) does not interfere with other serpin/serine protease systems[1]. TM5275 at concentrations of 20 and 100 μM significantly prolongs the retention of tPA-GFP on VECs by inhibiting tPA-GFP-PAI-1 high-molecular-weight complex formation. TM5275 enhances the time-dependent accumulation of plasminogen as well as the dissolution of fibrin clots on and around the tPA-GFP-expressing cells[2]. Cell viability at 72 h treatment is decreased with 70-100 μM TM5275 in ES-2 and

	JHOC-9 cells. From 48 h up to 96 h, cell growth is suppressed with 100 μM TM5275. Active PAI-1 in cell culture media is significantly decreased in cells treated with 100 μM TM5275 compared to control treatment. TM5275 is suggested to exert anti-proliferative effects in ovarian cancer with high PAI-1 expression[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	TM5275 exhibits a favorable pharmacokinetics profile and very low toxicity to mice and rats. In rat thrombosis models. Blood clot weights are significantly lower in rats administered 10 and 50 mg/kg of TM5275 (60.9±3.0 and 56.8±2.8 mg, respectively) than in vehicle-treated rats (72.5±2.0 mg). The antithrombotic effectiveness of TM5275 (50 mg/kg) is equivalent to that of ticlopidine (500 mg/kg), a reference antithrombotic compound. Plasma concentration of TM5275 reaches 17.5±5.2 μM after a dose of 10 mg/kg. TM5275 (5 mg/kg) combined with tPA (0.3 mg/kg) significantly enhances the antithrombotic effect of tPA (0.3 mg/kg) alone and provides a benefit similar to that of a high tPA dose (3 mg/kg)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay	TM5275 exhibits a favorable pharmacokinetics profile and very low toxicity to mice and rats. In rat thrombosis models. Blood clot weights are significantly lower in rats administered 10 and 50 mg/kg of TM5275 (60.9±3.0 and 56.8±2.8 mg, respectively) than in vehicle-treated rats (72.5±2.0 mg). The antithrombotic effectiveness of TM5275 (50 mg/kg) is equivalent to that of ticlopidine (500 mg/kg), a reference antithrombotic compound. Plasma concentration of TM5275 reaches 17.5±5.2 μM after a dose of 10 mg/kg. TM5275 (5 mg/kg) combined with tPA (0.3 mg/kg) significantly enhances the antithrombotic effect of tPA (0.3 mg/kg) alone and provides a benefit similar to that of a high tPA dose (3 mg/kg)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	ES2 cells are treated with DMSO (control) or 100 μM TM5275 for the indicated periods (24, 48, 72, 96 hour). Cell growth is determined by CellTiter-Glo assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats: Thrombus formation in arteriovenous shunts is achieved in male CD rats. Either TM5275 (10 and 50 mg/kg, n=9) or ticlopidine (500 mg/kg, n=6), suspended in 0.5% CMC solution, is administered orally by gavage 90 mins before the study. Control rats are administered only a 0.5% CMC solution (n=10). Blood is allowed to circulate through the shunt for 30 mins. The wet weight of the thrombus covering the silk thread is eventually measured[1]. Mice: TM5275 is administered orally by gavage to male ICR mice (50 mg/kg). Heparinized blood samples are collected from the vein before (0 h) and 1, 2, 6, and 24 h after oral drug administration. Plasma drug concentration is determined on a reverse-phase high-performance liquid chromatography[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Stem Cell Res Ther. 2021 Dec 20;12(1):608.
- Cells. 2023 May 16, 12(10), 1402.
- FASEB J. 2022 Jun;36(6):e22368.
- Integr Biol (Camb). 2022 Feb 19;zyac001.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Izuhara Y, et al. A novel inhibitor of plasminogen activator inhibitor-1 provides antithrombotic benefits devoid of bleeding effect in nonhuman primates. J Cereb Blood Flow Metab. 2010 May;30(5):904-12.

[2]. Yasui H, et al. TM5275 prolongs secreted tissue plasminogen activator retention and enhances fibrinolysis on vascular endothelial cells. Thromb Res. 2013 Jul;132(1):100-5.

[3]. Mashiko S, et al. Inhibition of plasminogen activator inhibitor-1 is a potential therapeutic strategy in ovarian cancer. Cancer Biol Ther. 2015;16(2):253-60.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA