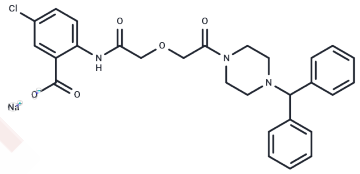
Data Sheet (Cat.No.T4255)

TargetMol

TM5275 sodium

Chemical Properties



CAS No. : 1103926-82-4

Formula: C28H27ClN3NaO5

Molecular Weight: 543.98

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	TM5275 sodium (TM5275 sodium salt) is an inhibitor of plasminogen activator inhibitor 1 (PAI-1).
Targets(IC50)	PAI-1
In vitro	1.TM5275 inhibits formation of a complex consisting of tissue plasminogen activator (tPA), PAI-1, and GFP on vascular endothelial cells (VECs) in vitro, prolonging the time that tPA is retained on VECs. It also enhances fibrin clot dissolution and plasminogen accumulation in vitro and has antithrombotic effects in rat models of thrombosis.2. 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. 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. 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
In vivo	1.TM5275 (10 and 50 mg/kg) decreases blood clot weight in an arteriovenous shunt thrombosis model and increases the time to primary occlusion in a ferric chloride-treated carotid artery thrombosis model when used at doses of 1 and 3 mg/kg. In a cynomolgus monkey model of photochemical-induced arterial thrombosis, TM5275 (10 mg/kg) increases the time to primary occlusion. It does not affect platelet activity, activated partial thromboplastin time, prothrombin time, or prolong bleeding time.2. 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)

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).
Cell Research	TM5275 is prepared in DMSO.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.
Animal Research	TM5275 is suspended in 0.5% carboxymethyl cellulose sodium salt (CMC).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.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

Solubility Information

Solubility	DMSO: 45 mg/mL (82.72 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.68 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8383 mL	9.1915 mL	18.383 mL
5 mM	0.3677 mL	1.8383 mL	3.6766 mL
10 mM	0.1838 mL	0.9192 mL	1.8383 mL
50 mM	0.0368 mL	0.1838 mL	0.3677 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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.
Liu Y, Shu L, Jiang X, et al.The development of nasal polyps involves early middle meatus mucous remodeling via TGF-β1 mediated PAI-1 reduction.Brazilian Journal of Otorhinolaryngology.2023
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.
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.