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产品名称：TM5275 (sodium)
产品别名：TM5275 sodium

生物活性：

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].
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].
Solvent&Solubility	***In Vitro:*** **DMSO： ≥ 100 mg/mL (183.49 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8349 mL	9.1746 mL	18.3493 mL
5 mM	0.3670 mL	1.8349 mL	3.6699 mL
10 mM	0.1835 mL	0.9175 mL	1.8349 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

	1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (4.59 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.59 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (4.59 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.59 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.59 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.59 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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].
Animal Administration	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].
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].
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