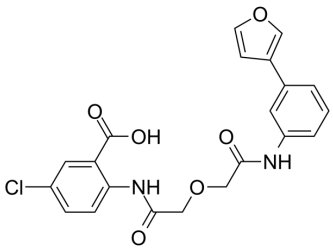
TM5441

Cat. No.:	HY-101761
CAS No.:	1190221-43-2
Molecular Formula:	$C_{21}H_{17}ClN_2O_6$
Molecular Weight:	428.82
Target:	PAI-1; Apoptosis
Pathway:	Metabolic Enzyme/Protease; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (233.20 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3320 mL	11.6599 mL	23.3198 mL
	5 mM	0.4664 mL	2.3320 mL	4.6640 mL
	10 mM	0.2332 mL	1.1660 mL	2.3320 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 (5.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TM5441 is an orally bioavailable inhibitor of plasminogen activator inhibitor-1 (PAI-1), has IC_{50} values between 13.9 and 51.1 μM and induces intrinsic apoptosis in several human cancer cell lines. TM5441 attenuates Nω-nitro-l-arginine methyl ester-induced cardiac hypertension and vascular senescence[1][2].

IC_{50} & Target

IC50: 13.9~51.1 μM (Tumor cell lines)[1]

In Vitro

TM5441 dose-dependently decreases HT1080, HCT116, Daoy, MDA-MB-231 and Jurkat cells with an IC_{50} ranging between 13.9 and 51.1 μM[1].
TM5441 increases caspase 3/7 activity for both HT1080 and HCT116 cells in a dose dependant manner. TM5441 increases apoptosis in HT1080 and HCT116 cells[1].

	TM5441 induces mitochondrial depolarization[1]. In mouse proximal tubular epithelial cells, TM5441 effectively inhibits PAI-1-induced mRNA expression of fibrosis and inflammation markers and also reverses PAI-1-induced inhibition of plasmin activity[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral administration of TM5441 (20 mg/kg daily) to HT1080 and HCT116 xenotransplanted mice increases tumor cell apoptosis and has a significant disruptive effect on the tumor vasculature that is associated with a decrease in tumor growth and an increase in survival. The average peak plasma concentration is 11.4 μM one hour after oral administration and undetectable levels 23 hours after administration[1]. TM5441 attenuates Nω-nitro-l-arginine methyl ester-induced cardiac hypertension and vascular senescence, prolongs lifespan in klotho null mice and elicits anti-tumorigenic and anti-angiogenic activities in cancer[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	HT1080, HCT116, Daoy, MDA-MB-231 and Jurkat cells are treated with 0-100 μM TM5441 for 48 hours at 37°C. Cell viability is measured by MTT assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice: TM5275 at 50 mg/kg/day and TM5441 at 10 mg/kg/day were orally administered in control and diabetic mice for 16 weeks. Mice were monitored at least once a day. At the end, blood is collected for measurement of plasma glucose and creatinine, urine for protein measurement, and kidneys for immunohistochemical analysis[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Kidney Int. 2023 Jun 23;S0085-2538(23)00425-8.
- Sci Rep. 2023 Sep 27;13(1):16210.
- Eur J Pharm Sci. 2020 Feb 15;143:105195.
- Biol Pharm Bull. 2023 Oct 10;46(12):1753-1760.
- bioRxiv. 2023 Nov 26.

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REFERENCES

[1]. Placencio VR, et al. Small Molecule Inhibitors of Plasminogen Activator Inhibitor-1 Elicit Anti-Tumorigenic and Anti-Angiogenic Activity. PLoS One. 2015 Jul 24;10(7):e0133786.

[2]. Jeong BY, et al. Novel Plasminogen Activator Inhibitor-1 Inhibitors Prevent Diabetic Kidney Injury in a Mouse Model. PLoS One. 2016 Jun 3;11(6):e0157012.

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

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