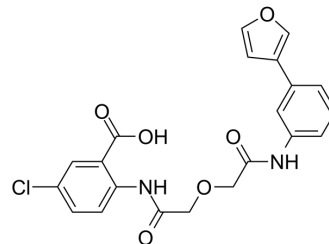


TM5441

Cat. No.:	HY-101761		
CAS No.:	1190221-43-2		
Molecular Formula:	C ₂₁ H ₁₇ ClN ₂ O 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)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	Preparing Stock Solutions	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	<ol style="list-style-type: none"> 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 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]} .
IC₅₀ & Target	IC ₅₀ : 13.9~51.1 μM (Tumor cell lines) ^[1]
In Vitro	<p>TM5441 dose-dependently decreases HT1080, HCT116, Daoy, MDA-MB-231 and Jurkat cells with an IC₅₀ ranging between 13.9 and 51.1 μM^[1].</p> <p>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].</p>

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 μ M one hour after oral administration and undetectable levels 23 hours after administration^[1].
TM5441 attenuates N ω -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 μ M 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