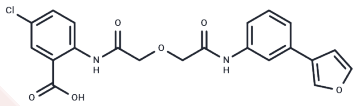
Data Sheet (Cat.No.T4254)

TargetMol

TM5441

Chemical Properties



CAS No. : 1190221-43-2

Formula: C21H17ClN2O6

Molecular Weight: 428.82

Storage: Store at low temperature
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	TM5441 is an orally bioavailable fibrinogen activator inhibitor-1 inhibitor that inhibits several cancer cell lines with IC50 values ranging from 13.9 to 51.1 μM.It induces intrinsic cell death in several human cancer cells and attenuates Nω-nitro-1-arginine methyl ester-induced cardiac hypertension and vascular senescence.
Targets(IC50)	Apoptosis,PAI-1
In vitro	**METHODS**: TM5441 (1-100μM) was used to further study the survival of HT1080, HCT116, Daoy, MDA-MB-231 and Jurkat. **RESULTS** Cell viability treated with TM5441 significantly decreased in a dose-dependent manner by 50%, ranging between 13.9 and 51.1μM.[2] **METHODS**: Cultures of human endothelial cells EA.hy926 were pretreated with TM5441 (10 μM) for 24 h and then treated with doxorubicin (Dox) in triplicate for 4 days. Total protein and RNA were collected from three independently treated wells and combined to explore the protective effect of TM5441 on Dox-induced cellular senescence. **RESULTS** TM5441 treatment inhibited Dox-induced expression levels of p53, PAI-1, p16, p21 and IGFBP3 in human endothelial cells. [3]
In vivo	**METHODS**: High-fat diet (HFD)-fed C57BL/6J mice were treated with 20 mg/kg of TM5441 daily to study the effect of TM5441, an oral PAI-1 inhibitor that lacks bleeding risk, on HFD-induced NAFLD. **RESULTS** Early and delayed treatment with TM5441 reduced hepatic steatosis, and both strategies abolished hepatic insulin resistance and mitochondrial dysfunction, manifested by enhanced p-Akt and p-GSK3β, reduced p-JNK signaling, and p-AMPK and PGC-1α activation. [1]
Kinase Assay	TM5441 is dissolved with DMSO at a stock concentration of 50 mM.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.
Animal Research	TM5441 is prepared in 0.5% carboxymethyl cellulose.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.

Solubility Information

Solubility	DMSO: 5.67 mg/mL (13.22 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Saline: < 10 mg/mL (23.32 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 10 mg/mL (23.32 mM),Solution. *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	2.332 mL	11.6599 mL	23.3198 mL
5 mM	0.4664 mL	2.332 mL	4.664 mL
10 mM	0.2332 mL	1.166 mL	2.332 mL
50 mM	0.0466 mL	0.2332 mL	0.4664 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

Lee SM,et al. TM5441, a plasminogen activator inhibitor-1 inhibitor, protects against high fat diet-induced non-alcoholic fatty liver disease. Oncotarget. 2017 Sep 21;8(52):89746-89760.
Zhang W, Yang S, Chen D, et al. SOX2-OT induced by PAI-1 promotes triple-negative breast cancer cells metastasis by sponging miR-942-5p and activating PI3K/Akt signaling. Cellular and Molecular Life Sciences. 2022, 79(1): 1-16.
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.
Ghosh AK, et al. A small molecule inhibitor of PAI-1 protects against doxorubicin-induced cellular senescence. Oncotarget. 2016 Nov 8;7(45):72443-72457.
Lee SM,etal.TM5441, a plasminogen activator inhibitor-1 inhibitor, protects against high fat diet-induced non-alcoholic fatty liver disease.Oncotarget. 2017 Sep 21;8(52):89746-89760.
Eren M,etal.PAI-1-regulated extracellular proteolysis governs senescence and survival in Klotho mice.Proc Natl Acad Sci U S A. 2014 May 13;111(19):7090-5.