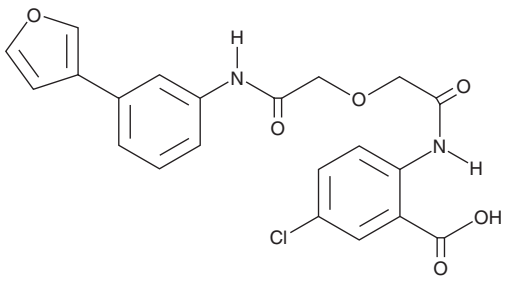
PRODUCT INFORMATION

TM5441

Item No. 22965

CAS Registry No.:	1190221-43-2
Formal Name:	5-chloro-2-[[2-[2-[[3-(3-furanyl)phenyl]amino]-2-oxoethoxy]acetyl]amino]-benzoic acid
MF:	$C_{21}H_{17}ClN_2O_6$
FW:	428.8
Purity:	≥98%
UV/Vis.:	λ_{max}: 226 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

TM5441 is supplied as a crystalline solid. A stock solution may be made by dissolving the TM5441 in the solvent of choice. TM5441 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of TM5441 in these solvents is approximately 20 and 33 mg/ml, respectively.

TM5441 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, TM5441 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. TM5441 has a solubility of approximately 0.14 mg/ml in a 1:6 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

TM5441 is an orally bioavailable inhibitor of plasminogen activator inhibitor 1 (PAI-1), a serine-protease inhibitor involved in thrombosis.[1,2] It decreases survival of HT1080, HCT116, Daoy, MDA-MB-231, and Jurkat cancer cells with IC_{50} values ranging from 13.9 to 51.1 µM.[1] TM5441 inhibits branching of human umbilical vein endothelial cells (HUVECs) in a vasculature assay *in vitro* when used at a concentration of 50 µM but does not affect HUVEC survival or apoptosis. It also disrupts tumor vasculature in HT1080 and HCT116 mouse xenograft models when used at a dose of 20 mg/kg per day. TM5441 prevents hypertension and cardiac hypertrophy and reduces periaortic fibrosis induced by L-NAME (Item No. 80210).[2] It protects against high-fat diet-induced non-alcoholic fatty liver disease (NAFLD) in mice when administered concurrently with a high-fat diet or after glucose tolerance has developed.[3] TM5441 also increases median lifespan by 4-fold and reduces signs of senescence in Klotho-deficient mice, a mouse model of aging.[4]

References

1. Placencio, V.R., Ichimura, A., Miyata, T., *et al.* Small molecule inhibitors of plasminogen activator inhibitor-1 elicit anti-tumorigenic and anti-angiogenic activity. *PLoS One* **10(7)**, e0133786 (2015).
2. Boe, A.E., Eren, M., Murphy, S.B., *et al.* Plasminogen activator inhibitor-1 antagonist TM5441 attenuates Nω-nitro-L-arginine methyl ester-induced hypertension and vascular senescence. *Circulation* **128(21)**, 2318-2324 (2013).
3. Lee, S.M., Dorotea, D., Jung, I., *et al.* TM5441, a plasminogen activator inhibitor-1 inhibitor, protects against high fat diet-induced non-alcoholic fatty liver disease. *Oncotarget* **8(52)**, 89746-89760 (2017).
4. Eren, M., Boe, A.E., Murphy, S.B., *et al.* PAI-1-regulated extracellular proteolysis governs senescence and survival in Klotho mice. *Proc. Natl. Acad. Sci. U.S.A.* **111(19)**, 7090-7095 (2014).

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