TG 100572

Cat. No.: HY-10184

CAS No.: 867334-05-2

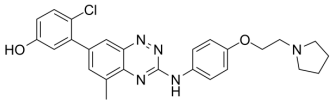
Molecular Formula: $C_{26}H_{26}ClN_5O_2$

Molecular Weight: 475.97

Target: Src; VEGFR; PDGFR; FGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 150 mg/mL (315.15 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	2.1010 mL	10.5049 mL	21.0097 mL
	5 mM	0.4202 mL	2.1010 mL	4.2019 mL
	10 mM	0.2101 mL	1.0505 mL	2.1010 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

TG 100572 is a multi-targeted kinase inhibitor which inhibits receptor tyrosine kinases and Src kinases; has IC_{50}s of 2, 7, 2, 16, 13, 5, 0.5, 6, 0.1, 0.4, 1, 0.2 nM for VEGFR1, VEGFR2, FGFR1, FGFR2, PDGFRβ, Fgr, Fyn, Hck, Lck, Lyn, Src, Yes, respectively.

IC_{50} & Target

VEGFR1 2 nM (IC_{50})	VEGFR2 7 nM (IC_{50})	FGFR1 2 nM (IC_{50})	FGFR2 16 nM (IC_{50})
PDGFRβ 13 nM (IC_{50})			

In Vitro

TG 100572 shows sub-nanomolar activity against the Src family as well as RTK such as VEGFR1 and R2, FGFR1 and R2, and PDGFRβ. TG 100572 inhibits vascular endothelial cell proliferation (ED_{50}=610±71 nM) and blocks VEGF-induced phosphorylation of extracellular signal-regulated kinase. TG 100572 induces apoptosis in rapidly proliferating, but not quiescent, endothelial cell cultures[1]. TG 100572 is shown to inhibit hRMVEC cell proliferation, with an IC_{50} of 610±72 nM. This suggests that TG 100572 has the therapeutic potential to inhibit VEGF function in ocular endothelial cells, a contributing factor to pathological angiogenesis in diseases such as AMD and PDR[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	Systemic delivery of TG 100572 in a murine model of laser-induced choroidal neovascularization (CNV) causes significant suppression of CNV, but with an associated weight loss suggestive of systemic toxicity[1]. A concentration of 23.4 μM (C_{max}) of TG 100572 is reached in 30 min (T_{max})=0.5 h) in the choroid and the sclera. However, the levels of TG 100572 in the retina are relatively low. The half-life of TG 100572 in ocular tissues is very short; hence, the compound is administered topically minimum t.i.d. to maintain appropriate drug levels in the eye. The maximum concentration one can achieve in formulations using TG 100572 is 0.7% w/v[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For proliferation assays, human retinal microvascular EC plated in 96-well cluster plates are cultured for 48 hr in the presence of either TG 100572 (2 nM-5 μM) or DMSO; medium contained 10% FBS, 50 μg/mL heparin, and 50 ng/mL rhVEGF. Cell numbers are then assessed using an XTT-based assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: C57BL/6 mice (15-20 g) are dosed i.p. twice daily for 4 days with 5 mg/ kg TG 100572, followed by a single dose on Day 5, 5 hr after which plasma samples are taken, animals euthanized, and eyes explanted. Alternatively, mice are dosed topically with either TG 100572 or related prodrugs (e.g., TG 100801) by delivering a single 10 μL drop to both eyes for a total of two days, and both plasma and eyes harvested prior to or 0.5, 1, 3, 5, or 7 hr after the Day 2 dosing[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Am J Pathol. 2019 Oct;189(10):2090-2101.

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REFERENCES

[1]. Doukas J, et al. Topical administration of a multi-targeted kinase inhibitor suppresses choroidal neovascularization and retinal edema. J Cell Physiol. 2008 Jul;216(1):29-37.

[2]. Palanki MS, et al. Development of prodrug 4-chloro-3-(5-methyl-3-{[4-(2-pyrrolidin-1-ylethoxy)phenyl]amino}-1,2,4-benzotriazin-7-yl)phenyl benzoate (TG100801): a topically administered therapeutic candidate in clinical trials for the treatment of age-related macular degeneration. J Med Chem. 2008 Mar 27;51(6):1546-59.

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