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产品名称：TG 100572 (Hydrochloride)
产品别名：TG 100572 Hydrochloride

生物活性：

Description

TG 100572 Hydrochloride is a multi-targeted kinase inhibitor which inhibits receptor tyrosine kinases and Src kinases; has IC50s 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	VEGFR2	FGFR1	FGFR2	PDGFRβ
2 nM (IC_{50})	7 nM (IC_{50})	2 nM (IC_{50})	16 nM (IC_{50})	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 (ED50=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 IC50 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].

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].

Solvent&Solubility

In Vitro:

DMSO : ≥ 44 mg/mL (85.87 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9515 mL	9.7574 mL	19.5149 mL
	5 mM	0.3903 mL	1.9515 mL	3.9030 mL
	10 mM	0.1951 mL	0.9757 mL	1.9515 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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.

实验参考：

Cell Assay	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].
Animal Administration	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].
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.