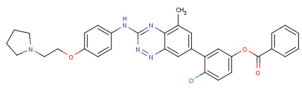
Data Sheet (Cat.No.T13157)

TargetMol
A DRUG SCREENING EXPERT

TG 100801

Chemical Properties



CAS No.:	867331-82-6
Formula:	C33H30ClN5O3
Molecular Weight:	580.08
Appearance:	N/A
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	TG 100801 is a prodrug to treat age-related macular degeneration. TG 100572 is a inhibitor of multi-targeted kinase(IC50s of 2, 7, 2, 16, 13, 5, 0.5, 6, 0.1, 0.4, 1, 0.2 for VEGFR1, VEGFR2, FGFR1, FGFR2, PDGFRβ, Fgr, Fyn, Hck, Lck, Lyn, Src, Yes, respectively).
Targets(IC_{50})	VEGFR1: 2 nM VEGFR2: 7 nM FGFR1: 2 nM FGFR2: 16 nM PDGFRβ: 13 nM
In vitro	TG 100801 is readily converted to the active TG 100572 in the eye.TG 100572 is shown to inhibit hRMVEC cell proliferation(IC50 of 610±72 nM)[1]. TG 100801 is formed by derivitization of a phenolic moiety in TG100572 to yield an ester. It displays excellent balance of stability (physical and chemical) with hydrolysis rate. On its own, TG 100801 does not display meaningful anti-kinase activity, as the ester group blocks key interactions with kinase active sites, however exposure to esterases (abundant in mammalian tissues) rapidly liberates active TG100572.TG 100572 shows sub-nanomolar activity against the Src family as well as RTK such as VEGFR1 and R2, FGFR1 and R2, and PDGFRβ. vascular endothelial cell proliferation with ED50 of 610±71 nM inhibited by TG 100572 and blocks VEGF-induced phosphorylation of extracellular signal-regulated kinase[2].
In vivo	A concentration of 23.4 μM (Cmax) of TG 100572 is reached in 30 min (Tmax)=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[1]. TG 100801 nor TG100572 are detectable in plasma following topical delivery of TG 100801, and adverse safety signals (such as weight loss) are not observed even with prolonged dosing schedules. Topical TG 100801 significantly suppresses laser-induced choroidal neovascularlization in mice, and reduces fluorescein leakage from the vasculature and retinal thickening measured by optical coherence tomography in a rat model or retinal vein occlusion.In a murine model of laser-induced choroidal neovascularization (CNV),Systemic delivery of TG 100572 causes significant suppression of CNV, but with an associated weight loss suggestive of systemic toxicity[2].

Solubility Information

Solubility	DMSO: 5.56 mg/mL (9.58 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.724 mL	8.62 mL	17.239 mL
5 mM	0.345 mL	1.724 mL	3.448 mL
10 mM	0.172 mL	0.862 mL	1.724 mL
50 mM	0.034 mL	0.172 mL	0.345 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. 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.

2. Doukas, John, et al. Topical administration of a multi-targeted kinase inhibitor suppresses choroidal neovascularization and retinal edema. Journal of Cellular Physiology (2008), 216(1), 29-37.

Tel:781-999-4286 E-mail:info@targetmol.com Address:36 Washington Street,Wellesley Hills,MA 02481