ZM323881 hydrochloride

Cat. No.: HY-15467A

CAS No.: 193000-39-4

Molecular Formula: $C_{22}H_{19}ClFN_3O_2$

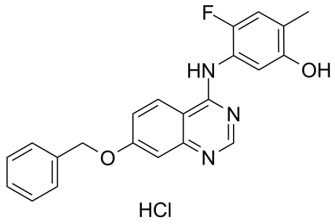
Molecular Weight: 411.86

Target: VEGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (121.40 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4280 mL	12.1400 mL	24.2801 mL
5 mM	0.4856 mL	2.4280 mL	4.8560 mL
10 mM	0.2428 mL	1.2140 mL	2.4280 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.07 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ZM323881 hydrochloride is a potent and selective VEGFR2 inhibitor with an IC_{50} of less than 2 nM.

IC_{50} & Target

VEGFR2

2 nM (IC_{50})

In Vitro

ZM323881 is an anilinoquinazoline that potently inhibits VEGFR2 (KDR) tyrosine kinase activity anddemonstrates excellent selectivity versus other receptor tyrosine kinases, including PDGFRβ, FGFR1, EGFR and erbB2 (IC_{50}>50 μM). ZM323881

inhibits VEGF-A-induced endothelial cell proliferation(IC_{50}=8 nM) and VEGFR2 tyrosine phosphorylation[1]. ZM323881 inhibits activation of VEGFR-2, but not of VEGFR-1, epidermal growth factor receptor (EGFR), platelet-derived growth factor receptor (PDGFR), or hepatocyte growth factor (HGF) receptor. In HAECs, ZM323881 completely inhibits VEGF-induced ERK phosphorylation at 1 μM[2]

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

PROTOCOL

Kinase Assay [1]

Compounds (ZM323881) are incubated (20 minutes, room temperature) with enzyme in an N-2-hydroxyethylpiperazine-N'-2-ethanesulphonate (HEPES) (pH 7.5) buffered solution containing 10 mM $MnCl_2$ and 2 μM ATP, in96-well plates coated with a poly(Glu, Ala, Tyr) 6:3:1 random copolymer substrate. Phosphorylated tyrosine is then detected bysequential incubation with mouse IgG anti-phosphotyrosine antibody a horseradish peroxidase(HRP)-linked sheep anti-mouse Ig antibody and 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid). IC_{50} data are interpolated by nonlin-ear regression[1].

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

Cell Assay [1]

HUVEC cells isolated from umbilical cords are plated (at passage 2–8) in 96-wellplates (1000 cells/well) and dosed with ZM323881±VEGF-A (3 ng/mL), EGF (3 ng/mL), or basicfibroblast growth factor (bFGF, 0.3 ng/mL). The cultures are then incubated for 4 days. On day 4, the cultures are pulsed with 1 μCi/well of ^3H-thymidine and reincubated for 4 hours. The cells are then harvested and assayed for the incorporation of tritium by using a beta-counter. IC_{50} data are interpolated[1].

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

CUSTOMER VALIDATION

- Front Physiol. 2018 Nov 30;9:1718.
- Oncotarget. 2016 Sep 27;7(39):63839-63855.

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REFERENCES

[1]. Whittles CE, et al. ZM323881, a novel inhibitor of vascular endothelial growth factor-receptor-2 tyrosine kinase activity. Microcirculation. 2002 Dec;9(6):513-22.

[2]. Endo A, et al. Selective inhibition of vascular endothelial growth factor receptor-2 (VEGFR-2) identifies a central role for VEGFR-2 in human aortic endothelial cell responses to VEGF. J Recept Signal Transduct Res. 2003;23(2-3):239-54.

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