Cabozantinib S-malate

Cat. No.: HY-12044

CAS No.: 1140909-48-3

Molecular Formula: $C_{32}H_{30}FN_3O_{10}$

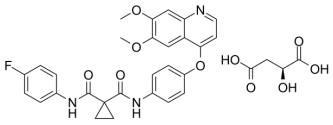
Molecular Weight: 635.59

Target: VEGFR; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (157.33 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5733 mL	7.8667 mL	15.7334 mL
5 mM	0.3147 mL	1.5733 mL	3.1467 mL
10 mM	0.1573 mL	0.7867 mL	1.5733 mL

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

BIOLOGICAL ACTIVITY

Description

Cabozantinib S-malate (XL184 S-malate) is a potent multiple receptor tyrosine kinases inhibitor that inhibits VEGFR2, c-Met, Kit, Axl and Flt3 with IC_{50}s of 0.035, 1.3, 4.6, 7 and 11.3 nM, respectively.

IC_{50} & Target

VEGFR2

0.035 nM (IC_{50})

In Vitro

Cabozantinib (0.1-0.5μM) inhibits the constitutive and inducible MET phosphorylation and its resultant downstream signaling in all MPNST cells. Cabozantinib (> 0.1μM) elicits a significant MPNST cell growth inhibition; higher Cabozantinib doses are needed to inhibit NSC growth. Cabozantinib treatment blocks HGF-induced MPNST motility and invasion (a similar effect of found on NSC)[2]. In cellular assays, cabozantinib inhibits phosphorylation of MET and VEGFR2, as well as KIT, FLT3, and AXL with IC_{50} values of 7.8, 1.9, 5.0, 7.5, and 42 μM, respectively. Cabozantinib also inhibits tubule formation in response to conditioned media derived from cultures of MDA-MB-231 (IC_{50}=5.1 nM), A431 (IC_{50}=4.1 nM), HT1080 (IC_{50}=7.7 nM), and B16F10 (IC_{50}=4.7 nM) cells[3].

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

In Vivo	Cabozantinib (60 mg/kg, i.p.) decreases the tumor vascularity with reductions ranging from 67% at 3 mg/kg to 83% at 30 mg/kg for 7 days in animals. Tumors in RIP-Tag2 mice treated for 7 days beginning at age 10 weeks are 40% smaller after XL880 and 35% smaller after Cabozantinib, compared to corresponding values for vehicle[1]. Cabozantinib (30 mg/kg) significantly decreases the microvessel density in mice[2]. Cabozantinib (100 mg/kg, p.o.) inhibits in vivo stimulation of MET phosphorylation by HGF in liver hepatocytes and VEGF-stimulated phosphorylation of FLK1 with inhibition of both targets sustained through 8 hours postdose. Cabozantinib (100 mg/kg, p.o.) disrupts tumor vasculature and promotes tumor and endothelial cell death. Cabozantinib (1-60 mg/kg, p.o.) inhibits tumor growth and promotes tumor regression in vivo[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [3]	The inhibition profile of cabozantinib against a broad panel of 270 human kinases is determined using luciferase-coupled chemiluminescence, ^{33}P-phosphoryl transfer, or AlphaScreen technology. Recombinant human full-length, glutathione S-transferase tag, or histidine tag fusion proteins are used, and half maximal inhibitory concentration (IC_{50}) values are determined by measuring phosphorylation of peptide substrate poly (Glu, Tyr) at ATP concentrations at or below the K_m for each respective kinase. The mechanism of kinase inhibition is evaluated using the AlphaScreen Assay by determining the IC_{50} values over a range of ATP concentrations. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [3]	Cells are seeded in triplicate overnight in media containing 10% FBS. The next day, cells are treated with serial dilutions of cabozantinib for 48 hours, followed by analysis of proliferation using Cell Proliferation ELISA, BrdUrd. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	H441 cells (3×10^6) are implanted intradermally into the hind flank and when tumors reach approximately 150 mg, tumor weight is calculated using the formula: (tumor volume=length (mm) × width^2 (mm^2)]/2, mice are randomized (n=5 per group) and orally administered a single 100 mg/kg dose of cabozantinib or vehicle. Tumors are collected at the indicated time points. Pooled tumor lysates are subjected to immunoprecipitation with anti-MET (SC161) and Western blotting with anti-phosphotyrosine MET (pY1230/34/35). After blot stripping, total MET is quantitated as a loading control. In a separate experiment, naive mice (n=5 per group) are administered a single 100 mg/kg dose of cabozantinib or vehicle, followed by intravenous administration of HGF (10 μg per mouse) 10 minutes before liver collection. Analysis of MET phosphorylation in liver lysates is as described above. In a separate experiment, naive mice (n=5 per group) are administered a single 100 mg/kg dose of cabozantinib or vehicle, followed by intravenous administration of VEGF (10 μg per mouse) 30 minutes before lung collection. Pooled lung lysates are subjected to immunoprecipitation with FLK1 (SC6251) and Western blotting with anti-phosphotyrosine (4G10). After blot stripping, total FLK1 is quantitated as a loading control. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Discov. 2021 Jan;11(1):126-141.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Biomaterials. 16 September 2022.
- Adv Healthc Mater. 2023 Aug 21;e2302046.
- Cancer Lett. 2019 Apr 10;447:105-114.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. You WK, et al. VEGF and c-Met blockade amplify angiogenesis inhibition in pancreatic islet cancer. Cancer Res, 2011, 71(14), 4758-4768.

[2]. Torres KE, et al. Activated MET is a molecular prognosticator and potential therapeutic target for malignant peripheral nerve sheath tumors. Clin Cancer Res, 2011, 17(12), 3943-3955.

[3]. Yakes FM, et al. Cabozantinib (XL184), a novel MET and VEGFR2 inhibitor, simultaneously suppresses metastasis, angiogenesis, and tumor growth. Mol Cancer Ther, 2011, 10(12), 2298-2308.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA