Cabozantinib

Cat. No.: HY-13016

CAS No.: 849217-68-1

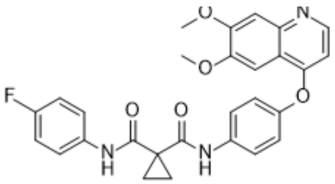
Molecular Formula: $C_{28}H_{24}FN_3O_5$

Molecular Weight: 501.51

Target: VEGFR; c-Met/HGFR; c-Kit; TAM Receptor; FLT3; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (49.85 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9940 mL	9.9699 mL	19.9398 mL
5 mM	0.3988 mL	1.9940 mL	3.9880 mL
10 mM	0.1994 mL	0.9970 mL	1.9940 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC/saline water
   Solubility: 2.5 mg/mL (4.98 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.98 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.15 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.15 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cabozantinib is a potent and orally active inhibitor of VEGFR2 and MET, with IC_{50} values of 0.035, and 1.3 nM, respectively. Cabozantinib displays strong inhibition of KIT, RET, AXL, TIE2, and FLT3 (IC_{50}=4.6, 5.2, 7, 14.3, and 11.3 nM, respectively). Cabozantinib shows antiangiogenic activity. Cabozantinib disrupts tumor vasculature and promotes tumor and endothelial

	cell apoptosis[1][2].

IC_{50} & Target				
	VEGFR2 0.035 nM (IC_{50})	Flt-4 6 nM (IC_{50})	Flt-1 12 nM (IC_{50})	Met 1.3 ± 1.2 nM (IC_{50})

In Vitro

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[1].
Cabozantinib (4.6 nM) inhibits tubule formation with no evidence of cytotoxicity, with IC_{50} values of 6.7, 5.1, 4.1, 7.7, and 4.7 nM in HMVEC, MDA-MB-231, A431, HT1080, and B16F10 cells, respectively[1].
Cabozantinib (0-370 nM, 24 h) inhibits cellular migration and invasion[1].
Cabozantinib (48 h) inhibits tumor cell proliferation in a variety of tumor types[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay

Cell Line:	SNU-5, Hs746T, SNU-1, SNU-16, MDA-MB-231, U87MG, H441, H69, and PC3 cells[1]
Concentration:	
Incubation Time:	48 hours
Result:	Inhibited tumor cell proliferation, with IC_{50} of 19, 9.9, 5223, 1149, 6421, 1851, 21700, 20200, and 10800 nM, respectively.

Cell Migration Assay

Cell Line:	B16F10 cells[1]
Concentration:	0, 41, 123, and 370 nM
Incubation Time:	24 hours
Result:	Potently inhibited HGF-induced migration (IC_{50} = 31 nM) of B16F10 cells.

Cell Invasion Assay

Cell Line:	B16F10 cells[1]
Concentration:	0, 1.5, 14, and 123 nM
Incubation Time:	24 hours
Result:	Potently inhibited HGF-induced invasion (IC_{50} = 9 nM) of B16F10 cells.

In Vivo

Cabozantinib (100 mg/kg, Orally, once) inhibits MET and VEGFR2 phosphorylation in mice[1].
Cabozantinib (100 mg/kg, Orally, once) significantly increases tumor hypoxia and apoptosis[1].
Cabozantinib (0-60 mg/kg, Orally, once daily for 14 days) inhibits tumor growth in a dose-dependent manner[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female mice bearing MBA-MB-231 tumor (5 per group)[1]
Dosage:	0, 100 mg/kg
Administration:	Orally, once
Result:	Inhibited MET and VEGFR2 phosphorylation.

Animal Model:	Mice bearing MBA-MB-231 tumor[1]
Dosage:	1, 3, 10, 30, 60 mg/kg
Administration:	Orally, once daily for 14 days
Result:	Inhibited tumor growth in a dose-dependent manner.

CUSTOMER VALIDATION

- Cancer Discov. 2021 Jan;11(1):126-141.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Biomaterials. 16 September 2022.
- Cancer Lett. 2019 Apr 10;447:105-114.
- J Pharm Anal. 2021 Jun 19.

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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]. 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.

[3]. Fuse MA, et al. Combination Therapy With c-Met and Src Inhibitors Induces Caspase-Dependent Apoptosis of Merlin-Deficient Schwann Cells and Suppresses Growth of Schwannoma Cells. Mol Cancer Ther. Mol Cancer Ther. 2017 Nov;16(11):2387-2398.

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