Fruquintinib

Cat. No.: HY-19912

CAS No.: 1194506-26-7

Molecular Formula: $C_{21}H_{19}N_3O_5$

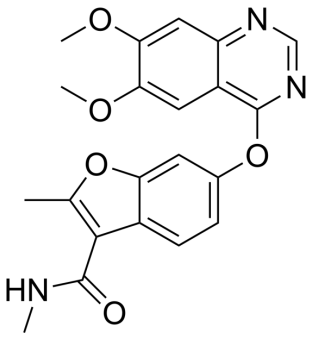
Molecular Weight: 393.39

Target: VEGFR

Pathway: Protein Tyrosine Kinase/RTK

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 : 10 mg/mL (25.42 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5420 mL	12.7100 mL	25.4201 mL
5 mM	0.5084 mL	2.5420 mL	5.0840 mL
10 mM	0.2542 mL	1.2710 mL	2.5420 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: ≥ 0.59 mg/mL (1.50 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.59 mg/mL (1.50 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.59 mg/mL (1.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Fruquintinib (HMPL-013) is a highly potent and selective VEGFR 1/2/3 inhibitor with IC_{50}s of 33, 0.35, and 35 nM, respectively.

IC_{50} & Target

VEGFR1	VEGFR2	VEGFR3
33 nM (IC_{50})	35 nM (IC_{50})	0.5 nM (IC_{50})

In Vitro

Fruquintinib demonstrates potent inhibition on VEGF-A dependent KDR phosphorylation in HEK293-KDR cells and VEGF-A induced proliferation in primary HUVECs with IC_{50}s of 0.6±0.2 nM and 1.7 nM, respectively. Similarly, potent VEGFR3

	attenuation by fruquintinib is observed in primary HLECs, with IC_{50}s of 1.5 nM and 4.2 nM for VEGF-C stimulated VEGFR3 phosphorylation and proliferation, respectively. Fruquintinib suppresses the tube branching, tube length and area in a concentration-dependent manner. The tubule length of primary HUVECs decreased by 74% and 94% at 0.03 and 0.3 μM of fruquintinib, respectively. Fruquintinib inhibits HUVEC tubule growth and CAM angiogenesis. Tube formation is suppressed significantly after treatment with fruquintinib at 0.3 μM for 18 hours[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Gastric cancer BGC-823 model is found to be most sensitive to fruquintinib. In this model, fruquintinib inhibits tumor growth by 62.3% and 95.4%98.6%, at 0.5 and 2 mg/kg once daily dosing, respectively. When the dose is elevated to 5 mg/kg and 20 mg/kg, the tumors regress by 24.1% and 48.6%, respectively. The level of anti-tumor growth activity of fruquintinib varies in different tumor xenograft models. Fruquintinib significantly decreases the micro-vessel density even at the lowest dose of 0.8 mg/kg[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Primary HUVECs or HLECs in exponential phase are suspended in 100 μL of RPMI-1640 media containing 0.5% FBS, and seeded at 5000 cell/well in 96-well plates pre-coated with 0.2% gelatin or fibronectin, and incubated overnight in a 5% CO_2, 37°C incubator. Fruquintinib and VEGF-A165 or VEGF-C (50 ng/mL) are added and incubated for 48 hours. Viability of the cells is determined using CCK-8 assay format[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: The patient derived xenograft models are established after the primary tumor adopted serial passages in vivo. Once tumors have grown to 100-300 mm^3, the animals are randomly assigned with 6-8 animals per group. The mice are treated orally with the vehicle (control group) or fruquintinib at a dose range of 0.5-20 mg/kg suspended in the vehicle (treated group) once daily for 3 weeks. In combination studies, docetaxel (Taxotere, 5 mg/kg) or oxaliplatin (10 mg/kg) is administered to nude mouse via intravenous injection, once a week. Tumor size and body weights are measured 3 times a week. Tumor volumes (TV) are calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Syst Biol. 2023 Dec 18.
- Eur J Med Chem. 2023 Nov 5, 259, 115703.
- Chemotherapy. 2023 Jan 9.
- Biochem Biophys Res Commun. 2023 Apr 10.
- Cell Reprogram. 2021 Jun 2.

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REFERENCES

[1]. Sun Q, et al. Discovery of fruquintinib, a potent and highly selective small molecule inhibitor of VEGFR 1, 2, 3 tyrosine kinases for cancer therapy. Cancer Biol Ther. 2014;15(12):1635-45.

Caution: Product has not been fully validated for medical applications. For research use only.

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