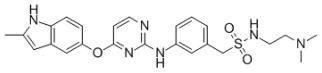
Sulfatinib

Cat. No.:	HY-12297
CAS No.:	1308672-74-3
Molecular Formula:	$C_{24}H_{28}N_6O_3S$
Molecular Weight:	480.58
Target:	FGFR; VEGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (208.08 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0808 mL	10.4041 mL	20.8082 mL
5 mM	0.4162 mL	2.0808 mL	4.1616 mL
10 mM	0.2081 mL	1.0404 mL	2.0808 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 (5.20 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.5 mg/mL (5.20 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.5 mg/mL (5.20 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Sulfatinib (HMPL-012) is a potent and highly selective tyrosine kinase inhibitor against **VEGFR1/2/3**, **FGFR1** and **CSF1R** with **IC_{50}**s of in a range of 1 to 24 nM.

IC_{50} & Target	VEGFR1	VEGFR2	VEGFR3	FGFR1

	CSF1R
In Vitro	Sulfatinib inhibits VEGFR1, 2, and 3, FGFR1 and CSF1R kinases with IC_{50}s in a range of 1 to 24 nM, and it strongly blocks VEGF induced VEGFR2 phosphorylation in HEK293KDR cells and CSF1 stimulated CSF1R phosphorylation in RAW264.7 cells with IC_{50} of 2 and 79 nM, respectively. Sulfatinib also attenuates VEGF or FGF stimulated HUVEC cells proliferation with IC_{50}< 50 nM[1]. Also, it is a hERG inhibitor with **IC_{50}** of 6.8 μM in CHO cell[2].
In Vivo	In animal studies, a single oral dosing of Sulfatinib inhibits VEGF stimulated VEGFR2 phosphorylation in lung tissues of nude mice in an exposure-dependent manner. Furthermore, elevation of FGF23 levels in plasma 24 hours post dosing suggests suppression of FGFR signaling. Sulfatinib demonstrates potent tumor growth inhibition in multiple human xenograft models and decreases CD31 expression remarkably, suggesting strong inhibition on angiogenesis through VEGFR and FGFR signaling. In a syngeneic murine colon cancer model CT-26, Sulfatinib demonstrates moderate tumor growth inhibition after single agent treatment[1]. After oral dosing of 10 mg/kg, the AUC and C_{max} are 397 ng/mL and 138ng/mL in the mouse, respectively[1].

PROTOCOL

Kinase Assay [2]	The KDR kinase inhibition activity is tested using the the Z-lyte assay kit. The testing system contains 300 ng/mL of recombinant human KDR catalytic domain, 10 μM of ATP, 1 μM of substrate peptide, and a test compound (Sulfatinib) at a series of different concentrations in 384-well plate; total volume is 10 μL. The enzyme inhibition proceeds at room temperature (25°C), for 1 hour at room temperature on the shaker. 5 μL of stop solution is added to stop the reaction[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	The phamacokinetics of Sulfatinib are studied with male ICR mice (n=6 for each group, weight 20-30g) after a single intraveneous and oral dosing at 2.5 and 10mg/kg, respectively. For i.v. dosing formulation, Sulfatinib is dissolved in DMSO (0.25%)-solutol(10%)-ethanol(10%)-physiological saline(79.75%) at the concentration of 0.25 mg/mL. And the p.o. Dosing formulation (1mg/mL) is prepared with 0.5% CMC-Na. After i.v. Or p.o. Dosing, blood samples are collected via the ophthalmic vein at 0 (pre-close), 5, 15, 30 min and 1, 1.5, 2, 4, 8, 24 h, anti-coagulated with heparin-Na. After centrifugation, plasma samples are seprated and protein precipitated with acetonitrilel containing internal standard[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. PCT Int. Appl. (2011), WO 2011060746 A1 20110526.

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