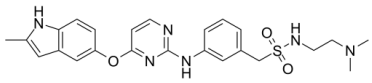
Data Sheet

Product Name:	Sulfatinib
Cat. No.:	CS-5949
CAS No.:	1308672-74-3
Molecular Formula:	C24H28N6O3S
Molecular Weight:	480.58
Target:	FGFR; VEGFR
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 100 mg/mL (208.08 mM)



BIOLOGICAL ACTIVITY:

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. **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 (Extracted from published papers and Only for reference)

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]. **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].

References:

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

CAIndexNames:

Benzenemethanesulfonamide, N-[2-(dimethylamino)ethyl]-3-[[4-[(2-methyl-1H-indol-5-yl)oxy]-2-pyrimidinyl]amino]-

SMILES:

O=S(CC1=CC=CC(NC2=NC=CC(OC3=CC4=C(NC(C)=C4)C=C3)=N2)=C1)(NCCN(C)C)=O

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

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