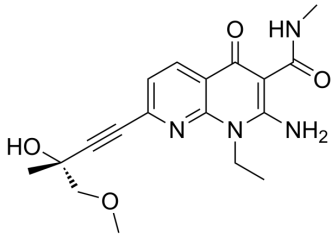
SAR131675

Cat. No.:	HY-15458
CAS No.:	1433953-83-3
Molecular Formula:	$C_{18}H_{22}N_4O_4$
Molecular Weight:	358.39
Target:	VEGFR
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (279.03 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7903 mL	13.9513 mL	27.9026 mL
	5 mM	0.5581 mL	2.7903 mL	5.5805 mL
	10 mM	0.2790 mL	1.3951 mL	2.7903 mL

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 10 mg/mL (27.90 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.43 mg/mL (3.99 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.43 mg/mL (3.99 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.43 mg/mL (3.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SAR131675 is a potent and selective VEGFR3 inhibitor with an IC_{50} of 23 nM. SAR131675 is a click chemistry reagent, it contains an Alkyne group and can undergo copper-catalyzed azide-alkyne cycloaddition (CuAAc) with molecules containing Azide groups.

IC_{50} & Target

VEGFR3

	23 nM (IC_{50})
In Vitro	AR131675 is highly selective for VEGFR-3. However, it is moderately active on VEGFR-2 with a VEGFR-3/VEGFR-2 ratio of about 10. SAR131675 inhibits VEGFR-3 tyrosine kinase activity and VEGFR-3 autophosphorylation in HEK cells with IC_{50} values of 20 and 45 nM, respectively. SAR131675 dose dependently inhibits the proliferation of primary human lymphatic cells, induced by the VEGFR-3 ligands VEGFC and VEGFD, with an IC_{50} of about 20 nM. SSAR131675 has no antiproliferative activity on a panel of 30 tumors and primary cells, further showing its high specificity and indicating that SAR131675 is not a cytotoxic or cytostatic agent[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SAR131675 is very well tolerated in mice and shows a potent antitumoral effect in several orthotopic and syngenic models, including mammary 4T1 carcinoma and RIP1.Tag2 tumors. Interestingly, it significantly reduces lymph node invasion and lung metastasis, showing its antilymphangiogenic activity in vivo. SAR131675 significantly reduces TAM infiltration and aggregation in 4T1 tumors[1]. Despite the promising findings, SAR131675 development was terminated during preclinical development due to adverse metabolic effects[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Multiwell plates are precoated with a synthetic polymer substrate poly-Glu-Tyr (polyGT 4:1). The reaction is carried out in the presence of kinase buffer (10×: 50 mM HEPES buffer, pH 7.4, 20 mM $MgCl_2$, 0.1 mM $MnCl_2$, and 0.2 mM Na_3VO_4) supplemented with ATP and dimethyl sulfoxide (DMSO) for the positive control (C+) or SAR131675 (ranging from 3-1,000 nM). ATP is used at 30 µM for VEGFR-1 and VEGFR-3 and at 15 µM for VEGFR-2. The phosphorylated poly-GT is probed with a phosphotyrosine specific monoclonal antibody (mAb) conjugated to horseradish peroxidase and developed in the dark with the HRP chromogenic substrate (OPD). The reaction is then stopped by the addition of 100 µL 1.25 mol/L H_2SO_4, and absorbance is determined using an Envision spectrophotometer at 492 nm[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	HLMVECs are seeded in 96-well plates coated with 0.3% gelatin (5000 cells per well). Cells are incubated in RPMI 0.1% FCS with VEGFA (10 ng/mL) VEGFC (300 ng/mL), VEGFD (300 ng/mL), or FGF2 (10 ng/mL) in the absence or presence of SAR131675. Five days later, viable cells are quantified with the cell Titer-glo luminescent cell viability assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mouse: Sterile sponge disks impregnated with 200 µg of FGF2 or PBS are subcutaneously introduced on the back of anaesthetized mice. FGF2 is reinjected into the sponges the first 2 days. Daily oral treatment with SAR131675 (30, 100, and 300 mg/kg/d) started the day of sponge implantation. Seven days later, the animals are euthanatized and the sponges are removed, harvested, and lysed in RIPA buffer at 4°C. After a centrifugation at 6,000 × g, the supernatants are collected for further analysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Elife. 2020 Dec 7;9:e61405.
- Stem Cell Res Ther. 2022 Sep 5;13(1):448.
- Transl Stroke Res. 2021 Dec;12(6):991-1017.
- J Cell Biochem. 2020 Mar;121(3):2343-2353.
- Research Square Preprint. 2023 Nov 14.

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REFERENCES

[1]. Paillasse MR, Esquerré M, Bertrand FA, et al. Targeting Tumor Angiogenesis with the Selective VEGFR-3 Inhibitor EVT801 in Combination with Cancer Immunotherapy. Cancer Res Commun. 2022;2(11):1504-1519.

[2]. Alam A, et al. SAR131675, a potent and selective VEGFR-3-TK inhibitor with antilymphangiogenic, antitumoral, and antimetastatic activities. Mol Cancer Ther. 2012 Aug;11(8):1637-49.

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