CEP-33779

Cat. No.: HY-15343

CAS No.: 1257704-57-6

Molecular Formula: $C_{24}H_{26}N_6O_2S$

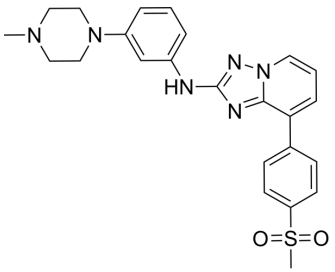
Molecular Weight: 462.57

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt

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 : 8.33 mg/mL (18.01 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1618 mL	10.8092 mL	21.6183 mL
5 mM	0.4324 mL	2.1618 mL	4.3237 mL
10 mM	0.2162 mL	1.0809 mL	2.1618 mL

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

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (21.62 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CEP-33779 is a novel, selective, and orally bioavailable inhibitor of JAK2 with an IC_{50} of 1.8±0.6 nM.

IC_{50} & Target

JAK2	JAK3
1.8 nM (IC_{50})	150 nM (IC_{50})

In Vitro	CEP-33779, at nontoxic concentrations, significantly sensitizes overexpression of P-glycoprotein overexpressing multidrug resistance cells to its anticancer substrates. CEP-33779 significantly increases intracellular accumulation and decreases the efflux of doxorubicin by inhibiting the overexpression of P-glycoprotein transport function[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CEP-33779 exhibits a favorable PK profile in nude mice, an iv half-life of 1 h, moderate distribution (Vd=2.6 L/kg), and measurable oral exposure with an estimated bioavailability of 33%. It demonstrates antitumor efficacy in the CWR22 xenograft model; oral dosing for 14 days at 30 mg/kg bid results in tumor stasis and partial regressions in 5/10 animals[1]. CEP-33779 administration results in an almost complete shrinkage of tumors in most animals; few remaining tumor nodules were small, poorly vascularized, and had a necrotic appearance. CEP-33779 suppressed activation of NF-κB in tumors[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The kinase activity of baculovirus-expressed human JAK1, JAK2, or JAK3 is measured. Each 96-well Costar high binding plate is coated with 100 µL/well of 10 µg/mL neutravidin in TBS at 37 °C for 2 h, followed by 100 µL/well of 1 µg/mL 15-mer peptide substrate at 37 °C for 1 h. The kinase assay mixture (total volume=100 µL/well) consisting of 20 mM HEPES (pH 7.2), ATP (0.2 µM ATP for JAK1 and JAK2 and 0.1 µM ATP for JAK3), 1 mM $MnCl_2$, 0.1% BSA, and CEP-33779 (diluted in DMSO, 2.5% DMSO final in assay) is added to the assay plate. Enzyme is added and the reaction is allowed to proceed for 20 min at room temperature. Detection of the phosphorylated product is performed by adding 100 µL/well of diluted Eu-N1 labeled PY100 antibody. Samples are incubated at RT for 1 h, followed by addition of 100 µL enhancement solution. Plates are agitated for 10 min, and the fluorescence of the resulting solution is measured. IC_{50} values are determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Nude mice bearing CWR22 xenografts are dosed orally with 55 mg/kg of CEP-33779 or a vehicle (PEG400). At 2, 6, and 24 h after dosing animals (3/group) are sacrificed, tumors are excised and plasma samples are prepared. Tumor extracts are prepared using Triton-based extraction buffer supplemented with inhibitors of proteases and phosphatases. Equal amounts of extracts are resolved on SDS-PAGE gels and STAT3 phosphorylation and expression are analyzed by Western blot using specific antibodies[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Rep. 2021 Jul 28;11(1):15319.
- Patent. US20180263995A1.

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REFERENCES

[1]. Dugan BJ, et al. A selective, orally bioavailable 1,2,4-triazolo[1,5-a]pyridine-based inhibitor of Janus kinase 2 for use in anticancer therapy: discovery of CEP-33779. J Med Chem. 2012 Jun 14;55(11):5243-54.

[2]. Seavey MM, et al. Therapeutic efficacy of CEP-33779, a novel selective JAK2 inhibitor, in a mouse model of colitis-induced colorectal cancer. Mol Cancer Ther. 2012 Apr;11(4):984-93.

[3]. Tang SJ, et al. CEP-33779 antagonizes ATP-binding cassette subfamily B member 1 mediated multidrug resistance by inhibiting its transport function. Biochem Pharmacol. 2014 Sep 15;91(2):144-56.

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

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