KW-2449

Cat. No.: HY-10339

CAS No.: 1000669-72-6

Molecular Formula: $C_{20}H_{20}N_4O$

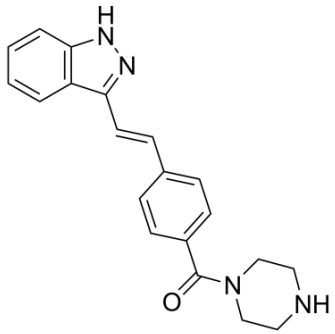
Molecular Weight: 332.4

Target: FLT3; FGFR; Bcr-Abl; Aurora Kinase; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Cell Cycle/DNA Damage; Epigenetics; Apoptosis

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 : ≥ 50 mg/mL (150.42 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0084 mL	15.0421 mL	30.0842 mL
5 mM	0.6017 mL	3.0084 mL	6.0168 mL
10 mM	0.3008 mL	1.5042 mL	3.0084 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 (7.52 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.52 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.52 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

KW-2449 is a multi-targeted kinase inhibitor of FLT3, ABL, ABL^{T315I} and Aurora kinase with IC_{50}s of 6.6, 14, 4 and 48 nM, respectively.

IC_{50} & Target

Abl 4 nM (IC_{50})	ABL-T315I 14 nM (IC_{50})	FGFR1 36 nM (IC_{50})	Aurora A 48 nM (IC_{50})
FLT3/D835Y	FLT3	JAK2	SRC

	1 nM (IC_{50})	6.6 nM (IC_{50})	150 nM (IC_{50})	400 nM (IC_{50})
	PDFGRα 1700 nM (IC_{50})			
In Vitro	KW-2449 shows growth inhibitory activities against FLT3/ITD-, FLT3/D835Y-, and wt-FLT3/FL-expressing 32D cells, MOLM-13 and MV4;11 with GI_{50} values of 0.024, 0.046, 0.014, 0.024, and 0.011 μM, respectively. KW-2449 suppresses the phosphorylations of FLT3 (P-FLT3) and its downstream molecule phospho-STAT5 (P-STAT5) in MOLM-13 cells in a dose-dependent manner. KW-2449 increases the percentage of cells in the G1 phase of the cell cycle and reciprocally reduced the percentage of cells in the S phase, resulting in the increase of apoptotic cell population[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			
In Vivo	Oral administration of KW-2449 shows dose-dependent and significant tumor growth inhibition in FLT3-mutated xenograft model with minimum bone marrow suppression. In FLT3 wild-type human leukemia, it induces the reduction of phosphorylated histone H3, G2/M arrest, and apoptosis. In imatinib-resistant leukemia, KW-2449 contributes to release of the resistance by the simultaneous down-regulation of BCR/ABL and Aurora kinases. Furthermore, the antiproliferative activity of KW-2449 is confirmed in primary samples from AML and imatinib-resistant patients. The inhibitory activity of KW-2449 is not affected by the presence of human plasma protein, such as α1-acid glycoprotein[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			

PROTOCOL

Cell Assay [1]	Cell viability is determined by the sodium 3′-[1-(phenylaminocarbonyl)-3, 4-tetrazolium]-bis (4-methoxy-6-nitro) benzene sulfonic acid hydrate assay after incubation with or without KW-2449 for 72 hours at 37°C. The number of viable cells is determined using the Cell Proliferation Kit II[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: SCID mice are subcutaneously inoculated with MOLM-13 cells. Five days after inoculation, tumor volume is measured using the Antitumor test system II. The 25 mice with tumors ranging from 90 to 130 mm^3 are selected and randomized using the Antitumor test system II. From the day of randomization, vehicle (0.5 wt/vol% MC400) or KW-2449 (2.5, 5.0, 10, and 20 mg/kg) is orally administered to mice twice a day for 14 days. Tumor volume is measured twice a week during the treatment [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Biochem Pharmacol. 2021, 114542.
- Int J Mol Sci. 2019 Apr 29;20(9):2112.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Shiotsu Y, et al. KW-2449, a novel multikinase inhibitor, suppresses the growth of leukemia cells with FLT3 mutations or T315I-mutated BCR/ABL translocation. Blood. 2009 Aug 20;114(8):1607-17.

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

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