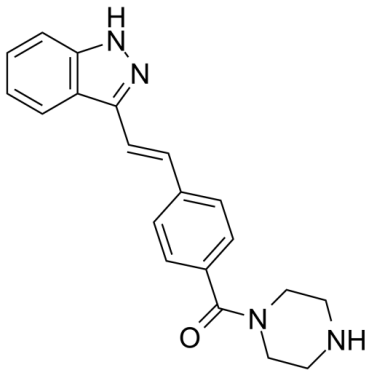
Data Sheet

Product Name:	KW-2449
Cat. No.:	CS-0231
CAS No.:	1000669-72-6
Molecular Formula:	$C_{20}H_{20}N_4O$
Molecular Weight:	332.40
Target:	Apoptosis; Aurora Kinase; Bcr-Abl; FGFR; FLT3
Pathway:	Apoptosis; Cell Cycle/DNA Damage; Epigenetics; Protein Tyrosine Kinase/RTK
Solubility:	DMSO : ≥ 50 mg/mL (150.42 mM)



BIOLOGICAL ACTIVITY:

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. IC50 & Target: IC50: 6.6 nM (FLT3), 14 nM (ABL), 4 nM (ABL^{T315I}), 48 nM (Aurora kinase)[1] **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **Animal Administration:** KW-2449 is prepared in 0.5 wt/vol% MC400[1].[1]Mouse: 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].

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.

CAIndexNames:

Methanone, [4-[2-(1H-indazol-3-yl)ethenyl]phenyl]-1-piperazinyl-

SMILES:

O=C(C1=CC=C(/C=C/C2=NNC3=C2C=CC=C3)C=C1)N4CCNCC4

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

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