Product Name: KW 2449

Revision Date: 6/30/2018

Product Data Sheet

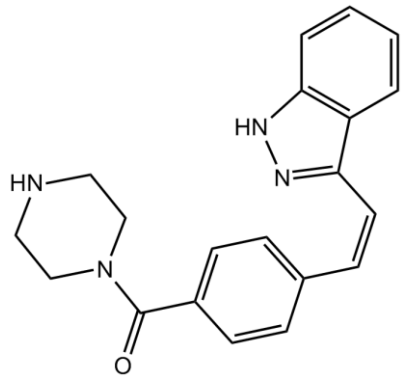
Chemical Properties

Product Name: KW 2449

Cas No.: 1000669-72-6

M.Wt: 332.4

Formula: C20H20N4O



Chemical Name: [4-[(E)-2-(1H-indazol-3-yl)ethenyl]phenyl]-piperazin-1-ylmethanone

Canonical SMILES: C1CN(CCN1)C(=O)C2=CC=C(C=C2)C=CC3=NNC4=CC=CC=C43

Solubility: ≥16.6 mg/mL in DMSO, <2.25 mg/mL in EtOH, <2.39 mg/mL in H2O

Storage: Store at -20°C

General tips: For obtaining a higher solubility , please warm the tube at 37° C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20° C for several months.

Shopping Condition: Evaluation sample solution : ship with blue ice
All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets : Tyrosine Kinase

Pathways: FLT3

Description:

KW 2449 is a multikinase inhibitor of FLT3, ABL, ABL-T315I, and Aurora kinase with IC50 values of 6.6nM, 14nM, 4nM and 48nM, respectively [1].
KW-2449 is a potent kinase inhibitor against FLT3, ABL, T315I-mutant ABL (ABL-T315I) tyrosine kinases as well as Aurora kinase. In vitro assay shows KW-2449 has the potency of growth inhibition with different mechanisms. In leukemia cells with FLT3 mutations, KW-2449 down-regulates phosphorylated-FLT3/STAT5, induces G1 arrest and apoptosis. KW-2449 also inhibits tumor growth in FLT3-mutated xenograft model. While in leukemia cells with wild-type

FLT3, KW-2449 reduces phosphorylated histone H3, induces G2/M arrest and apoptosis. However, it is reported that the AML patients treated with LT3 inhibitors, such as KW-2449, have only partial FLT3 inhibition in vivo. And the plasma level of FL (the ligand of FLT3) appears to rise after chemotherapy, which impeding the efficacy of the FLT3 inhibitors [1, 2].

***Reference**:*
[1] Shiotsu Y, Kiyoi H, Ishikawa Y, Tanizaki R, Shimizu M, Umehara H, Ishii K, Mori Y, Ozeki K, Minami Y, Abe A, Maeda H, Akiyama T, Kanda Y, Sato Y, Akinaga S, Naoe T. 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.
[2] Sato T, Yang X, Knapper S, White P, Smith BD, Galkin S, Small D, Burnett A, Levis M. FLT3 ligand impedes the efficacy of FLT3 inhibitors in vitro and in vivo. Blood. 2011 Mar 24;117(12):3286-93.

Protocol

Cell experiment:

Cell lines	MOLM-13 cells
Preparation method	The solubility of this compound in DMSO is >16.6mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting conditions	
Applications	In MOLM-13 cells, KW-2449 inhibited the phosphorylation of FLT3 (P-FLT3) and its downstream molecule phospho-STAT5 (P-STAT5) in a dose-dependent way. Furthermore, KW-2449 increased the percentage of cells in the G1 phase and reduced the percentage of cells in the S phase, resulting in the increase of apoptotic cell population.

Animal experiment [3]:

Animal models	SCID mice bearing the subcutaneous MOLM-13 tumor
Dosage form	2.5, 5.0, 10, and 20 mg/kg; orally administered; twice a day for 14 days
Applications	In SCID mice bearing the subcutaneous MOLM-13 tumor, KW-2449 completely reduced the levels of P-FLT3 and P-STAT5 in the tumor from 4 to 12 hours. While the phosphorylation of FLT3 and STAT5 returned to almost the basal level at 24 hours. KW-2449 showed a potent and significant antitumor effect in a dose-dependent way.

Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:
[1] Shiotsu Y, Kiyoi H, Ishikawa Y, Tanizaki R, Shimizu M, Umehara H, Ishii K, Mori Y, Ozeki K, Minami Y, Abe A, Maeda H, Akiyama T, Kanda Y, Sato Y, Akinaga S, Naoe T. 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

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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