BAY 61-3606 dihydrochloride

Cat. No.: HY-14985

CAS No.: 648903-57-5

Molecular Formula: $C_{20}H_{20}Cl_2N_6O_3$

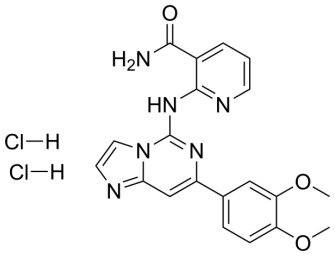
Molecular Weight: 463.32

Target: Syk; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage: -20°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

H_2O : 4.55 mg/mL (9.82 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1583 mL	10.7917 mL	21.5834 mL
	5 mM	0.4317 mL	2.1583 mL	4.3167 mL
	10 mM	---	---	---

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: ≥ 0.71 mg/mL (1.53 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.71 mg/mL (1.53 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BAY 61-3606 dihydrochloride is an orally available, ATP-competitive, reversible and highly selective Syk inhibitor with a K_i of 7.5 nM an IC_{50} of 10 nM[1]. BAY 61-3606 dihydrochloride reduces ERK1/2 and Akt phosphorylation in neuroblastoma cell[2]. BAY 61-3606 dihydrochloride induces a large decrease of Syk phosphorylation in K-rn cell lysates[3]. Bay 61-3606 dihydrochloride sensitizes TRAIL-induced apoptosis by downregulating Mcl-1 in breast cancer cells[4].

IC_{50} & Target

Ki: 7.5 nM (Syk)[1]
IC50: 10 nM (Syk)[1]

In Vitro

BAY 61-3606 (0.01-10 μM ; 48 hours) significantly reduces the cell viability of SYK-positive SH-SY5Y and SYK-negative SK-N-BE cells in a dose-dependent matter. SH-SY5Y cells expressing high SYK levels are significantly more sensitive to BAY 61-3606 in comparison to SK-N-BEcells expressing very low or no SYK[2].

BAY 61-3606 (0.4 and 0.8 μM; 4 or 24 hours) inhibits SYK activity by reducing ERK1/2 and Akt phosphorylation in neuroblastoma cell SH-SY5Y[2].
BAY 61-3606 (2 μM; 2 hours) induces a large decrease of Syk phosphorylation in K-rn cell lysates[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	SYK-positive SH-SY5Y and SYK-negative SK-N-BE cells
Concentration:	0.01, 0.1, 1, and 10 μM
Incubation Time:	48 hours
Result:	Significantly reduced the cell viability of both cell lines in a dose-dependent matter.

Cell Proliferation Assay[2]

Cell Line:	SH-SY5Y cells
Concentration:	0.4 and 0.8 μM
Incubation Time:	4 or 24 hours
Result:	Reduced the phosphorylation of ERK1/2 and Akt after a 4 or 24 h treatment.

Western Blot Analysis[3]

Cell Line:	K-rn cell lysates
Concentration:	2 μM
Incubation Time:	2 hours
Result:	Induced a large decrease of Syk phosphorylation.

In Vivo

Bay 61-3606 (50 mg/kg; administered twice a week for two weeks by intraperitoneal injection) alone leads to more efficacious reductions than that of TNF-related apoptosis-inducing ligand (TRAIL; 10 mg/kg) alone in MCF-7 tumor xenograft-bearing BALB/c nude mice. Bay 61-3606 administered in TRAIL combination significantly reduces the volume of the xenografted tumor[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female BALB/c nude mice (5 weeks old) bearing MCF-7 tumor xenograft[4]
Dosage:	50 mg/kg
Administration:	Injected intraperitoneally twice a week with Bay 61–3606 (50 mg/kg), TRAIL (10 mg/kg) or a combination of Bay 61-3606 (50 mg/kg) and TRAIL (10 mg/kg); TRAIL was given 2 h after the injection of Bay 61-3606; for two weeks
Result:	Led to efficacious reductions in tumor growth.

CUSTOMER VALIDATION

- Neuro Oncol. 2018 Apr 9;20(5):621-631.
- Proc Natl Acad Sci U S A. 2022 Oct 25;119(43):e2207280119.

- Front Immunol. 2018 Feb 15;9:249.
- Int J Mol Sci. 2021, 22(7), 3323.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Yamamoto N, et al. The orally available spleen tyrosine kinase inhibitor 2-[7-(3,4-dimethoxyphenyl)-imidazo[1,2-c]pyrimidin-5-ylamino]nicotinamide dihydrochloride (BAY 61-3606) blocks antigen-induced airway inflammation in rodents. J Pharmacol Exp Ther. 2003 Sep;306(3):1174-81.

[2]. Tümmler C, et al. SYK Inhibition Potentiates the Effect of Chemotherapeutic Drugs on Neuroblastoma Cells in Vitro. Cancers (Basel). 2019 Feb 10;11(2). pii: E202.

[3]. Gioia R, et al. Quantitative phosphoproteomics revealed interplay between Syk and Lyn in the resistance to AMN107 in chronic myeloid leukemia cells. Blood. 2011 Aug 25;118(8):2211-21.

[4]. Kim SY, et al. Bay 61-3606 Sensitizes TRAIL-Induced Apoptosis by Downregulating Mcl-1 in Breast Cancer Cells. PLoS One. 2015 Dec 31;10(12):e0146073.

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