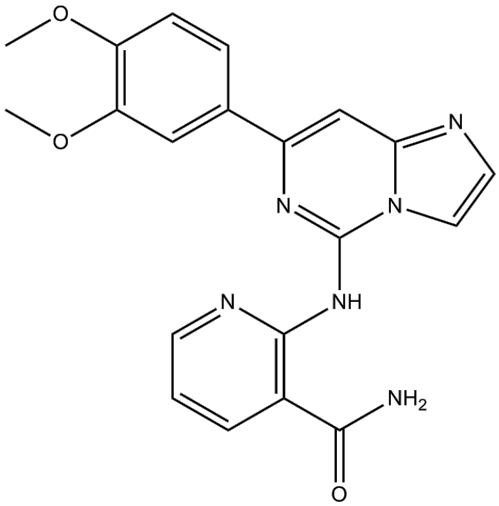
Product Data Sheet

Product Name: BAY 61-3606
Cat. No.: GC16389

Chemical Properties

Cas. No.	732983-37-8		
Chemical Name	2-[[7-(3,4-dimethoxyphenyl)imidazo[1,2-c]pyrimidin-5-yl]amino]pyridine-3-carboxamide		
SMILES	COC1=C(C=C(C=C1)C2=CC3=NC=CN3C(=N2)NC4=C(C=CC=N4)C(=O)N)OC.Cl		
Formula	$C_{20}H_{18}N_6O_3$	M.Wt	390.4
Solubility	DMSO: 30 mg/mL	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.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines SH-SY5Y cells

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Preparation Method	SH-SY5Y cells were cultivated in RPMI-1640 medium containing L-glutamine and sodium bicarbonate supplemented with 10% heat-inactivated fetal bovine serum (FBS) at 37°C in an incubator with 5% CO_2. Cells were seeded in 96-well plates at 3000 cells/well. After 24 hours, BAY 61-3606 was added in a concentration series of 0.1, 0.2, 0.4, 0.6, 0.8 and 1.0μM. Three technical replicates were carried out. Cells were incubated with the addition of BAY 61-3606 for 24 hours before assessing cell viability.
Reaction Conditions	0.1, 0.2, 0.4, 0.6, 0.8 and 1.0μM; 24h
Applications	BAY 61-3606 treatment inhibited cell viability of SH-SY5Y cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	Male C57BL/10ScNJ mice

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Preparation Method	Male C57BL/10ScNJ mice, aged 8 weeks with weights of 23.02±1.64g, were maintained in a controlled environment at 22±3°C and 60% relative humidity under a 12h light/dark cycle, and were given free access to standard rodent nutrition and water. After anesthesia with 5% isoflurane in oxygen with a delivery rate of 0.5l/min for induction and 2% isoflurane for maintenance, the mice were placed onto a stereotaxic apparatus platform. Sterile procedures were adhered to and an incision was first made along the midline. Subsequently, a $3mm^2$ craniotomy was performed at the following specific location: Left hemisphere; 1mm anterior-λ; 1mm left-midline; and 1 mm post-bregma. In total, $3mm^2$ of the skull was removed avoiding damage to the dura mater. The cerebral cortex extract (CCE) parameters were as follows: i) Deformation depth, 1mm; ii) impact speed, 3.5m/sec and iii) duration, 400msec. The incision was then sutured and the mice were placed on a 36-37°C heat pad. Mice were administered with BAY 61-3606 (3mg/kg/day) intraperitoneally for 7 days after TBI insult. The locomotor ability and balance function of mice were evaluated.
Dosage form	3mg/kg/day for 7 days; i.p.
Applications	BAY 61-3606 treatment improved locomotor ability and balance function in mice with TBI.

References:

[1] Tümmler C, Dumitriu G, Wickström M, et al. SYK inhibition potentiates the effect of chemotherapeutic drugs on neuroblastoma cells in vitro[J]. Cancers, 2019, 11(2): 202.
[2] He X, Huang Y, Liu Y, et al. BAY61-3606 attenuates neuroinflammation and neurofunctional damage by inhibiting microglial Mincle/Syk signaling response after traumatic brain injury[J]. International journal of molecular medicine, 2022, 49(1): 1-13.

Background

BAY 61-3606 is a potent and selective inhibitor of Syk kinase with a K_i value of 7.5nM [1]. BAY 61-3606 can downregulate MDM2 phosphorylation, upregulate P53 level and induce PARP cleavage as

well as the degradation of IKZF1 and IKZF3 proteins[2]. BAY 61-3606 has been widely used to inhibit the growth of various cancer cells and enhance the sensitivity of cancer cells to apoptosis induced by TRAIL[3].

In vitro, BAY 61-3606 treatment (0.8μM) for 24 hours significantly inhibited the viability of SH-SY5Y cells and decreased the phosphorylation levels of ERK1/2 and Akt[4]. Treatment with 10nM BAY 61-3606 for 48 hours significantly caused morphological changes, DNA fragmentation and cell death in human vestibular schwannomas (VS) cells, and significantly reduced the total and phosphorylated levels of pRb protein[5]. Treatment with 1μM BAY 61-3606 for 72 hours significantly inhibited human cytomegalovirus (HCMV) infection of human foreskin fibroblast (HFF), reduced IKKα kinase activity, and inhibited the accumulation of H3K9ac, H3K18ac and H3K27ac[6].

In vivo, BAY 61-3606 treatment via daily intraperitoneal injection at a dose of 3mg/kg for 7 days significantly alleviated the neuroglial dysfunction and reduced the neuroinflammation in mice with traumatic brain injury (TBI)[7]. One hour after zymosan (ZYM) injection (500mg/kg; i.p.), a single administration of BAY 61-3606 (3mg/kg; i.p.) could reverse the blood pressure drop and heart rate increase induced by ZYM in rats[8].

References:
[1] Yamamoto N, Takeshita K, Shichijo M, 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]. The Journal of pharmacology and experimental therapeutics, 2003, 306(3): 1174-1181.
[2] Li S, Fu J, Wu J, et al. SYK-Inhibitor Bay 61-3606 Induces Cell Cycle Arrest and Apoptosis in Multiple Myeloma Cells Independent of SYK Inhibitory Effects but Via Degradation of IKZF1/3[J]. Blood, 2016, 128(22): 4477.
[3] Kim S Y, Park S E, Shim S M, et al. Bay 61-3606 sensitizes TRAIL-induced apoptosis by downregulating Mcl-1 in breast cancer cells[J]. PLoS One, 2015, 10(12): e0146073.
[4] Tümmler C, Dumitriu G, Wickström M, et al. SYK inhibition potentiates the effect of chemotherapeutic drugs on neuroblastoma cells in vitro[J]. Cancers, 2019, 11(2): 202.
[5] Mitra R, Bhagavatula I D, Gope R. BAY 61-3606, CDKi, and sodium butyrate treatments alter gene expression in human vestibular schwannomas and cause cell death in vitro[J]. ecancermedicalscience, 2012, 6: 285.

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[6] Ho C M K, Donovan-Banfield I Z, Tan L, et al. Inhibition of IKKα by BAY61-3606 reveals IKKα-dependent histone H3 phosphorylation in human cytomegalovirus infected cells[J]. PloS one, 2016, 11(3): e0150339.
[7] He X, Huang Y, Liu Y, et al. BAY61-3606 attenuates neuroinflammation and neurofunctional damage by inhibiting microglial Mincle/Syk signaling response after traumatic brain injury[J]. International journal of molecular medicine, 2022, 49(1): 1-13.
[8] Unsal D, Kacan M, Temiz-Resitoglu M, et al. The role of Syk/IκB-α/NF-κB pathway activation in the reversal effect of BAY 61-3606, a selective Syk inhibitor, on hypotension and inflammation in a rat model of zymosan-induced non-septic shock[J]. Clinical and Experimental Pharmacology and Physiology, 2018, 45(2): 155-165.

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