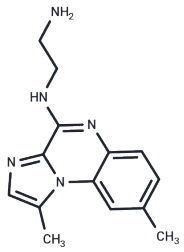
Data Sheet (Cat.No.T6326)

TargetMol

BMS-345541

Chemical Properties



CAS No. : 445430-58-0

Formula: C14H17N5

Molecular Weight: 255.32

Appearance: no data available

Storage: store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	BMS-345541 (IKK Inhibitor III) is a highly selective inhibitor of the catalytic subunits of IKK-2 and IKK-1 with IC50 of 0.3 μM and 4 μM, respectively.
Targets(IC50)	IκB/IKK
In vitro	Tumor-bearing mice treated with 75 mg/kg of BMS-345541 exhibited effective growth inhibition against SK-MEL-5, A375, and Hs 294T, with inhibition rates of 86%, 69%, and 67%, respectively, compared to the control group. At a dosage of 100 mg/kg, BMS-345541 reduced cumulative arthritis damage scores from 4.4 to 0, accompanied by lower degrees of tibial joint degeneration, severity of inflammation, synovial proliferation, bone absorption, and cartilage erosion. BMS-345541 dose-dependently inhibited IL-1β signaling, with animals in the 100 mg/kg dosage group displaying levels comparable to disease-free control animals. Oral administration of 100 mg/kg BMS-345541 reduced the weight ratio, clinical intestinal scores, average damage scores, and average inflammation scores in mice induced with dextran sulfate sodium colitis, which were 0.86 (vs the control group's 0.77), 1.0 (vs the control group's 2.5), 5.66 (vs the control group's 8.52), and 6.82 (vs the control group's 12.33), respectively.
In vivo	Treatment with 5 μM BMS-345541 induced cell cycle arrest at the G2/M phase in BE-13 and DND-41 cells and hindered RPMI-8402 cells from staying in the sub-G1 phase. This concentration, after 16 hours, led to an increase in apoptotic cells, along with time-dependent cleavage of procaspase-8, procaspase-3, and poly(ADP-ribose). Furthermore, 5 μM BMS-345541 triggered time-dependent dephosphorylation of IκBα and p65. At a concentration of 10 μM, BMS-345541 inhibited the growth of normal human epidermal melanocytes and metastatic melanoma cells (SK-MEL-5, A375, and HS294T), with inhibition rates of 96% and 99% after 72 hours, respectively. This dosage also reduced IKK activity by 76%, NF-kB activity by 95%, and diminished CXCL1 production. Dose-dependently, BMS-345541 inhibited the phosphorylation of IκBα stimulated by TNF-α in THP-1 monocytes, with an IC50 of 4 μM. In human umbilical vein endothelial cells, it suppressed the expression of TNFα-induced ICAM-1 and VCAM-1, with an IC50 of 5 μM. BMS-345541 binds to the allosteric sites of IKK-1 and IKK-2, affecting the activity sites of different subunits. It impacted various mitotic cell cycle transitions, including entry into mitosis, progression from early to late stages, and cytokinesis. Adding BMS-345541 to cells resulted in arrest at the G phase and inhibited the activation of Aurora A, B, and C, Cdk1, and the phosphorylation of histone H3.

	Treatment with BMS-34554 led to nuclear translocation of FOXO3a in T-ALL cells, including the regulation of p21 CIP1 gene expression levels. BMS-345541 also inhibited the growth of primary T-ALL cells from pediatric patients, with an IC50 of 2-6 μM.
Kinase Assay	Enzyme Assays: Assays measuring the enzyme-catalyzed phosphorylation of GST-IκBα are performed by adding enzyme (a final concentration of 0.5 μg/mL) at 30 ℃ to solutions of 100 μg/mL GST- IκBα and 5 μM [33P]ATP in 40 mM Tris HCl, pH 7.5, containing 4 mM MgCl2, 34 mM sodium phosphate, 3 mM NaCl, 0.6 mM potassium phosphate, 1 mM KCl, 1 mM dithiothreitol, 3% (w/v) glycerol, and 250 μg/mL bovine serum albumin. The specific activity of [33P]ATP used in the assay is 100 Ci/mmol. After 5 min, the kinase reactions are stopped by the addition of 2× Laemmli sample buffer and heat-treated at 90 ℃ for 1 min. The samples are then loaded on to NuPAGE 10% BisTris gels. After completion of SDS-PAGE, gels are dried on a slab gel dryer. The bands are then detected using a 445Si PhosphorImager, and the radioactivity is quantified using ImageQuant software. Under these conditions, the degree of phosphorylation of GST-IκBα is linear with time and concentration of enzyme.
Cell Research	1×105 cells per well are plated in six-well plates with 10% fetal bovine serum medium overnight to allow cell adhesion. Cells ae cultured in medium containing BMS-345541 for 72 hours of treatment. Cells are counted with a hemocytometer.(Only for Reference)

Solubility Information

Solubility	DMSO: 9 mg/mL (35.25 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.9167 mL	19.5833 mL	39.1665 mL
5 mM	0.7833 mL	3.9167 mL	7.8333 mL
10 mM	0.3917 mL	1.9583 mL	3.9167 mL
50 mM	0.0783 mL	0.3917 mL	0.7833 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Burke JR, et al. J Biol Chem, 2003, 278(3), 1450-1456.
Chen J, Liu G, Wang X, et al. Glioblastoma stem cell-specific histamine secretion drives pro-angiogenic tumor microenvironment remodeling. Cell Stem Cell. 2022
Blazkova H, et al. Cell Cycle, 2007, 6(20), 2531-2540.
Yang J, et al. Clin Cancer Res, 2006, 12(3 Pt 1), 950-960.
Buontempo F, et al. Cell Cycle, 2012, 11(13), 2467-2475.
MacMaster JF, et al. Inflamm Res, 2003, 52(12), 508-511.