产品名称：BMS-345541 free base
产品别名：BMS-345541

生物活性：

Description	BMS-345541 is a selective inhibitor of the catalytic subunits of IKK (IKK-2 IC_{50}=0.3 μM, IKK-1 IC_{50}=4 μM). BMS-345541 binds at an allosteric site of IKK.
IC_{50} & Target [1]	IKK-2: 0.3 μM (IC_{50}); IKK-1: 4 μM (IC_{50})
In Vitro	BMS-345541 selectively inhibits the stimulated phosphorylation of IκBα in cells (IC_{50}=4 μM). Consistent with the role of IKK/NF-κB in the regulation of cytokine transcription, BMS-345541 inhibits lipopolysaccharide-stimulated tumor necrosis factor α, interleukin-1β, interleukin-8, and interleukin-6 in THP-1 cells with IC_{50} values in the 1 to 5 μM range[1]. BMS-345541 treatment results in a concentration-dependent inhibition of melanoma cell proliferation in SK-MEL-5, A375, and Hs 294T cells. BMS-345541 (0, 100 μM) shows apoptotic features as revealed by TUNEL staining and nuclear condensation[2].
In Vivo	BMS-345541 (10 mg/kg, p.o.) results in prolonged serum drug levels, with concentrations sustained at or above 1 μM for many hours in mice. BMS-345541 dose-dependently inhibits the production of TNFα measured in the serum of animals challenged with an intraperitoneal administration of LPS[1]. BMS-345541 (0, 10, 25, and 75 mg/kg, p.o.) effectively inhibits SK-MEL-5 tumor growth in a dose-dependent manner in the mice. Tumor-bearing mice treated with 75 mg/kg of BMS-345541 show effective inhibition of growth of SK-MEL-5, A375, and Hs 294T tumors by 86±2.8%, 69±11% and 67±3.4%, respectively[2].

Solvent&Solubility

In Vitro:

DMSO : 10 mg/mL (**39.17 mM**; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 1 mg/mL (3.92 mM); Clear solution

此方案可获得 ≥ 1 mg/mL (3.92 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；

	向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 1 mg/mL (3.92 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (3.92 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 1 mg/mL (3.92 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (3.92 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Burke JR, et al. BMS-345541 is a highly selective inhibitor of I kappa B kinase that binds at an allosteric site of the enzyme and blocks NF-kappa B-dependent transcription in mice. J Biol Chem, 2003, 278(3), 1450-1456. [2]. Yang J, et al. BMS-345541 targets inhibitor of kappaB kinase and induces apoptosis in melanoma: involvement of nuclear factor kappaB and mitochondria pathways. Clin Cancer Res, 2006, 12(3 Pt 1), 950-960. [3]. MacMaster JF, et al. An inhibitor of IkappaB kinase, BMS-345541, blocks endothelial cell adhesion molecule expression and reduces the severity of dextran sulfate sodium-induced colitis in mice. Inflamm Res, 2003, 52(12), 508-511.

实验参考：

Cell Assay	SK-MEL-5 cells are treated with BMS-345541 at different concentrations (0, 1.0, 10, and 100 μM) for different time periods. The cells are collected by trypsinization, fixed in 70% ethanol for 2 hours on ice and stained with PI solution (PBS containing 2 μg/mL PI, 0.1% Triton X-100, and 125 units/mL RNase A) at 37°C for 30 minutes. Cell fluorescence is measured by flow cytometry with 488 nm excitation and 620 nm emission filters and resulting data are analyzed using the software program MultiCycle[2].
Animal Administration	Mice[1] BMS-345541 is administered either by intravenous tail vein injection or by peroral gavage to groups of three 18-22 g female BALB/c mice. BMS-345541 is formulated as a 2 mg/mL solution in 3% Tween 80, water. Mice receive either a 2 mg/kg (1 mL/kg) intravenous bolus or a 10 mg/kg (5 mL/kg) peroral gavage. Whole blood samples are taken from individual mice by orbital bleed and cardiac puncture at 0, 0.05, 0.25, 0.5, 1.0, 3.0, 6.0, and 8.0 h after dosing. Whole blood is centrifuged at $20\times10^3\times g$ for 5 min. Serum is stored at -20°C until analysis.
Kinase Assay	Assays measuring the enzyme-catalyzed phosphorylation of GST-IκBα are performed by adding enzyme (IKK-2, IKK-1, or IKK-ε, typically to a final concentration of 0.5 μg/mL) at 30°C to solutions of 100 μg/mL GST-IκBα and 5 μM [^{33}P]ATP in 40 mM Tris-HCl, pH 7.5, containing 4 mM $MgCl_2$, 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 [^{33}P]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°C 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 [1].
References	[1]. Burke JR, et al. BMS-345541 is a highly selective inhibitor of I kappa B kinase that binds at an allosteric site of the enzyme and blocks NF-kappa B-dependent transcription in mice. J Biol Chem, 2003, 278(3), 1450-1456. [2]. Yang J, et al. BMS-345541 targets inhibitor of kappaB kinase and induces apoptosis in melanoma: involvement of nuclear factor kappaB and mitochondria pathways. Clin Cancer Res, 2006, 12(3 Pt 1), 950-960. [3]. MacMaster JF, et al. An inhibitor of IkappaB kinase, BMS-345541, blocks endothelial cell adhesion molecule expression and reduces the severity of dextran sulfate sodium-induced colitis in mice. Inflamm Res, 2003, 52(12), 508-511.

源叶生物