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产品名称: **BMS-345541**
产品别名: **BMS-345541 hydrochloride**

生物活性:

Description	BMS-345541 hydrochloride 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	IKK-2	IKK-1			
	0.3 μM (IC ₅₀)	4 μM (IC ₅₀)			
In Vitro	BMS-345541 inhibits IKK-2 and IKK-1 in dose-dependent manner. BMS-345541 fails to inhibit a panel of both serine/threonine and tyrosine kinases at concentrations as high as 100 μM. MS-345541 at concentrations as high as 100 μM fails to block both the anisomycin-stimulated phosphorylation of c-Jun and LPS-stimulated activation of MAPKAP K2 in THP-1 cells, as well as the EGF-stimulated phosphorylation of STAT3 in H292 cells[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]. BMS-345541 (30 and 100 mg/kg, p.o.) is effective in blocking both clinical and histological endpoints of inflammation and injury in mice[3].				
Solvent&Solubility	In Vitro: DMSO : 20 mg/mL (68.54 mM; Need ultrasonic)				
	Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg	10 mg
		1 mM	3.4272 mL	17.1362 mL	34.2724 mL
		5 mM	0.6854 mL	3.4272 mL	6.8545 mL
		10 mM	0.3427 mL	1.7136 mL	3.4272 mL
	<p>*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。</p> <p>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。</p> <p>In Vivo:</p> <p>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:</p> <p>——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</p> <p>1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p>				



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	<p>Solubility: ≥ 2 mg/mL (6.85 mM); Clear solution</p> <p>此方案可获得 ≥ 2 mg/mL (6.85 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 μL 20.0 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。</p> <p>2. 请依序添加每种溶剂: 10% DMSO \rightarrow 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2 mg/mL (6.85 mM); Clear solution</p> <p>此方案可获得 ≥ 2 mg/mL (6.85 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 μL 20.0 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。</p> <p>3. 请依序添加每种溶剂: 10% DMSO \rightarrow 90% corn oil</p> <p>Solubility: ≥ 2 mg/mL (6.85 mM); Clear solution</p> <p>此方案可获得 ≥ 2 mg/mL (6.85 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。</p> <p>以 1 mL 工作液为例, 取 100 μL 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。</p>
References	<p>[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.</p> <p>[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.</p> <p>[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.</p>
实验参考:	
Cell Assay	<p>Briefly, SK-MEL-5 cells are treated with BMS-345541 at different concentrations or 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]</p>
Animal Administration	<p>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 $20 \times 10^3 \times g$ for 5 min. Serum is stored at -20°C until analysis. [1]</p>
	<p>Assays measuring the enzyme-catalyzed phosphorylation of GST-IkBa 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-IkBa and 5 μM [32P]ATP in 40 mM Tris-HCl, pH 7.5, containing 4 mM MgCl₂, 34</p>



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Kinase Assay	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	<p>[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.</p> <p>[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.</p> <p>[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.</p>