

产品名称: **BMS-536924**

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生物活性:

Description

BMS-536924 is an ATP-competitive IGF-1R/IR inhibitor with IC₅₀ of 100 nM/73 nM. IC₅₀ value: 100 nM (IGF-1R); 73 nM (IR) [1] Target: IGF-1R; IR in vitro: BMS-536924 also inhibits FAK and Lck with IC₅₀ of 150 nM and 341 nM, respectively. BMS-536924 inhibits cellular proliferation and disrupts Akt and MAPK phosphorylation [1]. BMS-536924 inhibits IGF-I-stimulated IGF-1R signaling in MCF10A cells and blocks constitutive IGF-1R activity in CD8-IGF-1R-MCF10A. Preincubation of MCF10A cells with 1 μM BMS-536924 completely blocks the ability of IGF-I to stimulate IGF-1R phosphorylation. IGF-I stimulation results in increased phosphorylation of ERK1/2, GSK3β, and Akt. BMS-536924 inhibits this ligand-induced phosphorylation. Treatment of the CD8-IGF-1R-MCF10A cells with BMS-536924 results in a dose-dependent inhibition of phosphorylation with partial inhibition at 0.01 μM and 0.1 μM, but complete receptor inhibition at a concentration of 1 μM. Maximal inhibition of phosphorylated IGF-1R is observed as early as 10 minutes following incubation. BMS-536924 retains its ability to inhibit IGF-1R phosphorylation for up to 48 hours. Addition of BMS-536924 time-dependently inhibits Akt phosphorylation starting at 1 hour. By 48 hours, Akt activation is completely blocked [2]. in vivo: Oral administration of BMS-536924 at 100-300 mpk strongly inhibits IGR-1R Sal tumor model. Efficacy is also observed in the nonengineered Colo205 human colon carcinoma mode. Oral administration of 3 on a once a day schedule (100-300 mpk) or a twice a day schedule (50, 100 mpk) demonstrates antitumor activity in this tumor model. Oral glucose tolerance test (OGTT) shows 100 mpk (b.i.d.) causes a significant elevation in glucose levels after glucose challenge. The pharmacokinetic parameters of BMS-536924, administered orally in poly(ethylene glycol) 400 and water (80:20 v/v), are determined in mouse, rat, dog, and monkey. Good bioavailability is evident in all species. Significant nonlinear pharmacokinetics is observed in rodents at increasing p.o. dose [1]. Oral administration of 70 mg/kg BMS-536924 significantly inhibits tumor growth (TGBC-1TKB cells) inoculated in nude mice. BMS-536924 up regulates apoptosis in xenografts tumors. The treatment doesn't have adverse effects on the body weight of mice or the glucose levels at the time of death, suggesting tolerable toxicity [3].

In Vitro:

DMSO : 50 mg/mL (104.18 mM; Need ultrasonic)

H₂O : < 0.1 mg/mL (insoluble)

	Solvent	Mass	1 mg	5 mg	10 mg
	Concentration				
Preparing	1 mM		2.0835 mL	10.4175 mL	20.8351 mL
Stock Solutions	5 mM		0.4167 mL	2.0835 mL	4.1670 mL
	10 mM		0.2084 mL	1.0418 mL	2.0835 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℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 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

Solvent&Solubility

	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: ≥ 2.5 mg/mL (5.21 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.21 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.25 mg/mL (4.69 mM); Clear solution 此方案可获得 ≥ 2.25 mg/mL (4.69 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 22.5 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: ≥ 2.5 mg/mL (5.21 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.21 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Wittman M, et al. Discovery of a (1H-benzoimidazol-2-yl)-1H-pyridin-2-one (BMS-536924) inhibitor of insulin-like growth factor I receptor kinase with in vivo antitumor activity. J Med Chem. 2005 Sep 8;48(18):5639-43. [2]. Litzenburger BC, et al. BMS-536924 reverses IGF-IR-induced transformation of mammary epithelial cells and causes growth inhibition and polarization of MCF7 cells. Clin Cancer Res. 2009 Jan 1;15(1):226-37. [3]. Ohashi H, et al. Insulin-like growth factor receptor expression is associated with aggressive phenotypes and has therapeutic activity in biliary tract cancers. Cancer Sci. 2012 Feb;103(2):252-61.

源叶生物