产品名称：SB743921
产品别名：SB-743921

生物活性：

Description	SB-743921 is a potent inhibitor of the mitotic kinesin KSP (Eg5), with a K_i of 0.1 nM.
IC_{50} & Target	Eg5
	0.1 nM (Ki)
In Vitro	SB-743921 is a potent inhibitor of Eg5, with a Ki of 0.1 nM[1]. SB-743921 (1 nM) potently inhibits colony forming cell (CFC) formation of chronic myeloid leukemia (CML) primary cells, but exhibits slight inhibitory activities on the colony-forming ability of normal bone marrow progenitors. SB-743921 (1, 3 nM) induces apoptosis of CML primary CD34 + cells, and shows slight effect on normal CD34 + cells. SB-743921 (2 nM) in combination with imatinib displays additive anti-proliferative effect in KCL22 and CML CD34 + cells. Furthermore, SB-743921 overcomes imatinib resistance in CML cells. SB-743921 (0.5 nM, 1 nM, 3 nM) inhibits MEK/ERK and AKT signaling in CML cells[2].
In Vivo	SB-743921 has good oral bioavailability and pharmacokinetics and induces complete tumor regression in nude mice bearing lung cancer patient xenografts[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (180.66 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8066 mL	9.0331 mL	18.0662 mL
	5 mM	0.3613 mL	1.8066 mL	3.6132 mL
	10 mM	0.1807 mL	0.9033 mL	1.8066 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: ≥ 2.5 mg/mL (4.52 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.52 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: ≥ 2.5 mg/mL (4.52 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.52 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 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 (4.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.52 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]. Jeffrey R. Jackson, et al. A second generation KSP inhibitor, SB-743921, is a highly potent and active therapeutic in preclinical models of cancer. First AACR International Conference on Molecular Diagnostics in Cancer Therapeutic Development, Sep 12-15, 2006. [2]. Yin Y, et al. Kinesin spindle protein inhibitor SB743921 induces mitotic arrest and apoptosis and overcomes imatinib resistance of chronic myeloid leukemia cells. Leuk Lymphoma. 2015 Jun;56(6):1813-20. [3]. Good JA, et al. Optimized S-trityl-L-cysteine-based inhibitors of kinesin spindle protein with potent in vivo antitumor activity in lung cancer xenograft models. J Med Chem. 2013 Mar 14;56(5):1878-93.

实验参考：

Cell Assay	K562 and KCL22 cells are seeded in six-well plates at a number of 5 × 10^5 in 2 mL RPMI-1640 mediumsupplemented with 10% FBS in a 5% CO_2 atmosphere at 37°C, and are treated with control (2% DMSO), 50 nM imatinib, 2 nM SB-743921 and 50 nM imatinib + 2 nM SB-743921, respectively. Cell number and viability are determined every 24 h. Results are plotted for live cells against time to generate a growth curve[2]
Animal Administration	The animal experiments are performed with female NMRI nu/nu mice. Tumor fragments are obtained from xenografts in serial passage in nude mice. Mice are randomized to the various groups, and dosing is started when the required number of mice carries a tumor of 50-250 mm^3 volume, preferably 80-200 mm^3. Vehicle for 1: 10% ethanol, 10% cremophor, 80% D5W (dextrose 5%); vehicle for all other compounds (including SB-743921): 8% DMSO, 2% Tween 80, distilled water (pH 5). All treatments are given intraperitoneally. Vehicle control mice (group 1) are treated with 10 mL/kg vehicle on days 0, 3, 6, 8, 10, 13, 20, 22, 24, 29, 31, 34, 36, 38, 48, 51, 55, 58, 62, 65, and 69[3]
References	[1]. Jeffrey R. Jackson, et al. A second generation KSP inhibitor, SB-743921, is a highly potent and active therapeutic in preclinical models of cancer. First AACR International Conference on Molecular Diagnostics in Cancer Therapeutic Development, Sep 12-15, 2006. [2]. Yin Y, et al. Kinesin spindle protein inhibitor SB743921 induces mitotic arrest and apoptosis and overcomes imatinib resistance of chronic myeloid leukemia cells. Leuk Lymphoma. 2015 Jun;56(6):1813-20. [3]. Good JA, et al. Optimized S-trityl-L-cysteine-based inhibitors of kinesin spindle protein with potent in vivo antitumor activity in lung cancer xenograft models. J Med Chem. 2013 Mar 14;56(5):1878-93.