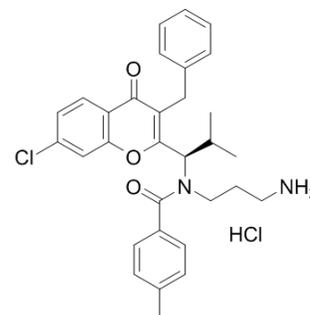


SB-743921

Cat. No.:	HY-12069		
CAS No.:	940929-33-9		
Molecular Formula:	C ₃₁ H ₃₄ Cl ₂ N ₂ O ₃		
Molecular Weight:	553.52		
Target:	Kinesin		
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



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	

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (4.52 mM); Clear solution

BIOLOGICAL ACTIVITY

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 (K _i)

In Vitro	SB-743921 is a potent inhibitor of Eg5, with a K_i 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] .

PROTOCOL

Cell Assay ^[2]	K562 and KCL22 cells are seeded in six-well plates at a number of 5×10^5 in 2 mL RPMI-1640 medium supplemented 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] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration ^[3]	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] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA