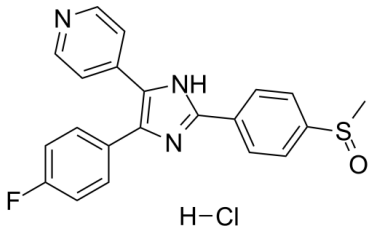
Data Sheet

Product Name:	SB 203580 (hydrochloride)
Cat. No.:	CS-1880
CAS No.:	869185-85-3
Molecular Formula:	C21H17ClFN3OS
Molecular Weight:	413.90
Target:	Autophagy; Mitophagy; p38 MAPK
Pathway:	Autophagy; MAPK/ERK Pathway
Solubility:	H2O : 8.43 mg/mL (20.37 mM; Need ultrasonic and warming); DMSO : 100 mg/mL (241.60 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

SB 203580 hydrochloride (RWJ 64809 hydrochloride) is a widely used **p38 MAPK** inhibitor. SB 203580 hydrochloride (RWJ 64809 hydrochloride) inhibits **SAPK2a/p38** and **SAPK2b/p38β2**, with **IC_{50}**s of 50 nM and 500 nM, respectively. LCK, GSK3β and PKBα are also inhibited by SB 203580 hydrochloride (RWJ 64809 hydrochloride), but the IC_{50}s are 100-500-fold higher than that for SAPK2a/p38[1].
In Vitro: SB 203580 (preincubated with 0-30 μM for 1 h and cultured for 24 h in the presence of 20 ng/mL IL-2) prevents the IL-2-induced proliferation of primary human T cells, murine CT6 T cells, or BAF F7 B cells with an IC_{50} of 3-5 μM[1].
SB203580 blocks PKB phosphorylation (IC_{50} 3-5 μM). SB203580 inhibitsthe phosphorylation of Ser473 in a dose-dependent manner in both CT6 and activated human T cells and IL-2-responsive BA/F3 F7 B cells[1]. **In Vivo:** SB203580 (5 mg/kg/day; intra peritoneal injected daily for 16 consecutive days, in female atymic Nu/Nu mice) treatment, p38WT tumors show a significantly smaller tumor burden when compared with p38TM tumors that were treated in parallel[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: SB 203580 is dissolved in DMSO and stored, and then diluted with appropriate medium before use[2].[2]Phosphorylation of p38, JNK1/2, and ERK1/2 is analysed by Western blotting. Briefly, TF-1 cells are cultured for 16 h in RPMI 1640 containing 0.1% FBS and subsequently stimulated for various periods of time with medium or OA (30 ng/mL) or SB 203580(1 μM, 5 μM, 10 μM) plus OA. After harvesting, total cell extracts are prepared by resuspending the cells in 500 μL 1× sample buffer (containing 2% SDS, 10% glycerol, 2% β-mercaptoethanol, 60 mM Tris-HCl (pH 6.8) and bromophenol blue) and lysing the cells by passing them through a 23G1 needle (three times). Cell extracts are directly boiled for 10 min and stored at −20°C. Before loading, samples are again boiled for 5 min and cell extracts are resolved by running 1/10th volume on a SDS/12.5%PAGE gel (acryla-mide:bisacrylamide is 173:1) and transferred to cellulosenitrate membrane. Immunoblotting with the antibodies is performed by standard procedures and detection is performed[2]. **Animal Administration:** SB 203580 is dissolved in vehicle (PBS) (Mice)[3].[3]Mice[3]
In survival studies, **C57BL/6J mice** weighing 20 g to 30 g are briefly anesthetized with isoflurane and challenged with 0.05 mL of IT normal saline (NS, noninfected controls) or E. coli (15×10^9 CFU/kg). One hour before NS challenge, mice (n = 24) receive either **intraperitoneal SB203580 (100 mg/kg in 0.25 mL)** or diluent only (placebo).
Infected animals receive **SB203580** in doses of **100, 10, 1, or 0.1 mg/kg** or placebo 1 hour before IT E. coli (n = 241); SB203580 100 or 0.1 mg/kg or placebo 1 hour after E. coli (n = 121); or SB203580 100 mg/kg or placebo 12 hours after E. coli (n = 72). All animals receive ceftriaxone (100 mg/kg in 0.1 mL, subcutaneously) for 4 days and NS (0.5 mL, subcutaneously) for 1 day beginning 4 hours after challenge. Animals were observed every 2 hours for the initial 48 hours, every 4 hours from 48 hours to 72 hours, every 8 hours from 72 hours to 96 hours, and then twice daily until study completion (168 hours)[3].

References:

[1]. Davies SP, et al. Specificity and mechanism of action of some commonly used protein kinase inhibitors. Biochem J. 2000 Oct 1;351(Pt 1):95-105.

[2]. Lali FV, et al. The pyridinyl imidazole inhibitor SB203580 blocks phosphoinositide-dependent protein kinase activity, protein kinase B phosphorylation, and retinoblastoma hyperphosphorylation in interleukin-2-stimulated T cells independently of p38 mitogen-activated protein kinase. J Biol Chem. 2000 Mar 10;275(10):7395-402.

[3]. Leelahavanichkul K, et al. A role for p38 MAPK in head and neck cancer cell growth and tumor-induced angiogenesis and lymphangiogenesis. Mol Oncol. 2014 Feb;8(1):105-18.

CAIndexNames:

Pyridine, 4-[4-(4-fluorophenyl)-2-[4-(methylsulfinyl)phenyl]-1H-imidazol-5-yl]-, hydrochloride (1:1)

SMILES:

O=S(C1=CC=C(C2=NC(C3=CC=C(F)C=C3)=C(C4=CC=NC=C4)N2)C=C1)C.[H]Cl

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