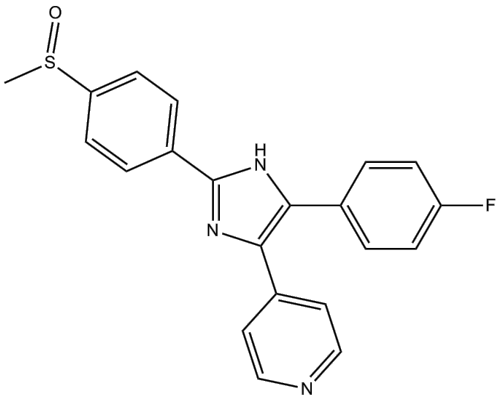
Product Data Sheet

Product Name: SB 203580
Cat. No.: GC13595

Chemical Properties

Cas. No.	152121-47-6		
Chemical Name	4-[4-(4-fluorophenyl)-2-(4-methylsulfinylphenyl)-1H-imidazol-5-yl]pyridine		
SMILES	CS(=O)C1=CC=C(C=C1)C2=NC(=C(N2)C3=CC=NC=C3)C4=CC=C(C=C4)F		
Formula	$C_{21}H_{16}FN_3OS$	M.Wt	377.44
Solubility	≥ 18.872mg/mL in DMSO, ≥ 3.28 mg/mL in EtOH with ultrasonic	Storage	Desiccate at 4°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines MDA-MB-231 human breast cancer cell line

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Preparation Method	Cells were treated at the logarithmic phase of the growth with various doses of SB 203580 (0.1, 0.5, 1, 5, 10, 25, 50, 100 μM) for 24 h
Reaction Conditions	0.1, 0.5, 1, 5, 10, 25, 50, 100 μM for 24 h
Applications	SB 203580 did not cause significant cytotoxicity on human MDA-MB-231 breast cancer cell line at low concentrations (0.1-10 μM) as compared to vehicle-treated (0.5% DMSO) control cells. However, the cytotoxic effects of both inhibitors were observed with higher concentrations of 25, 50 and 100 μM..

Animal experiment [2]:

Animal models	Male Balb/c mice
Preparation Method	Treatments with 2% DMSO alone or SB 203580 dissolved in 2% DMSO were given 1 h before and 1 h and 24 h after DENV infection intravenously. The volume of all injections was 0.4 ml. At 7 days after infection, the mice were euthanized with an overdose intraperitoneal injection of sodium pentobarbital anesthesia.
Dosage form	5 mg/kg/d for 7 days, infection intravenously
Applications	After the DENV-infected mice were treated with SB 203580, their liver AST levels were significantly reduced, but the changes in ALT were failed to reach statistical significance

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

[1]: Duzgun SA, Yerlikaya A, Zeren S, Bayhan Z, Okur E, Boyaci I. Differential effects of p38 MAP kinase inhibitors SB 203580 and SB202190 on growth and migration of human MDA-MB-231 cancer cell line. Cytotechnology. 2017;69(4):711-24.
[2]: Sreekanth GP, Chuncharunee A, Sirimontaporn A, Panaampon J, Noisakran S, Yenchitsomanus PT, et al. SB 203580 modulates p38 MAPK signaling and Dengue virus-induced liver injury by reducing MAPKAPK2, HSP27, and ATF2 phosphorylation. PLoS One. 2016;11:e0149486.

Background

SB 203580 is a specific inhibitor of p38-MAPK (Mitogen-activated Protein Kinase) pathway [1,2]. SB 203580 inhibits p38 kinase in a manner competitive with ATP with a Ki of 21 nm [2].

SB 203580 inhibit the proliferation of human breast cancer cell line MDA-MB-231 with the IC50 value of was 85.1 μM [3]. SB 203580 inhibited IL-10 production by monocytic WEHI 274.3 cells expressing WT-p38α MAPK in a dose-dependent manner with greater than 95% inhibition at 5 μm and with an IC_{50} of 0.1μM [4]. IL-2-induced proliferation of primary human T cells, murine CT6 T cells, or BAF F7 B cells is prevented by the p38 MAP kinase inhibitor SB 203580 with an IC50 of 3-5μM [5].

SB-203580 demonstrated moderate to high clearance in all species tested in vivo, with non-linear elimination observed in the rat at plasma concentrations > 1000ng ml -1. Although good solution bioavailability was observed in non-rodents (78% in dog, 32% in monkey), lower and more variable bioavailability was observed in the rat and mouse (3-48%) [6]. SB 203580 treatment significantly improve the white blood cell (WBC) and platelet counts decreased significantly in the DENV-infected mice, suggesting leucopenia and thrombocytopenia, respectively [7].

References:
[1]. Barancik M, Bohacova V, Kvackajova J, Hudecova S, Krizanova O, Breier A: SB 203580, a specific inhibitor of p38-MAPK pathway, is a new reversal agent of P-glycoprotein-mediated multidrug resistance. Eur J Pharm Sci. 2001, 14: 29-36. 10.1016/S0928-0987(01)00139-7.
[2]. Peter R. Young, Megan M. McLaughlin, Sanjay Kumar, et al. Pyridinyl Imidazole Inhibitors of p38

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Mitogen-activated Protein Kinase Bind in the ATP Site. The Journal of Biological Chemistry, 1997, 272(18): 12116-12121.
[3]. Duzgun SA, Yerlikaya A, Zeren S, Bayhan Z, Okur E, Boyaci I. Differential effects of p38 MAP kinase inhibitors SB 203580 and SB202190 on growth and migration of human MDA-MB-231 cancer cell line. Cytotechnology. 2017;69(4):711-24.
[4]. Guo, X., R.E. Gerl, and J.W. Schrader. 2003. Defining the involvement of p38alpha MAPK in the production of anti- and proinflammatory cytokines using an SB 203580-resistant form of the kinase. J. Biol. Chem. 278:22237-22242.
[5]. Lali, F. V., Hunt, A. E., Turner, S. J., and Foxwell, B. M. The pyridinyl imidazole inhibitor SB 203580 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.,275: 7395-7402,?2000
[6]. Ward KW, Prokscht JW, Azzaranot LM, et al. Preclinical pharmacokinetics of SB-203580, a potent inhibitor of p38 mitogen-activated protein kinase. Xenobiotica 2001; 31: 783-97
[7]. Sreekanth GP, Chuncharunee A, Sirimontaporn A, Panaampon J, Noisakran S, Yenchitsomanus PT, et al. SB 203580 modulates p38 MAPK signaling and Dengue virus-induced liver injury by reducing MAPKAPK2, HSP27, and ATF2 phosphorylation. PLoS One. 2016;11:e0149486.

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