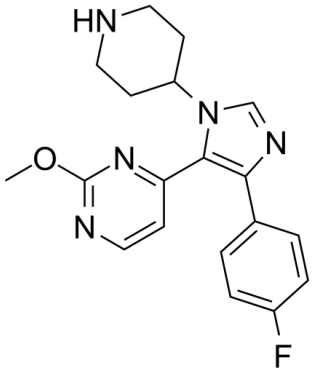
Data Sheet

Product Name:	SB 242235
Cat. No.:	CS-2097
CAS No.:	193746-75-7
Molecular Formula:	C19H20FN5O
Molecular Weight:	353.39
Target:	Autophagy; p38 MAPK
Pathway:	Autophagy; MAPK/ERK Pathway
Solubility:	DMSO : ≥ 48 mg/mL (135.83 mM)



BIOLOGICAL ACTIVITY:

SB-242235 is a potent and selective **p38 MAP kinase** inhibitor, with an **IC_{50}** of 1.0 μM in primary human chondrocytes[1]. IC50 & Target: IC50: 1.0 μM (p38 MAPK, primary human chondrocytes)[1] **In Vitro:** SB 242235 (0-10 μM) dose-dependently inhibits the activation of MAPKAP K2 with an IC_{50} of 1.0 μM in human chondrocytes stimulated with IL-1β[1].
SB 242235 inhibits intracellular p38 activity, MAPKAP K2 was then isolated from these cells and assayed using HSP27 as a substrate[1].
In Vivo: SB242235 (100 mg/kg; p.o.) abolishes MAP-KAPK-2 activity and HSP27 phosphorylation[2].
SB242235 inhibits expression of the pro-inflammatory cytokines interleukin (IL)-6 and KC (murine IL-8) and COX-2[2].
SB-242235 is demonstrated non-linear elimination kinetics that manifested as a decrease in clearance with increasing dose and apparent oral bioavailability > 100% at high oral doses in rat and monkey[3].

PROTOCOL (Extracted from published papers and Only for reference)

Enzyme assay [1] Human chondrocytes (1×107 cells) were established in 10 cm tissue culture petri dishes in DMEM with 10% FBS and stimulated with 20 ng/ml of IL-1 for varying periods of time. Immune complex kinase assays were performed essentially as described previously.11 Briefly, the cells were washed twice in PBS and then solubilized on ice in lysis buffer (20 mM Tris-HCl pH 7.4, 150 mM NaCl, 1% Triton X-100, 10% glycerol, 2 mM EDTA, 25 mM -glycerophosphate, 20 mM NaF, 1 mM sodium orthovanadate, 2 mM sodium pyrophosphate, 1 mM phenylmethylsulfonyl fluoride, 10 g/ml leupeptin, 5 U/ml aprotinin) and centrifuged at 15 000×g for 20 min at 4°C. Endogenous kinases were precipitated from cell lysates using anti-p381 or anti-MAPKAP kinase-2 antibodies (kindly supplied by Dr Jacques Landry, Quebec, Canada) bound to protein-A agarose for 4 h at 4°C. The beads were washed twice with lysis buffer and twice with kinase buffer (25 mM Hepes pH 7.4, 25 mM MgCl2, 25 mM -glycerophosphate, 100 mM sodium orthovanadate, 2 mM DTT). The immune-complex kinase assays were initiated by the addition of 25 l of kinase buffer containing 2 g of GSTATF2 for p38 or 2 g of the small heat shock protein 27 (HSP27, StressGen Biotechnology, Ontario, Canada) for MAPKAP kinase-2 as substrate and 50 μM [γ-32P] ATP (20 Ci/mmol, Amersham). After 30 min at 30°C, the reaction was stopped by the addition of SDS sample buffer and the hosphorylated products were resolved by SDS-PAGE and visualized by Phosphorimaging (Molecular Dynamics). For inhibition in intact cells, the cells were pre-treated with different concentrations of SB 242235 for 30 min prior to stimulation with IL-1. Recombinant GST-ATF2 was expressed in E. coli and purified over Glutathione sepharose 4B (Pharmacia) chromatography according to manufacturer's instructions.

References:

[1]. Badger, A.M., et al., Differential effects of SB 242235, a selective p38 mitogen-activated protein kinase inhibitor, on IL-1 treated bovine and human cartilage/chondrocyte cultures. Osteoarthritis Cartilage, 2000. 8(6): p. 434-43.

[2]. Kim AL , et al. Role of p38 MAPK in UVB-induced inflammatory responses in the skin of SKH-1 hairless mice. J Invest Dermatol. 2005 Jun;124(6):1318-25.

[3]. Ward, K.W., et al., SB-242235, a selective inhibitor of p38 mitogen-activated protein kinase. I: preclinical pharmacokinetics. Xenobiotica, 2002. 32(3): p. 221-33.

CAIndexNames:

Pyrimidine, 4-[4-(4-fluorophenyl)-1-(4-piperidinyl)-1H-imidazol-5-yl]-2-methoxy-

SMILES:

COC1=NC=CC(C2=C(C3=CC=C(F)C=C3)N=CN2C4CCNCC4)=N1

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