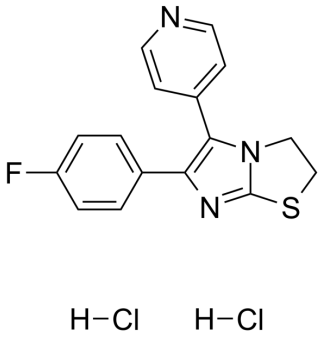
SKF-86002 dihydrochloride

Cat. No.:	HY-108641
CAS No.:	116339-68-5
Molecular Formula:	$C_{16}H_{14}Cl_2FN_3S$
Molecular Weight:	370.27
Target:	p38 MAPK
Pathway:	MAPK/ERK Pathway
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

SKF-86002 dihydrochloride is an orally active p38 MAPK inhibitor, with anti-inflammatory, anti-arthritic and analgesic activities. SKF-86002 dihydrochloride inhibits lipopolysaccharide (LPS)-stimulate human monocyte IL-1 and TNF-α production (IC_{50} = 1 μM). SKF-86002 dihydrochloride inhibits lipoxygenase- and cyclooxygenase-mediated metabolism of arachidonic acid[1][2][3].

In Vitro

SKF-86002 dihydrochloride (10 μM; 1 hour) inhibits apoptosis induced by stress stimulation with UV irradiation (UV)[1].
SKF-86002 dihydrochloride does not inhibit UV-induced apoptosis in undifferentiated HL-60 cells[1].
SKF-86002 dihydrochloride (10 μM; 72 hours) prevent IL-4-induced monocyte or U937 cell CD23 surface expression and protein formation with no effect on CD23 mRNA levels[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[4]

Cell Line:	U937 cells
Concentration:	10 μM
Incubation Time:	72 hours
Result:	Reduced CD23 levels on IL-4-treated U937 cells.

In Vivo

SKF-86002 dihydrochloride (10-90 mg/kg; p.o.; daily; for 22 days) has antiarthritic activity[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Lewis rats, with adjuvant-induced arthritis (AA)[5]
Dosage:	10 mg/kg, 30 mg/kg, 90 mg/kg
Administration:	Oral administration, daily, for 22 days
Result:	Significantly decreased hindleg volumes after injection of adjuvant.

REFERENCES

[1]. Frasch SC, et al. p38 mitogen-activated protein kinase-dependent and -independent intracellular signal transduction pathways leading to apoptosis in human neutrophils. J Biol Chem. 1998 Apr 3;273(14):8389-97.

[2]. Griswold DE, et al. SK&F 86002: a structurally novel anti-inflammatory agent that inhibits lipoxygenase- and cyclooxygenase-mediated metabolism of arachidonic acid. Biochem Pharmacol. 1987 Oct 15;36(20):3463-70.

[3]. Lee JC, et al. A protein kinase involved in the regulation of inflammatory cytokine biosynthesis. Nature. 1994;372(6508):739-746.

[4]. L A Marshall, et al. Inhibitors of the p38 mitogen-activated kinase modulate IL-4 induction of low affinity IgE receptor (CD23) in human monocytes. J Immunol. 1998 Dec 1;161(11):6005-13.

[5]. M J DiMartino, et al. Pharmacologic characterization of the antiinflammatory properties of a new dual inhibitor of lipoxygenase and cyclooxygenase. Agents Actions. 1987 Feb;20(1-2):113-23.

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