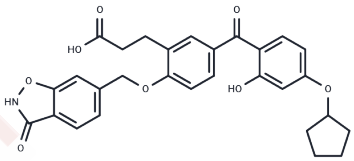
Data Sheet (Cat.No.T5416)

TargetMol

T-5224

Chemical Properties



CAS No. : 530141-72-1

Formula: C29H27NO8

Molecular Weight: 517.53

Storage: Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	T-5224 is a transcription factor c-Fos/AP-1 inhibitor that specifically inhibits the DNA-binding activity of c-Fos/c-Jun without affecting other transcription factors.
Targets(IC50)	MMP,DNA/RNA Synthesis
In vitro	In vitro production of the synovial cell mediators MMP-1, MMP-3, IL-6 and TNFα by IL-1b-stimulated human synovial SW982 cells was inhibited by T-5224. This was also the case for the chondrocyte inflammatory mediators MMP-3 and MMP-13 in IL-1b-stimulated human chondrocyte SW1353 cells. The IC50 values were ~10 μM for most of the cellular assays [1]. Vasopressin selectively stimulates an increase CDS1 mRNA that is dependent on protein kinase C and can be inhibited by the AP-1 inhibitor, T-5224 [3]. T-5224 significantly inhibited the invasion, migration, and MMP activity of HNSCC cells in a dose-dependent manner; there was no significant influence on cell proliferation [4].
In vivo	T-5224 efficiently inhibited the development of collagen-induced arthritis (CIA) when administered once daily from day 21, before the onset of arthritis. Arthritis on day 50 was inhibited by 64% and 91%, by 3 and 30 mg/kg of T-5224, respectively. The body weight of mice treated with T-5224 steadily recovered. X-ray studies showed that joint destruction was inhibited in treated but not in untreated arthritis controls, and notably, the joint was totally protected from destruction by 30 mg/kg of T-5224 [1]. Administration of T-5224 (300 mg/kg, p.o.) after intraperitoneal injection of LPS imparted appreciable protection against acute elevations in serum levels of TNFα, HMGB1, ALT/AST as well as in liver tissue levels of MIP-1α and MCP-1, and reduced the lethality (27 %) [2]. T-5224 (150 mg/kg) or vehicle was given orally every day for 4 weeks. The rate of cervical lymph node metastasis in the model was 40.0% in the T-5224-treated group versus 74.1% in the vehicle-treated group [4].
Kinase Assay	The DNA binding activity of transcription factors was measured using the TransAM kits. Nuclear extracts containing factors such as c-Fos/AP-1, c-Jun/AP-1, ATF-2, C/EBPa, MyoD, Sp-1 or NF-kB/p65 and various concentrations of T-5224 were added in the multi-well plates precoated with respective consensus double-stranded (ds)DNA oligomers. After incubation for 1 h, the transcription factor bound to its respective consensus dsDNA sequences was detected by using antibodies reactive against the respective transcription factors according to the manufacturer's protocol [1].

Cell Research	NIH/3T3 cells were transiently transfected with the luciferase reporter plasmids pAP-1-Luc (× 7 TGACTAA), pNF-kB-Luc (× 5 TGGGGACTTTCCGC) or control phRL-TK, and cultured overnight. Cells were incubated in 0.5% FBS/DMEM containing T-5224 for 1 h, and then stimulated with PMA (10 ng/ml) or TNFa (10 ng/ml), and then cultured for 3 h, followed by measurement of lysate by using dual-luciferase reporter assay system [1].
Animal Research	Mice were housed in an SPF (specific pathogen-free) grade environment and provided food and water ad libitum with a 12 h:12 h light/dark cycle. Male 8-week-old DBA/1J mice were immunized with bovine type II collagen emulsified in Freund's complete adjuvant on days 0 and 21. T-5224, MTX and LEF were orally administered once per day. Arthritis was assessed in a blind fashion for four paws per mouse using the following score: 0, uninvolved; 1, swelling of ≤2 toes or slight swelling in ankles and wrists; 2, swelling of ≥3 toes or moderate swelling in ankles and wrists; 3, extensive swelling of total paw. X-ray films of four paws taken using Softex were assessed for joint destruction in 2nd to 5th proximal interphalangeal joints and five metatarsophalangeal joints of four paws, the carpal joints of the forepaws, and the tarsal and calcaneal joints of the hind paws. Score was: 0, no change; 1, partial erosion; 2, complete erosion for joints; and 0, negative; 0.5, positive for osteoporosis. IL-1β (500 ng per unilateral hind paw) was administered into the footpads. The mice with ≥1 arthritis score were treated with either anti-TNFα antibody at 50 or 250 μg/mouse, intraperitoneally (i.p.) twice a week and/or with 3 mg/kg T-5224, orally once daily [1].

Solubility Information

Solubility	H2O: Insoluble, DMSO: 240 mg/mL (463.74 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (9.66 mM),Suspension. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.9323 mL	9.6613 mL	19.3226 mL
5 mM	0.3865 mL	1.9323 mL	3.8645 mL
10 mM	0.1932 mL	0.9661 mL	1.9323 mL
50 mM	0.0386 mL	0.1932 mL	0.3865 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Aikawa Y, et al. Treatment of arthritis with a selective inhibitor of c-Fos/activator protein-1. Nat Biotechnol. 2008 Jul;26(7):817-23.

Wang X, Li K, Cheng M, et al.RNPS1 stabilizes NAT10 protein to facilitate translation in cancer via tRNA ac4C modification.bioRxiv.2023: 2023.02. 11.528122.

Zhang Q, Hui M, Chen G, et al.Curcumin-Piperlongumine Hybrid Molecule Increases Cell Cycle Arrest and Apoptosis in Lung Cancer through JNK/c-Jun Signaling Pathway.Journal of Agricultural and Food Chemistry.2024

Izuta S, et al. T-5224, a selective inhibitor of c-Fos/activator protein-1, attenuates lipopolysaccharide-induced liver injury in mice. Biotechnol Lett. 2012 Dec;34(12):2175-82.

Blunsom NJ, et al. Sustained phospholipase C stimulation of H9c2 cardiomyoblasts by vasopressin induces an increase in CDP-diacylglycerol synthase 1 (CDS1) through protein kinase C and cFos. Biochim Biophys Acta Mol Cell Biol Lipids. 2019 Jul;1864(7):1072-1082.

Kamide D, et al. Selective activator protein-1 inhibitor T-5224 prevents lymph node metastasis in an oral cancer model. Cancer Sci. 2016 May;107(5):666-73.