

Product Data Sheet

Product Name: T-5224
Cat. No.: GC16165

Chemical Properties

Cas. No. 530141-72-1

Chemical Name 3-(5-(4-(cyclopentyloxy)-2-hydroxybenzoyl)-2-((3-oxo-2,3-dihydrobenzo[d]isoxazol-6-yl) methoxy)phenyl)propanoic acid

SMILES O=C1NOC2=CC(COC(C=CC(C(C3=C(O)C=C(OC4CCCC4)C=C3)=O)=C5)=C5CCC(O)=O)=CC=C12

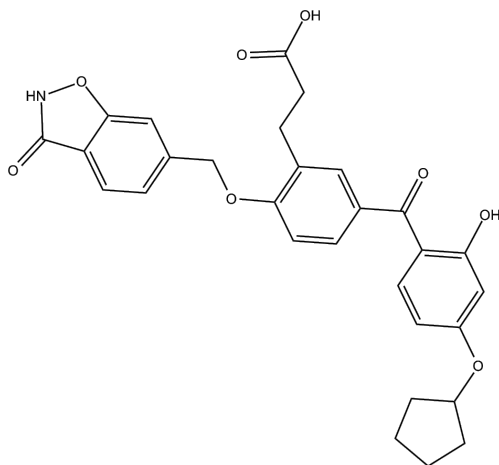
Formula $C_{29}H_{27}NO_8$ M.Wt 517.53

Solubility $\geq 25.88\text{mg/mL}$ in DMSO Storage Store at -20°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]:

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Cell lines	ARP1 cells
Preparation Method	ARP1 cells were cultured in RPMI-1640 medium, supplemented with 10% fetal bovine serum (FBS), 1% penicillin-streptomycin at 37°C in an incubator with 5% CO ₂ . Cells were seeded in a 96-well plate at a density of 5×10^4 cells/well for 24h. Cells were treated with different concentrations of T-5224 (0, 1, 10, 20, 50, and 100μM). After 24h of treatment, the cell viability was determined.
Reaction Conditions	0, 1, 10, 20, 50, and 100μM; 24h
Applications	T-5224 treatment inhibited the cell viability of ARP1 cells in a dose-dependent manner.
Animal experiment [2]:	
Animal models	Male C57BL/6 mice
Preparation Method	Male C57BL/6 mice (6 weeks old) were maintained in a controlled environment at 21±1°C and 60% relative humidity under a 12h light/dark cycle, and were given free access to food and water. One group of mice (n=8) was treated for 3 weeks with T-5224 at a concentration of 30mg/kg once daily by oral gavage and injected with bleomycin. The mice with subcutaneous injections of 100μl 0.9% NaCl, the solvent for bleomycin, were used as controls. Collect the skin tissues of mice for analysis.
Dosage form	30mg/kg/day; 3 weeks; p.o.

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Applications	T-5224 treatment significantly reduced bleomycin-induced accumulation of thickened collagen bundles and decreased dermal thickening in the skin tissues of mice.
References: [1] Tang S, Liu J, Li F, et al. AP-1 inhibitor induces ferroptosis via the PI3K/AKT pathway in multiple myeloma cells[J]. Heliyon, 2024, 10(14). [2] Avouac J, Palumbo K, Tomcik M, et al. Inhibition of activator protein 1 signaling abrogates transforming growth factor β-mediated activation of fibroblasts and prevents experimental fibrosis[J]. Arthritis & Rheumatism, 2012, 64(5): 1642-1652.	

Background

T-5224 is a non-peptidic small molecule inhibitor of c-Fos/AP-1 that specifically inhibits DNA binding activity of c-Fos/c-Jun^[1]. T-5224 regulates mast cell (MC) via a c-Fos/EGR1/IL-4 axis, reduces Fc ϵ RI-mediated MC degranulation, and diminishes EGR1 and IL-4 expression^[2]. T-5224 has been widely used to suppress inflammation and improve skin barrier function in a murine atopic dermatitis-like dermatitis^[3].

In vitro, T-5224 treatment for 24 hours notably restrained the proliferation of ARP1 cells and RPMI8226 cells, with IC₅₀ values of 9.24 μ M and 11.41 μ M, respectively^[4]. T-5224 treatment (10 μ M) for 24 hours significantly inhibited the IL-1 β -stimulated production of MMP-1, MMP-3, IL-6, and TNF α in SW982 cells^[5]. Treatment with 80 μ M T-5224 for 48 hours markedly decreased the invasive activity and migratory ability of HSC-3-M3 cells and altered cell morphology^[6].

In vivo, T-5224 treatment via a single oral dose of 300mg/kg, inhibited the lipopolysaccharide (LPS)-induced increase in TNF- α levels in mouse serum and alleviated kidney damage in mice within 48 hours^[7]. Oral administration of T-5224 at a dose of 30mg/kg daily for three consecutive weeks prevented bleomycin-induced experimental skin fibrosis and reduced dermal thickening in mice^[8].

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References:

- [1] Ye N, Ding Y, Wild C, et al. Small molecule inhibitors targeting activator protein 1 (AP-1): Miniperspective[J]. Journal of medicinal chemistry, 2014, 57(16): 6930.
- [2] Wang H N, Ji K, Zhang L N, et al. Inhibition of c-Fos expression attenuates IgE-mediated mast cell activation and allergic inflammation by counteracting an inhibitory AP1/Egr1/IL-4 axis[J]. Journal of translational medicine, 2021, 19(1): 261.
- [3] Sasakura M, Urakami H, Tachibana K, et al. Topical application of activator protein-1 inhibitor T-5224 suppresses inflammation and improves skin barrier function in a murine atopic dermatitis-like dermatitis[J]. Allergology International, 2024, 73(2): 323-331.
- [4] Tang S, Liu J, Li F, et al. AP-1 inhibitor induces ferroptosis via the PI3K/AKT pathway in multiple myeloma cells[J]. Heliyon, 2024, 10(14).
- [5] Aikawa Y, Morimoto K, Yamamoto T, et al. Treatment of arthritis with a selective inhibitor of c-Fos/activator protein-1[J]. Nature biotechnology, 2008, 26(7): 817-823.
- [6] Kamide D, Yamashita T, Araki K, et al. Selective activator protein-1 inhibitor T-5224 prevents lymph node metastasis in an oral cancer model[J]. Cancer science, 2016, 107(5): 666-673.
- [7] Miyazaki H, Morishita J, Ueki M, et al. The effects of a selective inhibitor of c-Fos/activator protein-1 on endotoxin-induced acute kidney injury in mice[J]. BMC nephrology, 2012, 13(1): 153.
- [8] Avouac J, Palumbo K, Tomcik M, et al. Inhibition of activator protein 1 signaling abrogates transforming growth factor β -mediated activation of fibroblasts and prevents experimental fibrosis[J]. Arthritis & Rheumatism, 2012, 64(5): 1642-1652.

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