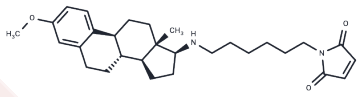
Data Sheet (Cat.No.T6243)

TargetMol

U-73122

Chemical Properties



CAS No. : 112648-68-7

Formula: C29H40N2O3

Molecular Weight: 464.64

Storage: Store under nitrogen
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	U-73122 (U73122) , an effective PLC inhibitor, reduces agonist-induced Ca2+ increases in platelets and PMN.
Targets(IC50)	Ferroptosis,Lipoxygenase,Phospholipase
In vitro	At a concentration of 0.1 mg/ml, U73122 inhibits the accumulation of 74% of lymphocytes and 65% of macrophages induced by carrageenan in the subcutaneous cavity of dogs. When administered at 30 mg/kg intraperitoneally (i.p.), U73122 blocks 65% and 80% of carrageenan-induced paw edema in rats 1 hour and 3 hours post-treatment, respectively. Furthermore, it completely inhibits the infiltration of macrophages and lymphocytes, as well as 80% of prostaglandin E2 production, in a mouse model of peritonitis triggered by lipopolysaccharides. U73122 also suppresses the swelling of mouse ears induced by 12-O-tetradecanoylphorbol-13-acetate.
In vivo	U-73122 inhibits the production of thromboxane B induced by collagen, where collagen induces this effect by inhibiting receptor-coupled arachidonic acid transfer. U-73122 also suppresses the aggregation of human polymorphonuclear neutrophils and the associated production of IP3 and diacylglycerol induced by FMLP. It notably inhibits the aggregation of human platelets induced by various agonists, including thrombin, collagen, ADP, and arachidonic acid (IC50 of 1-5 μM). Thrombin or U-46619 induces the production of IP3 and a subsequent rapid increase in intracellular Ca2+ by inhibiting the hydrolysis of platelet-soluble components catalyzed phosphatidylinositol [3H]mannose and phosphatidylinositol [3H]bisphosphate 4,5-diphosphate (Ki: 9/40 μM), which is inhibited by 10 μM of U-73122.
Kinase Assay	PMNs (4×107/4 mL) are incubated with U-73122 according to protocols. The reactions are stopped with cold calcium-free PBS. The cells are centrifuged at 750 × g (4°C) and resuspended in 1 mL of Triton X-100-free extraction buffer (50 mM Tris, pH 7.5, 50 mM fimercaptoethanol, 2 mM EGTA, 1 mM phenylmethylsulfonyl fluoride and 4 μg/mL of leupeptin, soybean trypsin inhibitor and aprotinin), and then sonicated for 10- and 5-sec consecutive bursts at 20% output. The lysates are centrifuged at 240 × g (4°C) for 20 mm in a TL-100 ultracentrifuge with the supernatant designated as the cytosol fraction. The pellet is resuspended in 1% Triton-containing extraction buffer, sonicated, shaken for 30 mm at 4°C and centrifuged (240 × g for 20 mm at 4°C). The supernatant constitutes the extractable particulate fraction, and the pellet is sonicated in extraction buffer with

Kinase Assay	Triton and constituted the nonextractable particulate fraction.
Cell Research	U-73122 is dissolved in DMSO. Agonist-induced production of IP3 in PMN is measured by use of the competitive radiobinding assy. PMN (2 x 106-107) in 0.2 mL of phosphate-buffered saline, pH 7.4 [NaC1 (138 mM), Na2HPO4 (8.1 mM), KH2PO4 (1.5 mM), KCI (2.7 mM), CaCl2 (1.0 mM), MgC12 (1.0 mM) and glucose (0.1%, w/v)] are incubated in conical polypropylene tubes at 37°C in a shaking water bath. U-73122 or U-73343 is added (in 1 µL of DMSO) 3 min before the addition of agonist, FMLP (0.1 µM) plus cytochalasin B (5 µg/mL). FMLP and cytochalasin B are added in 1 µL each of DMSO and ethanol, respectively. Appropriate vehicle controls are included in each experiment. PMN incubation mixtures are quenched with the addition of 0.07 mL of ice-cold TCA (20%, w/v) and a portion (0.2 mL) of the TCA extract is processed for the measurement of IP3 by competitive radiobinding as described above for platelets.

Solubility Information

Solubility	DMSO: 8 mg/mL (17.22 mM),Sonication and heating are recommended. H2O: < 0.1 mg/mL (insoluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1.25 mg/mL (2.69 mM),Solution. *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	2.1522 mL	10.761 mL	21.522 mL
5 mM	0.4304 mL	2.1522 mL	4.3044 mL
10 mM	0.2152 mL	1.0761 mL	2.1522 mL
50 mM	0.043 mL	0.2152 mL	0.4304 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

Bleasdale JE, et al. J Pharmacol Exp Ther, 1990, 255(2), 756-768.
Wang X, Cai J, Lin B, et al. GPR34-mediated sensing of lysophosphatidylserine released by apoptotic neutrophils activates type 3 innate lymphoid cells to mediate tissue repair. Immunity. 2021, 54(6): 1123-1136. e8.
Yan J, Zhang C, Xu Y, et al.GPR34 is a metabolic immune checkpoint for ILC1-mediated antitumor immunity.Nature immunology.2024: 1-11.
Sudi S, Chin Y Z, Wasli N S, et al. Carpaine Promotes Proliferation and Repair of H9c2 Cardiomyocytes after Oxidative Insults. Pharmaceuticals. 2022, 15(2): 230.
Smith RJ, et al. J Pharmacol Exp Ther, 1990, 253(2), 688-697.
Hou C, et al. J Pharmacol Exp Ther, 2004, 309(2), 697-704.
Ma L, Gong F, Xu J, et al. Uncarboxylated osteocalcin reverses the high glucose-induced inhibition of the osteogenic differentiation of MC3T3E1 cells via the GPRC6A/cAMP/PKA/AMPK signaling pathway. International Journal of Molecular Medicine. 2021 May;47(5):91. doi: 10.3892/ijmm.2021.4924. Epub 2021 Mar 31.
Zhu H, Liu X, Wang X, et al.Gβγ subunit inhibitor decreases DOM-induced head twitch response via the PLCβ/IP3/Ca2+/ERK and cAMP signaling pathways.European Journal of Pharmacology.2023: 176038.
Jin W, et al. Brain Res, 1994, 642(1-2), 237-243.
Yule DI, et al. J Biol Chem, 1992, 267(20), 13830-13835.
Cui S, Suo N, Yang Y, et al.The aminosteroid U73122 promotes oligodendrocytes generation and myelin formation. Acta Pharmacologica Sinica.2023: 1-12.
Ma L, Gong F, Xu J, et al. Uncarboxylated osteocalcin reverses the high glucose-induced inhibition of the osteogenic differentiation of MC3T3E1 cells via the GPRC6A/cAMP/PKA/AMPK signaling pathway[J]. International Journal of Molecular Medicine. 2021, 47(5): 1-11
Zhang Z, Zhou H, Gu W, et al.CGI1746 targets σ1R to modulate ferroptosis through mitochondria-associated membranes.Nature Chemical Biology.2024: 1-11.
Zhong T, Chen S, Deng K, et al.Magnesium alleviates extracellular histone-induced apoptosis and defective bacterial phagocytosis in macrophages by regulating intracellular calcium signal.International Immunopharmacology.2024, 132: 111870.
Gu Y P, Wang J M, Tian S, et al.Activation of TAS2R4 signaling attenuates podocyte injury induced by high glucose. Biochemical Pharmacology.2024: 116392.
Lin B, Zhou Y, Huang Z, et al.GPR34 senses demyelination to promote neuroinflammation and pathologies.Cellular & Molecular Immunology.2024: 1-14.