

Product Data Sheet

Product Name: R 59-022

Cat. No.: GC14583

Chemical Properties

Cas. No. 93076-89-2

Chemical Name 6-(2-(4-((4-fluorophenyl)(phenyl)methylene)piperidin-1-yl)ethyl)-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one

SMILES FC1=CC=C(C=C1)/C(C2=CC=CC=C2)=C3CCN(CCC4=C(C)N=C5SC=CN5C4=O)CC/3

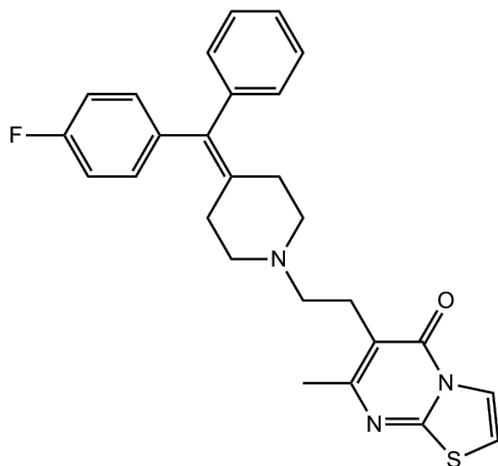
Formula $C_{27}H_{26}FN_3OS$ M.Wt 459.58

Solubility DMF: 20 mg/ml, DMF:PBS(pH7.2) (1:2): 0.25 mg/ml, DMSO: 5 mg/ml, Ethanol: 5 mg/ml
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	VeroE6 cells
Preparation Method	VeroE6 cells were seeded in clear bottom, black well tissue culture plates to be 80% confluent at the time of infection. The cells were treated with different concentrations of R 59-022 and infected with EBOV, expressing enhanced-GFP, at a multiplicity of infection of 0.1.
Reaction Conditions	2μM, 4μM; 4h
Applications	R 59-022 efficiently blocks EBOV GP-mediated entry into Vero cells.

Animal experiment [2]:

Animal models	Glioblastoma xenograft therapy model
Preparation Method	100,000 U87 GBM cells were implanted in 10μL of Dulbecco's Modified Eagle Medium. Beginning at 7 days postimplantation of tumor cells, mice were given daily intraperitoneal injections with either DMSO (v:v), 2mg/kg, or 10mg/kg of R 59-022 dissolved in DMSO in 50μL volume.
Dosage form	2mg/kg, 10mg/kg; ip; 13d
Applications	After daily intraperitoneal injection of the inhibitor R 59-022, the average tumor volume of the treated mice was significantly smaller than that of the control mice.

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References:

- [1]. Stewart CM, Dorion SS, Ottenbrite MA, et al. A diacylglycerol kinase inhibitor, R-59-022, blocks filovirus internalization in host cells. *Viruses*. 2019 Mar 1; 11(3): 206.
- [2]. Dominguez CL, Floyd DH, Xiao A, et al. Diacylglycerol kinase γ is a critical signaling node and novel therapeutic target in glioblastoma and other cancers. *Cancer discovery*. 2013 Jul 1; 3(7): 782-797.

Background

R 59-022 is a diacylglycerol kinase inhibitor ($IC_{50} = 2.8\mu M$) [1]. R 59-022 can inhibit diacylglycerol kinase on the human erythrocyte membrane, resulting in a significant increase in diacylglycerol levels, a decrease in phosphatidic acid formation, and an increase in protein kinase C activity [1-2]. R 59-022 is often used to treat cancer [3-4].

In MCF10A cells, R 59-022 ($1\mu M$, $10\mu M$, $100\mu M$; 72h) reduces the survival rate of SCRIB-knockdown H-RAS G^{12V} -expressing human mammary epithelial cells [4]. In VeroE6 cells, R 59-022 ($2\mu M$, $4\mu M$; 4h) efficiently blocks EBOV GP-mediated entry into Vero cells [5]. In adrenal chromaffin cells, nicotine and potassium depolarization-induced calcium influx is blocked by R 59-022 ($30\mu M$; 10min) [6]. In Swiss 3T3 cells, R 59-022 ($5\mu M$; 4h) enhances bombesin-stimulated protein kinase C activity and DNA synthesis [7].

In glioblastoma xenograft therapy model, after daily intraperitoneal injection of the inhibitor R 59-022 ($2mg/kg$, $10mg/kg$; ip; 13d), the average tumor volume of the treated mice was significantly smaller than that of the control mice [8]. In LCMV-infected $Sh2d1a^{-/-}$ mice, R 59-022 ($2mg/kg$; ip; 4d) reduces the numbers of activated virus-specific $CD8^{+}$ T cells [9].

References:

- [1]. de Courcelles DD, Roevens P, Van Belle H. R 59 022, a diacylglycerol kinase inhibitor. Its effect on diacylglycerol and thrombin-induced C kinase activation in the intact platelet. *Journal of Biological Chemistry*. 1985 Dec 15;260(29):15762-70.
- [2]. Nunn DL, Watson SP. A diacylglycerol kinase inhibitor, R59022, potentiates secretion by and aggregation of thrombin-stimulated human platelets. *Biochemical Journal*. 1987 May 1;243(3):809-

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- [3]. Liu K, Kunii N, Sakuma M, et al. A novel diacylglycerol kinase α -selective inhibitor, CU-3, induces cancer cell apoptosis and enhances immune response [S]. Journal of Lipid Research. 2016 Mar 1; 57(3):368-379.
- [4]. La Marca JE, Ely RW, Diepstraten ST, et al. A Drosophila chemical screen reveals synergistic effect of MEK and DGK α inhibition in Ras-driven cancer. Disease Models & Mechanisms. 2023 Mar 1; 16(3): dmm049769.
- [5]. Stewart CM, Dorion SS, Ottenbrite MA, et al. A diacylglycerol kinase inhibitor, R-59-022, blocks filovirus internalization in host cells. Viruses. 2019 Mar 1; 11(3): 206.
- [6]. Owen PJ, Jones JA, Boarder MR. Phosphatidic acid accumulation and catecholamine release in adrenal chromaffin cells: stimulation by high potassium and by nicotine, and effect of a diacylglycerol kinase inhibitor R 59 022. Journal of neurochemistry. 1991 Sep; 57(3): 769-774.
- [7]. Morris C, Rice P, Rozengurt E. The diacylglycerol kinase inhibitor R 59022 potentiates bombesin stimulation of protein kinase C activity and DNA synthesis in Swiss 3T3 cells. Biochemical and biophysical research communications. 1988 Sep 15; 155(2): 561-568.
- [8]. Dominguez CL, Floyd DH, Xiao A, et al. Diacylglycerol kinase α is a critical signaling node and novel therapeutic target in glioblastoma and other cancers. Cancer discovery. 2013 Jul 1; 3(7): 782-797.
- [9]. Ruffo E, Malacarne V, Larsen SE, et al. Inhibition of diacylglycerol kinase α restores restimulation-induced cell death and reduces immunopathology in XLP-1. Science translational medicine. 2016 Jan 13; 8(321): 321ra7.

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