R 59-022 hydrochloride

Cat. No.: HY-107613A

CAS No.: 93076-98-3

Molecular Formula: $C_{27}H_{27}ClFN_3OS$

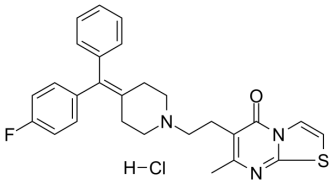
Molecular Weight: 496.04

Target: PKC; 5-HT Receptor

Pathway: Epigenetics; TGF-beta/Smad; GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (50.40 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0160 mL	10.0798 mL	20.1597 mL
	5 mM	0.4032 mL	2.0160 mL	4.0319 mL
	10 mM	0.2016 mL	1.0080 mL	2.0160 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.04 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.04 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.04 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

R 59-022 (DKGI-I) hydrochloride is a DGK inhibitor (IC_{50}: 2.8 μM). R 59-022 hydrochloride inhibits the phosphorylation of OAG to OAPA. R 59-022 hydrochloride is a 5-HT Receptor antagonist, and activates protein kinase C (PKC). R 59-022 hydrochloride potentiates thrombin-induced diacylglycerol production in platelets and inhibits phosphatidic acid production in neutrophils[1][2][3][4].

IC_{50} & Target			
	PKC	serotonin	DGK 2.8 μM (IC_{50})

In Vitro

R 59-022 (10 μM, 1 min) hydrochloride potentiates aggregation, but not shape change induced by sub-maximal concentrations of thrombin[2].
R 59-022 (30 μM, 0-60 min) hydrochloride increases release of Noradrenaline in chromaffin cells[3].
R 59-022 (40 μM, 30 min) hydrochloride activates PKC in HeLa and U87 cells[4].
R 59-022 (0-10 μM, 4 h) hydrochloride blocks EBOV GP-mediated entry into Vero cells[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[4]

Cell Line:	HeLa cells
Concentration:	40 uM
Incubation Time:	30 min
Result:	Increased the phosphorylation of PKC downstream targets by about 2.5-fold.

In Vivo

R 59-022 (2 mg/kg, i.p., 12 days) hydrochloride significantly increases median survival in SCID mice implanted with U87 GBM cells[6].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SCID mice implanted with U87 GBM cells[6]
Dosage:	10 mg/kg
Administration:	Intraperitoneal injection (i.p.)
Result:	Increased median survival and decreased tumor volume.

CUSTOMER VALIDATION

- Cancer Res. 2022 Aug 16;82(16):2887-2903.

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REFERENCES

[1]. de Chaffoy de Courcelles, D.C., et al. R 59 022, a diacylglycerol kinase inhibitor. Its effect on diacylglycerol and thrombin-induced C kinase activation in the intact platelet. J. Biol. Chem. 260(29), 15762-15770 (1985).

[2]. Nunn DL, et al. A diacylglycerol kinase inhibitor, R59022, potentiates secretion by and aggregation of thrombin-stimulated human platelets. Biochem J. 1987 May 1;243(3):809-13.

[3]. Jones JA, et al. Influence of phorbol esters, and diacylglycerol kinase and lipase inhibitors on noradrenalinerelease and phosphoinositide hydrolysis in chromaffin cells. Br J Pharmacol. 1990 Nov;101(3):521-6.

[4]. Boroda S, et al. Dual activities of ritanserin and R59022 as DGKα inhibitors and serotonin receptor antagonists. Biochem Pharmacol. 2017 Jan 1;123:29-39.

[5]. Stewart CM, et al. A Diacylglycerol Kinase Inhibitor, R-59-022, Blocks Filovirus Internalization in Host Cells. Viruses. 2019 Mar 1;11(3). pii: E206.

[6]. Dominguez CL, et al. Diacylglycerol kinase α is a critical signaling node and novel therapeutic target in glioblastoma and other cancers. Cancer Discov. 2013 Jul;3(7):782-97.

Caution: Product has not been fully validated for medical applications. For research use only.

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