RWJ-56110 dihydrochloride

Cat. No.: HY-108556A

CAS No.: 2387505-58-8

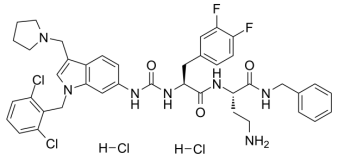
Molecular Formula: $C_{41}H_{45}Cl_4F_2N_7O_3$

Molecular Weight: 863.65

Target: Protease-Activated Receptor (PAR); Apoptosis

Pathway: GPCR/G Protein; Apoptosis

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 200 mg/mL (231.58 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.1579 mL	5.7894 mL	11.5788 mL
	5 mM	0.2316 mL	1.1579 mL	2.3158 mL
	10 mM	0.1158 mL	0.5789 mL	1.1579 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: ≥ 5 mg/mL (5.79 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (5.79 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (5.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RWJ-56110 dihydrochloride is a potent, selective, peptide-mimetic inhibitor of PAR-1 activation and internalization (binding IC_{50}=0.44 uM) and shows no effect on PAR-2, PAR-3, or PAR-4. RWJ-56110 dihydrochloride inhibits the aggregation of human platelets induced by both SFLLRN-NH2 (IC_{50}=0.16 μM) and thrombin (IC_{50}=0.34 μM), quite selective relative to U46619 (HY-108566). RWJ-56110 dihydrochloride blocks angiogenesis and blocks the formation of new vessels in vivo. RWJ-56110 dihydrochloride induces cell apoptosis[1][2].

IC_{50} & Target

IC50: 0.44 uM (PAR-1)
IC50: 0.16 μM (the aggregation of human platelets induced by SFLLRN-NH2)

	IC50: 0.34 μM (the aggregation of human platelets induced by thrombin)[1][2]
In Vitro	Proteinase-activated receptors (PARs) are a family of G protein-coupled receptors activated by the proteolytic cleavage of their N-terminal extracellular domain, exposing a new amino terminal sequence that functions as a tethered ligand to activate the receptors. RWJ56110 inhibits the aggregation of human platelets induced by both SFLLRN-NH2 (IC_{50}=0.16 μM) and thrombin (IC_{50}=0.34 μM) while being quite selective relative to collagen and the thromboxane mimetic U46619 (HY-108566)[1]. RWJ-56110 dihydrochloride is fully inhibits thrombin-induced RASMC proliferation with an IC_{50} value of 3.5 μM. RWJ-56110 dihydrochloride shows blockade of thrombin's action with RASMC calcium mobilization (IC_{50}=0.12 μM), as well as with HMVEC (IC_{50}=0.13 μM) and HASMC calcium mobilization (IC_{50}=0.17 μM)[1]. RWJ56110 (0.1-10 μM; 24-96 hours) inhibits endothelial cell growth dose-dependently, with half-maximal inhibitory concentration of RWJ56110 is approximately 10 μM[2]. RWJ56110 (0.1-10 μM; 6 hours) inhibits DNA synthesis of endothelial cells in a thymidine incorporation assays. Endothelial cells are in fast-growing state (50-60% confluence), RWJ56110 inhibits cell DNA synthesis in a dose-dependent manner, but when cells that are in the quiescent state (100% confluent), the inhibitory effect of PAR-1 antagonists is much less pronounced[2]. RWJ56110 (0.1-10 μM; pretreatment for 15 min) inhibits thrombin-induced Erk1/2 activation in a concentration-dependent manner. However, when endothelial cells are stimulated by FBS (final concentration 4%), it reduces partially the activated levels of Erk1/2[2]. RWJ56110 (30 μM; 24 hours) has an inhibitory effect on endothelial cell cycle progression. It reduces the percentage of cells in the S phase, while alterations in the percentages of G1 and G2/M cells are less pronounced[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

Cell Line:	Endothelial cells
Concentration:	0 μM; 3 μM; 1 μM; 3 μM; 10 μM
Incubation Time:	Pretreatment for 15 min
Result:	Resulted in MAPK activation in Endothelial cells.

Cell Cycle Analysis[2]

Cell Line:	Endothelial cells
Concentration:	0 μM; 3 μM; 1 μM; 3 μM; 10 μM
Incubation Time:	Pretreatment for 15 min
Result:	Reduced cell number in S phase.

REFERENCES

[1]. Andrade-Gordon, et al.Design, synthesis, and biological characterization of a peptide-mimetic antagonist for a tethered-ligand receptor. oc Natl Acad Sci U S A. 1999 Oct 26;96(22):12257-62.

[2]. Panagiota Zania, et al. Blockade of angiogenesis by small molecule antagonists to protease-activated receptor-1: association with endothelial cell growth suppression and induction of apoptosis. J Pharmacol Exp Ther. 2006 Jul;318(1):246-54.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA