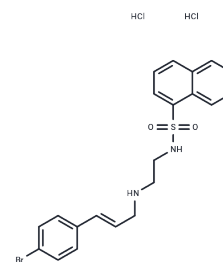


H-89 dihydrochloride

Chemical Properties

CAS No. :	130964-39-5
Formula:	C ₂₀ H ₂₀ BrN ₃ O ₂ S·2HCl
Molecular Weight:	519.28
Storage:	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	H-89 dihydrochloride (5-Isoquinolinesulfonamide) is a potent inhibitor of protein kinase A (PKA; IC ₅₀ : 0.14 μM, K _i : 48 nM).
Targets(IC ₅₀)	Autophagy,PKA,S6 Kinase
In vitro	H-89 was shown to have a potent and selective inhibitory action against protein kinase A, with K _i of 0.048 microM. Pretreatment with H-89 led to a dose-dependent inhibition of the forskolin-induced protein phosphorylation, with no decrease in intracellular cyclic AMP levels in PC12D cells, and the NGF-induced protein phosphorylation was not inhibited. H-89 also significantly inhibited the forskolin-induced neurite outgrowth from PC12D cells. This inhibition also occurred when H-89 was added before the addition of dibutyryl cAMP. Pretreatment of PC12D cells with H-89 (30 microM) inhibited significantly cAMP-dependent histone IIb phosphorylation activity in cell lysates but did not affect other protein phosphorylation activity [1]. H-89 also inhibits S6K1, MSK1, ROCK-II, PKBα, and MAPKAP-K1b with IC ₅₀ values of 0.08, 0.12, 0.27, 2.6, and 2.8 μM, respectively [2]. In skinned EDL fibers of the rat, force responses to depolarization (by ion substitution) were inhibited only slightly by 10 microM H-89, a concentration more than sufficient to fully inhibit PKA. At 1-2 microM, H-89 significantly slowed the repriming rate in rat skinned fibers. With 100 microM H-89, the force response to depolarization by ion substitution was completely abolished. In intact single fibers of the flexor digitorum longus (FDB) muscle of the mouse, 1-3 microM H-89 had no noticeable effect on action-potential-mediated Ca ²⁺ transients [3].
In vivo	Different doses of H-89 (0.05, 0.1, 0.2 mg/100g) were administered intraperitoneally (i. p.), 30 min before intravenous (i.v.) infusion of PTZ (0.5% w/v). Intraperitoneal administration of H-89 (0.2 mg/100g) significantly increased seizure latency and threshold in PTZ-treated animals. Pretreatment of animals with PTX (50 and 100 mg/kg) attenuated the anticonvulsant effect of H-89 (0.2 mg/100g) in PTZ-exposed animals. H-89 (0.05, 0.2 mg/100g) prevented the epileptogenic activity of bucladesine (300 nM) with a significant increase of seizure latency and seizure threshold [4]. Treatment with H89 (10 mg/kg, administered i.p.) significantly inhibited AHR in OVA-sensitized/challenged mice, whereas it had no effect on airway responses in control mice. Treatment with H89 decreased eosinophil numbers by 80%, neutrophil numbers by 64% and lymphocyte numbers by 74% without any effect on macrophage. In the moderate model, the cell infiltrate consisted of 39.3% eosinophils, 58.5% macrophages, 1.9% neutrophils, and 0.3% lymphocytes and was entirely inhibited by H89 [5].

Kinase Assay	All protein kinase activities were linear with respect to time in every incubation. Assays were performed either manually for 10 min at 30 °C in 50 µl incubations using [γ - ³² P]ATP or with a Biomek 2000 Laboratory Automation Workstation in a 96-well format for 40 min at ambient temperature in 25 µl incubations using [γ - ³³ P]ATP. The concentrations of ATP and magnesium acetate were 0.1 mM and 10 mM respectively unless stated otherwise. This concentration of ATP is 5–10-fold higher than the K_m for ATP of most of the protein kinases studied in the present paper, but lower than the normal intracellular concentration, which is in the millimolar range. All assays were initiated with MgATP. Manual assays were terminated by spotting aliquots of each incubation on to phosphocellulose paper, followed by immersion in 50 mM phosphoric acid. Robotic assays were terminated by the addition of 5 µl of 0.5 M phosphoric acid before spotting aliquots on to P30 filter mats. All papers were then washed four times in 50 mM phosphoric acid to remove ATP, once in acetone (manual incubations) or methanol (robotic incubations), and then dried and counted for radioactivity [2].
Cell Research	After 48 h in culture, PCL2D cells are cultured in a test medium containing 30 µM H-89 for 1 h and then exposed to a fresh medium that contained both 10 µM forskolin and 30 µM H-89. Cells are scraped off with a rubber policeman and sonicated in the presence of 0.5 mL of 6% trichloroacetic acid. To extract trichloroacetic acid, 2 mL of petroleum ether is added, the preparation mixed and centrifuged at 3000 rpm for 10 min. After aspiration of the upper layer, the residue sample solution is used for determination [1].
Animal Research	H89 (N-[2-(p-Bromocinnamylamino)ethyl]-5-isoquinolinesulfonamide], di-HCl Salt) (10 mg/kg) suspended in 5% DMSO in saline was administered i.p. two hours before each OVA challenge (or two hours before the last OVA challenge). Control animals received equivalent volumes (200 µl) of 5% DMSO in saline [5].

Solubility Information

Solubility	H ₂ O: < 1 mg/mL (insoluble or slightly soluble) DMSO: 104 mg/mL (200.28 mM), Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	5% DMSO+95% Saline: 3.16 mg/mL (6.09 mM), Solution. <i>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.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.9257 mL	9.6287 mL	19.2574 mL
5 mM	0.3851 mL	1.9257 mL	3.8515 mL
10 mM	0.1926 mL	0.9629 mL	1.9257 mL
50 mM	0.0385 mL	0.1926 mL	0.3851 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

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