H-89 dihydrochloride

Cat. No.: HY-15979A

CAS No.: 130964-39-5

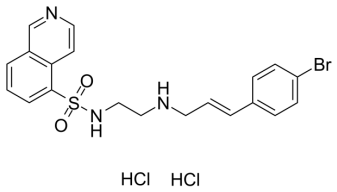
Molecular Formula: $C_{20}H_{22}BrCl_2N_3O_2S$

Molecular Weight: 519.28

Target: PKA; Autophagy

Pathway: Stem Cell/Wnt; TGF-beta/Smad; Autophagy

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (192.57 mM; Need ultrasonic)
H_2O : 5 mg/mL (9.63 mM; ultrasonic and warming and heat to 80°C)

Preparing Stock Solutions

Mass / Solvent / Concentration	1 mg	5 mg	10 mg
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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% saline
   Solubility: 5 mg/mL (9.63 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.75 mg/mL (5.30 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (5.30 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.81 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.81 mM); Clear solution
6. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.81 mM); Clear solution
7. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: ≥ 0.55 mg/mL (1.06 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	H-89 dihydrochloride is a potent and selective inhibitor of protein kinase A (PKA) with an IC_{50} of 48 nM and has weak inhibition on PKG, PKC, Casein Kinase.
IC_{50} & Target	IC50: 48 nM (protein kinase A)
In Vitro	H-89 inhibits protein kinase A, in competitive fashion against ATP. H-89 causes a dose-dependent inhibition of the forskolin-induced protein phosphorylation, with no decrease in intracellular cyclic AMP levels in PC12D cells. H-89 significantly inhibits the forskolin-induced neurite outgrowth from PC12D cells. H-89 (30 μM) inhibits significantly cAMP-dependent histone IIb phosphorylation activity in PC12D cell lysates[1]. H-89 (1-2 μM) significantly slows the repriming rate in rat skinned fibres, most likely due to it deleteriously affecting the T-system potential. H-89 (10-100 μM) inhibits net Ca^{2+} uptake by the SR and affectes the Ca^{2+}-sensitivity of the contractile apparatus in rat skinned fibres[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	H-89 (0.2 mg/100g, i.p.) significantly increases seizure latency and threshold in PTZ-treated animals. H-89 (0.05, 0.2 mg/100 g, i.p.) prevents the epileptogenic activity of bucladesine (300 nM) with significant increase of seizure latency and seizure threshold[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	After 48 h in culture, PCl2D cells are cultured in test medium containing 30 μM H-89 for 1 h and then exposed to 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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male albino mice weighing 20-25 g are obtained. BL-191 (25, 50, 100 mg/kg), bucladesine (50, 100, 300 nM/mouse) and H-89 (0.05, 0.1, 0.2 mg/100 g) are administered intraperitoneally (i.p.) 30 min before intravenous (i.v.) infusion of PTZ. In combination groups, the first and second components are injected 45 and 30 min before PTZ infusion. In all groups, the respective control animalsreceive an appropriate volume of vehicle. For the i.v. infusion, the needle is inserted into the lateral tail vein, fixed to the tail vein by a narrow piece of adhesive tape, and the animal is allowed to move freely. PTZ solution is infused at a concentration rate of 1 mL/min. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2023 Aug 9;8(1):290.
- Cell Metab. 2021 Sep 8;S1550-4131(21)00375-2.
- Cell Metab. 2021 Mar 2;33(3):565-580.e7.
- Cell Mol Immunol. 2023 Jan 5.
- Nat Commun. 2023 May 31;14(1):3159.

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REFERENCES

[1]. Chijiwa T, et al. Inhibition of forskolin-induced neurite outgrowth and protein phosphorylation by a newly synthesized selective inhibitor of cyclic AMP-dependent protein kinase, N-[2-(p-bromocinnamylamino)ethyl]-5-isoquinolinesulfonamide (H-89), of PC12D

[2]. Blazev R, et al. Effects of the PKA inhibitor H-89 on excitation-contraction coupling in skinned and intact skeletal muscle fibres. J Muscle Res Cell Motil. 2001;22(3):277-86.

[3]. Hosseini-Zare MS, et al. Effects of BL-191 and H-89 on epileptogenic activity of bucladesine in pentylenetetrazol-treated mice. Eur J Pharmacol. 2011 Nov 30;670(2-3):464-70.

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