**Proteins** 

# **HC-070**

Cat. No.: HY-112302 CAS No.: 1628291-95-1 Molecular Formula:  $\mathsf{C_{22}H_{20}Cl_2N_4O_4}$ 

Molecular Weight: 475.32

Target: TRP Channel

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: Powder -20°C 3 years

4°C 2 years

In solvent -80°C 6 months

> -20°C 1 month

**Product** Data Sheet

## **SOLVENT & SOLUBILITY**

In Vitro DMSO:  $\geq$  62.5 mg/mL (131.49 mM)

\* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg
	1 mM	2.1038 mL	10.5192 mL	21.0385 mL
	5 mM	0.4208 mL	2.1038 mL	4.2077 mL
	10 mM	0.2104 mL	1.0519 mL	2.1038 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 (5.26 mM); Clear solution
- 2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.26 mM); Clear solution

### **BIOLOGICAL ACTIVITY**

Description	HC-070 is an antagonist of TRPC4/TRPC5, with IC <sub>50</sub> s of 9.3 nm and 46 nm for nTRPC5 and nTRPC4 in cells, respectively.	
IC <sub>50</sub> & Target	IC50: 9.3 nM (hTRPC5, cell assay), 46 nM (hTRPC4, cell assay) <sup>[1]</sup>	
In Vitro	HC-070 is an antagonist of TRPC4/TRPC5, with IC $_{50}$ s of 9.3 nM and 46 nM for hTRPC5 and hTRPC4, respectively. HC-070 weakly inhibits TRPC3 (IC $_{50}$ , 1 $\mu$ M), and is at least 400-fold selective for human TRPC4 and TRPC5-containing channels versus the other channels examined. HC-070 inhibits lanthanum-activated hTRPC5-, mTRPC5-, rTRPC5-mediated currents with IC $_{50}$ s of 0.52 nM, 0.55 nM, and 0.32 nM in whole-cell manual patch clamp. Furthermore, HC-070 blocks M2R-activated human TRPC1/TRPC4 channels with an IC $_{50}$ of 1.3 nM and La $^{3+}$ - and M1R-activated human TRPC1/5 channels with IC $_{50}$ s of 1.4 nM	

and 4.4 nM. HC-070 inhibits human TRPC5 currents activated via muscarinic type 1 (M1R) with an IC<sub>50</sub> of 2.0 nM. HC-070 also suppresses hTRPC4 currents via M2R with an IC<sub>50</sub> of 0.49 nM. HC-070 (20 nM) reduces CCK-4 evoked neuronal activity in the amygdala slices<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

HC-070 (1 mg/kg, p.o.) affects mice with increased evoked anxiety (CCK-4), but shows no effects in the absence of CCK-4. HC-070 (0.3, 1 or 3 mg/kg, p.o.) decreases anxiety in a standard EPM (more light/high anxiety). HC-070 (1 mg/kg) reduces the increased capacity for fear memory in mice subjected to chronic social stress on days 1-15. In addition, HC-070 (1, 3, 10 mg/kg, p.o.) causes reduction in marble burying behavior. HC-070 (0.3, 1, 3, 10 mg/kg, p.o.) also reduces time of immobility in a tail suspension test but does not impact locomotor activity in mice<sup>[1]</sup>.

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#### **PROTOCOL**

# Animal Administration [1]

#### Mice<sup>[1]</sup>

The room is illuminated with fluorescent lighting on a 12-hour light/dark cycle. The light cycle is reversed, so that the dark cycle is from 6 am-6 pm daily and studies are performed when animals are more active. Groups of male C57/BL6 mice (10 weeks old) are dosed PO with 0.5% methyl cellulose or HC-070 at 0.3, 1 or 3 mg/kg (n = 10). The positive control, 1.5 mg/kg diazepam, is administered IP 30 minutes prior to testing (n = 10). Immediately following dosing, mice are returned to their home cage. At 60 minutes post vehicle or HC-070 administration, and 30 minutes post diazepam administration, mice are placed onto the elevated plus maze, one at a time, and their session recorded for 5 minutes. Videos are manually scored for number of open arm entries by a scorer blinded to treatment. All animals that fall off the maze during the test are removed from analysis<sup>[1]</sup>.

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#### **CUSTOMER VALIDATION**

- Sci Transl Med. 2021 May 26;13(595):eabd7702.
- bioRxiv. 2020 Jul.

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# REFERENCES

[1]. Just S, et al. Treatment with HC-070, a potent inhibitor of TRPC4 and TRPC5, leads to anxiolytic and antidepressant effects in mice. PLoS One. 2018 Jan 31:13(1):e0191225.

 $\label{lem:caution:Product} \textbf{Caution: Product has not been fully validated for medical applications. For research use only.}$ 

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Page 3 of 3 www.MedChemExpress.com