SB-705498

Cat. No.: HY-10633

CAS No.: 501951-42-4

Molecular Formula: $C_{17}H_{16}BrF_3N_4O$

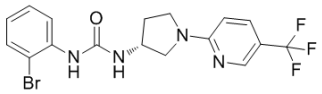
Molecular Weight: 429.23

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (232.98 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3298 mL	11.6488 mL	23.2975 mL
5 mM	0.4660 mL	2.3298 mL	4.6595 mL
10 mM	0.2330 mL	1.1649 mL	2.3298 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SB-705498 is a potent, selective and orally bioavailable transient receptor potential vanilloid 1 (TRPV1) receptor antagonist with a pIC_{50} of 7.1.

IC_{50} & Target

pIC50: 7.1

In Vitro

SB705498 (0.3 nM-1 μM) potently inhibits capsaicin-induced activation of human TRPV1 expressed in 1321N1 cells or HEK293 cells with apparent pK_i of 7.5 or 7.6, respectively. Coapplication of 100 nM SB705498 rapidly, completely and reversibly inhibits hTRPV1 expressed in HEK293 cells. SB705498 has no significant effect on endogenous [Ca^{2+}] responses in HEK293 cells produced by muscarinic acetylcholine receptor activation with carbachol or store-operated channel-mediated Ca^{2+} entry after depletion of intracellular stores with the Ca^{2+} pump inhibitor thapsigargin. SB705498 (10 pM-1 μM) also has no

	significant antagonist effect versus the close TRPV1 receptor paralog TRPV4 transiently expressed in HEK293 cells and activated using the synthetic ligand 4α-phorbol-12,13-didecanoate (10 μM). SB705498 reveals good antagonist potency against both the rat and guinea pig TRPV1. SB705498 antagonizes rat and guinea pig TRPV1 with pK_i of 7.5 and 7.3, respectively. Coapplication of 100 nM to 10 μM SB705498 to the steady state of a maintained capsaicin response leads to rapid and complete inhibition of hTRPV1 at -70 mV. SB705498 inhibits capsaicin-mediated activation of hTRPV1 with IC_{50} of 3 nM and 17 nM at positive and negative holding potentials (-70 mV and + 70 mV), respectively. Coapplication of 1 μM SB705498 to the plateau period of the response produces complete and reversible inhibition of the TRPV1-mediated conductance[1]. SB705498 shows approximately equal activity versus multiple and diverse chemical and physical modes of TRPV1 receptor activation. SB705498 shows little or no activity versus a wide range of ion channels, receptors and enzymes. SB705498 produces full blockade of heat as well as pH activation of hTRPV1[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SB705498 exhibits potent and reversible blockade against the multiple modes of TRPV1 activation, namely the vanilloid (capsaicin), heat- and acid-mediated activation of the receptor. SB705498 displays excellent activity at 10 and 30 mg/kg po with good reversal of allodynia. SB705498 (10 mg/kg p.o.) gives 80% reversal of allodynia in the guinea pig FCA model[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Rep. 2016 Jul 20;6:30168.

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REFERENCES

[1]. Martin J. Gunthorpe, et al. Characterization of SB-705498, a Potent and Selective Vanilloid Receptor-1 (VR1/TRPV1) Antagonist That Inhibits the Capsaicin-, Acid-, and Heat-Mediated Activation of the Receptor. JPET June 2007 vol. 321 no. 3 1183-1192.

[2]. Rami HK, et al. Discovery of SB-705498: a potent, selective and orally bioavailable TRPV1 antagonist suitable for clinical development. Bioorg Med Chem Lett. 2006 Jun 15;16(12):3287-91.

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

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