SSD114 hydrochloride

Cat. No.: HY-103668A

CAS No.: 2319790-02-6

Molecular Formula: $C_{18}H_{21}ClF_3N_3O$

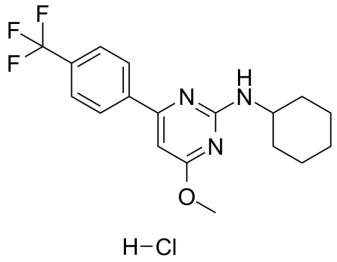
Molecular Weight: 387.83

Target: GABA Receptor

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 130 mg/mL (335.20 mM; Need ultrasonic)

H_2O : 2 mg/mL (5.16 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5784 mL	12.8922 mL	25.7845 mL
5 mM	0.5157 mL	2.5784 mL	5.1569 mL
10 mM	0.2578 mL	1.2892 mL	2.5784 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: ≥ 3.25 mg/mL (8.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 3.25 mg/mL (8.38 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.25 mg/mL (8.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SSD114 hydrochloride is a novel $GABA_B$ receptor positive allosteric modulator.

IC_{50} & Target

$GABA_B$ receptor[1]

In Vitro

In the presence of 10 μM GABA, SSD114 hydrochloride at 25 μM significantly increases (to approximately 170% above basal levels) the [^{35}S]GTPγS stimulation induced by GABA alone. SSD114 hydrochloride, added at 15 and 30 μM, induces a leftward shift of the GABA concentration-response curve with a slight concomitant increase of maximal GABA stimulation at the highest concentration. In the presence of both 15 and 30 μM SSD114 hydrochloride, the EC_{50} for GABA decreases by 2 and

	2.5 fold, respectively, while the maximal stimulation (Emax) is potentiated only at the concentration of 30 μM, reaching 161±5.09% over the basal value[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The onset of loss of righting reflex (LORR) is reduced by pretreatment with SSD114 hydrochloride [$F_{(5,30)}$=4.55, P<0.005]. Post hoc analysis indicates that the onset of LORR is significantly lower in mouse groups pretreated with doses of SSD114 hydrochloride equal to or higher than 10 mg/kg than in vehicle-treated mice. The duration of LORR is increased by pretreatment with SSD114 hydrochloride [$F_{(5,30)}$=4.81, P<0.005]. Post hoc analysis indicates that the duration of LORR is significantly longer in mouse groups pretreated with 10 and 100 mg/kg SSD114 hydrochloride than in vehicle-treated mice[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells are transfected and seeded into 96-well microplates. 24 h after transfection, cells are washed twice with PBS and incubated in the presence or absence of SSD114 hydrochloride (different concentrations) for 15 min before substrate addition in a 96-well microplate. The Bioluminescence resonance energy transfer (BRET) ratio is calculated as the emission of YFP (530 to 570 nm) over the emission of RLuc (370 to 470 nm). The curves are fitted using Graph Pad Prism 5.0. The amplitude-weighted mean time constant is obtained by fitting the BRET recovery phase to a double exponential function. Δ BRET is calculated as the difference between the basal and the plateau of the BRET signal[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male Sprague-Dawley rats and DBA mice, weighing 200 to 250 and 20 to 25 g, respectively, are used. On the test day, mice are divided into six groups (n=6 each) matched by body weight. Mice are treated acutely and intraperitoneally with 0, 1, 3, 10, 30, and 100 mg/kg SSD114 hydrochloride and sedation/hypnosis is measured. Specifically, after baclofen injection, each mouse is placed on its back once every 60 s until it is unable to right itself within 60 s. The time between baclofen injection and the start of the 60-s interval during which the mouse is unable to right itself is measured as the onset of loss of righting reflex (LORR). Each mouse is then left undisturbed on its back until it spontaneously regained its righting reflex (determined as having at least three paws under its body). Complete recovery of the righting reflex is defined as the mouse being able to turn itself upright twice more within 60 s. If this criterion is not fulfilled, the mouse is left undisturbed until it spontaneously regained its righting reflex. The time between loss and recovery of righting reflex is monitored in each mouse and defined as the duration of LORR. Observations are conducted by an operator unaware of the drug treatment[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Porcu A, et al. In vitro and in vivo pharmacological characterization of SSD114, a novel GABAB positive allosteric modulator. Eur J Pharmacol. 2016 Nov 15;791:115-123.

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