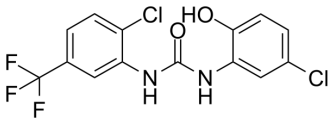
NS 1738

Cat. No.:	HY-12151
CAS No.:	501684-93-1
Molecular Formula:	$C_{14}H_9Cl_2F_3N_2O_2$
Molecular Weight:	365.13
Target:	nAChR
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (273.88 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.7388 mL	13.6938 mL	27.3875 mL
5 mM	0.5478 mL	2.7388 mL	5.4775 mL
10 mM	0.2739 mL	1.3694 mL	2.7388 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 (6.85 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.85 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.85 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NS 1738 (NSC 213859) is a novel positive allosteric modulator of the α7 nAChR, with respect to positive modulation of α7 nAChR (EC_{50}=3.4 μM in oocyte experiments).

IC_{50} & Target

EC50: 3.4 μM (α7 nAChR, in oocyte experiments)[1]

In Vitro

NS 1738 acts by increasing the peak amplitude of acetylcholine (ACh)-evoked currents at all concentrations; thus, it

	increased the maximal efficacy of ACh. Plotting peak current amplitude against the logarithm of the NS 1738 concentration used for preincubation reveals a sigmoidal concentration-response relationship that is well fit by the Hill equation (EC_{50}=3.4 μM). Under similar experimental conditions, NS 1738 shows comparable efficacy and potency at the rat α7 nAChR (EC_{50}=3.9 μM)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To estimate the ability of NS 1738 to permeate the blood-brain barrier, rats are administered 10 mg/kg NS 1738 intraperitoneally. Peak brain concentrations are measured approximately 30 min after injection, and they amount to ~80 ng/mL (~200 nM) at this dose. The ratio between the amount of compound entering the brain and that in plasma is AUC_{brain} /AUC_{plasma}=0.50. The half-life in plasma is estimated to 42 min. Incubation of NS1738 with isolated liver microsomes in vitro indicates that approximately 60 and 75% of NS 1738 is metabolized via the cytochrome P450 system in mouse and rat, respectively, within 1 h. Adult rats administered NS 1738 at 10 and 30 mg/kg i.p. immediately following the initial exposure to a juvenile rat (T1) display significant decreases in the investigative duration of a subsequent exposure to the same juvenile (T2) 2 h later (T2/T1 ratio of 0.69±0.13 and 0.61±0.07, respectively)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats[1] Sprague-Dawley rats are used. Adult (2-4 months; 400-450 g) and juvenile (50-60 g) animals are allowed to acclimate to the test room for 90 to 120 min before starting. After acclimation, adult rats are placed alone in their respective test cages. After a brief habituation period (30 min), they are allowed to interact for 5 min with a juvenile rat (trial; T1). During the interactive trial, the adult exhibits investigative behaviors that include close following, grooming, and/or sniffing of the juvenile for as much as 40 to 50% of the trial duration. The time of the investigative interaction is recorded in seconds. The juvenile rat is then removed, and the adult rats are immediately administered varying doses of NS 1738 (10 and 30 mg/kg NS-1738 i.p.) [prepared in 5% ethanol/95% hydroxypropyl-B-cyclodextrin (34% solution); 2.0 mL/kg i.p.] or Nicotine (0.1 mg/kg i.p.), and then they are returned to their home cage. A second 5-min interactive trial (T2) is conducted 120 min later in the same test cage, and investigative behavior of the adult rat is again monitored and the time is recorded. Recognition ratios of time spent investing the familiar juvenile in T2 divided by time spent investigating the juvenile in T1 are calculated. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Timmermann DB, et al. An allosteric modulator of the alpha7 nicotinic acetylcholine receptor possessing cognition-enhancing properties in vivo. J Pharmacol Exp Ther. 2007 Oct;323(1):294-307.

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