Dizocilpine maleate

Cat. No.: HY-15084

CAS No.: 77086-22-7

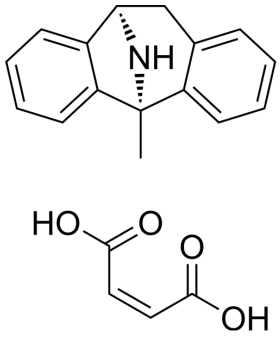
Molecular Formula: $C_{20}H_{19}NO_4$

Molecular Weight: 337.37

Target: iGluR

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

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 : 133.33 mg/mL (395.20 mM; Need ultrasonic)
Ethanol : 25 mg/mL (74.10 mM; Need ultrasonic)
H_2O : 7.69 mg/mL (22.79 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.9641 mL	14.8205 mL	29.6410 mL
5 mM	0.5928 mL	2.9641 mL	5.9282 mL
10 mM	0.2964 mL	1.4821 mL	2.9641 mL

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

In Vivo

1. Add each solvent one by one: Saline
   Solubility: 3.45 mg/mL (10.23 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.41 mM); Clear solution
3. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.41 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.19 mg/mL (6.49 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.17 mM); Clear solution
6. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Dizocilpine maleate (MK-801 maleate) is a potent, selective and non-competitive NMDA receptor antagonist with K_d of 37.2 nM in rat brain membranes.
IC_{50} & Target	NMDA Receptor
In Vitro	[^{3}H]Dizocilpine maleate binds with NMDA receptor with a K_d of 37.2±2.7 nM in rat cerebral cortical membranes[1]. Dizocilpine maleate causes a progressive, long-lasting blockade of current induced by N-Me-D-Asp[3]. Dizocilpine maleate progressively suppresses of current induced by NMDA. Mg^{2+} (10 mM) prevents Dizocilpine from blocking the N-Me-D-Asp-induced current, even when Dizocilpine (MK-801) is applied for a long time in the presence of NMDA. Dizocilpine blocks NMDA-activated single-channel activity in outside-out patches[3]. Dizocilpine maleate (< 500 μM) inhibits activation of microglia induced by LPS with increased Cox-2 protein expression in BV-2 cells. Dizocilpine (MK-801; <500 μM) reduces microglial TNF-α output with an EC_{50} of 400 μM in BV-2 cells[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Dizocilpine maleate can be used in animal modeling to construct models of schizophrenia. Dizocilpine maleate (MK 801 maleate) (1 mg/kg) treatment before each METH injection reduces the extent of DA depletion by 55% in striatal of mice. Dizocilpine (MK 801) (1 mg/kg) also attenuates the effects of METH on microglial activation in striatal of mice[4]. Dizocilpine maleate (0.05, 0.2 mg/kg, i.p.) attenuates subsequent cocaine-primed reinstatement without disruption in rats. Dizocilpine maleate (0.2 mg/kg, i.p.) prior to two reactivation sessions in the home cage shows no suppression on subsequent cocaine-primed reinstatement[5]. Dizocilpine maleate (0.03, 0.1, 0.3 and 1 mg/kg, i.p.) significantly increases the ambulation of mice at 0.3 and 1 mg/kg, but not at 0.03 and 0.1 mg/kg[6].Dizocilpine maleate (0.2 mg/kg, i.p.) exhibits a half-time of 52.31 min, an AUC of 3185.48 nM·min and a clearance of 34 nM in Sprague-Dawley rats[2]. Induction of Schizophrenia Background The specific mechanism of schizophrenia induction is unclear. One hypothesis is that, Dizocilpine maleateleads to dysregulation of glutamatergic system through NMDA inhibition[2]. Specific Mmodeling Methods Rats: Sprague-Dawley • male • adult with weight of 250-300 g Administration: 0.4 mg/kg • i.p. • single dose. Note Dizocilpine maleate is dissolved in 0.9% sterile saline. Modeling Indicators Behavior: Increased spontaneous activity with obvious anxiety-like behavior, increased motor activity in longer diatance (hyperactivity), reduced time staying in central area (avoidance of central area). Prepulse Inhibition (PPI): Decreased PPI significantly. maze test:Avoided open arm entries in elevated plus maze test and reduced number of novel arm entries in Y maze test. □□□□: Phencyclidine □□□□:Clozapine (HY-14539); Haloperidol (HY-14538) MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [5]	Animals are given saline or Dizocilpine ((+)-MK 801) followed by cocaine 30 min later in the home cage instead of in the CPP apparatus for the two days of “reactivation.” This is done to determine whether reactivation of the memory for the cocaine-associated context by cocaine in the CPP context is necessary for the ability of Dizocilpine ((+)-MK 801) to disrupt reconsolidation. Animals undergo preconditioning, conditioning, testing, and extinction but animals are injected with saline or Dizocilpine ((+)-MK 801) (0.20 mg/kg, i.p.) 30 min prior to a cocaine injection (10 mg/kg, i.p.) in the home cage. Animals remain in the home cages, and the next day, the procedure from the first day of reactivation is repeated. The following day,

animals are tested for cocaine-primed reinstatement in their CPP box without any prior microinjection of saline or Dizocilpine ((+)-MK 801).

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

CUSTOMER VALIDATION

- Cell. 2023 Nov 22;186(24):5347-5362.e24.
- Cell Host Microbe. 2023 Nov 8;31(11):1792-1803.e7.
- Nat Neurosci. 2021 Dec 9.
- Mol Psychiatry. 2022 Jun 17.
- Cell Biosci. 2023 Mar 16;13(1):57.

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REFERENCES

[1]. Wong EH, et al. The anticonvulsant MK-801 is a potent N-Me-D-Asp antagonist. Proc Natl Acad Sci U S A. 1986 Sep;83(18):7104-8.

[2]. Vardhan Reddy KH, et al. Convergent Strategy to Dizocilpine MK-801 and Derivatives. J Org Chem. 2018 Apr 6;83(7):4264-4269.

[3]. Huettner JE, et al. Block of N-Me-D-Asp-activated current by the anticonvulsant MK-801: selective binding to open channels. Proc Natl Acad Sci U S A. 1988 Feb;85(4):1307-11.

[4]. Thomas DM, et al. MK-801 and dextromethorphan block microglial activation and protect against neurotoxicity. Brain Res. 2005 Jul 19;1050(1-2):190-8.

[5]. Brown TE, et al. The NMDA antagonist MK-801 disrupts reconsolidation of a cocaine-associated memory for conditioned place preference but not for self-administration in rats. Learn Mem. 2008 Dec 2;15(12):857-65.

[6]. Jiang L, et al. Decrease of growth and differentiation factor 10 contributes to neuropathic pain through N-Me-D-Asp receptor activation. Neuroreport. 2017 May 24;28(8):444-450.

[7]. Iijima Y, et al. Modification by MK-801 (dizocilpine), a noncompetitive NMDA receptor antagonist sensitization: evaluation by ambulation in mice. Nihon Shinkei Seishin Yakurigaku Zasshi. 1996 Feb;16(1):11-8.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA