MPTP hydrochloride

Cat. No.: HY-15608

CAS No.: 23007-85-4

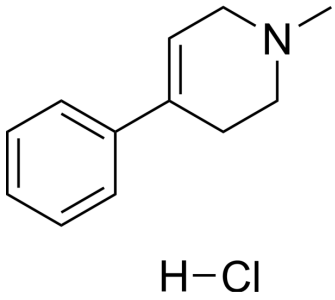
Molecular Formula: $C_{12}H_{16}ClN$

Molecular Weight: 209.72

Target: Dopamine Receptor; Apoptosis

Pathway: GPCR/G Protein; Neuronal Signaling; Apoptosis

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

H_2O : ≥ 100 mg/mL (476.83 mM)
DMSO : 12 mg/mL (57.22 mM; Need ultrasonic and warming)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.7683 mL	23.8413 mL	47.6826 mL
5 mM	0.9537 mL	4.7683 mL	9.5365 mL
10 mM	0.4768 mL	2.3841 mL	4.7683 mL

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

In Vivo

1. Add each solvent one by one: PBS
   Solubility: ≥ 100 mg/mL (476.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (7.96 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (7.96 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (7.96 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MPTP hydrochloride is a brain penetrant dopamine neurotoxin. MPTP hydrochloride can be used to induces Parkinson's Disease model. MPTP hydrochloride, a precusor of MPP^+, induces apoptosis[1][2][3]. MPTP hydrochloride has been verified by MCE with professional biological experiments.

In Vitro

Pretreatment with 50 mM 4-phenylpyridine, reduces IC_{50} (concentration for 50% inhibition of twitch amplitude) values of

MPTP from 53 to 18 mM and d-tubocurarine from 0.7 to 0.3 mM, respectively, in mouse phrenic nerve-diaphragm[2].

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

In Vivo

Although MPTP can be administered by a variety of different routes, including oral gavage and stereotaxic injection into the brain, the most common, and reproducible, results are obtained by systemic subcutaneous (s.c.) or intraperitoneal (i.p.) injection.

The commonly used protocols in the references are acute model (14-20 mg/kg, i.p., given every 2 hours within a day, a total of 4 times) and subacute model (30 mg/kg, i.p., once daily for 5 days).

MPTP is quickly metabolized to MPP^+ after injection, and MPP^+ has a half-life of about 6 days in sheep (serum). MPTP hydrochloride can be used in animal modeling to build Parkinson's syndrome models. MPTP reproduces the naturally occurring neurodegeneration and are useful for studying dopaminergic neuron neurodegeneration, mitochondrial dysfunction and neuroinflammation[8].

Induction of Parkinsonism model[4][5][6][7]

- Background

  MPTP is free to cross the blood-brain barrier and enter the brain, where it is metabolized by monoamine oxidase B (MAO-B) in astrocytes into MPP+, its active & toxic form. MPP+ is taken up by dopamine neurons via a dopamine transporter (DAT), blocking Complex I in the electron transport chain of mitochondria, triggering oxidative stress and mitochondrial breakdown, and finally leading to neuron apoptosis. In Parkinson's disease, it is the loss of neurons in the substantia nigra, the dopamine-producing part of the substantia nigrostriatum system, that causes the disease. Due to the toxic effects of MPTP, it will cause the death of dopamine neurons in the substantia nigra, causing symptoms similar to Parkinson's disease.

- Specific Mmodeling Methods

  Mice: C57BL/6 • male • 8-12 week-old (period: 2 weeks), older mice may be more sensitive

  Administration:

  Acute model: 14-20 mg/kg • ip • 4 times a day, two hours apart

  Sub-acute model: 30 mg/kg • ip • once daily for 5 days

  MPTP Hcl is dissolved in normal saline and configured when used.

  After administration, we can observe whether the mice have symptoms such as reduced activity, staggering walking, twitching, fried hair, increased urination, etc. This behavior may last for 24-48 hours, after which the mice behave basically normally.

  MPTP is usually sold as MPTP hydrochloride. The molecular weight of MPTP hydrochloride is 209.7. Therefore, it is recommended to take into account the presence of hydrochloride (HCl) when preparing injectable solutions. HCl has a molecular weight of 35.4 and accounts for 17% of MPTP. Thus, if a 20 mg/kg

dose of MPTP is to be prepared, the MPTP hydrochloride dose administered is 20 mg kg* 1.17% = 23.4 mg/kg.

If multiple injections are given within 1 day, it is best to alternate the injections on both sides. If injected every day, it should be done at the same time. Before each injection, the mice need to be weighed and the dosage volume should be adjusted.

Modeling mice may not show behavioral defects of Parkinson's disease. Mice may show individual differences, and the success rate of modeling is generally difficult to reach 100%. Therefore nigrostriatal damage associated with gliosis should be mainly monitored in MPTP mouse studies.

High drug dosage/mice weighing less than 22 g/mixing of drugs from different batches/mice not adapting in advance/animal room being too cold may result in a number of deaths, and it is recommended that the number of animals in each group be increased.

- Modeling Indicators

  Nigrostriatal injury: Tyrosine hydroxylase in the substantia nigra and striatum is reduced after successful modeling (IHC, IF, WB, etc.);

  Other markers: reduction of brain neurotransmitters (DA, DOPAC, 5-HT, HVA, etc.) (detected by HPLC);

  Nigrostriatal microglia (IBA1+ cells) and astrocytes (GFAP+ cells) are activated, and the number of α-syn aggregates in the substantia nigra .

- Opposite Product(s): L-Carnosine (HY-W013494)

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

PROTOCOL

Animal Administration [3]

For the preparation of the LPS rat model and the MPTP mouse model, the treatments of the animals are performed. Briefly, adult rats receive unilateral injections of LPS (0.5 μL of 10 μg/μL diluted in 0.9% saline) into the medial forebrain bundle (MFB) at the following coordinates, AP-4.2 mm, L 1.5 mm, and V 7.8 mm, and into the contralateral side with the same volume of 0.9% saline. Adult mice are administered intraperitoneal injections of MPTP of 25 mg/kg per day for five continuous days, and the same volume of saline is injected as a control. All the animals are sacrificed at week 1, 2, 3, or 4 after the LPS or MPTP injections. The brain samples are collected for the subsequent immunohistochemistry and western blot experiments.

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CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2021 Feb 24;6(1):77.
- Cell Death Dis. 2021 Feb 15;12(2):181.
- Cell Death Dis. 2019 Dec 16;10(12):952.
- J Med Chem. 2023 Aug 31.
- Antioxidants (Basel). 2023 Nov 13, 12(11), 1999.

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REFERENCES

[1]. Jackson-Lewis V, Przedborski S. Protocol for the MPTP mouse model of Parkinson's disease. Nat Protoc. 2007;2(1):141-51.

[2]. Rabaneda-Lombarte N, et al. The CD200R1 microglial inhibitory receptor as a therapeutic target in the MPTP model of Parkinson's disease. J Neuroinflammation. 2021 Apr 6;18(1):88.

[3]. Lee, et al. MPTP-driven NLRP3 inflammasome activation in microglia plays a central role in dopaminergic neurodegeneration. Cell Death Differ. 2019 Jan;26(2):213-228.

[4]. Zhang QS, et al. Reassessment of subacute MPTP-treated mice as animal model of Parkinson's disease. Acta Pharmacol Sin. 2017 Oct;38(10):1317-1328.

[5]. Hammock BD, et al., A sheep model for MPTP induced Parkinson-like symptoms. Life Sci. 1989;45(17):1601-8.

[6]. Langston J W, Irwin I. MPTP Neurotoxicity: An Overview and Characterization of Phases of Toxicity. II. Selective Accumulation of MPP in the Substantia Nigra: A Key to Neurotoxicity (Question). Life Sci., 1985, 36, No. 3, 201-12.

[7]. Hsu K S, et al. Potentiation of MPTP by 4-Phenylpyridine on the Neuromuscular Blockade in Mouse Phrenic Nerve-Diaphragm. Neuropharmacology, 1993, 32, No. 9, 877-83.

[8]. Sun XL, et al. Gas1 up-regulation is inducible and contributes to cell apoptosis in reactive astrocytes in the substantia nigra of LPS and MPTP models. J Neuroinflammation. 2016 Jul 8;13(1):180.

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

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