MLi-2

Cat. No.: HY-100411

CAS No.: 1627091-47-7

Molecular Formula: $C_{21}H_{25}N_5O_2$

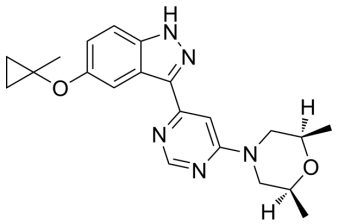
Molecular Weight: 379.46

Target: LRRK2

Pathway: Autophagy

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 : 50 mg/mL (131.77 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6353 mL	13.1766 mL	26.3532 mL
	5 mM	0.5271 mL	2.6353 mL	5.2706 mL
	10 mM	0.2635 mL	1.3177 mL	2.6353 mL

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

In Vivo

1. Add each solvent one by one: 30 % SBE-β-CD
   Solubility: 5 mg/mL (13.18 mM); Suspension solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.87 mg/mL (7.56 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.87 mg/mL (7.56 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.59 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MLi-2 is an orally active and highly selective LRRK2 inhibitor with an IC_{50} of 0.76 nM. MLi-2 has the potential for Parkinson's disease[1].

IC_{50} & Target	IC50: 0.76 nM (LRRK2)[1]
In Vitro	MLi-2 exhibits exceptional potency in a purified LRRK2 kinase assay in vitro(IC_{50}=0.76 nM), a cellular assay monitoring dephosphorylation of LRRK2 pSer935 LRRK2 (IC_{50}=1.4 nM), and a radioligand competition binding assay (IC_{50}=3.4 nM). MLi-2 has greater than 295-fold selectivity for over 300 kinases in addition to a diverse panel of receptors and ion channels[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Acute oral and subchronic dosing in MLi-2 mice results in dose-dependent central and peripheral target inhibition over a 24-hour period as measured by dephosphorylation of pSer935 LRRK2. Treatment of MitoPark mice with MLi-2 is well tolerated over a 15-week period at brain and plasma exposures. Morphologic changes in the lung, consistent with enlarged type II pneumocytes, are observed in MLi-2-treated MitoPark mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: MLi-2 is suspended in 30% Captisol and administered in a volume of 10 mL/kg. Dose calculations are on the basis of active moiety. Mice receive MLi-2 [1-100 mg/kg; by mouth (PO)], or vehicle 1 hour prior to euthanasia by excess CO2. Immediately following euthanasia, mouse brain cortex is dissected and frozen on a steel plate over dry ice for analysis of pSer935 LRRK2 via Western Blot. Plasma and brain samples are collected and frozen for determination of MLi-2 levels by LC-MS/MS[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2022 Jun 8;14(648):eabj2658.
- Acta Neuropathol. 2023 Jun 8.
- Stem Cell Reports. 2022 Sep 12;S2213-6711(22)00423-4.
- Exp Neurobiol. 2021 Jun 30;30(3):232-243.

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REFERENCES

[1]. Fell MJ, et al. MLi-2, a Potent, Selective, and Centrally Active Compound for Exploring the Therapeutic Potential and Safety of LRRK2 Kinase Inhibition. J Pharmacol Exp Ther. 2015 Dec;355(3):397-409.

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