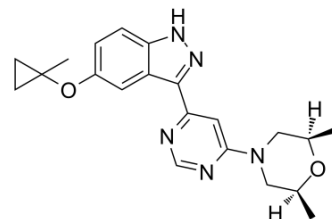


MLi-2

Cat. No.:	HY-100411		
CAS No.:	1627091-47-7		
Molecular Formula:	C ₂₁ H ₂₅ N ₅ O 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 : 60 mg/mL (158.12 mM; Need ultrasonic)

Concentration	Mass		
	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

- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 6 mg/mL (15.81 mM); Clear solution
- 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
- 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

BIOLOGICAL ACTIVITY

Description

MLi-2 is an orally active and highly selective LRRK2 inhibitor with an IC₅₀ of 0.76 nM. MLi-2 has the potential for Parkinson's disease^[1].

IC₅₀ & Target

IC₅₀: 0.76 nM (LRRK2)^[1]

In Vitro

MLi-2 exhibits exceptional potency in a purified LRRK2 kinase assay in vitro (IC₅₀=0.76 nM), a cellular assay monitoring dephosphorylation of LRRK2 pSer935 LRRK2 (IC₅₀=1.4 nM), and a radioligand competition binding assay (IC₅₀=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.

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.

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

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