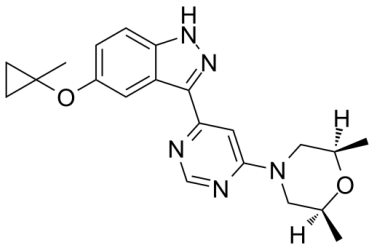
Data Sheet

Product Name:	MLi-2
Cat. No.:	CS-6349
CAS No.:	1627091-47-7
Molecular Formula:	C21H25N5O2
Molecular Weight:	379.46
Target:	LRRK2
Pathway:	Autophagy
Solubility:	DMSO : 60 mg/mL (158.12 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

MLi-2 is a potent, highly selective, orally available, brain penetrant inhibitor of **LRRK2** with an **IC_{50}** of 0.76 nM. IC50 & 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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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].

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.

CAIndexNames:

1H-Indazole, 3-[6-[(2R,6S)-2,6-dimethyl-4-morpholinyl]-4-pyrimidinyl]-5-[(1-methylcyclopropyl)oxy]-, rel-

SMILES:

C[C@@](C1)([H])O[C@](C)([H])CN1C2=CC(C3=NNC4=CC=C(OC5(C)CC5)C=C43)=NC=N2

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

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