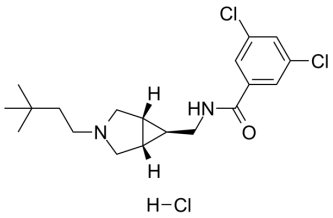
ML218 hydrochloride

Cat. No.:	HY-103309A
CAS No.:	2319922-08-0
Molecular Formula:	$C_{19}H_{27}Cl_3N_2O$
Molecular Weight:	405.79
Target:	Calcium Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	ML218 hydrochloride is a potent, selective and orally active T-type Ca^{2+} channels (Cav3.1, Cav3.2, Cav3.3) inhibitor with IC_{50}s of 310 nM and 270 nM for Cav3.2 and Cav3.3, respectively. ML218 hydrochloride inhibits the burst activity in subthalamic nucleus (STN) neurons. ML218 hydrochloride has no significant inhibition of L- or N-type calcium channels, K_{ATP} or hERG potassium channels. ML218 hydrochloride can penetrate the blood-brain barrier[1].
IC_{50} & Target	IC50: 310 nM (Cav3.2), 270 nM (Cav3.3), and 150 nM (Ca^{2+} flux)[1]
In Vitro	In plasma protein binding studies (equilibrium dialysis), ML218 possesses good free fraction in both rat and human. Intrinsic clearance experiments in liver microsomes indicated that ML218 is highly cleared in rat (CL_{int} = 115 mL/min/kg), but low to moderately cleared in human liver microsomes (CL_{int} = 12.7 mL/min/kg)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ML218 (0.03-30 mg/kg; oral administration; once; male Sprague-Dawley rats) treatment reverses cataleptic behavior in rats induced by a 0.75 mg/kg dose of haloperidol[1]. Free brain and plasma concentrations of ML218 increases in a dose proportional manner across the dose range (3 mg/kg: [plasma] = 98 nM, [brain] = 1.66 μM; 10 mg/kg: [plasma] = 282 nM, [brain] = 5.03 μM; 30 mg/kg: 1.2 μM, [brain] = 17.7 μM)[1]. Noncompartmental pharmacokinetic analysis indicates ML218 (1 mg/kg, IV) has a mean residence time (MRT) of nearly 7 h, a value which is consistent with its terminal half-life ($t_{1/2}$ = 7 h)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Sprague-Dawley rats (275-299 g) induced by haloperidol[1]
Dosage:	0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg, 30 mg/kg
Administration:	Oral administration; once
Result:	Reversed cataleptic behavior in rats induced by a 0.75 mg/kg dose of haloperidol.

REFERENCES

[1]. Xiang Z, et al. The Discovery and Characterization of ML218: A Novel, Centrally Active T-Type Calcium Channel Inhibitor with Robust Effects in STN Neurons and in a

Rodent Model of Parkinson's Disease. ACS Chem Neurosci. 2011 Dec 21;2(12):730-742.

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