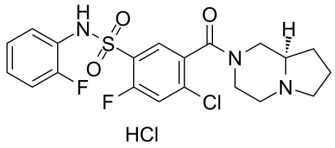
ABT-639 hydrochloride

Cat. No.:	HY-101616
CAS No.:	1235560-31-2
Molecular Formula:	$C_{20}H_{21}Cl_2F_2N_3O_3S$
Molecular Weight:	492.37
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	ABT-639 hydrochloride is a novel, peripherally acting, selective T-type Ca^{2+} channel blocker.
IC_{50} & Target	Ca^{2+} Channel[1]
In Vivo	ABT-639 blocks recombinant human T-type ($Ca_V3.2$) Ca^{2+} channels in a voltage-dependent fashion (IC_{50}=2 μM) and attenuates low voltage-activated (LVA) currents in rat DRG neurons (IC_{50}=8 μM). ABT-639 is significantly less active at other Ca^{2+} channels (e.g. $Ca_V1.2$ and $Ca_V2.2$) (IC_{50}>30 mM). ABT-639 has high oral bioavailability (%F=73), low protein binding (88.9%) and a low brain:plasma ratio (0.05:1) in rodents. Following oral administration ABT-639 produces dose-dependent antinociception in a rat model of knee joint pain (ED_{50}=2 mg/kg, p.o.). ABT-639 (10-100 mg/kg, p.o.) also increases tactile allodynia thresholds in multiple models of neuropathic pain (e.g. spinal nerve ligation, CCI, and vincristine-induced, and capsaicin secondary hypersensitivity). ABT-639 does not attenuate hyperalgesia in inflammatory pain models induced by complete Freund's adjuvant or carrageenan. At higher doses (e.g. 100-300 mg/kg) ABT-639 does not significantly alter hemodynamic or psychomotor function. The antinociceptive profile of ABT-639 provides novel insights into the role of peripheral T-type ($Ca_V3.2$) channels in chronic pain states[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats[1] The pharmacokinetic properties are determined in Sprague Dawley rats dosed intravenously with 5 μmol/kg ABT-639 prepared in 10% DMSO/90% poly ethylene glycol 400 (PEG400). The plasma levels of ABT-639 are determined using HPLC and mass spectrometry. Following oral administration (p.o.) of the ABT-639 (3, 10 and 30 mg/kg) prepared in 10% PEG400/10% Cremophor EL/80% Oleic Acid the levels of ABT-639 in plasma and brain are determined. Briefly, the brains are immediately removed and freed from blood vessels as much as possible. The resulting brain tissues are frozen at -20°C, followed by weighing and homogenization before analysis. The heparinized blood samples are also frozen (-20°C) until analysis. ABT-639 is separated from the blood and brain samples using protein precipitation with acetonitrile followed by quantification with liquid chromatography/mass spectroscopy. Plasma samples for concentration determinations from in vivo efficacy experiments are collected from each animal within 15 min following behavioral testing. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biomed Pharmacother. 2019 Dec;120:109475.
- Eur Rev Med Pharmacol Sci. 2020 Dec;24(24):12887-12895.

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REFERENCES

[1]. Jarvis MF, et al. A peripherally acting, selective T-type calcium channel blocker, ABT-639, effectively reduces nociceptive and neuropathic pain in rats. Biochem Pharmacol. 2014 Jun 15;89(4):536-44.

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