Azimilide

Cat. No.: HY-18600

CAS No.: 149908-53-2

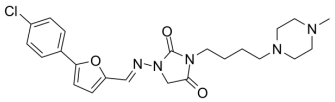
Molecular Formula: $C_{23}H_{28}ClN_5O_3$

Molecular Weight: 457.95

Target: Potassium Channel

Pathway: Membrane Transporter/Ion Channel

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Azimilide(NE-10064) is a class III antiarrhythmic compound, inhibits I(Ks) and I(Kr) in guinea-pig cardiac myocytes and I(Ks) (minK) channels expressed in Xenopus oocytes.IC50 value:Target: in vitro: Azimilide blocked HERG channels at 0.1 and 1 Hz with IC50s of 1.4 microM and 5.2 microM respectively. Azimilide blockade of HERG channels expressed in Xenopus oocytes and I(Kr) in mouse AT-1 cells was decreased under conditions of high [K+]e, whereas block of slowly activating I(Ks) channels was not affected by changes in [K+]e [1]. Azimilide suppressed the following currents (Kd in parenthesis): IKr (< 1 microM at -20 mV), IKs (1.8 microM at +30 mV), L-type Ca current (17.8 microM at +10 mV), and Na current (19 microM at -40 mV). Azimilide was a weak blocker of the transient outward and inward rectifier currents (Kd > or = 50 microM at +50 and -140 mV, respectively). Azimilide blocked IKr, IKs, and INa in a use-dependent manner. Furthermore, azimilide reduced a slowly inactivating component of Na current that might be important for maintaining the action potential plateau in canine ventricular myocytes [2]. In guinea pig ventricular myocytes, NE-10064 (0.3-3 microM) significantly prolonged action potential duration (APD) at 1 Hz. At 3 Hz, NE-10064 (0.3-1 microM) increased APD only slightly, and at 10 microM decreased APD and the plateau potential. NE-10064 potently blocked the rapidly activating component of the delayed rectifier, IKr (IC50 0.4 microM), and inhibited IKs (IC50 3 microM) with nearly 10-fold less potency [3].in vivo: NE-10064 (10 mg/kg intravenously, i.v.) reduced ($p < 0.05$) the incidence (8 of 12) of PES-induced ventricular tachycardia (VT). The cycle length of induced VT was not prolonged by NE-10064 (0.245 +/- 0.046 s predrug vs. 0.301 +/- 0.060 s postdrug). NE-10064 increased ventricular effective refractory period (VERP 166 +/- 5 ms predrug vs. 194 +/- 13 ms postdrug, $p = 0.013$), prolonged QTc interval (310 +/- 12 ms predrug vs. 350 +/- 16 ms postdrug, $p = 0.004$) and prolonged the effective refractory period (ERP) of noninfarcted myocardium ($p = 0.045$) [4].

CUSTOMER VALIDATION

- Biochem Biophys Res Commun. 2016 Apr 29;473(2):396-402.

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REFERENCES

[1]. Busch AE, et al. Blockade of HERG channels by the class III antiarrhythmic azimilide: mode of action. Br J Pharmacol. 1998 Jan;123(1):23-30.

[2]. Yao JA, et al. Azimilide (NE-10064) can prolong or shorten the action potential duration in canine ventricular myocytes: dependence on blockade of K, Ca, and Na

channels. J Cardiovasc Electrophysiol. 1997 Feb;8(2):184-98.

[3]. Fermini B, et al. Use-dependent effects of the class III antiarrhythmic agent NE-10064 (azimilide) on cardiac repolarization: block of delayed rectifier potassium and L-type calcium currents. J Cardiovasc Pharmacol. 1995 Aug;26(2):259-71.

[4]. Black SC, et al. Protection against programmed electrical stimulation-induced ventricular tachycardia and sudden cardiac death by NE-10064, a class III antiarrhythmic drug. J Cardiovasc Pharmacol. 1993 Dec;22(6):810-8.

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