NS3623

Cat. No.: HY-108586

CAS No.: 343630-41-1

Molecular Formula: $C_{15}H_{10}BrF_3N_6O$

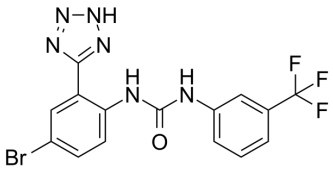
Molecular Weight: 427.18

Target: Potassium Channel

Pathway: Membrane Transporter/Ion Channel

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 : 250 mg/mL (585.23 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3409 mL	11.7047 mL	23.4093 mL
5 mM	0.4682 mL	2.3409 mL	4.6819 mL
10 mM	0.2341 mL	1.1705 mL	2.3409 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.87 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NS3623 is an activator of human ether-a-go-go-related gene (hERG1/K_V11.1) potassium channels. NS3623 activates the IKr and Ito currents and has antiarrhythmic effect. NS3623 has a dual mode of action, being an inhibitor of hERG1 channels[1][2][3].

In Vitro

In isolated canine cardiomyocytes, application of NS3623 (5 μM) greatly increases the size of the tail current confirming previous studies demonstrating this drug increased IKr. The effect of NS3623 on IKr recorded from cells kept in culture is evaluated. After 48 h, the magnitude of IKr is greatly reduced compared to freshly isolated cells. Peak IKr tail currents are 0.47 ± 0.08 pA/pF in freshly isolated myocytes and 0.28 ± 0.06 pA/pF in 2 day cultured myocytes. Application of NS3623 increases IKr in cultured Mid cells. Analysis of the current-voltage (I-V) relation of IKr tail current showed that NS3623 increased current density in both 1 day and 2 day cultured Mid cells. On a percentage basis, NS3623 increases IKr tail

currents (at +50 mV activating pulse) by 60% in normal Mid cells, and 68% in 48 h cultured cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

NS3623 (30 mg/kg; i.v.; lasting for 3 minutes) shortens the corrected QT interval by 25 +/- 4% in anaesthetized guinea pigs[1]. NS3623 (50 mg/kg) shortenes the QT interval by 30 +/- 6% in conscious guinea pigs. NS3623 (50 mg/kg) immediately decreases the QTcF interval and remains significantly shortened for approximately 30 minutes[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Anesthetized guinea pig[1]
Dosage:	30 mg/kg
Administration:	Intravenous injection; lasting for 3 minutes
Result:	Shortened the corrected QT interval by 25 +/- 4%.

REFERENCES

[1]. Hansen RS, et al. In vivo effects of the IKr agonist NS3623 on cardiac electrophysiology of the guinea pig. J Cardiovasc Pharmacol. 2008 Jul;52(1):35-41.

[2]. Diness JG, et al. Antiarrhythmic effect of IKr activation in a cellular model of LQT3. Heart Rhythm. 2009 Jan;6(1):100-6.

[3]. Calloe K, et al. A dual potassium channel activator improves repolarization reserve and normalizes ventricular action potentials. Biochem Pharmacol. 2016 May 15;108:36-46.

[4]. Hansen RS, et al. Biophysical characterization of the new human ether-a-go-go-related gene channel opener NS3623 [N-(4-bromo-2-(1H-tetrazol-5-yl)-phenyl)-N'-(3'-trifluoromethylphenyl)urea]. Mol Pharmacol. 2006 Oct;70(4):1319-29.

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